ADULT OBESITY: PERSONALITY TRAITS, EATING BEHAVIOUR, PHYSICAL ACTIVITY, *DRD2* POLYMORPHISMS AND HEALTH RELATED QUALITY OF LIFE IN A MALAYSIA PRIVATE UNIVERSITY

By

LIM ZHI MENG

A dissertation/thesis submitted,
Faculty of Science,
Universiti Tunku Abdul Rahman,
in partial fulfillment of the requirements for the degree of
Master of Science
February 2021

ABSTRACT

ADULT OBESITY: PERSONALITY TRAITS, EATING BEHAVIOUR, PHYSICAL ACTIVITY, *DRD2* POLYMORPHISMS AND HEALTH RELATED QUALITY OF LIFE IN A MALAYSIA PRIVATE UNIVERSITY.

Lim Zhi Meng

Obesity is a worldwide issue with high prevalence rate up to 64% and 65% of obese or overweight male and female population in Malaysia, respectively. National Health and Morbidity Survey 2019 reported that 50.1% of adults in Malaysia were overweight or obese, with 30.4% being overweight and 19.7% obese (NHMS 2019). This study aims to investigate the aetiology of obesity as obesity is believed to present a risk to health (chronic diseases and psychological disorders). It was hypothesized that there is a correlation of obesity with dopamine receptor D2 (*DRD2*) *Taq1* gene polymorphism, personality traits, eating behaviour, physical activity and quality of life. *DRD2* gene is selected as reduced D2 receptor activity generates a reward deficiency and alters appetitive motivation, which may induce compulsive eating and contributes to obesity (Beeler et al., 2016). The study cohort consisted of 394 subjects (125 males and 269 females) who studied or worked in University Tunku Abdul Rahman (UTAR), Malaysia. Personality traits, eating behaviours and physical activity were examined by using Mini International Personality Item Pool (IPIP), Three-Factor Eating Questionnaire-R18 (TFEQ-R18) and International Physical Activity Questionnaire (IPAQ), respectively. The Motives for Physical Activity Measure – Revised (MPAM-R) were used to

assess the strength of five motives for participating in physical activities. The Short Form General Health Questionnaire (SF-36) was used to examine the quality of life. Body mass index (BMI) of the participants was examined to evaluate obesity status. Genotyping of *Taq1* gene polymorphisms (*ANKK1/DRD2 Taq1A, DRD2 Taq1B and DRD2 Taq1D*) was performed by PCR-RFLP using the genomic DNAs extracted from mouthwash samples. Statistical analysis was done by using SPSS, AMOS and Stats Tools Package. Cognitive restraint (CR), uncontrolled eating (UE) and emotional eating (EE) showed significant correlations on neuroticism. UE and EE were significantly correlate with conscientiousness while EE was significantly correlated with extraversion. Extraversion trait was predominantly seen among underweight and normal BMI individuals and with positive correlation correlated with physical activity. Underweight and Normal individuals were more prone to emotional eating. Obesity is significantly associated with physical activity. *DRD2 Taq1A*, *Taq1B and Taq1D* polymorphisms did not exerted as the moderator in eating behaviour, physical activity and obesity. There is no significant difference between obesity and health related quality of life (HR-QoL). In conclusion, extraversion is correlated to being physically active and decreased emotional eating. Hence, people are encouraged to take the initiatives to forge meaningful connections with others and maintain an energetic lifestyle, which in turn lower the rate of obesity. In addition, *Taq1* genotypes showed significant differences on motives for participating in physical activities but not physical activity level. This suggested that innate genetic factor alone does not help in preventing obesity. Postnatal initiative is required for individuals to execute physical activities in order to achieve a healthy BMI.

ACKNOWLEDGMENT

I would like to take this opportunity to extend my gratitude to my supervisors, Dr. Teh Lai Kuan and Dr. Chie Qiu Ting for the guidance throughout the study. I greatly appreciate the assistance provided. Next, I would like to express my appreciation to Dr. Alia Azalea and Dr. Say Yee How, the ex-principal invigilator and supervisor of their earlier guidance as well as recruiting me as the master student for this project. Also, I would like to thank Universiti Tunku Abdul Rahman Research Fund (UTARRF) Without the monetary support, this project would not able to progress smoothly.

Secondly, I would like to thank to my friends who volunteered in helping me for the data collection. The project would not be accomplished in time without their contribution. Thirdly, thanks to my seniors, for providing me ideas and solutions throughout the obstacles I had faced. In addition, I would like to thank laboratory officers for their guidance besides supplying some materials needed for this study.

Last but not least, I would like to express my appreciation to all the participants who involved in this study. Without them, this study would never be completed.

DECLARATION

I LIM ZHI MENG hereby declare that the dissertation is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at UTAR or other institutions.

Name 
(LIM ZHI MENG)

Date 19 FEBRUARY 2021

APPROVAL SHEET

This dissertation/thesis entitled "**ADULT OBESITY: PERSONALITY TRAITS, EATING BEHAVIOUR, PHYSICAL ACTIVITY, *DRD2* POLYMORPHISMS AND HEALTH RELATED QUALITY OF LIFE IN A MALAYSIA PRIVATE UNIVERSITY"** was prepared by **LIM ZHI MENG** and submitted as partial fulfillment of the requirements for the degree of Master of Science at Universiti Tunku Abdul Rahman.

Approved by:

_____

(Dr. TEH LAI KUAN) Date:16.02.2021
Professor/Supervisor
Department of Allied Health Sciences
Faculty of Science
Universiti Tunku Abdul Rahman

_____

(Dr. CHIE QIU TING) Date:16.02.2021
Professor/Co-supervisor
Department of Psychology and Counselling
Faculty of Arts and Social Science
Universiti Tunku Abdul Rahman

FACULTY OF SCIENCE

UNIVERSITI TUNKU ABDUL RAHMAN

Date: 19 FEBRUARY 2021

SUBMISSION OF DISSERTATION

It is hereby certified that **LIM ZHI MENG** (ID No: **19ADM00073**) has completed this final year project/ dissertation/ thesis* entitled "ADULT OBESITY: PERSONALITY TRAITS, EATING BEHAVIOUR, PHYSICAL ACTIVITY, *DRD2* POLYMORPHISMS AND HEALTH RELATED QUALITY OF LIFE IN A MALAYSIA PRIVATE UNIVERSITY" under the supervision of Dr. Teh Lai Kuan (Supervisor) from the Department of Allied Health Sciences, Faculty of Science, and Dr. Chie Qiu Ting (Co-Supervisor) from the Department of Psychology and Counselling, Faculty of Arts and Social Science.

I understand that University will upload softcopy of my dissertation/thesis in pdf format into UTAR Institutional Repository, which may be made accessible to UTAR community and public.

Yours truly,

(LIM ZHI MENG)

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AGFI	Adjusted goodness of fit index
ALFA	Allele Frequency Aggregator
ANKK1	Ankyrin repeat and kinase domain containing 1
APD	Apomorphine administration
BED	Binge eating disorder
BMI	Body mass index
CDC	Centers for Disease Control and Prevention
CFI	Comparative Fit Index
CI	Confidence interval
CR	Cognitive restraint eating
CNS	Central nervous system
CTNNBL1	Catenin Beta Like 1
DALYs	Disability-adjusted life-years
DAT	Dopamine transporter
dH2O	Sterile deionized water
DNA	Deoxyribonucleic acid
dNTP	Deoxynucleoside triphosphate
DRD2/D2R	Dopamine receptor D2
EE	Emotional eating
EIGP	Excessive internet video gameplay
fMRI	Functional magnetic resonance imaging
FTO	Fat mass and obesity
GFI	Goodness of Fit

GH	Growth hormone
GWAS	Genome-wide association study
HRQoL	Health-related quality of life
HWE	Hardy-Weinberg equilibrium
IGD	Internet Gaming Disorder
IPAQ	International Physical Activity Questionnaire
KLF9	Kruppel Like Factor 9
MAF	Minor allele frequency
MPAM-R	Motives for Physical Activity Measure – Revised
MCS	Mental component summary
METs	Metabolic equivalent of task
Mini-IPIP	Mini-International Personality Item Pool Scales
NCBI	National Center for Biotechnology Information
NHMS	National Health and Morbidity Survey
NIH	National Institutes of Health
NPC1	Niemann-Pick disease, type C1
PCR	Polymerase chain reaction
PCR-RFLP	Restriction fragment length polymorphism
PROMIS	Patient-Reported Outcomes Measurement Information System
PCS	Physical component summary
QALY	Quality-adjusted life-year
QFS	Québec Family Study
RMSEA	Root Mean Square Error of Approximation
RDS	Reward Deficiency Syndrome
SEA	South East Asia

SF-36	Short Form 36 Health Survey Questionnaire
SNP	Single nucleotide polymorphism
SNpc	Substantia nigra pars compacta
SPSS	Statistical Package for the Social Sciences
TAD	Theory of self-determination
TFEQ-R18	Three-Factor Eating Questionnaire -R18
UE	Uncontrolled eating
UTAR	University Tunku Abdul Rahman
VTA	Ventral tegmental area
WHO	World Health Organisation

CHAPTER 1

INTRODUCTION

1.1 Background

Overweight and obesity are defined as abnormal or excessive fat accumulation (WHO, 2020). They are presented as a risk to health and a global pandemic resulting in an estimated 3.4 million deaths, 3.8% of life lost, and 3.8% of disability-adjusted life-years (DALYs) worldwide (Ng et al., 2013). Obesity is attributed as one of the major risk factors for various chronic diseases, such as heart diseases, type II diabetes, and cancer. In addition, obesity also brings autonomic nervous system dysfunction with symptoms including dizziness, urinary problems, and vision problems. Body mass index (BMI), a person's weight in kilograms divided by the square of height in meters, is a commonly used parameter in categorising obesity. Generally, a person with BMI equals to, or more than 25.0 kg/m^2 is considered overweight, and 30.0 kg/m^2 is considered obese (WHO, 2019).

Obesity is an issue worldwide with a high prevalence rate although countless health efforts have been made by governments and organisations, including the World Health Organisation, World Obesity, The Obesity Society, and etc. In a study by Ng and co-workers in 2014, Malaysia was ranked the first among South East Asia (SEA) countries with the highest obesity rate of 43.8% among men, 48.6% of women were overweight and obese (Ng et al., 2014). Despite countless efforts in controlling the obesity rate, Malaysia's obesity rate has become more severe. The prevalence of obesity in Malaysia was reported 50.1%

of adults (aged 18 years old and above) were overweight or obese, with 30.4% being overweight and 19.7% obese (NHMS 2019). Population in Malaysia holds the highest rate of overweight and obesity among Asian countries which up to 64% and 65% of obese or overweight male and female populations respectively (WHO, 2019).

Various factors such as psychology, environment, and genetics may play roles in causing overweight and obese, and subsequently affecting health-related quality of life (HRQoL). Big-five-personality traits made up of openness, conscientiousness, extraversion, agreeableness, neuroticism, and insalubrious eating behaviour and a sedentary lifestyle are major psychological and environmental factors contributing to obesity. Obesity results from an energy imbalance in our body where the energy intake is more than the energy expenditure. If an individual does not burn off the energy through physical activity, excessive energy from fats and sugars will be stored by the body as fat. Family genetic linkage studies have greatly aided in identifying many genetic events associated with obesity. Obesity may be induced by a mutation in a single gene (monogenic inheritance) or the presence of variants in multiple genes (polygenic inheritance). A study by Hinney and the team stated that the carrier of an obesity-associated genotype might further increase the susceptibility of being obese and the risk of obesity-related diseases (Hinney et al., 2010). Dopamine type 2 receptor genes (*DRD2*) *Taq1* gene which encodes for D2 dopamine receptors was selected as the targeted gene in this research study. This is because reduced D2 receptor activity is believed to generate a reward deficiency and alters appetitive motivation, which may induce compulsive

eating and contributes to obesity (Beeler et al., 2016). However, candidate gene variants *ANKK1/DRD2 Taq1A*, *DRD2 Taq1B* and *DRD2 Taq1D* are still lacking in studies in elucidating its role in BMI, eating behaviours, or tendency to participate in physical activity. Dopamine is found to modulate physical activity; but is still undetermined whether reduced D2 receptors contribute to obesity by changing in physical activity and energy expenditure and physical activity. Furthermore, although the A1 or B1 alleles of the *DRD2 Taq1A* and *Taq1B* have been associated with lower cognitive restraint and higher uncontrolled eating behaviours, further studies are still required for their contribution in obesity (Lek, Ong, & Say, 2017). Therefore, we anticipated to fill in the knowledge regarding the correlation of *DRD2 Taq1A*, *Taq1B* and *Taq1D* with those mentioned factors in leading to obesity.

1.2 Problem statement

To date, there is scarce study that provides evidence on psychological and environmental components in association of obesity in Malaysia. Furthermore, there are limited studies of the possible moderating role of dopamine receptor genotype in the relationship between eating behaviour and physical activity and obesity and the relationship between obesity and HRQoL. Hence, the aim of the study is to understand the association between dopamine receptor genotypes and the aetiology of obesity and investigate the role of dopamine receptor genotypes in moderating links between eating behaviours and physical activity, and consequently affecting HR-QoL.

1.3 Significance of study

This is an exploratory study which combines psychological and health components with genotypes as possible associates of obesity. This study also fills in the knowledge gap where most of the studies were not predominantly Southeast Asian, uniquely Malaysian, which was made up of multiple ethnicities. We are also looking at the possible moderating role of dopamine receptor genotype in the relationship between eating behaviour and physical activity and obesity. Therefore, the research is important as it might contribute to health awareness especially among Malaysian.

1.4 Research objectives

1. To explore the aetiology of obesity (i.e., personality traits, eating behaviour, physical activity, and dopamine receptor genotypes) among UTAR staff and students.
    i. To examine the correlation of personality traits (i.e., Extraversion, Agreeableness, Conscientiousness, Emotional Stability, and Openness), eating behaviour and physical activity.
    ii. To investigate the association of eating behaviour, physical activity associate and obesity.
    iii. To study whether the D2 dopamine receptor gene polymorphisms moderate the link between physical activity, eating behaviour, and obesity.
2. To compare the Health-Related Quality of Life of an individual among different BMI classes.

CHAPTER 2

LITERATURE REVIEW

2.1 Obesity

Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to body health (World Health Organization, 2020). Fat is accumulated as triacylglycerol form in adipocytes (fat cells) as an energy reservoir. Adipose tissue, or commonly known as body fat is usually deposited underlying the skin as subcutaneous fat, packed around internal organs as visceral fat, between muscles, within the bone marrow, and in breast tissue. To assess the obesity in an individual, body mass index (BMI), waist circumferences, and waist to hip ratio are taken. BMI, which is a person's weight in kilograms (kg) divided by the square of the person's height in metres (kg/m^2) is the most universal parameter being employed and accepted in health study. Classification of overweight and obese classification is shown in Table 2.1. Global BMI cut-off range and Asian criteria BMI cut-off range are different as Asian traditionally possess smaller body size than Caucasian.

Table 2.1: Classification of BMI cut-off range by WHO

(WHO in 2019)

	BMI cut-off (kg/m^2)	
Nutritional Status	**Global criteria**	**Asian criteria**
Underweight	<18.5	<18.5
Normal	18.5 – 24.9	18.5 – 22.9
Overweight	≥25.0	≥23.0
Pre-Obese	25 – 29.9	23 – 24.9
Obese	≥30	≥25
Obese Type 1	30.0 - 34.9	25-29.9
Obese Type 2	35.0 - 39.9	≥30
Obese Type 3	≥40.0	

2.1.1 Prevalence of Obesity

Until now, overweight and obesity are consistently an issue even though uncountable efforts have been made by health organisations throughout the world to raise a public health concern. The public may be aware about the consequences of obesity, but yet most people are uncaring, and insensitivity, leading to the increase of overweight and obesity from year to year. The worldwide obesity prevalence nearly trebled between 1975 and 2016 (World Health Organization, 2020). Figure 2.1 illustrates the share of adults ages ≥18 years that are overweight or obese in 2016.

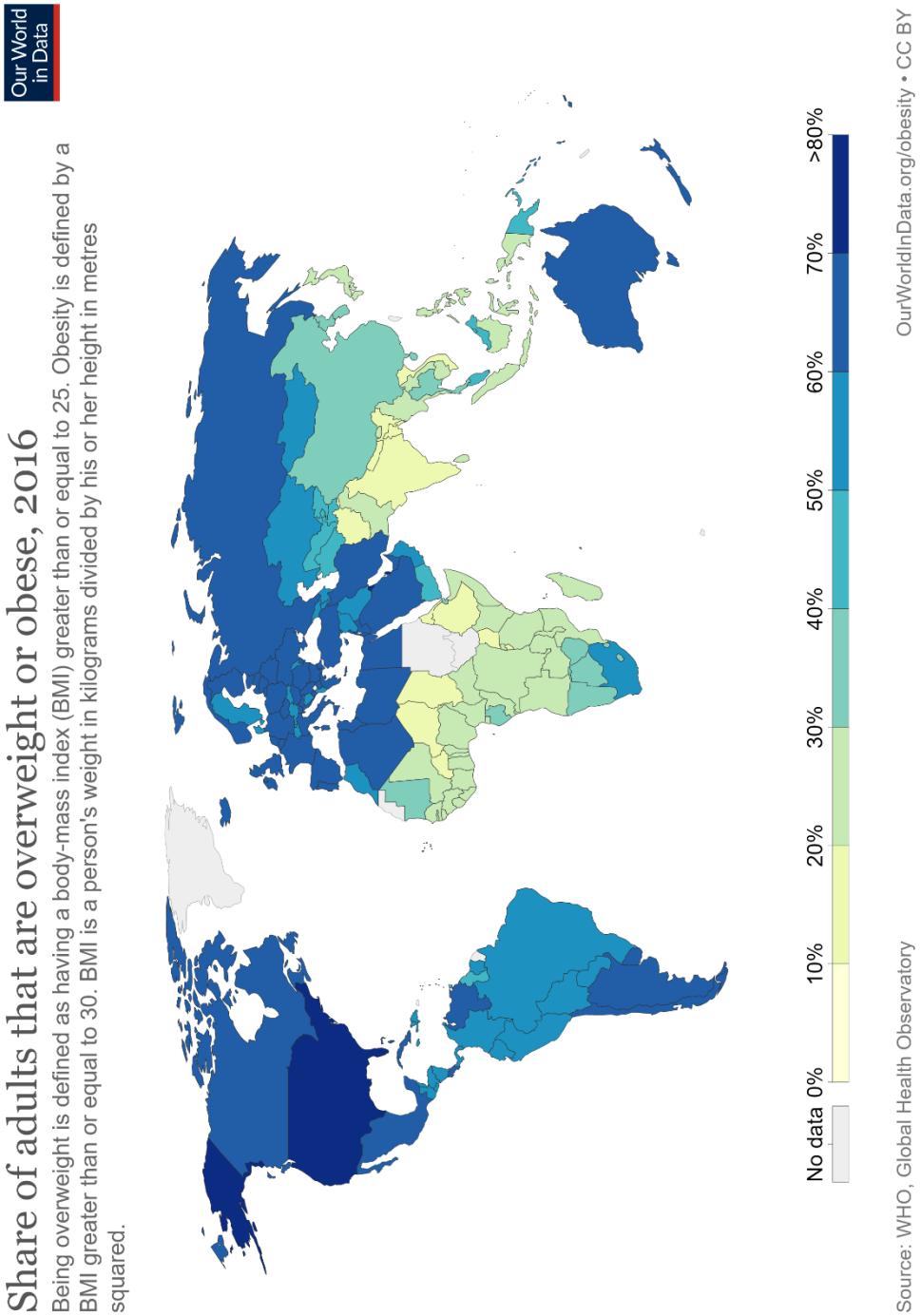


Figure 2.1: Share of adults ages ≥18 years that are overweight or obese in 2016 (Ritchie and Roser, 2017).

South-east Asia had the lowest prevalence rate of obesity (3%) and overweight (14%) globally (Ng et al., 2014). Malaysia had the highest prevalence rate of obesity (14%) (Cheong, 2014), followed by Thailand (8.8%). As reported by National Health and Morbidity Survey of 2015 (NHMS 2015), the prevalence rate of overweight and obesity in Malaysia was 48.6% in women and 43.8% in men, and the prevalence of obesity for women (16.7%) was greater than men (11.4%) (Institute of Public Health, 2015). To date, Malaysia has the highest obesity rate among adults in SEA (15.6%). It was then followed by Brunei (14.1 %), Thailand (10.0 %), and Indonesia (6.9 %) (World Population Review, 2020). NHMS 2019 reported 50.1% of the obesity rate in Malaysia adults. From the figure, 30.4% of them were overweight and 19.7% obese. As predicted, the growth of overweight and obesity continue to ascend compared to previous findings. Apart from adults, overweight and obesity disease has been generalised at a younger age. Among children from 5 to17 years old, 15.0% and 14.8% were overweight and obese, respectively (Institute of Public Health, 2019). The polarised imbalance distribution of weight growth should be concerned. Therefore, this study aims to investigate how environmental factors (personality traits, eating behaviours, and physical activity level) and genetic factors (dopamine receptor gene) as elements of obesity which then affect HRQoL.

2.2 Theoretical and conceptual framework of obesity study

Homeostatic theory by Marks, 2015 can be used to discuss obesity physiologically. Homeostatic obesity imbalance is ascribed to a positive or negative feedback to weight increment, body discontent, negative affect and energy consumption (Marks, 2015). Understanding the theory of obesity would help in reducing the obesity epidemic as individuals would be conscious of their behaviours in regulating the homeostasis of obesity. Figure 2.2 presents a clearer picture of the theory of the homeostasis of obesity to daily life (Ghanemi et al., 2018):

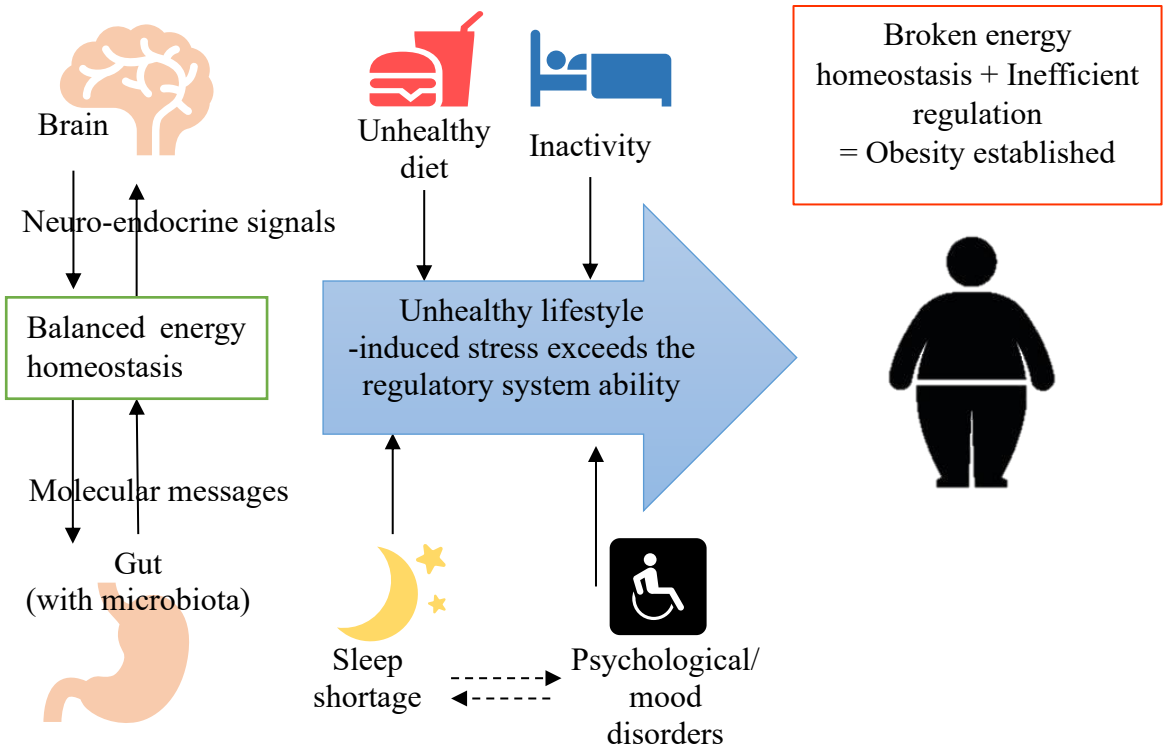


Figure 2.2: Homeostasis of obesity (Ghanemi et al., 2018)

As in Figure 2.2, energy balance and feedback regulation such as diet choice, physical activity level, rest and mental state would bring an outcome to a person's weight, either optimal BMI or obesity. Apropos of the homeostasis

theory of obesity, obesity establishment is somewhat 'controllable' if a person implements healthy performance (feedback). Therefore, to verify this hypothesis, our study, looked into eating behaviours, physical activity level, personality traits, and the dopamine receptor gene, which plays a role in energy balance. This will fill in the knowledge gap and to create a health awareness to the public.

Despite the vast literature in obesity studies, there is still a lack of exploration of it regarding the association of personality traits with eating behaviour and physical activity. Inconsistent findings across various international studies have made it difficult to state conclusively whether personality traits have an influence on eating behaviour and participation in physical activity or vice versa. The cultural demographic of Malaysia and differences in lifestyle factors across urban and rural areas despite rapid modernisation and development could yield some interesting findings in regards to eating behaviour (Lek et al., 2018). Differences in lifestyle factors such as living environment, work professions and individual lifestyle choices play a role in the risk of obesity and subsequently, HRQoL. Thus, this study will attempt to investigate the association of personality traits (openness, conscientiousness, extraversion, agreeableness, neuroticism) with eating behaviour and physical activity in a cohort of Malaysian. Furthermore, sampling obese and non-obese individuals would allow a clear comparison of HRQoL in a local context. In the field of genetics, family studies, animal models, and the advancements in research technology have greatly helped identify many genetic events associated with obesity (Xia and Grant, 2013). However, the combined results of linkage and candidate genes

have provided very little explanation for the variance in BMI, eating behaviours or tendency to participate in physical activity. For instance, dopamine is recognized for its effect in modulating the physical activity. It is still undetermined whether fewer D2 receptors would contribute to obesity by changing in physical activity and energy expenditure. Furthermore, although the A1 or B1 alleles of the dopamine receptor genes have been associated with lower cognitive restraint and higher uncontrolled eating behaviours, further studies are required for their contribution in obesity (Lek et al., 2018). This suggests that further investigation still needs to be done.

2.3 Environmental factors of obesity

There were plenty of research studies showing that environmental changes play a role in leading to an increase of overweight and obesity. The main factor is the loss of energy balance as the calorie intake exceeds the body's requirements (Claussnitzer et al., 2015). Excessive calorie intake will lead to a positive energy balance and result in adipose tissue formation for energy storage in the triglyceride form. The adipose tissue composed of adipose stem cells will ultimately escalate the lipid accumulation, and new adipocytes will be produced in the human body. Nonetheless, enlarged adipocytes will secrete paracrine growth factors which may induce terminal differentiation of neighbouring preadipocytes. Preadipocytes differentiate into mature adipocytes and eventually strengthen the adipose tissue reservoir (Sorisky et al., 2000).

The link between personality traits and body weight showed three aspects: cognitive, behavioural, and psycho-physiological (Bogg and Roberts, 2004).

For instance, conscientiousness-related traits demonstrated a negative relationship to unhealthy behaviours that may cause obese (e.g., unhealthy diet, low activity level and alcoholism). Also, there has been increasing research interest in the association of body weight or obesity with personality traits, which may appear to be a risk factor or protective factor (Gerlach et al., 2015). For instance, individuals with personality traits more conscious of what they eat, calculate the food calorie and the nutritional value, this would become a protective factor for them in increasing body weight. Conversely, individuals with personality traits without restriction on what they are consuming, personality traits have now become a risk factor for them to put on weight. Eating behaviour and physical activity level always seem to be inseparable with the loss of energy balance. Individuals who have a binge and emotional eating will have their weight increase as they eat excessively than their body needs.

Physical inactivity or sedentary lifestyle may result in the increase of overweight and obesity as individuals with limited or no physical activity have less energy expenditure which leads to the energy imbalance if the individual exceeds the energy intake. The generalised internet and social networking and modernisation of technologies have further severe physical inactivity problems. A previous study discussed the negative effect of watching television and food commercials on the increment of obesity among adults and children (Rosiek et al., 2015). Surfing the internet, movies, and dramas watching, as well as video gaming, have now become common individuals' preferences in leisure time, and all these activities can be done in a sedentary mode.

The role of excessive food consumption and physical inactivity towards the aetiology of obesity has been largely documented through cross-sectional studies investigating the relationship of eating behaviour and physical activity with obesity or reviews of health interventions to increase weight loss in obese individuals. Unhealthy eating behaviour and low physical activity are considered to be the main risk factors for overweight and obesity (National Nutrition Surveillance Centre 2009; Al-Nakeeb et al., 2014; Psouni et al., 2016). Therefore, individuals should control their diet and carry out physical activity to reduce excessive weight. Weight loss from dietary restriction alone leads to the reduction in energy expenditure, whereas physical activity leads to incremental energy expenditure. A combination of both (dietary restriction and physical activity) results in weight loss, without a subsequent reduction in resting energy expenditure (National Nutrition Surveillance Centre 2009). In a nutshell, environmental factors that may contribute to overweight and obesity in our research study include personality traits, eating behaviours, and physical activity.

2.3.1 Personality traits and behavioural aspects of obesity (eating behaviour and physical activity).

Personality has been considered as one of the most impactful topics in psychological research. This is because personality traits might act as a predictor for health, social status, well-being, academic and job performance, relationships, political attitudes, and online behaviours (Azucar et al., 2018). Big Five personality traits (also known as the five-factor model) is one of the most well studied and widely accepted theoretical frameworks of personality. This is comprised of openness (O), conscientiousness (C), extraversion (E), agreeableness (A), and neuroticism (N) (McCrae and Costa 1987; McCrae and John, 1992). Therefore, the five factors model has also abbreviated in the acronyms OCEAN.

Openness is shorthand for 'openness to experience'. It indicates how open-minded a person is when involved in new things, incidents, and the environment. People with a high level of openness in a personality test enjoy the adventure for instance travel to a new place and live in an area with different cultures and practices (Pappas, 2017). They are imaginative, curious, and appreciate art. Open individuals allow and do not resist the 'variety of life'. On the other hand, people who are low in openness prefer sticking to their habits and things that they are familiar with and avoid fresh-new experiences.

Conscientiousness is the personality trait of being careful, self-responsible, or diligent. Conscientious individuals are organised and have a robust sense of duty. They are disciplined, dependable, and accomplishment-focused. However,

individuals who are low in conscientiousness are more spontaneous and may be more prone to carelessness. Individuals with high levels of conscientiousness were relatively reliable due to their organized tendencies which affected their surroundings (Arthur and Graziano, 1996). A recent study showed that a high level of conscientiousness would be more empathetic towards others (Melchers et al., 2016).

Extraversion versus introversion is possibly the most markable personality trait of the Big Five. People who score high on the extraversion category in personality tests are the life of the party. They are sociable, enjoy being with people, and are full of energy. They tend to be confident and animated in social interactions. Au contraire, introverts need a lot of solitary time. Introversion is frequently confused with shyness, but they are conceptually distinct from each other. Social shyness usually implies a fear of social interactions or discomfort and inhibition in the presence of others (Briggs 1988). However, introverts can be perfectly fine at parties, yet they just prefer alone or small-group activities.

Agreeableness measures the extent of a person's warmth, harmony, and tactfulness. Individuals who score high on agreeableness are more likely to be trusting, helpful, and benevolent. They generally have an optimistic view of human nature and get along well with others. Disagreeable people, on the other hand, are often cold and suspicious of others. They are less motivated to maintain positive relationships with others (Graziano and Tobin, 2009).

Neuroticism refers to a relatively enduring tendency or disposition to respond with negative emotional states (Widiger, 2009). Individuals with neuroticism

score respond poorly to environmental stress and easily slip into anxiety and depression as they are readily to interpret ordinary situations as threatening (Widiger, 2009). They are more likely than the average to experience moody, fear, envy, jealousy, anger, guilt, loneliness, and depression. They are often shy and self-conscious. Also, they may have difficulty in controlling impulses and urges impulses when they are overwhelmed with upset (Widiger, 2009). Neuroticism may be a predictor of several mental and physical disorders. Undeniably, neuroticism can result in the quality and longevity of their lives (Lahey, 2009).

In broad respects of animal and human studies, there is a common acknowledgement that personality is organised into a variety of fundamental facets, with characteristic discriminating a vast behavioural approach against avoidance motivation appearing in almost all personality models. In humans, approach and an avoidance system, and a general disinhibition and constraint motivational systems are corresponding to introversion (versus extraversion) and neuroticism (versus emotionally stable) (Fischer et al., 2018). Available literature exploring the link between personality traits and body weight showed that three aspects are involved: (a) cognitive, (b) behavioural and (c) psycho-physiological (Bogg and Roberts, 2004). However, this study will focus on the association between personality traits and behavioural aspects of body weight (eating behaviour and physical activity). There has been increasing research interest in the association of body weight or obesity with personality traits, which appears to be a risk factor as well as protective factor (Gerlach, Herpertz & Loeber, 2015).

Neuroticism is a trait in which the person may react more aggressively towards anxious stimuli. The individual has a higher tendency in refraining from unusual situations and potentially unpleasant stimuli (Fischer et al., 2018). Therefore, it is a trait greatly moderated by avoidance motivation behaviour. However, as mentioned, the personality traits may become a protective or a risk factor of overweight and obesity. For instance, a study by Reshadat showed that neuroticism is predictive of unhealthy eating behaviours (Reshadat et al., 2017). This is because neuroticism is associated with less restrained eating but enhanced emotional eating (Provencher et al., 2008; Lee-Winn et al., 2016). A recent multidimensional analysis statistically evidenced impulsiveness (a facet of neuroticism) showed an increase of the impulse response from gorging to binge (Micanti et al., 2017). They revealed the relationship between impulsiveness and overeating, particularly the link with external eating. This psychopathological factor promotes unhealthy eating behaviour further accelerate the risk of being overweight and obese. As individuals who are high in neuroticism are prone to binge or emotional eating, and this may lead to overweight and obesity in the long run. Personality traits may associate with obesity through eating behaviour and physical activity as a medium.

Extraversion is characterised by a motivation to engage in prototypical situations, highly sociable, and positive emotionality. Individuals who have high extraversion scores usually allow the novel behavioural approach. Extraversion is linked to a tendency of becoming overweight (Gerlach et al., 2015) as these 'social-favoured-traits' may cause an individual to be the life of the party or participate more in social interaction. Undeniably, these occasions usually

require the individual to drink or eat more, and we call this situation social eating or social drinking. On the other perspective, if an extravert who prefer mixing with people who implement healthy lifestyle such as good eating habit and maintain a high physical activity level, extraversion is now a protective factor for the individual to become overweight or obese. Also, there were studies showed that extraversion was correlates of physical activity (Rhodes and Smith, 2006); hence people who have high extraversion score may have a lower chance of becoming overweight and obese due to a high physical activity rate.

Conscientiousness appears to function more as a protective factor against obesity (Jokela et al., 2013). This is because conscientious individuals are more cautious in controlling their diet, as well as the frequency of physical activity (Rhodes and Smith 2006; Wilson and Dishman, 2015). Individuals with high in conscientiousness demonstrated positive engagement in behaviors which give rise to adaptive outcomes. For instance, they are more likely to take part in physical activity (Hagger, 2019). However, there is a downside of the conscientiousness trait as it might turn into an eating disorder such as anorexia nervosa. Conscientiousness and neuroticism are strongly correlated with dysfunctional eating. The differences were most pronounced for cognitive restraint and emotional eating. Also, emotional eating occurred more often in females than in males, resulting in greater weight control difficulties among female patients (Gade et al., 2014). For agreeableness and openness, studies focusing on these traits were unable to indicate a clear and solid association with obesity (Gerlach et al., 2015).

As countries developed, a lack of physical activity has become a critical risk factor for obesity (Rhodes and Boudreau, 2017). As such, physical exercise is an important component of the treatment of obesity. In accordance with the health-behaviour model by Wiebe and Smith, it was hypothesised that the principal effect of personality on physical activity is through the quality of our health practices, i.e. the frequency and intensity of physical exercise (Wiebe and Smith, 1997). A meta-analysis by Rhodes and Smith on the relationship between personality and physical activity showed that conscientiousness, extraversion, and neuroticism were correlates of physical activity. However, openness and agreeableness were not associated with physical activity (Rhodes and Smith, 2006). A subsequent meta-analysis by Wilson and Dishman found similar results but additionally indicated that conscientiousness was linked more to the frequency of physical activity compared to other personality traits. Also, a small but significant relationship was found between openness and physical activity (Wilson and Dishman, 2015). Along with the development of technologies as well as the generalisation of the internet and smartphone or other mobile devices, a sedentary lifestyle has become an unavoidable issue. Personality traits such as high neuroticism, psychoticism, sensational seeking (high extraversion) and low self-directedness (low conscientiousness) as well as temperament traits such as reward dependence which associated with Internet Gaming Disorder (IGD) (Paik et al., 2012) have indirectly led to overweight and obesity while increasing people sitting time. However, the correlated relationship of personality and physical activity across time is lack of exploration. As such, longitudinal research that would allow researchers to investigate whether physical activity practices shape personality could be a promising future research direction. For

instance, some longitudinal studies of personality change in adulthood showed that physically active adults have their personality traits scores of openness, conscientiousness, extraversion, and agreeableness incline significantly in comparing to those who were less physically active (Stephan et al., 2014).

Personality traits may vary between and within populations (Schmitt et al., 2007; Allik et al., 2017). For example, Asians have a lower mean of extraversion than European and North American, whereas Southern European, South American, and East Asian populations manifested higher neuroticism means (Fischer et al., 2018). There is a shortage of studies in Malaysia, and hence the study may widen the view and bring some impact to the Malaysian community.

2.3.2 Eating behaviour and obesity

Eating behaviour is meant for food preference and motives, eating pattern, dieting, feeding practices, and eating-related problems of an individual, including eating and feeding disorders. Our study study on eating patterns and eating-related problems (obesity) using Three-Factor Eating Questionnaire - R18 (TFEQ-R18). This is to evaluate cognitive restraint eating (CR), uncontrolled eating (UE) and emotional eating (EE) to measure eating behaviour. Restraint is defined as a tendency to restrict the food intake consciously and constantly with physiological cues, hunger, and satiety, as moderator of food intake. Restrained eating is distinct from normal dieting. Restrained eaters may eat less food than they desired and less than they require to maintain the energy balance. On the other hand, uncontrolled eating is a tendency to overeat; while emotional eating demonstrates the tendency to

consume in response to negative emotions (Anglé et al., 2009).

The relationship between unhealthy eating behaviour and excessive BMI was inseparable (Al-Nakeeb, 2014). A review by Nicholls et al. (2016) reported binge eating disorder (BED)-obesity was significantly associated with emotional eating. In Mexico, a previous study by Lazarevich et al. (2013) demonstrated a strong significant association between eating behaviour and obesity, particularly in individuals who constantly feel hungry and overeating and difficulty in stopping eating. Therefore, it is important to possess a healthy eating behaviour to maintain a good body weight. This was shown in a previous study reported individuals with healthy eating behaviours tended to have more positive attitudes and intentions for healthy eating, and hence engendered a healthy body weight (Psouni et al., 2016).

2.3.3 Physical activity and obesity

Physical activity is defined as any body movement produced by skeletal muscles that require energy expenditure (WHO, 2020). The common ways to stay active are through walking, cycling, recreation, and sports. Regular and adequate levels of physical activity can bring numerous benefits, including: i) improve muscular, skeletal, and cardio-respiratory strength, ii) improve functional health and iii) reduce the risk of common diseases such as coronary heart disease, stroke, hypertension, diabetes, and depression (WHO, 2020).

Physical activity is not just solely meant for exercise. Exercise is a subcategory of physical activity that is structured, repetitive, and intents to improve or

maintain physical health. Besides exercise, any other physical activity that is executed during leisure time, or as part of work are considered health beneficial (WHO, 2020). WHO recommends an at least 150 min/week of moderate-intense physical activity for adults aged 18 to 64 years old, or accumulating a minimum 75 min/week of vigorous-intense physical activity, or a corresponding combination of both (World Health Organization, 2018).

Back to the 19th century, many ways were used for the assessment of physical activity. The application of metabolic equivalents (METs) was introduced later in the late 19th century (Sallis et al., 1985) and became more developed. Later in the 20th century, METs were used in quantifying and tracking the 'volume' of physical activity. METs measures the proportion of the rate at which an individual expends energy, relative to the mass of the individual. METs are also known as the ratio of the metabolic work rate to the resting metabolic rate. Table 2.2 represents the physical activities and their respective METs score.

Table 2.2: METs score on respective physical activity

Physical activity	**MET**
Light intensity activities	< 3
Resting	0.9
Typing	1.8
Slow walking	2.9
Moderate intensity activities	3 to 6
Walking	3.3
Moderate workout	3.5
Bicycling	5.5
Vigorous intensity activities	**> 6**
Jogging	7.0
High-intensity training	8.0
Running	8.0
Rope skipping	10.0

(Jetté et al., 1990)

For large health survey research, METs are used to measure the physical activity practice of communities. Data on the distribution of activity practices and detecting changes in the activities over time can be obtained to allow the comparison with other epidemiologic studies of physical activity.

Low physical activity is considered as one of the main risk factors for an excessive BMI (Al-Nakeeb et al., 2014). A study by Psouni et al., (2016) on 361 Greek individuals indicated that people with healthy BMIs had higher levels of leisure time activity and more years of exercise participation. Similarly, a previous study showed that BMI was found to be significantly higher among individuals with the lowest level of physical activity in their leisure time

(Stefanov et al., 2011). In addition, there was a review by the National Nutrition Surveillance Centre (2009) of national and international research related to obesity in Ireland concluded that there is a synergistic relationship between obesity, physical activity and practice of controlled eating behaviour. This demonstrated physical activity is sufficient to exert an impact on obesity solely.

According to NHMS 2019, the overall prevalence of physically inactive adults in Malaysia was 25.1%. Females (28.2%) were found to be more inactive than males (22.1%). The physical inactivity level increased from 55-59 years old to ≥75 years old. The rural population demonstrated a lower prevalence of physical inactivity (20.3%) compared to the urban population (26.5%). Malaysian-Chinese reported the highest level of physical inactivity (32.5%), followed by Malays (25.7%) and Malaysian-Indians (25.0%). From the perspective of education background, adults with no formal education (29.4%) and tertiary education (28.1%) were found to be more physically inactive. This shows that education does not bring much impact to the physical activity level, but possibly self-awareness and health concerns are the main factors for an individual to carry out physical activities. Furthermore, plenty of leisure time is also significant as non-working adults (43.6%), and students (38.9%) demonstrated a higher level of physical inactivity (Institute of Public Health, 2019). The level of physical inactivity among Malaysian adults was moderate as reported in NHMS 2011 and NHMS 2015. Additionally, most of the adults noticed physical activity information from television and the internet (Institute of Public Health, 2019).

Lacking motivation in doing physical activity has become an unavoidable issue in the current era as we can see from these reported data that physical inactivity in Malaysia is relatively high. It was identified that people who lack the motivation to physical activity might due to competing demands in their time of educational, professional and family obligations in each category of life (Korkiakangas et al., 2009). Exercise could be time and resources consuming which leads them to be unmotivated, with no intention of being more physically active or insufficiently motivated in spending their time in doing physical activity. Although people are aware of the importance of physical activity for health, a large number of individuals are still unmotivated or are not motivated sufficiently to be physically active or are inadequately motivated to sustained activity as shown in the NHMS report.

2.4 Genetic factors of obesity

Apart from environmental factors (eating behaviour and physical activity), genetic predisposition also plays a critical role in overweight and obesity through affecting energy intake and energy expenditure. According to WHO, obesity was found commonly resulted from excessive food intake, lack of physical activity, and genetic predisposition (WHO, 2020). The risk of developing obesity, obesity-promoting behaviours, and obesity-related phenotypes depend on the genes of an individual when exposed to a shared or similar environment (Faith and Kral, 2006). According to Pérusse et al., obesity-related phenotypes include physiological and metabolic measures, peptides and hormones, and behavioural traits (Pérusse et al., 2005). These phenotypes can be inherited from the ancestor to the next generations. Maes and colleagues have

demonstrated the heritability of obesity-related phenotypes (BMI and fat mass) in family studies, adoption studies and twin studies (Maes et al., 1997). Twins studies presented the highest similarity of BMI (50-90%) followed by family studies (20-80%) and adoption studies (20-60%). Study of twins reared apart (i.e., two individuals with the same genetic constitution reared in two different environments) produce predicted heritability at approximately 65- 75% for BMI (Stunkard et al., 1990). Therefore, these studies demonstrated that genetic predisposition is a vital factor in causing overweight and obesity despite the fact that they may be multifactorial.

From the aspects of genetic study, obesity is generally categorised into two groups which are monogenic obesity or polygenic obesity based on the number of genes involved in obesity development. Monogenic obesity is an uncommon and severe early-onset obesity with abnormal eating behaviour as well as endocrine disorders. Monogenic obesity is particularly caused by autosomal recessive mutations in the genes which are related to the leptin-melanocortin pathway that contributes to the hypothalamic control of food intake (Huvenne et al., 2016). In contrast, polygenic obesity is caused by the defect of multiple common and interacting alleles. Each allele may play a role in a minor effect, which is either additive or non-additive (Reich and Lander, 2001).

2.4.1 Genome-wide association study of obesity

Genome-wide association study (GWAS) had been studied on obesity to explore the candidate gene. 24 rare and high-risk genetic variants were discovered contributing to monogenic obesity and 200 low-risk common genetic variants involving polygenic obesity (Loos and Janssens, 2017). To date, up to 3305 candidate genes have been documented in National Center for Biotechnology Information (NCBI) and over 250 loci associated with BMI and obesity have been identified via GWAS. High expression of BMI or obesity susceptibility genes located in the insula and substantia nigra, which are two brain regions that are involved in the addiction and rewarding pathway (Ndiaye et al., 2019). The susceptibility to obesity genes may affect eating addiction for the first exposure, and rewarding behaviour after the expression of the obesity genes in substantia nigra and insula is enriched, at the end leading to hyperphagia (Ndiaye et al., 2019). Fat mass and obesity-associated (*FTO*) gene is the most well-known and was the first identified obesity-related gene by GWAS. *FTO* gene variants may increase the risk of obesity by modifying the food preference and consumption (Loos and Yeo, 2014). Additionally, the utilisation of GWAS also enhances the identification of other genes such as *CTNNBL1* which was strongly associated with BMI and fat mass (Liu et al., 2008), MAF for the transcription factor involved in insulin-glucagon regulation and adipogenesis, *NPC1* for the transportation of intracellular lipid (Hofker and Wijmenga, 2009), *CDKAL1* and *KLF9* which were found to be associated with BMI in the East Asian population (Okada et al., 2012) et cetera.

2.4.2 Dopamine receptor D2

Dopamine receptor gene encodes dopamine receptors which may induce obesity by affecting personality traits, eating behaviours, and physical activity level. In humans, there are five different subtypes of dopamine receptors (D1R-D5R). The dopamine receptor D2 (D2R) is a G protein-coupled receptor in postsynaptic dopaminergic neurons. Neurotransmitters (dopamine) are released from the presynaptic terminal to the postsynaptic terminal by dopamine receptors' uptake action. Figure 2.3 illustrates the dopaminergic synapse activity and Figure 2.4 illustrates the G protein-coupled receptor activity in resting state and stimulated state.

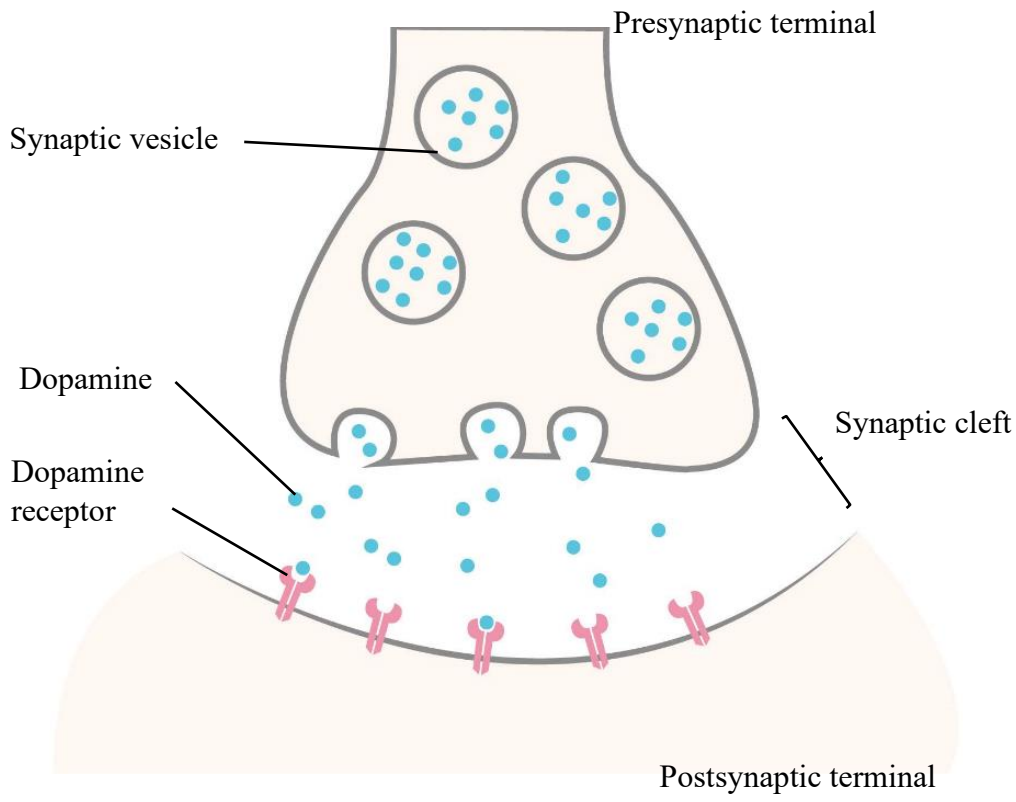
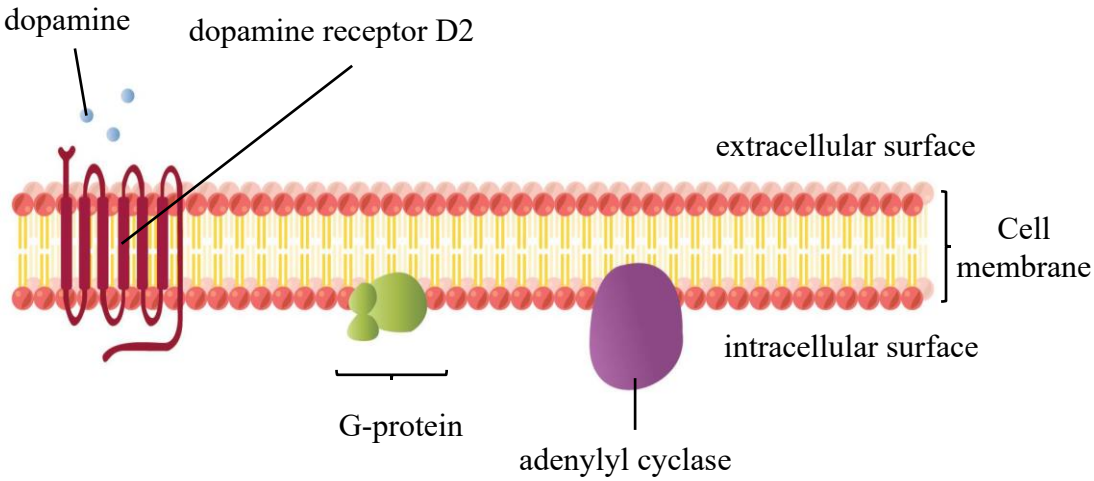


Figure 2.3: Dopaminergic synapse activity

Resting state



Stimulated state

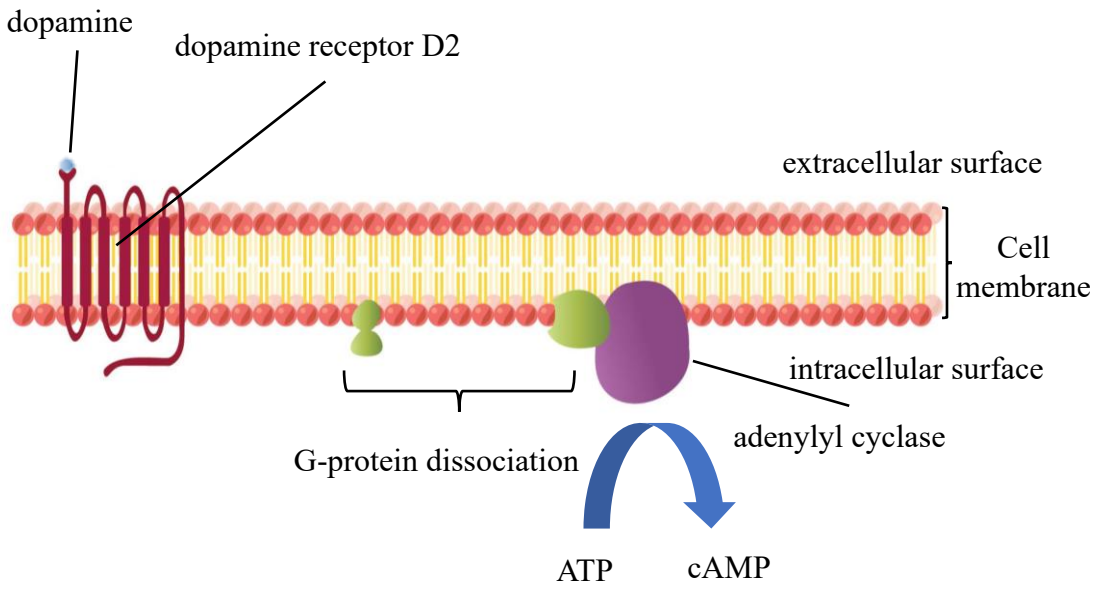


Figure 2.4: G protein-coupled receptor activity

Human dopaminergic neurons are localised in the ventral tegmental area (VTA), and substantia nigra pars compacta (SNpc), and they are in charge in the regulation of hormone secretion, motor activity, and behaviours in the central nervous system (CNS). Figure 2.5 shows the location of VTA and SNpc in the human brain.

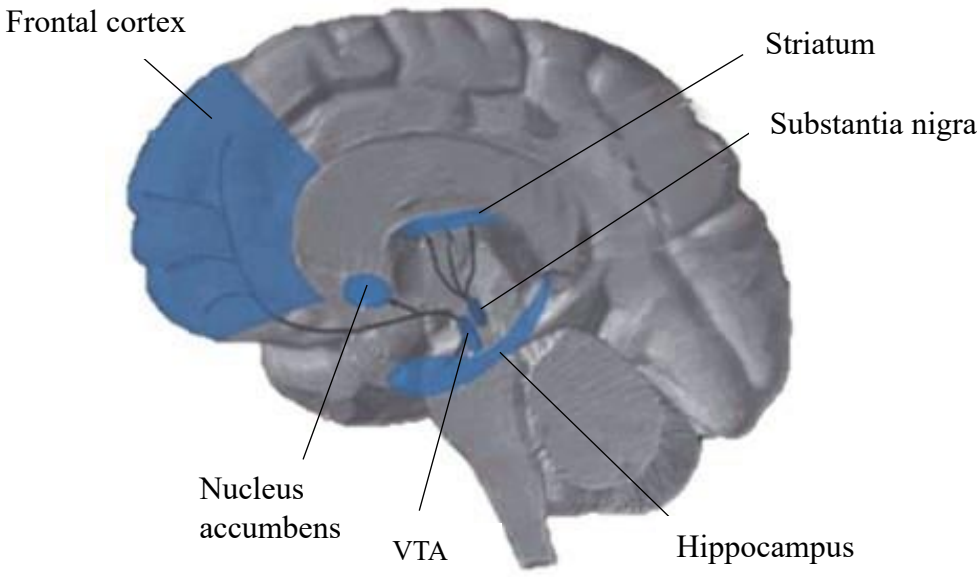


Figure 2.5: General view of the human brain (picture adapted from Wikipedia)

2.4.3 *DRD2* controls cognitive and behavioural approaches

Apart from causing an effect on overweight and obesity directly, obesity-related genes usually bring an impact or a modification to the environmental factors such as personality traits, eating behaviours, and physical activity level to induce overweight and obesity. Kirac et al. (2016) suggested the existence of the tendency to remain physically inactive through the involvement of biological systems. Also, behaviours like the preferences of food and beverage may be genetically determined. Likewise, the environmental factor, the genetic

component may also play a role in eating behaviours and the level of physical activity, and eventually affect obesity. Kirac et al. further explored the influence of gene mutations on obesity, eating behaviours, and physical activity levels. A study conducted on 100 obese patients and 100 controls demonstrated that gene mutations were no relation with the levels of physical activity. Inversely, good eating patterns were essential to prevent obesity (Kirac et al., 2016). Although various genes may contribute to overweight and obesity, personality traits, eating behaviours, and physical activity level, the dopamine receptor gene is chosen as the candidate gene in this study with its effect on the rewarding system pathway.

Genes regulate a dopaminergic brain system differently, especially in analysing, reinforcement learning, risk judgement, executing, and emotional decision making (Fischer et al., 2018). Dopamine is considered one of the major neurotransmitters in the control cognitive and behavioural approach system with various correlational and experimental procedures demonstrating dopamine association, especially with neuroticism-type and extraversion behavioural traits. Dopamine gene variants have shown an association with personality traits in general and clinical studies (Chen et al., 2012; Wacker and Smillie, 2015), but the stability and consistency of these associations are indistinct. This indicates the significance of paying greater concern to environmental factors that are possible to affect gene expression (Fischer et al., 2018). For instance, depressed patients ordinarily possess a higher score in their neuroticism. Additional evidence should be provided respecting the role of dopamine in depression, and therefore Pearson-Fuhrhop et al. examine the

combined effect and relation of dopamine-related polymorphisms and depressive symptom severity. Genetic risk score approach is employed. It sums the multiple polymorphisms effects in the same biological system. The genetic risk score used in the research captures genetic variation in a few aspects of the dopamine system. It consists of synaptic dopamine availability and dopamine receptor binding, and these proteins are rich in the cortical and subcortical structures in depressive disorder individuals. In a nutshell, Pearson-Fuhrhop et al. corroborated that genetic factors correlate with depressive symptomatology, with lower dopaminergic neurotransmission expecting higher levels of depression. Moreover, the result is a similar magnitude and in the expected direction within depressed adults and healthy adults' participants (Pearson-Fuhrhop et al., 2014). Along with that, there was a more recent study that showed that higher hypodopaminergic genetic risk scores positively predicted higher novelty-seeking scores (Conner et al., 2017), which represents the extraversion score in our study.

2.4.4 *DRD2 Taq1A*, *Taq1B* and *Taq1D*

Figure 2.6 shows the Dopamine receptor D2 gene (*DRD2*), which is localised on human chromosome 11 at the q arm region (q22- q23), and it has 9 exons.

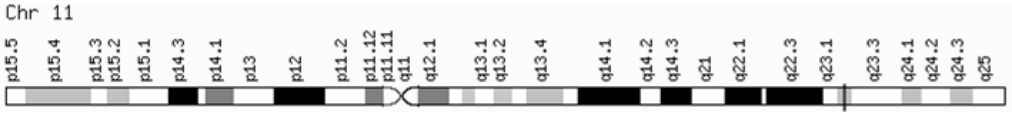


Figure 2.6: *DRD2* gene in genomic location (picture adapted from GeneCards ®, 2020)

Three single nucleotide polymorphisms (SNPs) of the *DRD2* gene are focused, which are *DRD2*/*ANKK1 Taq1A* (rs1800497), *DRD2 Taq1B* (rs1079597), and *DRD2 Taq1D* (rs1800498). *DRD2/ANKK1 Taq1A* (rs1800497) is located at

exon 8 of the ANKK1 gene in chromosome 11 as a transition from nitrogenous base guanine (G) to adenine (A), resulting as an missense variants. rs1800497 is found significant in the East Asian population with minor allele frequency (MAF) of 0.379 according to ALFA Allele Frequency in the release version: 20200227123210 in National Center for Biotechnology Information (NCBI). This SNP results in a substitution of amino acid glutamate to lysine. rs1800497 is unlikely to influence structural integrity, but it may bring impact to the substrate-binding specificity (Neville et al., 2004). *DRD2 Taq1B* (rs1079597) point mutation occurs in the intron site of the *DRD2* gene in chromosome 11, which is caused by the substitution of nitrogenous base cytosine (C) to thymine (T). According to ALFA, rs1079597 is found significant in the East Asian population with a MAF of 0.423; release version: 20200227123210 in NCBI. There is still a paucity of study for this SNP until today. *DRD2 Taq1D* (rs1800498) is also found in the intron site of the *DRD2* gene in chromosome 11. It is also a guanine (G) to adenine (A) point mutation. The East Asian MAF of rs1800498 is 0.1 according to ALFA; release version: 20200227123210 in NCBI. Similar to rs1079597, the study on rs1800498 is still inadequate.

2.4.4.1 *DRD2 Taq1A*, *Taq1B* and *Taq1D* polymorphism and obesity

The relationship between *DRD2* polymorphism and obesity is indivisible with the rewarding system. This is because *DRD2* polymorphisms alter the normal uptake function and efficacy of D2 receptors by affecting the substrate-binding specificity (Neville et al., 2004) as well as D2 receptor density (Benton and Young., 2016). A study from Benton and Young manifested that individuals who carry the *A1* variant of *DRD2 Taq1A*, either homozygous mutant (*A1/A1*) or heterozygous mutant (*A1/A2*) have a 30–40% lower density of D2 receptor (Benton and Young., 2016). This reflects that the decline of the efficacy in uptake action of D2 receptors caused by *DRD2* gene polymorphisms affects the population of D2 receptors situated in postsynaptic terminals. Supportive results were demonstrated by various studies showing that *DRD2 Taq1* polymorphisms were associated with altered function of the D2 receptor (Lucht et al., 2010; Kirsch et al., 2006).

Although there was abundance of studies on the utilisation of nutritional approaches to obesity-related health sequels, there is still a lack of study involving neurotransmitter (dopamine) manipulation involving the rewarding system coupled with genetic polymorphic identification and obesity. Reward Deficiency Syndrome (RDS), a disorder characterised by a clinically significant deficiency of the dopamine in the brain, which can be caused by either a low density of D2 receptor or a reduction of dopamine released from the presynaptic terminal, has been suggested to underlie multiple types of addiction, including overeating (Blum, 2014). The study by Guo et al. (2014) furthered justify the relationship between *DRD2* polymorphisms, obesity and reward deficiency by

reporting that obese individuals have alterations in dopamine neurocircuitry that may increase their susceptibility to opportunistic overeating while at the same time making food intake less rewarding, causing them to eat more to achieve satiety.

In the 20th century, high sugar beverages such as milk tea had become one of the youngsters' favourites. NHMS report showed when an individual is addicted to a certain type of unhealthy beverage or food, it will increase the risk of being overweight or obese. This addictive effect may be caused by *DRD2 Taq1A* polymorphism. Several findings support the role for genetic variants of the DRD1 gene towards addictive behaviours and food motivation (Comings et al., 1997; Dagher and Robbins, 2009; Baskerville and Douglas, 2010; Baik, 2013) but more research studies must be carried out to validate these theories especially in human subjects. In addition to food motivation, dopamine showed an important role in the increase of D2 receptors and glucose craving (Downs et al., 2009). Individuals who carry an A1 allele have a lower D2 receptors density than an individual who possesses both A2 alleles (wildtype), and a higher risk to manifest addictive behaviour or substance abuse (Blum et al., 2009). Evidence of the A1 allele has upheld the propounded role of D2 receptors in addiction and leads to obesity, which is a positive association that has been found between obesity and an increased risk of drug abuse (Wang et al., 2001). There were substantial studies that the parallel relationship between the A1 variant to increased risk of alcoholism, smoking, drugs dependence (opiate and cocaine), and food and beverages (Munafo et al., 2007; Munafò et al., 2009; Deng et al., 2015; Verdejo-Garcia et al., 2015). These results lead to the

prognosis that addiction reflects a low density of D2 receptors, then obesity. Therefore, individuals who carry the A1 allele should be at risk of overweight and obese development (Benton and Young, 2016). The findings from Wang et al. have their subjects in an average BMI of 51.2 kg/m^2, and those obese subjects were found to have fewer D2 receptors, suggested a homology with those possess addiction behaviour. Hence, this has matched the conjecture of reward system insensitivity will provoke the need to overeat to stimulate an increased amount of dopamine release to suffice the satiety (Wang, 2004). The over intake of palatable food stimulates the brain's reward centre's reward centre to compensate for the low D2 receptor density for dopamine uptake action. The brain now requires a higher degree of stimulation to experience the same degree of reward; i.e., additional food is consumed to prevent food cravings and withdrawal symptoms (Benton and Young., 2016).

Furthermore, the addiction to alcohol brought out by *A1* variants may indirectly increase weight. This is because besides the calories contained in alcohol itself, alcohol may increase an individual's appetite as well as reduce fat oxidation (Traversy et al., 2015), and aggravate the risk of overweight and obesity. This is supported by a finding from Bendsen et al. stated that high consumption of alcohol (more than 500 mL a day) might be positively associated with abdominal obesity as well as the consumption of alcoholic beer (for 21 to 126 days) generates weight gain (Bendsen et al., 2013).

On the other hand, *DRD2 Taq1B* polymorphism seems to have no association with substance dependence (Nacak et al., 2012) and dopaminergic reward

pathways (Suriyaprom et al., 2013). Another finding in Turkey showed no significant difference of genotypes and alleles of *DRD2 Taq1A* and *DRD2 Taq1B* polymorphism in obese individuals (Col Araz et al., 2012). However, conflicting results have been reported with the findings of the presence of the association between the *Taq1B* allele with low dopamine receptor D2 density. *Taq1A* and *Taql* B, but not *Taq1D* are in linkage disequilibrium with a functional allelic variant which impacts dopamine receptor D2 expression, and *Taq1B* SNP is significantly associated with 40% fewer D2 receptor binding sites (Ritchie and Noble, 2003). Also, Ritchie and Noble's study found that subjects who possess *DRD2 TaqlD* polymorphism have no significant allelic differences in the number of binding sites or binding affinity of the dopamine receptors D2 compared to subjects having the minor alleles at the *Taq1A* and *Taq1B*. On a local view, a study showed that the D1 allele might be the causative agent of obesity as this gene is correlated with increased preference in high-carbohydrate and oily diets (Lek et al., 2018).

In a nutshell, these results indicate that *DRD2 Taq1A* and *Taq1B* polymorphism might cause overweight and obesity by overeating as a compensation for the RDS, and by addiction to unhealthy food. Subjects with *DRD2 Taq1* minor allele would have higher odds in weight increment. Equivocal findings were shown between the association between *DRD2 Taq1B* and *Taq1D* polymorphism with dopamine receptor D2 as well as with obesity; therefore, our study focused on *Taq1* polymorphism might bring a clearer insight into this.

2.4.4.2 *DRD2 Taq1A*, *Taq1B* and *Taq1D* polymorphism and eating behaviour

Reduced activity in D2R is often associated with obesity. Reduced D2R activity may generate a reward deficiency and alters eating behaviour, which induces compulsive eating and contributes to obesity. An earlier study by Volkow et al. attempted to prove this by demonstrating that obese individuals have impairments in dopaminergic pathways and therefore have a defect in reward sensitivity, conditioning, and control (Volkow et al., 2011). Food consumption provides a pleasurable sensation (reward) which is regulated by the release of dopamine. When the dopamine pathways are impaired, the reward system is impaired, resulting in the individual unable to experience satisfying reward sensations from consuming a normal food portion. As such, there is an increased tendency for the individual to overeat. This insight has led to a later study by Davis et al. investigated binge eating disorder (an overeating disorder) with D2R genes (i.e. *DRD2/ANKK1 Taq1A*). Davis et al. demonstrated the presence of causal origins between binge-eating and hypersensitivity to reward, a condition that would be a predisposition to cause overeating (Davis et al., 2012). Binge-eating is believed to relate with strong dopamine signalling in the neurocircuitry which coordinates delightful and appetitive behaviours. Lek et al. examined the relationship between *DRD2 Taq1* gene and eating behaviour and obesity. They demonstrated ethnicities of Chinese and Indian and gender were not significantly different on eating behaviour scores. However, participants with A1 or B1 alleles were more likely to exhibit lower CR level and uncontrolled eating behaviours (Lek et al., 2018). From these findings, the researchers suggested that although the three *DRD2 Taq1* gene SNP has an

effect on eating behaviour, their role in overweight and obesity is still inconclusive.

2.4.4.3 *DRD2 Taq1A*, *Taq1B* and *Taq1D* polymorphism and physical activity

The level of physical activity has demonstrated a familial pattern, implying that the involvement in physical activity is not merely by environmental factors but also the familial genetic factors (Simonen et al., 2003). The dopamine system is the physiological pathway associated with rewarding and motivational behaviours such as eating and is also involved in regulating motor movement.

Studies involving the dopamine system or dopamine receptor genotypes and physical activity found that variations in the dopamine gene had been strongly correlated with physical activity levels in humans and rodents and is thus, correlated with increased longevity (Grady et al., 2013). A study by Simonen et al. suggested a correlation of *DRD2* gene polymorphism and the prevalence of physical activity. For instance, in exon 6, the TT genotype of the *DRD2* gene was associated with reduced level of long-term activity. Additionally, in the *DRD2* gene locus, the variation in the DNA sequence may result in long-term involvement in physical activity. Besides, it is believed that the proliferation of the dopamine level through exercise may arouse pleasurable feelings. Therefore, this may promote the increase of physical activity of individuals in order to seek for the pleasure sensation (Simonen et al., 2003). A study by Han et al. has investigated the association of genetic variants with reward dependency on excessive internet video gameplay (EIGP). Higher reward dependency and an increased prevalence of the *DRD2 Taq1 A1* have shown in EIGP subjects (Han

et al., 2007), though the study only included male adolescents who possibly manifested higher sensation-seeking risk-taking behaviour.

The influence of reduced D2R in obesity might not rely on the eating behaviours and increasing appetitive motivation generating compulsive eating, but most likely in regulating physical activity and energy expenditure, promoting reduced behavioural expenditure of energy (Beeler et al., 2016). Diminished dopamine reduces the willingness and enthusiasm to work for reward, including locomotor activity without altering free-feeding food preferences (Salamone et al., 2005). Besides regulating behavioural energy expenditure, dopamine also regulates behavioural choice (Beeler et al., 2012). To put it simply, if an individual has previously received compliments (rewards) of perfect body shape after putting in hard work in physical activity, the individual tends to remain disciplined even when facing a real delicacy. The individual will most likely exercise and control his or her diet in the future as compliments (prior reward) are more valuable than delicacy (current reward) for the individual, or vice versa depending on the prior reward or the personal preference in reward.

2.5 Health-Related Quality of Life (HRQoL) and obesity

Life expectancy and roots of life lost have been commonly employed as key indicators regarding the health status of the population. Although these indicators offer crucial information on populations' health, information pertaining to the quality of the physical, mental, and social aspects of life are not provided. The generic measure of health status, particularly those that comprise the quality-adjusted life-year (QALY) are emphasised to increase life

expectancy. The importance of assessing and improving populations' quality of life is then widely accepted by communities and recognised by WHO in 1995 (WHOQOL Group, 1995). When the quality of life has been taken in the framework of health and disease burden, it is usually referred to as health-related quality of life (HRQoL) to distinguish it from the other quality of life domains. HRQoL is a multidimensional notion that includes domains with respect to physical, mental, emotional, and social functioning (Ferrans, 2005). It highlighted the influence of health on quality of life and positive elements of an individual's life (e.g., life contentment and positive emotions) instead of a mere measurement on health status, life expectancy, and causes of life loss of population. Over the past decades, HRQoL and 'Well-Being Measures' have been commonly used as indicators by an organisation such as National Institutes of Health (NIH) and Centers for Disease Control and Prevention (CDC) to ascertain the impacts of chronic diseases, treatments, as well as short- and long-term disabilities (Healthy People 2020, 2010). There are multiple existing assessments of HRQoL and well-being (PROMIS, Well-Being Measures, Participation Measures, SF-36, etc.).

Although there were myriads of studies demonstrating the association between obesity with morbidity and mortality, the study regarding the effect of obesity on HRQoL is not well documented and incomprehensive. The assessment of the association between obesity and HRQoL can be classified into two categories: generic and disease-specific measures (Warkentin et al., 2014). Generic measures are designed to assess a broad spectrum of HRQoL, whereas disease-specific measures are used to assess a specific medical or clinical condition of

HRQoL. The generic measure was employed in our study, and it was clustered into two groups, which are physical component summary (PCS) and mental component summary (MCS) of subjects. Higher scores reflect better physical and mental health. A meta-analysis of cross-sectional differences among non-patient subgroups and patient subgroups by Van Nunen et al. demonstrated that obesity was associated with lower generic and obesity-specific HRQoL in patient subgroups who have undergone bariatric surgery for weight loss. Also, only physical functioning, a subscale under PCS of HRQoL, showed a consistent reduction for the patient against non-patient groups (Van Nunen et al., 2007). A meta-analysis later supports this result by Ul-Haq et al., which compared normal-weight adults with overweight or obese adults. A parallel relationship between BMI (≥25 kg/m^2) and reduced PCS scores. Contrarily, only class III obesity subjects (BMI (≥40 kg/m^2) showed significant association with MCS score (Ul-Haq et al., 2013). A recent review from Kolotkin and Andersen concluded a consistent relationship between improved HRQoL and weight loss after bariatric surgery. For non-surgical weight loss, improved HRQoL was also shown but inconsistent (Kolotkin and Andersen, 2017). However, as we can see from most of the studies mentioned above which show a significant association between obesity and HRQoL uses weight loss as a variable instead of the currently existing BMI or weight from the subjects. Therefore, our study that employs the comparison of healthy individuals' BMI as subjects to HRQoL might contribute some insights and impacts to the society, and perhaps create a healthier community.

CHAPTER 3

METHODOLOGY

3.1 Conceptual framework

This proposed study attempts to look into the association between dopamine receptor gene polymorphisms and the aetiology of obesity and investigate dopamine receptor genotypes' role in moderating links between eating behaviours and physical activity. The conceptual framework is presented in Figure 3.1.

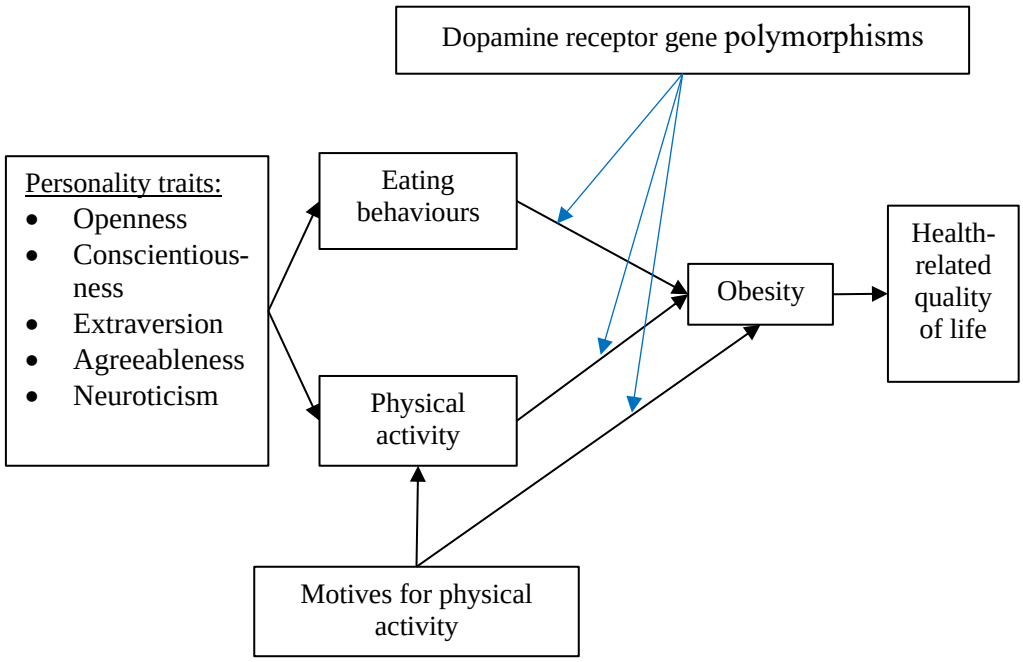


Figure 3.1: Conceptual framework

3.2 Study Design and sample size calculation

The study subjects were designed as cross-sectional study with recruitment based on convenient sampling. Participants were recruited from University Tunku Abdul Rahman (UTAR) Kampar campus, Perak, Malaysia. This is a retrospective study and the data was collected through questionnaires. The sample size was calculated using Raosoft sample size calculator with the formula: $x = Z(\frac{c}{100})^2 r(100\text{-}r)$ and $n = \frac{Nx}{(N-1)E^2 + x}$, where n is the number of sample sizes. Z(c/100) is the critical value (1.96 in this case with 95% confidence interval). r is the fraction of responses of interest (0.025 in this case with default set up of 50% response distribution). The margin of error was set to be 5% (E = 0.05). The number of x = 0.96 was obtained from the calculation with the first equation. N, which represents the number of population size, is set to 25000 (approximately 22000 students and 2200 staff according to the UTAR official website).

Sample size calculation:

$$n = \frac{Nx}{(N-1)E^2 + x}$$

$$= \frac{25000\ (0.96)}{(25000-1)0.05^2+0.96}$$

$$= \frac{24000}{63.4575}$$

$$= 378.20 \sim 379$$

3.3 Inclusion and exclusion criteria

Sampling was conducted based on the inclusion criteria of healthy staff and students of UTAR age ≥18 years old. Study subjects who did not meet the inclusion criteria would be excluded, such as those with:

i. major medical conditions such as diabetes, hypertension or diagnosed metabolic syndrome
ii. recent weight loss or dieting
iii. use of any medications known to affect the taste, bodyweight or appetite
iv. smoking more than one pack per week
v. chronic sinus problems, previous malabsorptive or restrictive intestinal surgery
vi. pregnant and breastfeeding.

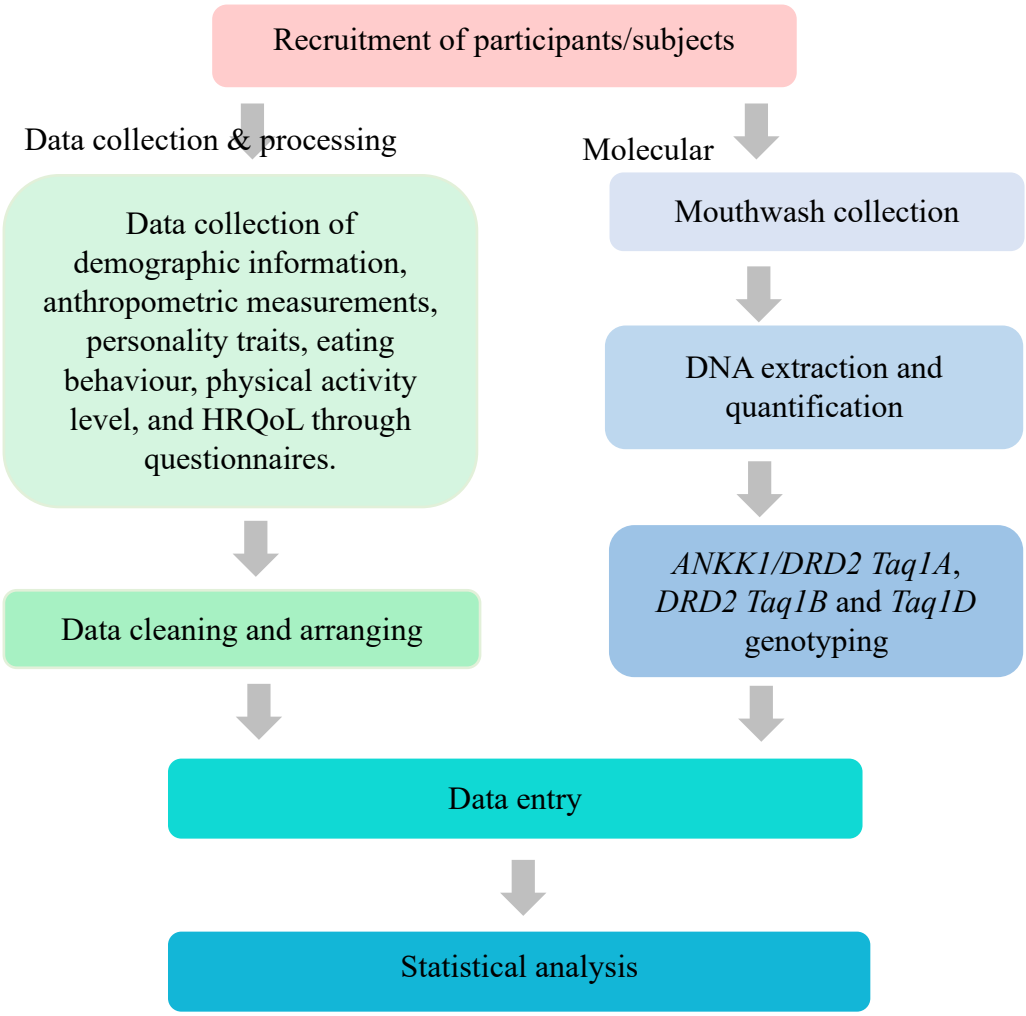
3.4 Ethical approval

The study was conducted after acquiring ethical approval from the UTAR Scientific and Ethical Review Committee (UTAR SERC approval number: U/SERC/97/2018]). Informed consent from subjects was obtained prior to sampling. Sampling procedures were conducted in accordance with the Helsinki Declaration.

3.5 Study design

Study was designed into two parts after recruitment of participants, which are social science and molecular analysis. The overview of the study's experimental design was summarised in a flowchart, as presented in Figure 3.2.

Figure 3.2: Experimental design



3.6 Survey and questionnaire

Data was collected through questionnaires, including demographic information (e.g., age, gender and ethnicity) and anthropometric measurements (height, weights, BMI, etc.). Participants' body mass index (BMI) was measured using the Omron Karada Scan HBF-375 Body Fat Composition Monitor. The questionnaires consisted of a few parts to assess personality traits, eating

behaviours, physical activity, motivation in doing physical activity and general health status. The questionnaires were included in the appendix.

3.6.1 Personality traits score

The Mini-International Personality Item Pool Scales (Mini-IPIP) was employed to obtain the subjects' personality traits score. Mini-IPIP consists of 20 questions related to the Big-Five personality traits (Donnellan et al., 2006). There are four items each to measure openness, conscientiousness, extraversion, agreeableness, and emotional stability. This self-rating scale asked the participants to rate themselves with a 5-point Likert scale, rated from 1 (strongly disagree) to 5 (strongly agree). Mini-IPIP has the lowest coefficient alpha of 0.64 on agreeableness and highest Cronbach's α-values of 0.90 on extraversion (Donnellan et al., 2006). After omitting the subjects that violated the inclusion criteria and data that contain missing values, data arranging was followed. For items 6, 7, 8, 9, 10, 15, 16, 17, 18, 19, and 20 in Mini-IPIP, reverse scoring was executed before assessing the five domains (openness, conscientiousness, extraversion, agreeableness, and neuroticism) with 1 = 5, 2 = 4, 3 = 3, 4 = 2, and 5 = 1. The five domains score was then obtained by averaging the items scores (Table 3.1).

Table 3.1: The scoring system of Mini-IPIP.

Scale	Number of items	Mean the following items
Neuroticism	4	4, 9r, 14, 19r
Extraversion	4	1, 6r, 11, 16r
Openness	4	5, 10r, 15r, 20r
Agreeableness	4	2, 7r, 12, 17r
Conscientiousness	4	3, 8r, 13, 18r

Note: r indicates reverse scoring of the particular item.

3.6.2 Eating behaviours score

In order to assess the eating behaviour score, the Three-Factor Eating Questionnaire (TFEQ-R18) was adopted (Fleurbaix Laventie Ville Sante Study Group, 2004). TFEQ-R18 with eighteen items related to eating behaviours in a person. The responses ranged from "definitely true", "mostly true", "mostly false" to "definitely false". The subscales of TFEQ-18 were cognitive restraint (CR), uncontrolled eating (UE) and emotional eating (EE). The reliability of the subscales was demonstrated through high coefficient alpha, with lowest α-values of 0.78 on EE of a teenager (Fleurbaix Laventie Ville Sante Study Group, 2004). Higher scores in the respective scales indicate greater CR, UE or EE. Table 3.2 shows the scoring system of TFEQ-R18.

Table 3.2: The scoring system of TFEQ-R18.

Scale	Number of items	Items
CR	6	2, 11, 12, 15, 16, 18r
UE	9	1, 4, 5, 7, 8, 9, 13, 14, 17
EE	3	3, 6, 10

Note: r indicates recode of the particular item where 1–2 scores were recoded to 1; 3–4 scores were recoded to 2; 5–6 scores were recoded to 3; 7–8 scores were recoded to 4.

In order to calculate the CR score, it was started with obtaining the raw score range. The possible raw score range of the six items (2, 11, 12, 15, 16, 18) was multiplied by four maximum scores (definitely true, mostly true, mostly false, definitely false): 6 * 4 = 24. The lowest possible raw score is obtained by multiplying six items and a minimum score of one: 6 * 1 = 6. The raw scale scores then are transformed to a 0 – 100 scale: [((raw score - lowest possible raw score)/possible raw score range) x 100]. After inserting the counted value,

a formula to calculate CR is obtained: [(sum of 2, 11, 12, 15, 16, 18r) – 6] / 24 * 100 = CR score of the particular subject.

Similar to CR, the calculation of UE score was started with obtaining the raw score range. Multiplication of the nine items (1, 4, 5, 7, 8, 9, 13, 14, 17) and four maximum scores (definitely true, mostly true, mostly false, definitely false) to acquire the possible raw score range: 9 * 4 = 36. In order to obtain the lowest possible raw score, nine items were multiplied by the minimum score of one: 9 * 1 = 9. The raw scale scores then are transformed to a 0 –100 scale: [((raw score - lowest possible raw score)/possible raw score range) * 100]. After interpolating the counted value, a formula to calculate UE is obtained: [(sum of 1, 4, 5, 7, 8, 9, 13, 14, 17) – 9] / 36 *100 = UE score of the particular subject.

EE scale which made up of three items (3, 6, 10) has a raw score of 12 after the multiplication of three with the maximum score of four (definitely true, mostly true, mostly false, definitely false): 3 * 4 = 12, and the lowest possible score of 3 by multiplying three to the minimum score of one: 3 * 1 = 3. The raw scale scores then are transformed to a 0 – 100 scale: [((raw score - lowest possible raw score)/possible raw score range) * 100]. After inserting the counted value, a formula to calculate EE is obtained: [(sum of 3, 6, 10) – 3] / 12 *100 = EE score of the particular subject.

3.6.3 Physical activity level score

Physical activity level was assessed using the International Physical Activity Questionnaire (IPAQ) (IPAQ Research Committee, 2005), consisting of 4

questionnaires. There are two IPAQ questionnaire versions, including long (5 activity domains asked independently) and short (4 generic items) questions. IPAQ-short last 7 days self-administered format was applied in this study. The questionnaire's validity and reliability have been tested to evaluate the intensity, frequency, and duration of physical activity during the preceding week before the survey. The total metabolic equivalent of task (MET-min/week) for vigorous-intense, moderate-intense and walking will be calculated to categorise the studied populations into three levels, which are active, moderately active and inactive, in line with the IPAQ scoring criteria. According to IPAQ scoring criteria, a physically active or moderately active person was considered a compiler to the WHO physical activity recommendations. The IPAQ questionnaire applies the metabolic equivalent of task (MET) in the assessment of physical activity, where there are 3.3 METs for walking, 4.0 METs for Moderate physical activity, and 8.0 METs for vigorous physical activity (IPAQ Research Committee, 2005). IPAQ continuous score is expressed as MET-min per week: MET level x minutes of activity/day x days per week. Hence, to calculate the physical activity score:

- Walking MET-minutes/week = 3.3 * walking minutes * walking days
- Moderate MET-minutes/week = 4.0 * moderate-intensity activity minutes * moderate days
- Vigorous MET-minutes/week = 8.0 * vigorous-intensity activity minutes * vigorous-intensity days

∴ Total MET-minutes/week = Walking (METs*min*days) + Moderate (METs*min*days) + Vigorous (METs*min*days)

3.6.4 The motives for physical activity measure domains

In order to assess motivation in doing physical activities, the Motives for Physical Activity Measure – Revised (MPAM-R) was employed (Richard et al., 1997). MPAM-R is a 7-point Likert scale rated from 1 (not at all true for me) to 7 (very true for me). The score comprises five domains (Interest/enjoyment, competence, appearance, fitness, social). A higher score indicates higher motivation of the particular domain in doing physical activity. The scoring system of MPAM-R is similar to Mini-IPIP, which averages the item's score. The score of the five domains was then obtained by averaging the items scores, as shown in Table 3.3.

Table 3.3: The scoring system of MPAM-R.

Scale	Number of items	Mean the following items
Interest/Enjoyment	7	2, 7, 11, 18, 22, 26, 29
Competence	7	3, 4, 8, 9, 12, 14, 25
Appearance	6	5, 10, 17, 20, 24, 27
Fitness	5	1, 13, 16, 19, 23
Social	5	6, 15, 21, 28, 30

3.6.5 HRQoL score arranging

The Short Form 36 Health Survey Questionnaire (SF-36), an indicator of general health status, was employed in this study to assess HRQoL (Ware et al., 2000). SF-36 assesses the quality of life in eight health domains:

i. physical functioning
ii. limitations in role activities because of physical health
iii. limitations in role activities because of emotional problems
iv. vitality (i.e., energy/fatigue)
v. general mental health (i.e., emotional well-being)

vi. social functioning

vii. bodily pain

viii. general health

The eight domains are collapsed to be classified into two components: physical component summary (PCS) and mental component summary (MCS). The SF-36 also has well-established internal consistency and validity. Overall reliability of the SF-36 has exceeded 0.78. The SF-36 scales are responsive for the treatment of numerous medical conditions, including obesity. This will allow researchers to compare the burdens imposed by obesity against populations with or without other associated disorders.

There are two main steps when applying SF-36: 1) value recoding and 2) averaging the recoded items. Table 3.4.1 shows the changes in the original response category to the new recorded value, and Table 3.4.2 shows the scoring system of HRQoL.

Table 3.4: The recoding system of HRQoL items.

Items	Original value		Recoded value
1, 2, 20, 22, 34, 36	1	→	100
	2	→	75
	3	→	50
	4	→	25
	5	→	0
3, 4, 5, 6, 7, 8, 9, 10, 11, 12	1	→	0
	2	→	50
	3	→	100
13, 14, 15, 16, 17, 18, 19	1	→	0
	2	→	100
21, 23, 26, 27, 30	1	→	100
	2	→	80
	3	→	60
	4	→	40
	5	→	20
	6	→	0
24, 25, 28, 29, 31	1	→	0
	2	→	20
	3	→	40
	4	→	60
	5	→	80
	6	→	100
32, 33, 35	1	→	0
	2	→	25
	3	→	50
	4	→	75
	5	→	100

Table 3.5: The scoring system of HRQoL.

Scale	Number of items	Average the following recoded HRQoL items
Physical functioning	10	3 4 5 6 7 8 9 10 11 12
Role limitations due to physical health	4	13 14 15 16
Role limitations due to emotional problems	3	17 18 19
Energy/fatigue	4	23 27 29 31
Emotional well-being	5	24 25 26 28 30
Social functioning	2	20 32
Pain	2	21 22
General health	5	1 33 34 35 36

The SF-36 eight subscale evaluate the quality of life in either physical health (PCS) or behavioural health (MCS). PCS is obtained by the summation of the recoded items of general health, pain, physical functioning, and role limitations due to physical health; where MCS is obtained by the summation of the recoded items of energy/fatigue, emotional well-being, social functioning, as well as role limitations due to emotional problems).

After data cleaning and arranging, data entry is carried out by importing all the numbers or figures into IBM SPSS software version 23, a software package employed for calculation and statistical analysis, for the subsequent statistical analysis (refer to section 3.6 Statistical analysis).

3.7 DNA extraction and quantification

Mouthwash samples were collected from the subjects. Genomic DNA was extracted from it by using GF-1 Nucleic Acid Extraction Kit (Vivantis, Malaysia). Genotyping of the three D2 gene variants (*DRD2/ANKK1 Taq1A*, *DRD2 Taq1B* and *DRD2 Taq1D*) were performed by using PCR-RFLP technique using three pairs of primers adopted (refer to Table 3.6) from a previous study (Vijayan et al., 2007). These primers have distinct specific target region site on the *ANKK1* gene or *DRD2* gene, as presented in Table 3.6. The rs1800497 (*Taq1A*), rs1079597 (*Taq1B*) and rs1800498 (*Taq1D*) were located at 11q23.2, exon 8 of *ANKK1*/*DRD2* gene at chromosome 11, as shown in Figure 3.3(a) and Figure 3.3(b). PCR was conducted in a final volume of 20 μL solution containing 50 ng DNA template, 1× PCR buffer (TransGen Biotech Co., Ltd, China), 0.2 mM deoxyribonucleotide triphosphates (dNTP) (TransGen

Biotech Co., Ltd, China), 2.5 units of *Taq* polymerase (TransGenges Biotech Co., Ltd, China) and 0.25 μM for each forward and reverse primer. Table 3.7 shows the concentration and volume of PCR reaction preparation for rs1800497, rs1079597 and rs1800498.

Table 3.6: Primer sequences for *DRD2* gene polymorphisms

***DRD2* SNP**	**Forward primer (5' – 3')**	**Reverse primer (5' – 3')**
Taq1A (rs1800497)	CCCTTCCTGAGTGTCATCA	CGGCTGGCCAAGTTGTCTA
Taq1B (rs1079597)	GATACCCACTTCAGGAAGTC	GATGTGTAGGAATTAGCCAGG
Taq1D (rs1800498)	CCCAGCAGGGAGAGGGAGTA	GACAAGTACTTGGTAAGCATG

(Vijayan et al., 2007)

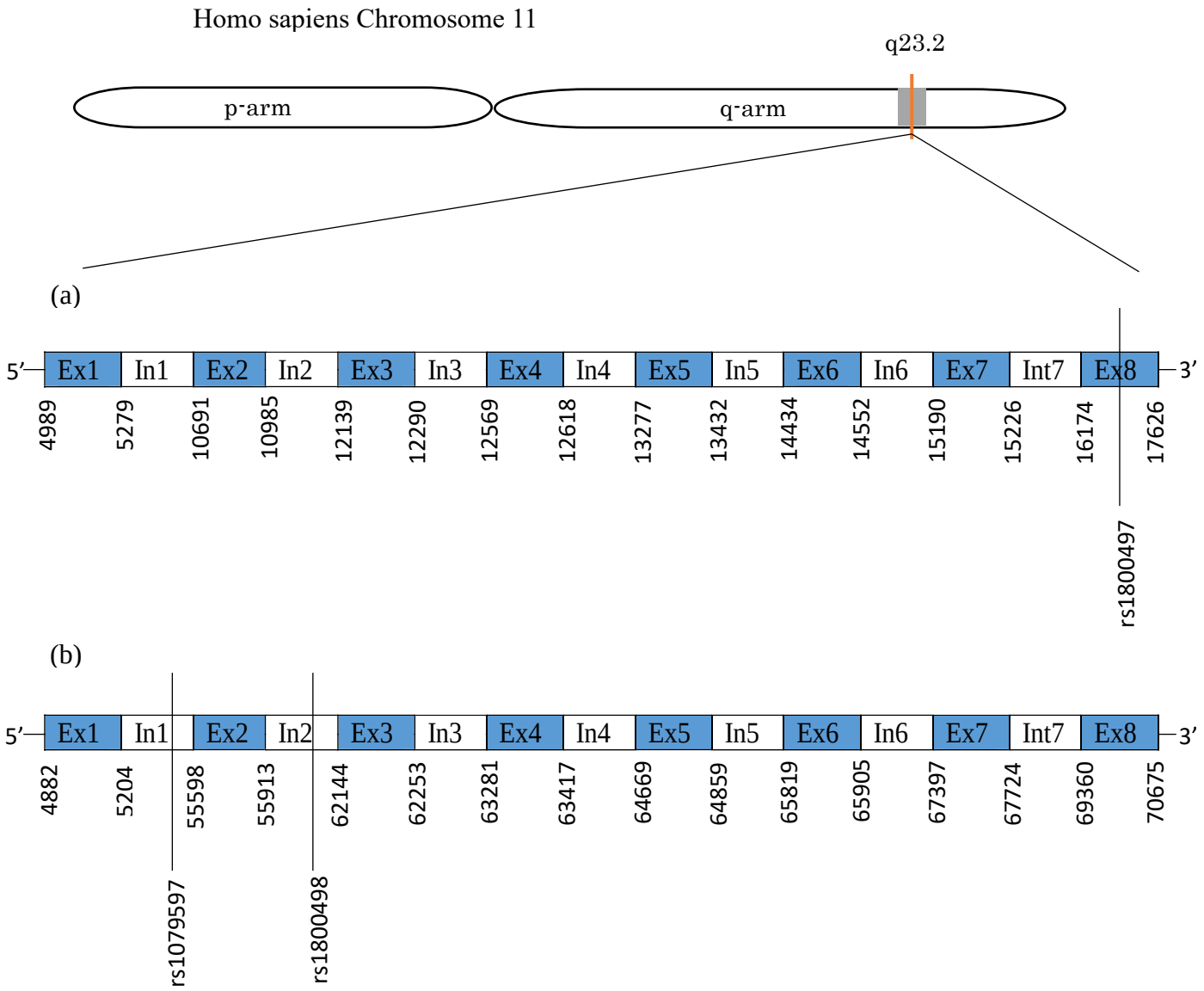


Figure 3.3: Schematic diagram showing the location of rs1800497, rs1079597 and rs1800498 polymorphism. (a) *ANKK1*. (b) *DRD2* gene

Table 3.7: Volume and concentration of PCR preparation

PCR components	**Stock concentration**	**Final concentration**	**Volume (µL)**
PCR buffer (with Mg^{2+})	10X; 20µM $MgCl_2$	1X; 2µM $MgCl_2$	2.0
dNTP	2.5 mM	0.2 mM	1.6
Taq Polymerase	5 units/µL	2.5 units	0.5
Primer (Forward)	10 µM	0.25 µM	0.5
Primer (Reverse)	10 µM	0.25 µM	0.5
Genomic DNA	10 ng/µL	50 ng/µL	5.0
dH_2O			9.9
Total			20.0

Table 3.8: PCR primers and amplicon for PCR used to detect different *DRD2* polymorphisms.

SNP	**Target region**	**Amplicon size (bp)**	**Fragment size after *TaqI* digestion (bp)**
Taq1A rs1800497	*DRD2/ANKK1* gene - exon 8	304	125, 176
Taq1B rs1079597	*DRD2* gene - intron 1	459	190, 269
Taq1D rs1800498	*DRD2* gene - intron 2	419	271, 148

The cycling condition was performed with an initial denaturation (94°C, 3 minutes), followed by 35 cycles of denaturation (94°C, 30 seconds), annealing (65°C and 45 seconds for *DRD2 Taq1A*), and extension (72°C for 60 seconds).

Final extension step (72°C for 5 minutes) was performed for the reannealing of the PCR product into double-stranded DNA (Table 3.9). After amplification, 5 µL of PCR product were digested with restriction enzyme *Taq*-1 in a final volume of 10 µL solution containing 5 µL PCR product, 1× Reaction buffer v5 (Vivantis, Malaysia), two units of *Taq*-1 restriction enzyme (Vivantis, Malaysia) and 3.5 µL of Double Distilled Water (ddH2O). The components of the reagent mix were as shown in Table 3.10. The solution was incubated for 1 hour at 65°C. Figure 3.4 illustrated the recognition site of *Taq*-1 restriction enzyme. The RFLP products were electrophoresed using 1.5% agarose gel. The amplicon was visualised with gel red staining using a gel documentation system (Gel Doc XR+ Gel Documentation System; Bio-Rad, Malaysia). Two fragments are produced for each SNP after *Taq*-1 digestion (Table 3.8). Each run of genotyping was performed for 14 samples in parallel with positive and negative control. Run with inappropriate control will be replicated. In addition, replication of PCR was conducted on PCR or RFLP products which showed unsatisfactory result (e.g., vague band). Roughly 50 DNA samples were randomly selected for PCR replication to ensure the replicability of the result.

Table 3.9: PCR setting of *DRD2 Taq1A*, *Taq1B* and *Taq1D*.

Steps	**Temperature (°C)**	**Duration (sec)**	**Cycles**
Initial denaturation	94	180	1
Denaturation	94	30	35
Annealing (*Taq1A*; *Taq1B*; *Taq1D*)	65; 60; 60	45	35
Extension	72	60	35
Final extension	72	300	1

Table 3.10: Reagent components for PCR-RFLP.

Steps	**Initial concentration**	**Final concentration**	**Volume (µL)**
Buffer v5	10X	1X	1.0
Taq-1	4 units/µL	2 units	0.5
PCR product			5.0
dH_2O			3.5
Final volume			10.0

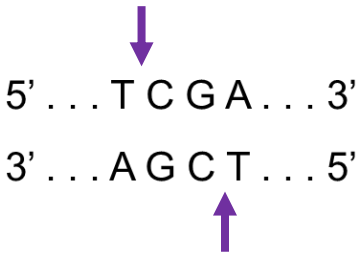


Figure 3.4: Recognition site of the *Taq-1* restriction enzyme

3.8 Statistical analysis

Statistical analysis was conducted to verify the proposed research hypotheses. Various analysis tests were conducted, including Chi-Square Test for Association, Spearman's Rank-Order Correlation, Kruskal-Wallis H Test and path analysis.

3.8.1 Research Hypotheses

i. There is a significant correlation between personality traits (extraversion, agreeableness, conscientiousness, emotional Stability, and openness) and eating behaviour and physical activity.

ii. There is a significant association between obesity and eating behaviour and physical activity

iii. Dopamine receptor D2 genotypes moderates the link of physical activity and eating behaviour on obesity.

iv. There is a significant relationship between health-related quality of life and BMI classes.

3.8.2 Data analysis tests

Genotypic and allelic frequencies of each *DRD2* gene polymorphisms were generated by SNPStats web tool. Hardy-Weinberg equilibrium (HWE) analysis was performed on *DRD2 Taq*1 genotype distribution where the observed and expected values were analysed using a chi-square test. Normality test was performed to examine the skewness and kurtosis level of the testing variables before analysing the variables. Classification of data was carried out.

Categorical variables: demographic distribution (gender and ethnicity), genotypes, and alleles; continuous variable: personality traits score, eating behaviour score, IPAQ score, and HRQoL score. The variables were analysed using Statistical Package for Social Scientists (SPSS) software version 23.0 (SPSS Inc., Chicago, IL, USA). Spearman's rank correlation coefficient was employed to determine the correlation between personality trait scores and eating behaviour scores and physical activity level score. The relationship between eating behaviour and obesity was investigated using regression analysis. Pearson's chi-squared test was used in the study of the association between physical activity and obesity. Kruskal Wallis test was used to compare the HRQoL of an individual with obesity. For the stratification of data, parametric One-Way ANOVA and non-parametric Kruskal Wallis test were employed to determine the means ± standard deviation or standard error of measurement (SEM). The statistical significance (p-value) was set at < 0.05 with confidence interval (CI) at 95%. To study the effect of *DRD2* genotypes in moderating the link between eating behaviour, physical activity, MPAM-R and obesity, IBM SPSS Amos 23 and Stats Tools Package was employed. The path analysis model was demonstrated by using IBM SPSS Amos 23. There are a few minimum criteria (model fit) need to be achieved before proceeding to the study of moderation effect of D2 genes: p-value >0.05; GFI ≥0.95 AGFI ≥0.90; ≥0.90; RMSEA <0.08. 'Regression weight results table' and 'Pairwise Parameter Comparisons' obtained from the path analysis will be interpolated into Stats Tools Package, under the category of 'Group Differences'. The Z-score value will be obtained after pressing 'Enter'. Any Z-score values that are higher than 1.96 (p-values < 0.05) represents a significant impact of the moderator

(Afthanorhan et al., 2014).

CHAPTER 4

RESULTS

4.1 Demographic, anthropometric characteristics and environmental exposures of subjects

This study successfully recruited 394 study subjects. Among the 394 study subjects, 125 (31.7%) were male, and 269 (68.3%) were female. Female subjects showed higher BMI with the minimum BMI at 14.2 kg/m^2 and maximum BMI at 53.8 kg/m^2. The minimum and maximum BMI for male subjects were found 14.8 kg/m^2 and 39.9 kg/m^2, respectively. Majority of the subjects were Malaysian-Chinese (n = 329, 83.5%), followed by Malaysian-Indians (n = 32, 8.1%), Malays (n = 32, 8.1%) and only one was aborigines (n = 1, 0.3%). Table 4.1 presents the distribution of BMI for the study subjects.

Table 4.1: BMI based on gender and ethnicity for 394 study subjects.

	Mean ± SD (BMI)	**Range (BMI)**
Gender		
Male (n=125)	23.10 ± 4.70	14.8 - 39.9
Female (n=269)	22.70 ± 5.36	14.2 – 53.8
Ethnicity		
Malay (n=32)	26.91 ± 8.62	17.3 – 53.8
Chinese (n=329)	22.25 ± 4.47	14.2 – 41.7
Indian (n=32)	24.52 ± 5.20	17.3 – 36.9
Aborigine (n=1)	28.1	-

4.2 Genotypic and allelic frequencies of dopamine receptor gene variants

Genotypic and allelic frequencies of the *DRD2/ANKK1 Taq1A* (rs1800497), *Taq1B* (rs1079597) and *Taq1D* (rs1079597) polymorphisms are presented in Table 4.2. For rs1800497, A1/A2 was the predominant genotype (n = 184; 47.0%), followed by A2/A2 (n = 153; 39.0%) and A1/A1 genotype (n = 57; 14.0%). A2 was the major allele at 62.0% and A1 was the minor allele at 38.0%. For rs1079597, B1/B2 genotype was the predominant genotype (n = 171; 43.0%), followed by B2/B2 (n = 155; 39.0%) and B1/B1 genotype (n = 68; 17.0%). B2 allele was expressed dominantly at 61.0% and B1 was the minor allele at 39.0%. For rs1800498, D2/D2 was the predominant genotype (n = 337; 85.0%), followed by D1/D2 (n = 52; 14.0%) and D1/D1 genotypes (n = 5; 1.0%). D2 allele was the major allele at 92.0% while D1 was the minor allele at 8%.

Table 4.2: Genotypic and allelic frequencies of *DRD2 Taq1A* (rs1800497), *Taq1B* (rs1079597) and *Taq1D* (rs1800498) polymorphisms.

***DRD2* Gene Variant**	**Genotypic frequencies n (%)**			**Allelic frequencies**	
				Major	**Minor**
Taq1A (rs1800497)	A2/A2	A1/A2	A1/A1	A2	A1
Total (n=394)	153 (0.39)	184 (0.47)	57 (0.14)	0.62	0.38
Taq1B (rs1079597)	B2/B2	B1/B2	B1/B1	B2	B1
Total (n=394)	155 (0.39)	171 (0.43)	68 (0.17)	0.61	0.39
Taq1D (rs1800498)	D2/D2	D1/D2	D1/D1	D2	D1
Total (n=394)	337 (0.85)	52 (0.14)	5 (0.01)	0.92	0.08

Parentheses value under the genotypic frequencies' column indicates the percentage within the same genetic variant.

4.3 Hardy-Weinberg equilibrium (HWE)

Table 4.3 demonstrated the distribution of *DRD2 Taq1* genotypes following Hardy-Weinberg Equilibrium (HWE). HWE is used to estimate the number of homozygous and heterozygous variant carriers in populations that are not evolving due to disturbing factors (e.g., mutations, natural selection, non-random mating, genetic drift, and gene flow) (Graffelman et al., 2017). Significant deviations from HWE have been used to detect genotyping errors, which can result in extreme heterozygote excess. The null hypothesis (H_0) was set as the observed genotype frequency is in HWE whereas the alternative hypothesis (H_1) was set as observed genotype frequency is not in HWE. The calculated χ^2 value for all three *DRD2 Taq1* genetic variants genotypes were less than 3.84 (0.0308 for *Taq1A*, 3.0157 for *Taq1B* and 3.0984 for *Taq1D*), indicating that the null hypothesis was not rejected. The genotype distribution of *DRD2 Taq1A*, *Taq1B* and *Taq1D* did not deviate from the HWE.

Table 4.3: A chi-square test of HWE for *DRD2 Taq1* genotype distribution.

Genotype	Observed	Expected	(O-E)	$(O-E)^2/E$
A2/A2	153	151.45	1.55	0.0159
A1/A2	184	185.65	-1.65	0.0147
A1/A1	57	56.89	0.11	0.0002
Total	394	394		χ^2 = 0.0308, *p*-value = 0.91
B2/B2	155	146.80	8.20	0.4577
B1/B2	171	187.40	-16.39	1.4343
B1/B1	68	59.80	8.20	1.1236
Total	394	394		χ^2 =3.0157, *p*-value = 0.09
D2/D2	337	333.48	3.52	0.0371
D1/D2	52	58.00	-6.00	0.6207
D1/D1	5	2.52	2.48	2.4406
Total	394	394		χ^2 = 3.0984, *p*-value = 0.08

4.4 Genotypic distribution of dopamine receptor genetic variants among different BMI classes

Table 4.4 demonstrates the distribution of dopamine receptor genotypes with BMI. The null hypothesis (H_0) was set as the observed genotypes and alleles have no significant association with BMI classes whereas the alternative hypothesis (H_1) was set as observed genotypes and alleles has significant association with BMI classes. From the association analysis, no significant association was found between BMI with three genetic variants and alleles. The rs1079597 demonstrated the strongest association with ($\chi^2 = 5.214$) at *p*-value = 0.517. The weakest association with BMI ($\chi^2 = 1.618$) at *p*-value = 0.951 was found in rs1800498. The association between rs1800497and BMI was 3.053, with p- value = 0.802. The rs1079597 alleles demonstrated the strongest association with BMI ($\chi^2 = 3.576$; *p*-value = 0.311) while rs1800498 showed the weakest association with BMI ($\chi^2 = 0.470$; *p*-value = 0.926). The null hypothesis was not rejected.

Table 4.4: Genotypic distributions of dopamine receptor genetic variants among body mass index (BMI) of subjects.

***DRD2* gene variant**	**Genotypes**	**BMI classes n (%)**				**χ2; *p*-value**
		Underweight	**Normal**	**Overweight**	**Obese**	
Taq1A	A2/A2	23 (5.8)	74 (18.8)	23 (5.8)	33 (8.4)	3.053;
rs1800497	A1/A2	27 (6.9)	89 (22.6)	22 (5.6)	46 (11.7)	0.802
Total	A1/A1	9 (2.3)	23 (5.8)	7 (1.8)	18 (4.6)	
(n=394)						
	A2	74 (9.4)	237 (30.1)	68 (8.6)	112 (14.2)	2.468;
	A1	44 (5.6)	135 (17.1)	36 (4.6)	82 (10.4)	0.481
Taq1B	B2/B2	24 (6.1)	77 (19.5)	21 (5.3)	33 (8.4)	5.214;
rs1079597	B1/B2	24 (6.1)	79 (20.1)	26 (6.6)	42 (10.7)	0.517
Total	B1/B1	11 (2.8)	30 (7.6)	5 (1.3)	22 (5.6)	
(n=394)						
	B2	72 (9.1)	233 (29.6)	68 (8.6)	108 (13.7)	3.576;
	B1	46 (5.8)	139 (17.6)	36 (4.6)	86 (10.9)	0.311
Taq1D	D2/D2	50 (12.7)	161 (40.9)	44 (11.2)	82 (20.8)	1.618;
rs1800498	D1/D2	8 (2.0)	23 (5.8)	8 (2.0)	13 (3.3)	0.951
Total	D1/D1	1 (0.3)	2 (0.5)	0 (0.0)	2 (0.5)	
(n=394)						
	D2	108 (13.7)	345 (43.8)	96 (12.2)	177 (22.5)	0.470;
	D1	10 (1.3)	27 (3.4)	8 (1.0)	17 (2.2)	0.926

Parentheses indicate the percentage within the same genetic variant. The analysis was done by comparing BMI with genotypes and alleles through Pearson's chi-squared test; **p*-value significant at < 0.05

4.5 *DRD2* gene polymorphisms with eating behaviours, physical activity and the motives for physical activity

Table 4.5 shows the comparison of the *DRD2* genetic variants and alleles with the three different eating behaviours (CR, UE and EE, respectively). The null hypothesis (H_0) was set as having no significant difference between genotypes and alleles with eating behaviours whereas the alternative hypothesis (H_1) was set as there was a significant difference between genotypes and alleles with eating behaviours.

No significant difference was found between genotypes among CR and UE. A significant difference was presented between EE with the *Taq1A* genotype (*p*-value = 0.040). However, no significant difference was found between *Taq1B* and *Taq1D* genotypes on EE with *p*-value at 0.075 and 0.855, respectively. There were no significant differences between all three *DRD2 Taq1* gene alleles CR, UE and EE either.

A Kruskal-Wallis test provided evidence of a difference ($p < 0.05$) between the mean ranks of at *DRD2 Taq1A* and EE. Dunn's pairwise tests were carried out for the three pairs of groups. *Post hoc* test showed that the *DRD2 Taq1A* heterozygote (A2/A1) and homozygote (A1/A1) differed significantly at adjusted *p*-value = 0.040 with mean rank difference of 42.12. EE showed significant difference in *DRD2 Taq1B* genotypes with *p*-value = 0.026 but with non-significant multiple pairwise comparisons. The *Taq1B* heterozygote (A2/A1) was not significantly different from the wildtype (A2/A2) and homozygote (A1/A1) group with adjusted *p*-value = 0.078 and 0.075,

respectively. The *Taq1B* wildtype (A2/A2) was not significantly different from the homozygote (A1/A1) group with adjusted *p*-value = 1.000.

Table 4.5: Distribution of the eating behaviour scores in different *DRD2* genotypes and alleles.

	Genotypes (mean ± SEM)			Alleles (mean ± SEM)	
Taq1A **rs1800497**	**A2/A2**	**A1/A2**	**A1/A1**	**A2**	**A1**
CR	37.88 ± 0.65	37.50 ± 0.63	38.82 ± 1.07	37.84 ± 0.37	38.09 ± 0.48
p-value		0.751		0.874	
UE	41.27 ± 0.81	39.58 ± 0.71	41.23 ± 1.10	40.65 ± 0.44	40.18 ± 0.53
p-value		0.197		0.441	
EE	48.97 ± 1.30	46.29 ± 1.23	52.92 ± 2.26	48.01 ± 0.74	48.74 ± 0.99
p-value		***0.040****		0.553	
Taq1B **rs1079597**	**B2/B2**	**B1/B2**	**B1/B1**	**B2**	**B1**
CR	37.96 ± 0.64	37.40 ± 0.67	38.66 ± 0.97	37.89 ± 0.37	37.99 ± 0.48
p-value		0.470		0.947	
UE	41.49 ± 0.76	39.46 ± 0.77	40.73 ± 1.04	40.77 ± 0.44	40.02 ± 0.54
p-value		0.085		0.146	
EE	49.90 ± 1.28	45.61 ± 1.30	51.35 ± 2.01	48.37 ± 0.75	48.15 ± 0.97
p-value		***0.026****		0.821	
Taq1D **rs1800498**	**D2/D2**	**D1/D2**	**D1/D1**	**D2**	**D1**
CR	37.91 ± 0.45	36.94 ± 1.14	42.50 ± 3.58	37.94 ± 0.31	37.84 ± 1.06
p-value		0.207		0.969	
UE	40.29 ± 0.50	41.51 ± 1.71	42.22 ± 4.51	40.38 ± 0.35	41.62 ± 1.51
p-value		0.624		0.328	
EE	48.42 ± 0.90	47.76 ± 2.55	45.00 ± 3.33	48.37 ± 0.62	47.31 ± 2.17
p-value		0.855		0.696	

CR = cognitive restraint eating; UE = uncontrolled eating; EE = emotional eating. The analysis was done by comparing eating behaviour with genotypes and alleles through Kruskal-Wallis Test; **p*-value significant at < 0.05

Table 4.6 demonstrates the comparison of the *DRD2* genetic variants and alleles with the respective total physical activity MET-minutes/week. The null hypothesis (H_0) was set as having no significant difference between genotypes and alleles with physical activity whereas the alternative hypothesis (H_1) was set as there was a significant difference between genotypes and alleles with physical activity. No significant difference was shown between *DRD2 Taq1* genotypes and total physical activity MET-minutes/week and between *DRD2 Taq1* alleles and total physical activity MET-minutes/week (p-value > 0.05). The null hypothesis was not rejected.

Table 4.6: Distribution of the physical activity scores in different *DRD2* genotypes and alleles.

	Genotypes (mean ± SEM)			Alleles (mean ± SEM)	
***Taq1A* rs1800497**	**A2/A2**	**A1/A2**	**A1/A1**	**A2**	**A1**
Walking METs	836.61 ± 120.14	796.80 ± 88.54	838.03 ± 162.12	819.99 ± 62.38	815.31 ± 70.04
p-value		0.932		0.639	
Moderate METs	321.63 ± 52.21	312.64 ± 49.26	296.14 ± 80.33	317.61 ± 29.45	307.36 ± 37.38
p-value		0.360		0.174	
Vigorous METs	468.50 ± 88.02	508.91 ± 88.54	442.11 ± 125.38	482.69 ± 50.96	484.98 ± 64.38
p-value		0.919		0.833	
Total METs	1626.74 ± 194.13	1618.35 ± 167.75	1576.27 ± 247.96	1620.29 ± 106.0	1607.65 ± 123.35
p-value		0.871		0.820	
***Taq1B* rs1079597**	**B2/B2**	**B1/B2**	**B1/B1**	**B2**	**B1**
Walking METs	796.55 ± 116.64	810.96 ± 89.91	885.90 ± 165.03	801.67 ± 61.86	844.16 ± 71.75
p-value		0.374		0.233	
Moderate METs	306.26 ± 49.38	317.93 ± 52.47	320.29 ± 77.66	310.41 ± 29.17	318.98 ± 37.91
p-value		0.741		0.527	
Vigorous METs	412.28 ± 84.38	529.45 ± 93.92	530.59 ± 121.70	453.94 ± 50.89	529.95 ± 64.45
p-value		0.509		0.230	
Total METs	1515.09 ± 187.52	1658.34 ± 173.62	1736.79 ± 257.41	1566.12 ± 105.24	1693.09 ± 125.54
p-value		0.456		0.197	

Table 4.6 continued.

	Genotypes (mean ± SEM)			Alleles (mean ± SEM)	
***Taq1D* rs1800498**	**D2/D2**	**D1/D2**	**D1/D1**	**D2**	**D1**
Walking METs	812.57 ± 71.59	760.27 ± 169.23	1801.80 ± 1059.58	808.83 ± 48.47	928.26 ± 185.37
p-value		0.746		0.977	
Moderate METs	322.48 ± 36.60	283.85 ± 71.59	36.00 ± 36.00	319.71 ± 24.54	243.87 ± 61.20
p-value		0.465		0.689	
Vigorous METs	506.16 ± 61.84	327.69 ± 146.95	580.80 ± 369.02	493.38 ± 41.92	368.52 ± 129.33
p-value		0.233		0.662	
Total METs	1641.21 ± 126.22	1371.81 ± 253.89	2418.60 ± 1396.07	1621.92 ± 84.77	1540.65 ± 261.24
p-value		0.828		0.943	

Walking, Moderate and Vigorous METs represents Walking, Moderate and Vigorous METs-minutes/week, respectively. Total METs represent total summation of walking, moderate and vigorous MET-minutes/week. The analysis was done by comparing physical activity level with genotypes and alleles through Kruskal-Wallis Test; **p*-value significant at < 0.05

Table 4.7 reveals the comparison of the *DRD2* genetic variants and alleles with the five domains of MPAM-R, respectively. The null hypothesis (H_0) was set as having no significant difference between genotypes and alleles with MPAM-R whereas the alternative hypothesis (H_1) was set as there was a significant difference between genotypes and alleles with MPAM-R. *DRD2 Taq1A* and *Taq1B* genotypes showed no significant difference on MPAM-R (*p*-value > 0.05). *DRD2 Taq1D* genotypes showed significant differences on all five domains of MPAM-R: interest/enjoyment, competence, appearance, fitness and social with a *p*-value of 0.031, 0.016, 0.011, 0.014 and 0.010, respectively. On the allele perspective, *DRD2 Taq1A* and *Taq1B* alleles showed a significant difference on interest/enjoyment with a *p*-value of 0.036 and 0.014 respectively, whereas *DRD2 Taq1D* alleles showed significant differences on competence,

appearance, fitness and social with a *p*-value of 0.025, 0.010, 0.015 and 0.019 respectively.

A Kruskal-Wallis test provided evidence of a difference ($p < 0.05$) between the mean ranks of *DRD2* genotype groups. Dunn's pairwise tests were carried out for the three pairs of groups. For interest/enjoyment, *post hoc* test showed that the *DRD2 Taq1D* wildtype (*A2/A2*) and homozygote (*A1/A1*) differed significantly at adjusted *p*-value = 0.025 with mean rank difference of 135.1; *Taq1D* heterozygote (*A2/A1*) and homozygote (*A1/A1*) differed significantly at adjusted *p*-value = 0.039 with mean rank difference of 132.4. The *Taq1D* wildtype (*A2/A2*) was not significantly different from the heterozygote (*A2/A1*) group with adjusted *p*-value = 1.000.

For competence, *post hoc* test showed that the *DRD2 Taq1D* wildtype (*A2/A2*) and homozygote (*A1/A1*) differed significantly at adjusted *p*-value = 0.016 with mean rank difference of 142.7; *Taq1D* heterozygote (*A2/A1*) and homozygote (*A1/A1*) differed significantly at adjusted *p*-value = 0.047 with mean rank difference of 128.9. The *Taq1D* wildtype (*A2/A2*) was not significantly different from the heterozygote (*A2/A1*) group with adjusted *p*-value = 1.000. For appearance, *post hoc* test showed that the *DRD2 Taq1D* wildtype (*A2/A2*) and homozygote (*A1/A1*) differed significantly at adjusted *p*-value = 0.014 with mean rank difference of 145.0. The *Taq1D* wildtype (A2/A2) and homozygote (*A1/A1*) were not significantly different from the heterozygote (*A2/A1*) group with adjusted *p*-value = 0.718 and 0.057, respectively.

For fitness, *post hoc* test showed that the *DRD2 Taq1D* wildtype (*A2/A2*) and homozygote (*A1/A1*) differed significantly at adjusted *p*-value = 0.016 with mean rank difference of 142.24. The *Taq1D* wildtype (*A2/A2*) and homozygote (*A1/A1*) were not significantly different from the heterozygote (*A2/A1*) group with adjusted *p*-value = 0.887 and 0.058, respectively. For social, *post hoc* test showed that the *DRD2 Taq1D* wildtype (*A2/A2*) and homozygote (*A1/A1*) differed significantly at adjusted *p*-value = 0.009 with mean rank difference of 151.29; *Taq1D* heterozygote (*A2/A1*) and homozygote (*A1/A1*) differed significantly at adjusted *p*-value = 0.030 with mean rank difference of 137.14. The *Taq1D* wildtype (*A2/A2*) was not significantly different from the heterozygote (*A2/A1*) group with adjusted *p*-value = 1.000.

Table 4.7: Distribution of the MPAM-R scores in different *DRD2* genotypes and alleles.

	Genotypes (mean ± SEM)			**Alleles (mean ± SEM)**	
***Taq1A* rs1800497**	**A2/A2**	**A1/A2**	**A1/A1**	**A2**	**A1**
Interest/Enjoyment	4.32 ± 0.12	4.53 ± 0.10	4.66 ± 0.18	4.40 ± 0.06	4.58 ± 0.08
p-value		0.142		***0.036****	
Competence	4.19 ± 0.11	4.31 ± 0.10	4.31 ± 0.19	4.23 ± 0.06	4.32 ± 0.08
p-value		0.703		0.349	
Appearance	4.64 ± 0.11	4.47 ± 0.10	4.18 ± 0.18	4.51 ± 0.06	43.6 ± 0.08
p-value		0.224		0.123	
Fitness	4.98 ± 0.11	4.96 ± 0.10	4.81 ± 0.16	4.97 ± 0.06	4.91 ± 0.07
p-value		0.536		0.345	
Social	3.54 ± 0.11	3.73 ± 0.09	3.57 ± 0.18	3.61 ± 0.06	3.67 ± 0.08
p-value		0.392		0.324	
***Taq1B* rs1079597**	**B2/B2**	**B1/B2**	**B1/B1**	**B2**	**B1**
Interest/Enjoyment	4.31 ± 0.12	4.51 ± 0.10	4.72 ± 0.16	4.38 ± 0.06	4.60 ± 0.08
p-value		0.063		***0.014****	
Competence	4.17 ± 0.12	4.35 ± 0.10	4.26 ± 0.17	4.23 ± 0.06	4.31 ± 0.08
p-value		0.506		0.371	
Appearance	4.50 ± 0.11	4.48 ± 0.10	4.30 ± 0.17	4.49 ± 0.06	4.40 ± 0.08
p-value		0.623		0.359	
Fitness	4.39 ± 0.11	4.97 ± 0.09	4.92 ± 0.16	4.94 ± 0.06	4.95 ± 0.07
p-value		0.975		0.827	
Social	3.57 ± 0.11	3.76 ± 0.09	3.45 ± 0.17	3.64 ± 0.06	3.63 ± 0.07
p-value		0.138		0.777	

Table 4.7 continued.

	Genotypes (mean ± SEM)			Alleles (mean ± SEM)	
***Taq1D* rs1800498**	**D2/D2**	**D1/D2**	**D1/D1**	**D2**	**D1**
Interest/Enjoyment	4.46 ± 0.07	4.41 ± 0.20	5.91 ± 0.21	4.45 ± 0.05	4.47 ± 0.18
p-value		***0.031****		0.113	
Competence	4.23 ± 0.08	4.32 ± 0.20	5.77 ± 0.17	4.24 ± 0.05	4.55 ± 0.18
p-value		***0.016****		***0.025****	
Appearance	4.41 ± 0.07	4.59 ± 0.20	6.07 ± 0.30	4.42 ± 0.05	4.83 ± 0.19
p-value		***0.011****		***0.010****	
Fitness	4.91 ± 0.07	5.03 ± 0.18	6.36 ± 0.21	4.92 ± 0.05	5.25 ± 0.17
p-value		***0.014****		***0.015****	
Social	3.58 ± 0.07	3.79 ± 0.17	5.36 ± 0.39	3.60 ± 0.05	4.04 ± 0.17
p-value		***0.010****		***0.019****	

The analysis was done by comparing physical activity level with genotypes and alleles through Kruskal-Wallis Test; **p*-value significant at < 0.05

4.6 Correlation of personality traits scores with eating behaviour scores and physical activity scores, respectively

Table 4.8 presents the correlation between personality traits scores and eating behaviour scores. The null hypothesis (H_0) was set as having no correlation between personality traits scores and eating behaviour scores whereas the alternative hypothesis (H_1) was set as there was a correlation between personality traits scores and eating behaviour scores. As shown in Table 4.8, extraversion showed a slight negative correlation (-0.101) with EE at *p*-value <0.05 (0.045) but no correlation with CR and UE. On the other hand, neuroticism was shown to be correlated to the factors in eating behaviour. Neuroticism exhibited a slightly negative correlation with CR (-0.136) at *p*-

value <0.01 (0.007) and with UE and EE (- 0.216; -0.268) at *p*-value <0.001. As shown in Table 4.8, conscientiousness showed a slight positive correlation (0.201) with UE at *p*-value <0.001 and with EE (0.147) at *p*-value <0.05 (0.003). Lastly, no correlation was found between openness and agreeableness with eating behaviours.

Table 4.8: Spearman's rank correlation coefficient between personality trait scores and eating behaviour scores.

Traits	**CR**		**UE**		**EE**	
	r_s	**p**	r_s	**p**	r_s	**p**
Openness	0.030	0.549	-0.025	0.620	0.003	0.957
Conscientiousness	0.063	0.212	0.201	***<0.001******	0.147	***<0.001******
Extraversion	-0.019	0.704	-0.054	0.281	-0.101	***0.045****
Agreeableness	-0.021	0.685	-0.015	0.760	-0.062	0.221
Neuroticism	-0.136	***0.007****	-0.216	***<0.001******	-0.268	***<0.001******

Note * indicates significant at the level 0.05; ** indicates significant at the level 0.01; *** indicates significant at the level <0.001.

Table 4.9 shows the correlation between personality traits scores and physical activity scores. The null hypothesis (H_0) was set as having no correlation between personality traits scores and physical activity scores whereas the alternative hypothesis (H_1) was set as there was a correlation between personality traits scores and physical activity scores. Extraversion exhibited a slight positive correlation (0.197) with total physical activity MET-minutes/week at *p*-value <0.001. In contrast, neuroticism, openness, agreeableness and conscientiousness observed no significant correlation with physical activity.

Table 4.9: Spearman's rank correlation coefficient between personality trait scores and physical activity scores.

Traits	Total physical activity MET-minutes/week	
	r_s	p
Openness	0.056	0.266
Conscientiousness	0.083	0.099
Extraversion	0.197	***<0.001******
Agreeableness	-0.005	0.929
Neuroticism	-0.044	0.388

Note * indicates significant at the level 0.05; ** indicates significant at the level 0.01; *** indicates significant at the level <0.001.

4.7 Relationship of eating behaviour and physical activity with obesity, respectively

Table 4.10 provides information comparing each BMI category group against the reference category (Obese BMI ≥ 25). The null hypothesis (H_0) was set as having no relationship between eating behaviour scores and obesity classes whereas the alternative hypothesis (H_1) was set as there was a relationship between eating behaviour scores and obesity classes. Only EE was a significant predictor ($p<0.05$) at the *p*-value of 0.012 for underweight. The odds ratio of 1.031 indicated that for every one-unit increase of EE, the odds of a person to be underweight changed by a factor of 1.031. Only EE was a significant predictor ($p<0.05$, *p*-value of 0.025) for normal weight. The odds ratio of 1.021 indicated that persons who were high in EE scores were more likely to fall in the normal weight than obese. For 'Underweight' and 'Normal weight', CR and UE are not significant predictors for obesity. For 'Pre-obese', CR, UE and EE are not significant predictors for obesity.

Table 4.10: Regression analysis of eating behaviour and obesity.

BMI category	Eating behaviour					
	CR		UE		EE	
	OR	***p*-value**	**OR**	***p*-value**	**OR**	***p*-value**
Underweight (BMI < 18.5)	1.032	0.136	0.989	0.610	1.031	***0.012****
Normal (BMI 18.5 – 22.9)	1.019	0.254	0.993	0.655	1.021	***0.025****
Pre-obese (BMI 23 – 24.9)	1.003	0.882	0.996	0.846	1.014	0.270

OR is odds ratio or known as a standardised beta coefficient; *p*-values by multinomial logistic regression test; * indicates significant at the level 0.05; ** indicates significant at the level 0.01; *** indicates significant at the level <0.001. Reference category is Obese (BMI ≥ 25).

Table 4.11 shows the distribution of total physical activity MET-minutes/week category with different BMI categories. The null hypothesis (H_0) was set as having no association between physical activity scores and obesity classes whereas the alternative hypothesis (H_1) was set as there was an association between physical activity scores and obesity classes. A Pearson's chi-squared test revealed that among the UTAR population, BMI classes and physical activity intensity are significantly associated, $X^2 = 19.09$, 6 df, *p*-value = 0.004. Pairwise comparisons *post hoc* test was conducted with Bonferroni corrections of the *p* value < 0.0042 is considered significant. Results demonstrated that underweight category was more likely to engage in low level of physical activity (*p*-value = 0.0021) and pre-obese category was more likely to engage in moderate level physical activity (*p*-value = 0.0042).

Table 4.11: Association of physical activity and obesity.

BMI category	Total physical activity MET-minutes/week n (%)			X^2; *p*-value
	Low (< 600)	Moderate (600-2999.99)	High (≥3000)	
Underweight (BMI < 18.5)	37 (9.4)	14 (3.6)	8 (2.0)	
Normal (BMI 18.5 – 22.9)	88 (22.3)	69 (17.5)	29 (7.4)	
Pre-obese (BMI 23 – 24.9)	14 (3.6)	30 (7.6)	8 (2.0)	
Obese (BMI ≥25)	36 (9.1)	43 (10.9)	18 (4.6)	
Total	175 (44.4)	156 (39.6)	63 (16.0)	19.09; ***0.004***

Parentheses indicate the percentage within the BMI category. The analysis was done by comparing BMI category with Total physical activity MET-minutes/week category through Pearson's chi-squared test; **p*-value significant at < 0.05; ** *p*-value significant at < 0.01; *** *p*-value significant at < 0.001. *Post hoc* Bonferroni corrections adjusted *p*-value significant at < 0.0042. Significant result was observed in the association of underweight and low intensity physical activity (*p*-value = 0.0021); and association of pre-obese and moderate intensity physical activity (*p*-value = 0.0042).

4.8 Path analysis study of eating behaviour, MPAM-R, Total METs and BMI in different *DRD2* genotypes

The variables of eating behaviours (CR, UE and EE), motives for physical activity (MPAM-R) and physical activity level (total METs) are examined and presented in Figure 4.1. Physical activity level (total METs) acted as a mediator variable and should be linked to endogenous (a variable caused by one or more variable) construct and connected with exogenous variable (a variable independent of another variable in the model), MPAM-R. Prerequisite model fit should be achieved where *p*-value >0.05; GFI ≥0.95 AGFI ≥0.90; CFI ≥0.90; RMSEA <0.08 before using path analysis for the assessment of the subsequent study (which is moderator effects of *DRD2 Taq1A*, *Taq1B* and *Taq1D* in this study). Figure 4.1 shows a representative illustration of the path analysis moderated mediation model. The subsequent moderated mediation models in which *DRD2 Taq1A*, *Taq1B* and *Taq1D* genotypes and alleles act as grouping variables were presented in Appendix G.

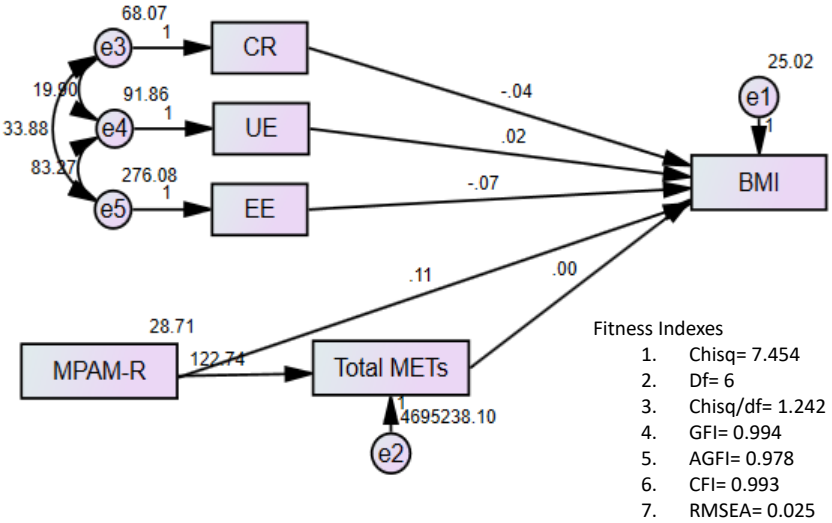


Figure 4.1: Path analysis study of eating behaviour, MPAM-R, Total METs and BMI (Chisq indicates Chi-square value, Df indicates degree of freedom, GFI indicates goodness of fit, CFI indicates comparative fit index, AGFI indicates adjusted goodness of fit index and RMSEA indicates Root Mean Square Error of Approximation. The value above the arrow indicates factor loading).

The value of z-score or z-test was presented to determine their significant impact. Z-score was obtained by importing the critical ratio of differences generated by AMOS into Stats Tools Packages (STP). The z-score more than 1.96 (*p*-values< 0.05) indicated the existence of significant impact. Table 4.12 shows the estimation for *Taq1A* homozygous wild-type (*A2/A2*) with *Taq1A* heterozygote (*A2/A1*) and homozygote (*A1/A1*) genotype with the z- score. *Taq1A* genotype had positively moderated the effect of MPAM-R on BMI at *p*-value < 0.05 (z-score 2.179) when compared to *Taq1A* homozygous WT (*A2/A2*) and *Taq1A* homozygote (*A1/A1*). On the other hand, the other path showed that *Taq1A* genotypes did not moderate the effect of independent variables (MPAM-R, CR, UE, EE, Total METs) on dependent variables (BMI).

Table 4.12: Moderated mediation table of *Taq1A* homozygous and heterozygous for eating behaviour, MPAM-R, Total METs, and BMI.

			Taq1A wild-type (*A2/A2)*		*Taq1A* heterozygote (*A2/A1*)		
			Estimate	P	Estimate	P	z-score
Total METs	←	Total MPAM-R	136.386	0.000***	138.338	0.000***	0.043
BMI	←	CR	-0.035	0.436	-0.057	0.187	-0.356
BMI	←	UE	0.039	0.342	0.016	0.720	-0.389
BMI	←	EE	-0.065	0.012*	-0.054	0.037*	0.280
BMI	←	Total METs	0.000	0.598	0.000	0.857	-0.233
BMI	←	Total MPAM-R	0.041	0.551	0.072	0.318	0.308
			Taq1A wild-type (*A2/A2)*		*Taq1A* homozygote (*A1/A1*)		
			Estimate	P	Estimate	P	z-score
Total METs	←	Total MPAM-R	136.386	0.000***	33.779	0.469	-1.786*
BMI	←	CR	-0.035	0.437	0.045	0.670	0.697
BMI	←	UE	0.039	0.343	-0.034	0.764	-0.608
BMI	←	EE	-0.065	0.013*	-0.128	0.027*	-1.002
BMI	←	Total METs	0.000	0.599	0.000	0.946	-0.243
BMI	←	Total MPAM-R	0.041	0.552	0.409	0.008***	***2.179****

For estimate, * indicates significant at the level 0.05; ** indicates significant at the level 0.01; *** indicates significant at the level 0.0. For z-score, * indicates *p*-value < 0.10; ** indicates *p*-value < 0.05; *** indicates *p*-value < 0.01.

Table 4.13 reveals that *Taq1B* genotype positively moderates the effect of MPAM-R on BMI when compared to *Taq1B* wild-type (*B2/B2*) and *Taq1B* homozygote (*B1/B1*) at *p*-value < 0.05 (z-score 2.089). No significant moderating effects of *Taq1B* were shown on total MPAM-R score to total METs score and CR, UE, EE scores and total METs to BMI score. *Taq1B* genotype had positively moderated the effect of MPAM-R on BMI at *p*-value < 0.05 (z-score 2.179)

Table 4.13: Moderated mediation table of *Taq1B* wild-type (*B2/B2*) with *Taq1B* homozygote genotype (*B1/B1*).

			Taq1B wild-type (*B2/B2*)		*Taq1B* homozygote (*B1/B1*)		
			Estimate	P	Estimate	P	z-score
Total METs	←	Total MPAM-R	123.748	0.000***	94.400	0.041*	-0.523
BMI	←	CR	-0.053	0.233	0.035	0.712	0.840
BMI	←	UE	0.034	0.418	-0.025	0.785	-0.586
BMI	←	EE	-0.042	0.096	-0.086	0.080	-0.796
BMI	←	Total METs	0.000	0.329	0.000	0.685	-0.767
BMI	←	Total MPAM-R	0.007	0.914	0.329	0.018*	***2.089*****

For estimate, * indicates significant at the level 0.05; ** indicates significant at the level 0.01; *** indicates significant at the level 0.0. For z-score, * indicates *p*-value < 0.10; ** indicates *p*-value < 0.05; *** indicates *p*-value < 0.01.

Table 4.14 shows no significant interaction between *Taq1D* wild-type (*D2/D2*) with *Taq1D* heterozygote (*D2/D1*) genotype according to the Z-score (*p*-value > 0.05).

Table 4.14: Moderated mediation table of *Taq1D* wild-type (*D2/D2*) with *Taq1D* heterozygote genotype (*D2/D1*).

			Taq1D wild-type (D*2/D2*)		*Taq1D* heterozygote (*D2/D1*)		
			Estimate	P	Estimate	P	z-score
Total METs	←	Total MPAM-R	125.395	0.000***	126.653	0.004**	0.025
BMI	←	CR	-0.029	0.397	0.030	0.760	0.568
BMI	←	UE	0.012	0.732	0.075	0.317	0.763
BMI	←	EE	-0.057	0.003**	-0.132	0.012*	-1.341
BMI	←	Total METs	0.000	0.932	0.000	0.300	-1.023
BMI	←	Total MPAM-R	0.128	0.015*	0.019	0.903	-0.672

For estimate, * indicates significant at the level 0.05; ** indicates significant at the level 0.01; *** indicates significant at the level 0.0. For z-score, * indicates *p*-value < 0.10; ** indicates *p*-value < 0.05; *** indicates *p*-value < 0.01.

From the perspectives of *Taq1* alleles, table 4.15 shows that *Taq1B* allele negatively moderates the effect of MPAM-R on BMI at *p*-value <0.05 (z-score= -2.280); whereas *Taq1A* and *Taq1D* alleles show no significant impact (*p*-value> 0.05) of allele as a moderator.

Table 4.15: Moderated mediation table of *Taq1A*, *Taq1B* and *Taq1D* alleles.

			Taq1A A2		*Taq1A A1*		
			Estimate	P	Estimate	P	z-score
Total METs	←	Total MPAM-R	97.391	0.000***	137.083	0.000***	1.350
BMI	←	CR	-0.024	0.553	-0.042	0.107	-0.375
BMI	←	UE	0.005	0.902	0.031	0.212	0.533
BMI	←	EE	-0.073	0.001**	-0.063	0.000***	0.368
BMI	←	Total METs	0.000	0.657	0.000	0.494	0.733
BMI	←	Total MPAM-R	0.195	0.002**	0.056	0.165	-1.858*
			Taq1B B2		*Taq1B B1*		
			Estimate	P	Estimate	P	z-score
Total METs	←	Total MPAM-R	114.711	0.000***	127.161	0.000***	0.420
BMI	←	CR	-0.005	0.891	-0.052	0.051	-0.975
BMI	←	UE	0.011	0.771	0.032	0.222	0.431
BMI	←	EE	-0.080	0.000***	-0.058	0.000***	0.843
BMI	←	Total METs	0.000	0.458	0.000	0.394	1.086
BMI	←	Total MPAM-R	0.213	0.000***	0.043	0.283	**-2.280****
			Taq1D D2		*Taq1D D1*		
			Estimate	P	Estimate	P	z-score
Total METs	←	Total MPAM-R	113.026	0.010**	125.045	0.000***	0.259
BMI	←	CR	-0.080	0.350	-0.031	0.187	0.556
BMI	←	UE	0.037	0.597	0.018	0.431	-0.251
BMI	←	EE	-0.122	0.015*	-0.063	0.000***	1.145
BMI	←	Total METs	0.000	0.171	0.000	0.884	-1.364
BMI	←	Total MPAM-R	-0.101	0.428	0.122	0.000***	-1.680*

For estimate, * indicates significant at the level 0.05; ** indicates significant at the level 0.01; *** indicates significant at the level 0.0. For z-score, * indicates *p*-value < 0.10; ** indicates *p*-value < 0.05; *** indicates p-value < 0.01.

4.9 Health-related quality of life among different BMI classes

Table 4.16 compares the eight domains of HRQoL that were classified into two components HRQoL with the four different BMI classes (underweight, normal, overweight and obese). The null hypothesis (H_0) was set as having no significant differences between HRQoL among all four different BMI classes whereas the alternative hypothesis (H_1) was set as there was a significant difference between HRQoL among all four different BMI classes. No significant differences were observed between PCS, MCS and total HRQoL among all four different BMI classes with *p*-value> 0.05. The null hypothesis was not rejected.

Table 4.16: Distribution of HRQoL scores in different BMI classes.

	BMI classes (mean ± SEM)				**X^2; *p*-value**
	Underweight	**Normal**	**Overweight**	**Obese**	
General health	55.42 ± 1.82	57.42 ± 1.24	61.44 ± 2.08	57.37 ± 1.68	4.559; 0.207
Pain	79.28 ± 2.51	75.71 ± 1.70	73.56 ± 2.94	73.10 ± 2.20	3.996; 0.262
Physical functioning	80.93 ± 2.57	85.83 ± 1.28	83.37 ± 3.03	80.10 ± 2.00	7.660; 0.054
Role limitations (P)	79.66 ± 4.34	85.08 ± 2.04	77.88 ± 4.21	78.87 ± 3.61	3.640; 0.303
PCS	73.82 ± 1.89	76.01 ± 1.05	74.06 ± 2.15	72.36 ± 1.61	3.668; 0.300
Energy/fatigue	53.22 ± 1.76	53.36 ± 0.97	54.52 ± 1.74	54.02 ± 1.49	0.518; 0.915
Emotional well-being	63.46 ± 1.88	63.08 ± 1.18	63.85 ± 2.39	63.75 ± 1.55	0.465; 0.926
Social functioning	71.82 ± 2.86	70.90 ± 1.53	76.44 ± 2.54	70.36 ± 2.05	3.214; 0.360
Role limitations (E)	77.97 ± 4.74	70.79 ± 2.88	79.49 ± 4.77	67.35 ± 4.14	5.703; 0.127
MCS	66.62 ± 2.02	65.53 ± 1.29	68.57 ± 2.05	63.87 ± 1.82	2.545; 0.467
Total HRQoL score	70.22 ± 1.66	70.27 ± 1.03	71.32 ± 1.87	68.12 ± 1.49	2.514; 0.473

PCS= physical component summary score, MCS= mental component summary score and Total HRQoL score are PCS+MCS divided by two. Role limitations (P) and (E) stand for role limitations due to physical health and emotional problems. The analysis was done by comparing eating behaviour with genotypes through Kruskal-Wallis Test; **p*-value significant at < 0.05.

CHAPTER 5

DISCUSSION

5.1 Genotypic and allelic frequencies of dopamine receptor gene variants

All three *DRD2* gene variants rs1800497 (*Taq1A*), rs1079597 (*Taq1B*) and rs1800498 (*Taq1D*) were reported as significant SNPs with the minor allele frequency (MAF) >0.05. The *Taq1A* MAF value showed inconsistency with the global MAF of 0.196 based on ALFA Allele Frequency, release version: 20200227123210. In the ALFA Allele Frequency, the MAF of *Taq1A* in European, African, Asian, East Asian and South Asian were reported as 0.190, 0.336, 0.404, 0.379, and 0.271, respectively. The present study reported 0.38 for the *Taq1A* MAF among Malaysians, which was concordant with the East Asian population. It was presumed that the gene flow of *ANKK1/DRD2 Taq1A* could be originated from the East Asian region down to Malaysia. For *Taq1B*, the MAF value of 0.39 was found, and was greater than the global MAF at 0.166. The MAF was reported at 0.151, 0.178, 0.429, 0.423 and 0.25 for regions such as European, African, Asian, East Asian and South Asian (ALFA Allele Frequency). The MAF was found significant for *Taq1D* (0.08). Globally, the MAF of *Taq1D* was reported at 0.576 (ALFA Allele Frequency). In European, African, Asian, East Asian and South Asian, MAF of *Taq1D* was found to be 0.598, 0.206, 0.08, 0.1 and 0.8 (ALFA Allele Frequency). We could observe that the Western population possesses higher MAF than Asian for *Taq1D*. From the *Taq1B* and 1D MAF value, the Malaysian population showed similarity to the Asian populations with consistently similar reported MAF. It could be due to

the factor of geographical location, in which the gene flow was most likely came from the similar progenitor. Inbreeding of the similar genotypes (i.e., Asian mates with Asian) might also be one of the reasons for the consistency of the MAF of Malaysian with Asian.

5.2 Genotypic distribution of dopamine receptor gene variants based on demographics and BMI class

DRD2 gene was highlighted in this present study as this gene plays a role in the dopaminergic system (the dopaminergic pathway) which affects the rewarding pathway, motivational behaviours as well as regulation of motor movement. The motivation of an individual to perform physical activities is greatly influenced by the dopamine system. This could be attributed to a dopamine level elevation in the brain that may induce a pleasant sensation, and therefore promote the seeking of the pleasure sensation from exercise (Simonen et al., 2003). Thus, lower motivation in performing physical activities is prone to increase body weight, leading to changes at the individual's BMI. The association between *DRD2* gene polymorphism and physical activity level had been shown by Simonen et al. (2003) and later in humans and rodents at *DRD4* gene instead of *DRD2* gene (Grady et al., 2013) which might indirectly aid in weight reduction. Therefore, with the previous ideas and findings of how dopamine genes bring impacts on obesity with rewarding pathways, we have chosen these three *DRD2* variants, which were associated with reward sensitivity in previous studies (Blum, 2014; Guo et al. 2014) to look into their association with obesity.

DRD2 DNA sequence changes may also result in a deterioration of *DRD2* receptors, which would be compensated through the rewarding pathway. Studies had reported genetic changes in *DRD2* resulted in the individual to show overeating behaviour and also indirectly lead to obesity (Heni et al., 2016; Sari and Wijaya, 2017). *Taq1A* polymorphism has an effect on the D2 receptor substrate-binding specificity (Noble, 2000). When the presence of A1 allele (rare allele), the receptor binding affinity is affected in which the neurotransmitters are not taken up the dopamine normally and with low dopamine receptor density in striatum (Ishiguro et al., 1998; Jönsson et al., 1999). Earlier study suggested that compensation mechanism by rewarding pathway resulted in a positive association between *Taq1A* with striatal dopamine D2 receptor density in contributing obesity (Benton and Young, 2016). However, contradicting findings were shown in our study with no association of the genotypes (and alleles) of *DRD2 Taq1A*, *Taq1B* and *Taq1D* with obesity. The *Taq1B* genotypes are relatively closely associated with BMI compared to *Taq1A* and *Taq1D* even though the association was not significant for all three genotypes. *Taq1A*, *Taq1B* and *Taq1D* alleles from *DRD2* gene variants also showed no association with BMI. The insignificant findings were concordance with some previous findings (Thomas et al., 2000; Col Araz et al., 2012; Hardman et al., 2014; Dang et al., 2016; Yeh et al., 2016), although most of them were focusing on other *DRD2* gene polymorphisms instead of *DRD2 Taq1A*, *Taq1B* and *Taq1D* gene polymorphism; nevertheless, their samples were foreigners. Consistent with a meta-analysis, there was no difference in BMI on *Taq1A A1* and *A2*, showing that *A1* allele was not beneficial to reduce weight (Benton and Young, 2016). To be more specific, *Taq1B* was reported to have no

association with the dopaminergic reward pathways (Suriyaprom et al., 2013). Thus, BMI was not influenced by any *DRD2* alleles and genotypes can be concluded. It could be other gene variants, alleles or SNP, giving the influential role to BMI changes. In addition, there is no support of the reward deficiency theory of food addiction due to *DRD2* SNP resulting in obesity.

In addition, there is a possible reason for the presence of other variants at the dopamine receptor gene that provide a significant effect on the aberrant D2 receptors function instead of the *Taq1A*, *Taq1B* and *Taq1D* polymorphisms. This is being demonstrated by the review by Ma et al. (2015) which reported two other polymorphisms (rs1076560 and rs6276) in dopamine receptor gene were significantly associated with the apomorphine administration (APD)-induced growth hormone (GH) response, in which GH response to APD reflected an altered function of D2 receptors. *DRD2* with risk allele of rs1076560 and rs6276 was associated with a reduced GH response to APD which was associated with reduced D2 receptor activity. Reduced D2 receptor activity generates a reward deficiency and alters appetitive motivation (Beeler et al., 2016). This will eventually result in obesity as overeating was performed to achieve satiety as a compensation in the dopaminergic rewarding system (Ma et al., 2015).

5.3 *DRD2* gene polymorphisms with eating behaviours, physical activity and motives for physical activity

Studies have shown that the *DRD2* gene was more directly related to the reward pathway in eating behaviours and motivation in doing a physical activity rather than to obesity. The reward pathway is activated and provides a pleasure feeling from food consumption when there is a dopamine release. *DRD2* gene polymorphisms could lead to a decrease in the density (Benton and Young., 2016) and affect the substrate-binding specificity of D2 receptors (Neville et al., 2004). Therefore, the dopamine D2 receptor activity is reduced. Dopamine D2 receptor activity reduction will give rise to a reward deficiency and affect the appetitive motivation which will lead to compulsive eating (Volkow et al., 2011). The impairment of dopamine release will lead to an extraordinary consumption of food and increase the tendency of overeating to satisfy the reward. In overall, the lack of D2 receptor has the tendency in causing individuals to consume more to achieve satiety as compared to normal individuals due to abnormal reception of dopamine firing from presynaptic neurons.

5.3.1 *DRD2* gene polymorphisms with eating behaviours

From the study, *DRD2 Taq1A* genotype has a significant influence on EE behaviours. This is found consistent with Davis et al., who found that the *A2/A2* genotype of the *Taq1A* variant had significantly higher scores on EE (Davis et al., 2012). EE showed significant difference in *DRD2 Taq1B* genotype groups with p-value = 0.026 but with non-significant multiple pairwise comparisons. This might be due to the existence of Type-I error. Emotions such as stress would bring an impact to individuals' appetite with the release of cortisol

hormone in response to stress and result in an elevation of dopamine activity (Wanat et al., 2008). The cortisol hormone will promote seeking and eating palatable food as a response to being excited by stress (Morris et al., 2015). Hence, from our findings, it showed that *DRD2 Taq1A* gene variant was associated with EE which could be caused by depression, poor emotion regulation skills and emotional control (van Strien, 2018; Takeuchi et al., 2015). Besides, *DRD2 Taq1B* and *Taq1D* revealed no significant difference in EE score. This can conclude that the changes of nucleotide from C to T in the intron region does not affect the translation mechanism in the synthesis of the D2 receptor, and therefore, the normal structural function of D2 receptors is not affected.

Another two eating behaviours, CR and UE in which CR is known as the voluntary cognitive control to restrict food intake while UE is the loss of control over the intake of food along with increased tendency to consume more than usual, as well as accompanied by subjective feelings of hunger. Both CR and UE are responsible for binge eating disorder (BED) (Volkow et al., 2011). In our study, all three *DRD2 Taq1* gene variants do not show significant differences in both CR and UE. The result is contradicting with the previous review which reported a relationship between maladaptive behaviours (e.g., uncontrolled eating) and reward sensitivity (Vainik et al., 2019). Food reward sensitivity elucidates individual differences in the propensity to seek and obtain pleasure from food cues (e.g., environment replete with highly appetizing foods). By the activation of the dopaminergic rewarding system, positive stimuli such as palatable foods, could potentially incite maladaptive behaviours (e.g., uncontrolled eating) (Saunders and Robinson, 2013). Greater stimulation of the

reward system may show stronger inducement salience of food cues, leading to loss of control (Vainik et al., 2019). The contradicting finding could be attributed to different populations with different ethnicities as earlier findings were mostly in western countries but not among Malaysian. Malaysia is made up of different ethnicities. This has been supported by Napolitano and Himes (2011) as well as Lydecker and Grilo (2016) that *DRD2 Taq1* allele frequencies differ significantly between different ethnicities. Thus, this study has shown the importance of emphasising on eating behaviour analysis in multi-ethnic populations. Besides, the insignificant finding could be reasoned by the relationship of CR and UE with the dopamine reward pathway might be affected by dopamine-releasing but not the uptake action by dopamine receptors. Thus, *DRD2 Taq1* gene variants which are only accountable for the formation of D2 receptors may not be responsible for the positive relationship of CR and UE with the dopaminergic rewarding pathway. However, future study is needed to verify this inference.

5.3.2 *DRD2* gene polymorphisms with physical activity

Ample studies demonstrated the contribution of dopamine pathways in the regulation of physical activity, yet the results were inconclusive (Huppertz et al., 2014). Our findings were observed that all three *ANKK1/DRD2 Taq1A*, *DRD2 Taq1B* and *Taq1D* genes showed no significant difference in physical activity. Diverse environmental factors and genetic factors may contribute to an inconsistency of physical activity level results. For genetic factors, it is unconfirmed whether the *DRD2 Taq1* gene has functional significance per se, or in the linkage disequilibrium with other DNA variants in the dopamine

receptor gene which will contribute an effect to different physical activity levels. The association of the *DRD2* genotype with the prevalence of physical activity might not be contributed by the *DRD2 Taq1A, Taq1B and Taq1D* but other SNPs such as rs6275 (Rosso et al., 2018). However, there are still obscure DNA variants in other genes that could be in linkage disequilibrium with the D2 receptor gene polymorphism. Dohrn et al. 2020 demonstrated a positive association between *DRD1* polymorphism and moderate-to-vigorous physical activity. *DRD2* gene polymorphism plays its role by influencing the effect of DRD1 on physical activity, together with DRD3 gene variants (Dohrn et al., 2020). Therefore, the *DRD2* gene variant seems to be more likely to play a supporting role in affecting physical activity indirectly instead of exerting a significant effect on physical activity level directly.

In addition, different assessing methods in physical activity level will yield various results. For instance, the study by Simonen et al. in 2002 showed a positive association between *DRD2* gene variants and physical activity when Québec Family Study (QFS) cohort was employed, whereas their study in 2003 showed no association between *DRD2* gene variants and physical activity when the methods of assessment had changed to three-day diary (Simonen et al., 2003). It may be because some of the assessing methods are insufficient in providing an exact estimate of an individual's accustomed physical activity level as there is periodicity variation in personal physical activity mode. As such, it is reasonable that our results which employed METs in assessing physical activity level show a distinct result in the association between physical inactivity and *DRD2 Taq1* genotypes and alleles. Even though the relationship between

DRD2 Taq1 gene variants and physical activity level was inclusive, the way of dopamine in affecting the physical activity level is yet speculative to a certain degree. As such, two hypotheses are suggested: *DRD2* gene plays a role in motor control in affecting motor skills, or it is involved in the rewarding system. The first hypothesis indicated defect in the dopamine system may result in diseases along with the different extent of locomotor impairment (Reynolds et al., 1999; Klein et al., 1999; Oliveri et al., 2000) such as Parkinson's disease and consequently, a decline in physical activity. Second hypothesis hypothesised that the elevation of dopamine levels in the brain due to exercise may raise the feeling of pleasure and therefore encourage the seeking of the sensation through exercise. This is similar to the drugs and alcohol addicts which find pleasurable sensation when they are consuming drugs or alcohol. Therefore, physical activity involvement may bring pleasurable feelings in giving rise to exercise adherence. Hence, this has led to the perception on that *DRD2* gene variants affect the motivation to carry out physical activity. This study suggested the relationship between motivation in doing physical activity and *DRD2 Taq1* gene variants should be considered.

5.3.3 *DRD2* gene polymorphisms with motives for physical activity

The role of *DRD2* gene in motivational salience has been demonstrated in various domains such as drug abuse, smoking, alcoholism, behaviour, study, performance, and so forth (Cools, 2008; Zuo et al., 2009; Frank and Fossella, 2011; Rhodes and Boudreau, 2017). The relationship between motivation in doing physical activity and *DRD2* gene and consequently results in obesity is still inconclusive. In this study, the total MPAM-R was used to act as an

indicator of the motivation level in doing physical activity. The factors in driving regular physical activity are complex. According to Ryan and Patrick, lack of motivation in conducting physical activity can be due to two main factors, competence and interest. For instance, some people may not feel competent in doing physical activity resulting in the perception that they are physically incapable or poorly skilled to execute the activity. Some people may show no interest in physical activity as they do not have special purpose or objectives of being physically active or just simply reluctant to practise it (Ryan and Patrick, 2009). Theory of self-determination (TAD) seems to be one of the most used methods to distinguish the intrinsic and extrinsic types of motivation that regulate an individual's behaviour (Faria et al., 2019).

For the genotypic association study of *DRD2 Taq1A, Taq1B* and *Taq1D* gene with motives for physical activity, only *DRD2 Taq1D* genotypes show significant differences on all five MPAM-R score (interest/enjoyment, competence, appearance, fitness, and social). The study of motives for physical activity is significant because it might provide a clearer idea of the relationship between physical activity and the dopaminergic system. The impact of dopamine on physical activity findings varied across studies (Marques et al., 2021). This might because of the potential effect of the reward-system-associated-genes (e.g., *DRD2* gene) are actually acting on the innate motivation for physical activity instead of directly exerting an effect on the physical activity level score. Inherent *DRD2 Taq1D* might exert a significant impact on the motivation for physical activity but not physical activity level, and hence the physical inactivity level was reported higher yearly in Malaysia (NHMS, 2019).

Various factors could lead to a sedentary lifestyle. For instance, lack of time, living in a low-income country, not having a job/studying, low socioeconomic status and level of knowledge about physical activity, living in an urban area, negative self-perception of health, using public transportation, etc. (Martins et al., 2021). Individuals might need to overcome the existing reality of life before enjoying a leisure time for exercise. Therefore, individuals might be motivated by their innate *DRD2* gene but in reality, they do not really carry out physical activity due to personal reasons.

Although *DRD2 Taq1A* and *Taq1B* genotypes show no significant difference on MPAM-R score, *DRD2 Taq1A* and *Taq1B* alleles show a significant difference on interest/enjoyment, present intrinsic motives. Intrinsically motivated action can be characterized by an individual's engagement in behaviour for one's own sake, with free-choice time on a task (Ng, 2018). However, little is known about the relationship between dopaminergic system and types of motivation (intrinsic or extrinsic). Our result suggested *DRD2 Taq1A* and *Taq1B* alleles may play a role for individuals in implementing their physical activity practice for personal satisfaction. This is support by a previous study stated dopamine system is a considered essential substance of intrinsic motivation, thus promoting attentiveness and behavioural engagement (Baik, 2013). As such, individuals were expected to voluntarily involved in the activity during a free choice time period or a self-determined choice condition (Ng, 2018). These findings indicate that *DRD2 Taq1* gene in dopaminergic system promotes intrinsic motivation. As such, physical activity might be a process that requires the reinforcement of synaptic functioning and is strongly regulated by *DRD2 Taq1* gene. Positive and

negative affect will also strengthen or weaken the individual's intrinsic motivation in a particular subject (physical activity in our case), thus influencing the attitude towards that subject (Ng, 2018). Intrinsic motivation is associated with dopaminergic system (DePasque and Tricomi, 2015). The brain striatum is responsible for the reinforcement learning as it receives nerve impulses from the midbrain dopamine neurons and generates adaptive behaviours (Ng, 2018). Striatum activity is associated with reward processing, indicating that an intrinsically motivated task could foster the individual's intrinsic motivation (Ng, 2018). As such, positive feedback was viewed as a rewarding outcome that can potentially promote intrinsic motivation of a desired behaviour. Therefore, *DRD2 Taq1* which plays a role in the dopaminergic rewarding system could exert an effect to a certain extent on intrinsic motivation (interest/enjoyment).

Similarly results can be observed on *DRD2 Taq1D* genotypes which showed a significant difference on interest/enjoyment. In addition, apart from interest/enjoyment, both *DRD2 Taq1D* genotypes and its alleles demonstrated a significant difference in competence score. Competence is also considered as an intrinsic motivation in doing physical activity. This suggests the ability to do something successfully or the sense of achievement is one of the key factors for individuals with different *DRD2 Taq1D* gene variants in order to trigger them to practise physical activities. In contrast to intrinsic motivation, extrinsic motivation is related to external factors and the sense of receiving some type of reward (Ryan and Deci, 2000). Some extrinsic motives are described as less self-determined motivation where, despite being able to be motivated in physical activity, people are unable to sustain motivation over time compared to

other types of more self-determined motivation. In contrast to activity which is more prone to self-approval or personally valued, people perform them because they value the outcome (e.g., maintaining a good health, becoming skilful or pro in particular sport, and receiving compliment or admiration from the others). Apropos of that, our results revealed that *DRD2 Taq1D* genotypes and alleles showed significant differences on appearance, fitness and social. Therefore, from our findings, we can conclude that *DRD2 Taq1D* gene variants were more responsible for the both internal and external motivation for physical activity while *DRD2 Taq1A* and *Taq1B* gene, particularly the alleles, were more responsible for the internal motivation for physical activity based on TAD.

Motivation may be intervened by other factors. Ego orientation is possible to impair intrinsic motivation. Individuals with high orientation towards ego (or goal-orientated) are more fascinated in the anticipated results rather than doing the activity itself (Faria et al., 2019). In other words, obtaining social approval and rewards and flaunting superior skill in a certain activity has become the priority. In this sense, individuals with high ego orientation are less prone to personal satisfaction, and thus, this might be the reason that *DRD2 Taq1D* alleles showed no significant differences in intrinsic motivation, particularly interest/enjoyment in our findings. Furthermore, goal-orientated can satisfy not only the need for personal autonomy but also the need for competence, since individuals with high goal orientation are less likely to feel incompetent (Ntoumanis, 2001). Perceptions of competence are fragile when an individual has a high ego orientation. This is because of the natural comparative characteristic of humans that seldom emphasise on self-reference criteria, and

this raises the doubt regarding the competence and makes an individual an unlikely candidate to become a self-determined athlete in sport (Ntoumanis, 2001). Therefore, the goal-orientated behaviour might play a larger role in affecting individuals' motivation for physical activity than inherent *DRD2 Taq1A* and *Taq1B*, and hence our results of *DRD2 Taq1A* and *Taq1B* genotypes and alleles present no significant difference on competence and other extrinsic motivation (appearance, fitness and social).

5.4 Correlation of personality traits and eating behaviour with physical activity

Extraversion is reported to be associated with being active, optimistic, gregarious and assertive (Keller and Siegrist, 2015). Consistent findings were observed in this study, in which extraversion, neuroticism and conscientiousness were correlated significantly with eating behaviours (CR, UE and EE). In this study, extraversion was correlated negatively with EE (rs = -0.10). Thus, individuals with high extraversion scores are less likely to have emotional eating. Therefore, this can postulate that extraversion is directly associated with external eating, as seen in the study by Keller and Siegrist (2015). Individuals with high scores in extraversion are more likely to be stimulated by external stimuli such as the presence of aromatic smell and appearance of food instead of emotions like negative feelings.

In this study, neuroticism score was found inversely proportional to CR, UE and EE score. Impulsiveness (one of the neuroticism facets) and low self-discipline represent poor self-control. High impulsiveness indicates difficulties in

declining reluctant things, while low self-discipline indicates failure to carry out things they always wanted to do (Elfhag and Morey, 2008). Poor self-control in eating behaviour can be compared to a previous study on immoderation (one of the IPIP neuroticism factors) and impatience (Heaven et al., 2001). This suggested that eating behaviours that are consistent with poor self-control and impulsiveness. Restraint eating implies an individual with a relatively stable emotion, and hence neuroticism is presented correlated negatively with CR. Since impulsiveness carries the most crucial neuroticism facet (Elfhag and Morey, 2008), this means a dejection is not exclusively responsible for emotional eating because they are more likely to relieve stress or sadness in another way which may be more impulsive. The chance of emotional eating is less likely to occur for individuals with high neuroticism scores. Therefore, individuals with high scores in neuroticism show a negative correlation to EE, indicating they might not be impulsive to cravings and urges, and they are able to resist the desire. Similar to UE, people with high scores in neuroticism have their impulsiveness constituted by other aspects of life (e.g., exercise) instead of food.

Besides neuroticism, conscientiousness is correlated with eating behaviour as conscientiousness exhibits positive correlation with CR and negative correlation with UE and EE (Heaven et al., 2001; Elfhag and Morey, 2008; Keller and Siegrist, 2015). However, our study demonstrates contradicting findings where conscientiousness shows a slight positive correlation with UE and a weak positive correlation with EE. The positive correlation of conscientiousness with UE and EE might be due to conscientious (restraint) eaters sometimes indulging

in excessive overeating caused by weakening of their self-control (such as through alcohol use or the experience of stressors). Diminished control and "disinhibited suppressed behaviour" may lead to excessive food intake (Heaven et al., 2001). Neurotransmitters such as serotonin (5-HT), a happy chemical in contributing to happiness and controlling of eating behaviour (Leibowitz, 1998). Therefore, restrained eaters who are not only prudent with self-efficacy but also sometimes suffer emotional problems such as depression and anxiety (Heaven et al., 2001). Thus, restrained eaters may experience uncontrolled eating and emotional eating. Negative emotions constitute overeating-inducing-disinhibitors in restrained eaters. These could be attributed as overeating neutralises dysphoria temporarily, expresses an approach to cope with negative emotions, and hence, a positive correlation is possible to found in conscientiousness with EE (Walther and Hilbert, 2015).

Under normal circumstances, eating behaviours can be influenced by other factors such as stress and hormonal levels. This could explain why openness and agreeableness show no correlation with eating behaviours, as well as other personality traits that showed contradict findings with previous studies. Consistently with the study by Epel et al. who demonstrated that stress-induced cortisol reactivity was in relation to increased caloric intake after exposure to a prototypical laboratory stressor (Epel et al., 2001). Besides psychological, physiological aspects, social variables, compensatory mechanisms, and heredity should be taken into account in assessing eating behaviour (De Castro, 2000). Specifically, heredity which contributes to a vast facet of food consumption regulation, such as the determination of body weight and size, the personal

preferences and social proclivities (De Castro, 2000).

In the study of personality traits and physical activity, only extraversion exhibited a slight positive correlation with total physical activity MET-minutes/week (p-value=0.000). This suggested extraversion was correlated with physical activity, leading to a high tendency to seek out intense sensory stimulation (such as physical activities) among extraverts while individuals who are more prone to introverted tend to avoid it. This is supported by the findings from Tolea et al., where extraversion was significantly correlated to muscle strength (Tolea et al., 2012). People who are high in extraversion are typically sociable and outgoing, making them physically active. Higher levels of physical activity among extraverts may fulfil a drive for stimulation and socialization (Wilson and Dishman, 2015). These are supported by a meta- analysis where extraversion revealed a weak positive correlation with physical activity (Rhodes and Smith, 2006). Although there were ample studies on the relationship between personality traits and physical activity internationally, our findings further strengthen these findings especially among Southeast Asian. Negative emotions (neuroticism) are prone to possess unhealthy lifestyles, and vice versa for subjects with high conscientiousness. Individuals with high neuroticism scores tend to avoid physical activity, while individuals with high conscientiousness are more likely to practice physical activity regularly to maintain healthy lifestyles. Although our results demonstrated a negative correlation of neuroticism and a positive correlation of conscientiousness to physical activity, the significant power is absent as the p-value is larger than 0.05.

5.5 Relationship of eating behaviour and physical activity with obesity

In the regression analysis of eating behaviour and obesity, CR and UE show no significant relationship with BMI while EE presented a significant relationship among 'Underweight' and 'Normal weight' individuals. This indicated that EE was a significant predictor for underweight and normal weight. EE should contribute to pre-obese or obese (Lazarevich et al., 2016; Spinosa et al., 2019; Jáuregui-Lobera and Montes-Martínez, 2020) but our result showed a contrasting finding. Generally, EE only assesses participants' experiences of their desire to eat in response to various emotions. It does not evaluate how much a person consumed when they experience this inclination, and hence, it is difficult to assess whether overeating occurs as the differences in appetite was always neglected. 'Underweight' and 'Normal weight' individuals might have more comfort eating event or eat more than usual during emotional states and situation, yet the portion is still lesser than the usual portion eats by pre-obese and obese individuals under normal circumstances. This is also supported as underweight individuals would have different eating portions in positive and negative states (Geliebter and Aversa, 2003; Nolan et al., 2010). This reflects assessment of obesity on emotional eating solely is not well to define obesity as there are so many unexpected external factors that will contribute to obesity. Wardle implied that obese individuals tend to possess higher responsiveness to external stimuli and lower responsiveness to internal stimuli (Wardle, 2007). This finding suggests that people become obese is highly affected by external stimuli (the smell and the appearance of palatable food) rather than internal cues (e.g., satiety and emotional feelings). Therefore, EE episodes commonly occur in underweight and normal weight categories is feasible.

The assessment of emotional eating using TFEQ-R18 in this study was mainly focused on negative feeling eating (e.g., eating when anxious, blue and lonely). However, positive emotional states and situations are being neglected in this study. Emotional eaters usually consume calories (foods or beverages) in response to feelings (either happy or sad). Therefore, the TFEQ-R18 questionnaire might not be absolute in assessing emotional eating score. This ambiguity might cause it strenuous to draw plans of the interventions to target EE and aid in improving weight loss (Frayn and Knäuper, 2018).

METs is employed in the present study to track the "volume" of physical activity better and precisely. Our result demonstrated a significant association between physical activity and obesity. As obesity is increased yearly among Malaysian (Institute for Public Health, 2019), the findings in this study may bring an impact and awareness to the public of the importance of exercise. As presented in Table 4.11, light intensity activity constitutes the largest number in total physical activity METs (44.4%), followed by moderate (39.6%) and vigorous (16.0%). This revealed the exercise-adherence of the participated population was still relatively low because common leisure exercise such as fast walking, slow cycling and slow jogging are categorised in moderate-intensity activity (3-6 METs) occupying 39.6% in our study. Obese manifests as the second-highest physical activity level in Table 4.11. This finding showed that those obese subjects were aware of their health issue and were trying to lose weight through physical activity. Despite the lack of moderate or vigorous physical activity of the study population, lighter amounts of physical activity (<3 METs) also help in reducing weight. A previous study suggested using numerous sessions of light

physical activity such as 10,000 steps/day is also efficient in increasing aerobic fitness (Chan et al., 2003). Individuals are not necessary to conduct moderate or vigorous physical activity in order to yield considerable health benefits. Increment of the light physical activity frequency will eventually reduce one's weight. This was supported by the previous study by Vanhecke et al. in which a low VO2 max (the maximum energy produced, or the maximum rate of oxygen consumption measured during incremental exercise and is expressed in ml/kg/min or METs) was associated with decreased steps per day of their study subjects (Vanhecke et al., 2009).

5.6 Moderating effect of dopamine receptor gene in the association between eating behaviour, physical activity, motives for physical activity and obesity

To study the moderating role of D2R genotypes on obesity, five variables are included: CR, UE, EE, Total physical activity MET-minutes/week (physical activity level) and total MPAM-R (the total summation score of the motives for physical activity measure domains which include interest/enjoyment, competence, appearance, fitness, social). All the *DRD2* genotypes groups were evaluated through estimation to determine which *DRD2* genotypes groups were more prominent to exert a more substantial effect on obesity. Five causal paths were selected (CR on BMI, UE on BMI, EE on BMI, Total METs on BMI and Total MPAM-R on BMI) and proceed to the subsequent procedure to identify the moderator role of *DRD2* genotypes. By using z-score in identifying the moderating role of *DRD2* genotypes, values more than 1.96 (p-values< 0.05) would indicate existence of significant impact. The moderating role of *DRD2*

genotypes as shown in tables 4.12 to 4.14 presented only one of the variables that demonstrated a significant impact on the causal path. The *ANKK1/DRD2 Taq1A* and *DRD2 Taq1B* moderated the effect of motivation (MPAM-R) on obesity (BMI) upon the multi-group analysis. The notation next to the values of z-score denotes the direction of the significant impact. This presented that *ANKK1/DRD2 Taq1A* and *DRD2 Taq1B* positively moderated the motivation on obesity. In contrast, the remaining path showed that the *DRD2* genotypes groups do not moderate the effect of CR, UE, EE and Total METs on BMI. Furthermore, in comparing *ANKK1/DRD2 Taq1A* wildtype (*A2/A2*) and *A1* homozygote, MPAM-R of *Taq1A A1* homozygote and *Taq1B B1* homozygote was more prominent to exhibit effect on BMI when compared to *Taq1A* and *Taq1B* wildtype group, respectively. This was because higher estimates were prone to *Taq1A A1* homozygous group (0.409) compare to *Taq1A* wildtype group (0.041), and *Taq1B B1* homozygous group (0.018) compare to *Taq1B* wildtype group (0.007).

However, the moderator effect of *DRD2* genotypes can only be observed when comparing the *DRD2* wildtype and minor homozygous group. This represents that a change in a single allele might not bring an impactful influence as a moderator to other variables. Additionally, before assessing the *DRD2* moderating role, application of AMOS in analysis required fulfilment of many criteria to obtain significant results. Therefore, the failure in achieving the criteria results in an incomplete comparison of *DRD2* genotypes, as shown in table 4.13 and table 4.14. Thus, the moderated mediation of *DRD2 Taq1A*, *Taq1B* and *Taq1D* alleles was introduced (table 4.15) to identify the moderating

role of D2R gene on the mentioned independent variables towards obesity. In the comparison of *DRD2 Taq1* alleles within their respective genotypes, no moderating effect was shown on eating behaviour and physical activity and obesity. In contrast, *DRD2 Taq1* alleles show a negative moderating effect of motivation (Total MPAM-R) on obesity (BMI), particularly *DRD2 Taq1B* allele with the z-score value of -2.28 (p-value < 0.05). To reduce the chances of obtaining a false-positive result, only z-score value with p-value <0.05 is employed. Therefore, the z-score value with p-value < 0.10 at the causal path of the MPAM-R on BMI for both *DRD2 Taq1A* and *Taq1D* in table 4.15 were neglected although an asterisk mark is present (asterisk marks were generated automatically by Stats Tools Package). *DRD2 Taq1* alleles bring a negative moderating effect of motivation on obesity with results suggesting the estimates of wild type alleles group (*A2*, *B2* and *D2*) is more pronounced compared to mutant alleles group (*A1*, *B1* and *D1*) towards obesity in the sense of motivation.

A significant negative moderating role of *DRD2 Taq1B* was observed in table 4.15 regarding the relationship between motives for physical activity (MPAM-R) and obesity (BMI) with z-score value -2.28. A decrease of the coefficient score (estimate) was observed from 0.213 (*B2* wild-type) to 0.043 (*B1* homozygote). This indicates that individuals who possess *B1* allele have lower motivation for physical activity compared to *B2* wild-type individuals. Individuals with *B1* allele of the *DRD2 Taq1B* polymorphism, either heterozygosity or homozygosity, is(are) associated with less dopamine receptor density (Jönsson et al., 1999). Subjects with *B1* allele might fail to detect, pursue or derive pleasure (reward) from the stimuli (physical activity in this case)

probably due to the alterations in reward sensitivity (Volkow et al., 2011). Therefore, they are less motivated in physical activities. In addition, all three *A1*, *B1* and *D1* alleles demonstrated a negative moderating role in the relationship of motivation for physical activity and BMI in table 4.15 (-1.858, -2.280 and -1.680, respectively). This reveals subjects carrying the *A1*, *B1* and *D1* allele are more prone to avoidance behaviour. A previous study by Kazantseva et al. (2011) has supported this inference by reporting a significant association between *DRD2 Taq1A* polymorphism with neuroticism (a personality trait with tendency to show emotional lability, anxiety and avoidance behaviour). However, the *B1* and *D1* allele are still lacking in the exploration of literature.

The impact of *DRD2 Taq1* gene polymorphisms on obesity can be observed from its effect on addictive behaviours. The most commonly seen examples are alcohol abuse, binge eating and unhealthy food choices (Rivera-Iñiguez et al., 2019), and they are all usually linked to the dopaminergic reward system (Benton and Young, 2016) in the process of achieving gratification. Although no significant moderating role of *DRD2 Taq1A*, *Taq1B* and *Taq1D* gene polymorphism was shown in the relationship of the interested variables (eating behaviours and physical activity) on BMI in table 4.15, several observations can still be remarked in the changes of the coefficients. For example, an increase of the coefficient of UE on *A1* allele and *B1* allele compared to *A2* allele and *B2* allele, respectively. This is because individuals with *A1* or *B1* allele are more prone to uncontrolled eating (Lek, et al., 2018) and binge eating (Manfredi et al., 2021).

In a nutshell, *DRD2 Taq1* gene, particularly *Taq1B*, plays a significant role as a moderator in the causal relationship of motivation for physical activity and obesity. Surprisingly, as shown in the results of moderated mediation of *DRD2 Taq1* gene as a moderator in tables 4.12 to 4.15, contradicting findings can be observed where *DRD2 Taq1* genotypes (except for *DRD2 Taq1D*) demonstrated a positive moderating effect while *DRD2 Taq1* alleles revealed a negative moderating effect on the causal path of MPAM-R on BMI. Therefore, further study is required on investigating how *DRD2 Taq1* gene contributes to its effect in the relationship of motivation for physical activity and obesity.

5.7 Distribution of the Health-Related Quality of Life (HRQoL) scores among different BMI classes

Inconsistent findings have been reported in previous studies on the HRQoL with obesity (Sendi et al., 2005; Driscoll et al., 2016; Kolotkin, and Andersen, 2017). HRQoL was classified into two categories which are Generic HRQoL instruments and specific instruments with different specificity. Specific instruments assess the quality of life specific to a particular disease, population, or clinical problem whereas generic provide a generalised assessment on the quality of life of the subjects (Fontaine and Barofsky, 2001). Our study employed SF-36 to evaluate the generic HRQoL of the Malaysian subjects. There are no significant differences in PCS, MCS and Total HRQoL among all four different BMI classes. This could be explained as the assessment of HRQoL with SF-36 is not entirely dependent on the differences in body weight (Van Nunen et al., 2007). The current SF-36 suggests that obese individual who encounters limitations in the daily activities as a result of physical health or

emotional problems is(are) not fully explained by the magnitude of excess weight. This had suggested that body weight alone is not sufficient to positively influence the physical health or mental health of these people. On the other perspective, previous studies showed a significant improved of HRQoL by obese populations. These are found consistent among obese patient who is seeking, receiving or underwent weight reduction surgical treatment instead of healthy subjects (Van Nunen et al., 2007; Magallares and Schomerus, 2015; Jumbe et al., 2016; Kolotkin, and Andersen, 2017). Therefore, our study, which comprises healthy subjects, manifested no significant relationship between HRQoL and BMI classes.

Previous studies revealed that obesity-associated decrements on HRQoL is relatively consistent and pronounced on physical functioning HRQoL (Fontaine and Barofsky, 2001; Kroes et al., 2016; Kolotkin, and Andersen, 2017). Consistently the findings in this study showed no significant difference between HRQoL and obesity classes. Physical functioning shows a marginally significant difference in BMI classes. This finding suggests that physical functioning may be highly dependent on body weight. Bariatric surgery reviews evidenced that the improvement of physical components HRQoL is much consistent and greater than mental aspects of HRQoL concerning body weight with the assessment of SF-36 (Lindekilde et al., 2015; Magallares and Schomerus, 2015; Driscoll et al., 2016). In conclusion, this study concluded that body weight contributes a pivotal impact in affecting the physical aspects of HRQoL regardless of their race and age. Hence, people are encouraged to take the initiatives in maintaining a heathier body weight to reduce the limitations in

physical activities, which in turn achieving a better quality of life.

5.8 Limitation and future studies

Firstly, self-selection bias might occur as this cross-sectional study adopted the convenience sampling method in obtaining participants' data. However, the convenience sampling method is considered as the most suitable and efficient sampling method in this exploratory quantitative study which combines genetic analysis protocol with psychological research variables within the UTAR population sample to examine the associations as proposed by the conceptual framework. Thus, convenience sampling was employed to achieve a breadth of understanding. The convenience sampling method is useful for investigating particular phenomenon (in this case, is genetics, health behaviours and HRQoL) in a given sample as this method primarily accentuate on generalizability, which means assuring the knowledge received is indicative of the population from which the sample was obtained (Etikan et al., 2016). Also, the convenient sampling method was adopted for convenient accessibility and proximity to researchers, especially the mouthwash samples must be collected and processed as soon as possible in the laboratory to avoid DNA degradation with time.

Secondly, the study sample was majorly constituted by female subjects. Although hierarchical multiple regression test was conducted demonstrating that sex is not a confounding variable in the study, equal number of the sample subjects' sex might increase the robustness and perhaps the results' precision. Thirdly, the study subjects were mainly comprised of Malaysian-Chinese. This could not represent the whole population in Malaysia as Malaysia is a

multiethnicity with different cognition, attitudes, lifestyle, eating habits (Hao et al., 2016). Equal study subjects of different ethnic could contribute to a more promising result. Lastly, the comparison of the prevalence of obesity among UTAR staff and students with the general population of Malaysia was not accomplished due to the insufficiency of a complete demographic data of UTAR population.

In the future studies, waist circumference could be employed as an index of obesity in the result analyses. This is because the use of BMI might neglect factors such as individuals with bulky muscle. For instance, a body builder could be high in BMI due to the muscle weight instead of fats. The use of waist circumference could be a better assessment of one's unhealthy weight as fats are usually deposited at the abdominal region. In addition, the evaluation of the significant difference of the races in Malaysia and genetic correlates of obesity as well as other modifier factors could be conducted in the future study. For the quality of life, we could further our study by using disease-specific instruments to examine whether the diseases and symptoms have an effect on the health, condition, and the capability to function in daily life of the particular patient population. This might allow us to make a comparison in the difference of the generic and disease-specific HRQoL for the particular population.

CHAPTER 6

CONCLUSION

From the total 394 study subjects, the MAF for *Taq1A* (rs1800497), *Taq1B* (rs1079597) and *Taq1D* (rs1800498) was 0.38, 0.39 and 0.08, respectively. The genotype distribution for *DRD2 Taq1A*, *Taq1B* and *Taq1D* were following HWE. No significant association was found between the three *DRD2 Taq1A*, *Taq1B* and *Taq1D* polymorphisms and BMI. This shows that a genetic factor alone was unable to exert a definite outcome of a person's body mass. Perhaps the role of environmental factors (or in combination with genetic factors) is more likely to contribute an impact on obesity.

Eating behaviours score (CR, UE and EE) was not significantly different between *DRD2 Taq1A*, *Taq1B* and *Taq1D* genotypes (and alleles). Only EE showed a significant difference with the *Taq1A* genotype. This suggested the possible role of the dopamine receptor gene, which in charge of RDS could influence individuals' eating behaviour (especially emotional eating).

Taq1D genotypes showed significant differences on all five domains of MPAM-R while *Taq1A* and *Taq1B* genotypes did not. *DRD2 Taq1A* and *Taq1B* alleles show a significant difference in interest/enjoyment, whereas *DRD2 Taq1D* alleles showed significant differences in competence, appearance, fitness and social. These results showed that the difference in *DRD2* gene variants did affect the motives and motivation in carrying out physical activity. For instance, the influence of *DRD2 Taq1A* and *Taq1B* alleles in carrying out physical activity is

more to do with self- pleasure, while *Taq1D* alleles contribute to external factors such as maintaining or improving appearance and competition. However, although *DRD2* gene plays a role in motive or motivation in doing physical activity, no significant difference was found between *DRD2 Taq1A*, *Taq1B* and *Taq1D* genotypes (and alleles) and total physical activity MET-minutes/week. This suggested that innate genetic factor alone does not result in individuals' action in practising physical activity. Perhaps acquired factors (e.g., determination, perseverance, stimuli and purpose) are more likely to play a role in it.

Extraversion showed a weak negative correlation with EE while neuroticism exhibited a weak negative correlation with CR, UE and EE. Conscientiousness showed a weak positive correlation with UE and EE. Openness and agreeableness were not correlated with eating behaviours. Based on the personality traits scores with physical activity, extraversion exhibited a slight positive correlation with total physical activity MET-minutes/week. Eating behaviour and physical activity showed relationships with obesity. EE was a significant predictor for individuals with 'Underweight" and 'Normal weight'. Total physical activity MET-minutes/week was significantly associated with BMI. In overall, extraversion, neuroticism and conscientiousness which correlated with EE might indirectly affect BMI of an individual. Extraversion, particularly, which correlates with both EE and physical activity is most likely to exert an impact on BMI. Future studies should include the correlation between personality traits and BMI to verify this hypothesis.

To study the moderating role of the dopamine receptor gene, *DRD2 Taq1A*, *Taq1B* and *Taq1D* genotypes (and alleles) were found to not moderate the effect of eating behaviours and physical activity on BMI. *DRD2 Taq1A* and *Taq1B* genotypes moderated the effect of MPAM-R on BMI positively. There was no significant impact of genotype as a moderating role for *Taq1D* genotype. *Taq1B* allele negatively moderates the effect of MPAM-R on BMI, whereas *Taq1A* and *Taq1D* alleles showed no significant impact of alleles as a moderator. From the results, it suggested that the *DRD2 Taq1* gene variants did not demonstrate a moderating role which will result in the difference in BMI of the individuals. However, the *DRD2 Taq1* gene, particularly *DRD2 Taq1B*, might indirectly exhibit an effect on obesity with its moderating effect in the motivation of doing physical activity to BMI.

For Health-Related Quality of Life of an individual with obesity, there were no significant differences found for PCS, MCS and total HRQoL among all four different BMI classes. This showed that body weight was unable to bring an impact to the HRQoL of individuals independently. However, a marginally significant difference was demonstrated in physical functioning of BMI classes. Therefore, we can conclude that the BMI difference is more likely to influence the quality of life physically but not mentally.

References

Afthanorhan, A., Ahmad, S. and Safee, S., 2014. Moderated mediation using covariance-based structural equation modeling with amos graphic: volunteerism program. *Advances in Natural and Applied Sciences*, 8(8), pp.108-116.

Al-Nakeeb, Y., Dodd, L.J., Lyons, M., Collins, P. and Al-Nuaim, A., 2014. A cluster analysis of lifestyle and health habits of youth from two geographically and culturally diverse countries. *Open Journal of Preventive Medicine*, 4(4), pp.193-203.

Anglé, S. et al., 2009. Three factor eating questionnaire-R18 as a measure of cognitive restraint, uncontrolled eating and emotional eating in a sample of young Finnish females. *International Journal of Behavioral Nutrition and Physical Activity*, 6(1), p.41.

Arthur Jr, W. and Graziano, W.G., 1996. The five‐factor model, conscientiousness, and driving accident involvement. *Journal of personality*, 64(3), pp.593-618.

Azucar, D., Marengo, D. and Settanni, M., 2018. Predicting the Big 5 personality traits from digital footprints on social media: A meta-analysis. *Personality and individual differences*, 124, pp.150-159.

Allik, J., Church, A.T., Ortiz, F.A., Rossier, J., Hřebíčková, M., De Fruyt, F., Realo, A. and McCrae, R.R., 2017. Mean profiles of the NEO personality inventory. *Journal of Cross-Cultural Psychology*, 48(3), pp.402-420.

Baik, J.H., 2013. Dopamine signaling in reward-related behaviors. *Frontiers in neural circuits*, 7, p.152.

Baskerville, T.A. and Douglas, A.J., 2010. Dopamine and oxytocin interactions underlying behaviors: potential contributions to behavioral disorders. *CNS neuroscience & therapeutics*, 16(3), pp.e92-e123.

Beeler, J.A., Frazier, C.R. and Zhuang, X., 2012. Putting desire on a budget: dopamine and energy expenditure, reconciling reward and resources. *Frontiers in integrative neuroscience*, 6, p.49.

Beeler, J.A., Faust, R.P., Turkson, S., Ye, H. and Zhuang, X., 2016. Low dopamine D2 receptor increases vulnerability to obesity via reduced physical activity, not increased appetitive motivation. *Biological psychiatry*, 79(11), pp.887-897.

Bendsen, N.T., Christensen, R., Bartels, E.M., Kok, F.J., Sierksma, A., Raben, A. and Astrup, A., 2013. Is beer consumption related to measures of abdominal and general obesity? A systematic review and meta-analysis. *Nutrition reviews*, 71(2), pp.67-87.

Benton, D. and Young, H.A., 2016. A meta-analysis of the relationship between brain dopamine receptors and obesity: a matter of changes in behavior rather than food addiction?. *International journal of obesity*, 40(S1), p.S12.

Blum, K. et al., 2009. Neurogenetics of dopaminergic receptor supersensitivity in activation of brain reward circuitry and relapse: proposing "deprivation-amplification relapse therapy"(DART). *Postgraduate medicine*, 121(6), pp.176-196.

Blum, K. et al., 2014. Hatching the behavioral addiction egg: Reward Deficiency Solution System (RDSS)™ as a function of dopaminergic neurogenetics and brain functional connectivity linking all addictions under a common rubric. *Journal of Behavioral Addictions*, 3(3), pp.149-156.

Briggs, S.R., 1988. Shyness: Introversion or neuroticism?. *Journal of Research in Personality*, 22(3), pp.290-307.

Bogg, T. and Roberts, B.W., 2004. Conscientiousness and health-related behaviors: a meta-analysis of the leading behavioral contributors to mortality. *Psychological bulletin*, 130(6), p.887.

Calati, R., Gressier, F., Balestri, M. and Serretti, A., 2013. Genetic modulation of borderline personality disorder: systematic review and meta-analysis. *Journal of psychiatric research*, 47(10), pp.1275-1287.

Chan, C.B., Spangler, E., Valcour, J. and Tudor‐Locke, C., 2003. Cross‐sectional relationship of pedometer‐determined ambulatory activity to indicators of health. *Obesity Research*, 11(12), pp.1563-1570.

Chen, C. et al., 2012. Genetic variations in the dopaminergic system and alcohol use: a system‐level analysis. *Addiction Biology*, 17(2), pp.479-489.

Chester, D.S. et al., 2016. Looking for reward in all the wrong places: Dopamine receptor gene polymorphisms indirectly affect aggression through sensation-seeking. *Social neuroscience*, 11(5), pp.487-494.

Childs, E. et al., 2008. Association between ADORA2A and DRD2 polymorphisms and caffeine- induced anxiety. *Neuropsychopharmacology*, 33(12), p.2791.

Claussnitzer, M. et al., 2015. FTO obesity variant circuitry and adipocyte browning in humans. *New England Journal of Medicine*, 373(10), pp.895-907.

Col Araz, N. et al., 2012. Childhood obesity and the role of dopamine D2 receptor and cannabinoid receptor-1 gene polymorphisms. *Genetic testing and molecular biomarkers*, 16(12), pp.1408-1412.

Comings, D.E. et al., 1997. Studies of the potential role of the dopamine D 1 receptor gene in addictive behaviors. *Molecular psychiatry*, 2(1), pp.44-56.

Conner, B.T., Hellemann, G.S., Demianczyk, A.C., Ritchie, T. and Noble, E.P., 2017. Using a Systems-Based Risk Score Approach to Examine Genetic Predisposition to Novelty Seeking. *Journal of Individual Differences*, pp.163-174.

Cools, R., 2008. Role of dopamine in the motivational and cognitive control of behavior. *The Neuroscientist*, 14(4), pp.381-395.

Dagher, A. and Robbins, T.W., 2009. Personality, addiction, dopamine: insights from Parkinson's disease. *Neuron*, 61(4), pp.502-510.

Dang, L.C. et al., 2016. Associations between dopamine D2 receptor availability and BMI depend on age. *Neuroimage*, 138, pp.176-183.

Davis, C. et al., 2012. Binge eating disorder and the dopamine D2 receptor: genotypes and sub-phenotypes. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 38(2), pp.328-335.

De Castro, J.M., 2000. Eating behavior: lessons from the real world of humans. *Nutrition*, 16(10), pp.800-813.

Deng, X.D. et al., 2015. Association between DRD2/ANKK1 TaqIA polymorphism and common illicit drug dependence: evidence from a meta-analysis. *Human immunology*, 76(1), pp.42-51.

DePasque, S. and Tricomi, E., 2015. Effects of intrinsic motivation on feedback processing during learning. *NeuroImage*, 119, pp.175-186.

Dohrn, I.M., Papenberg, G., Winkler, E. and Welmer, A.K., 2020. Impact of dopamine-related genetic variants on physical activity in old age–a cohort study. *International Journal of Behavioral Nutrition and Physical Activity*, 17, pp.1-8.

Donnellan, M.B., Oswald, F.L., Baird, B.M. and Lucas, R.E., 2006. The mini-IPIP scales: tiny-yet-effective measures of the Big Five factors of personality. *Psychological assessment*, 18(2), p.192.

Downs, B.W. et al., 2009. Nutrigenomic targeting of carbohydrate craving behavior: Can we manage obesity and aberrant craving behaviors with neurochemical pathway manipulation by Immunological Compatible Substances (nutrients) using a Genetic Positioning System (GPS) Map?. *Medical hypotheses*, 73(3), pp.427- 434.

Driscoll, S., Gregory, D.M., Fardy, J.M. and Twells, L.K., 2016. Long‐term health‐related quality of life in bariatric surgery patients: a systematic review and meta‐analysis. *Obesity*, 24(1), pp.60-70.

Elfhag, K. and Morey, L.C., 2008. Personality traits and eating behavior in the obese: poor self-control in emotional and external eating but personality assets in restrained eating. *Eating behaviors*, 9(3), pp.285-293.

Ellrott, T. and Pudel, V., 1998. *Adipositastherapie. Aktuelle Perspektiven*. Tabellen: Thieme.

Epel, E., Lapidus, R., McEwen, B. and Brownell, K., 2001. Stress may add bite to appetite in women: a laboratory study of stress-induced cortisol and eating behavior. *Psychoneuroendocrinology*, 26(1), pp.37-49.

Etikan, I., Musa, S.A. and Alkassim, R.S., 2016. Comparison of convenience sampling and purposive sampling. *American journal of theoretical and applied statistics*, 5(1), pp.1-4.

Faith, M.S. and Kral, T.V., 2006. Social environmental and genetic influences on obesity and obesity-promoting behaviors: Fostering research integration. In *Genes, behavior, and the social environment: Moving beyond the nature/nurture debate*. National Academies Press (US).

Faria, L.O., Ribeiro, T.L., Souza, T.F.D., Rennó, G.V.C. and Albuquerque, M.R., 2019. Motives for physical activity practice in skill-orientated sport: an example of taekwondo. *Revista Brasileira de Ciências do Esporte*, 41(2), pp.198-205.

Fontaine, K.R. and Barofsky, I., 2001. Obesity and health‐related quality of life. *Obesity reviews*, 2(3), pp.173-182.

Ferrans, C.E., 2005. Definitions and conceptual models of quality of life. Outcomes assessment in cancer: *Measures, methods, and applications*, pp.14-30.

Fischer, R., Lee, A. and Verzijden, M.N., 2018. Dopamine genes are linked to Extraversion and Neuroticism personality traits, but only in demanding climates. *Scientific reports*, 8(1), p.1733.

Fitzgerald, K.L. and Demakis, G.J., 2007. The neuropsychology of antisocial personality disorder. *Disease-a-month*, 53(3), pp.177-183.

Fleurbaix Laventie Ville Sante (FLVS) Study Group, 2004. The Three-Factor Eating Questionnaire-R18 is able to distinguish among different eating patterns in a general population. *The Journal of nutrition*, 134(9), pp.2372-2380.

Fontaine, K.R. and Barofsky, I., 2001. Obesity and health‐related quality of life. *Obesity reviews*, 2(3), pp.173-182.

Frank, M.J. and Fossella, J.A., 2011. Neurogenetics and pharmacology of learning, motivation, and cognition. *Neuropsychopharmacology*, 36(1), pp.133-152.

Frayn, M. and Knäuper, B., 2018. Emotional eating and weight in adults: a review. *Current Psychology*, 37(4), pp.924-933.

Gade, H., Rosenvinge, J.H., Hjelmesæth, J. and Friborg, O., 2014. Psychological correlates to dysfunctional eating patterns among morbidly obese

patients accepted for bariatric surgery. *Obesity Facts*, 7(2), pp.111-119.

Geliebter, A. and Aversa, A., 2003. Emotional eating in overweight, normal weight, and underweight individuals. *Eating behaviors*, 3(4), pp.341-347.

Gerlach, G., Herpertz, S. and Loeber, S., 2015. Personality traits and obesity: a systematic review. *Obesity reviews*, 16(1), pp.32-63.

Ghanemi, A., Yoshioka, M. and St-Amand, J., 2018. Broken energy homeostasis and obesity pathogenesis: the surrounding concepts. *Journal of clinical medicine*, 7(11), p.453.

Grady, D.L. et al., 2013. DRD4 genotype predicts longevity in mouse and human. *Journal of Neuroscience*, 33(1), pp.286-291.

Graffelman, J., Jain, D. and Weir, B., 2017. A genome-wide study of Hardy–Weinberg equilibrium with next generation sequence data. *Human genetics*, 136(6), pp.727-741.

Graziano, W. G. and Tobin, R. M., 2009. Agreeableness. In M. R. Leary & R. H. Hoyle (eds.), *Handbook of individual differences in social behavior*. The Guilford Press., pp. 46-61

Guo, J., Simmons, W.K., Herscovitch, P., Martin, A. and Hall, K.D., 2014. Striatal dopamine D2-like receptor correlation patterns with human obesity and opportunistic eating behavior. *Molecular psychiatry*, 19(10), pp.1078-1084.

Hagger, M.S., 2019. Habit and physical activity: Theoretical advances, practical implications, and agenda for future research. *Psychology of Sport and Exercise*, 42, pp.118-129.

Han, D.H. et al., 2007. Dopamine genes and reward dependence in adolescents with excessive internet video game play. *Journal of addiction medicine*, 1(3), pp.133-138.

Hao, J., Li, D., Peng, L., Peng, S. and Torelli, C.J., 2016. Advancing our understanding of culture mixing. *Journal of Cross-Cultural Psychology*, 47(10), pp.1257-1267.

Hardman, C.A., Rogers, P.J., Timpson, N.J. and Munafo, M.R., 2014. Lack of association between DRD2 and OPRM1 genotypes and adiposity. *International journal of obesity*, 38(5), pp.730-736.

Heaven, P.C., Mulligan, K., Merrilees, R., Woods, T. and Fairooz, Y., 2001. Neuroticism and conscientiousness as predictors of emotional, external, and restrained eating behaviors. *International Journal of Eating Disorders*, 30(2), pp.161-166.

Heni, M. et al., 2016. Interaction between the obesity-risk gene FTO and the dopamine D2 receptor gene ANKK1/TaqIA on insulin sensitivity. *Diabetologia*,

59(12), pp.2622-2631.

Hesselbrock, V.M. and Hesselbrock, M.N., 2006. Are there empirically supported and clinically useful subtypes of alcohol dependence?. *Addiction*, 101, pp.97-103.

Hinney, A., Vogel, C. I. G. and Hebebrand, J., 2010. From monogenic to polygenic obesity: recent advances. *European Child & Adolescent Psychiatry*, 19(3), pp. 297-310.

Hofker, M. and Wijmenga, C., 2009. A supersized list of obesity genes. *Nature genetics*, 41(2), pp.139-140.

Hovatta, I. and Barlow, C., 2008. Molecular genetics of anxiety in mice and men. *Annals of medicine*, 40(2), pp.92-109.

Huang, S.Y. et al., 2007. Monoamine oxidase-A polymorphisms might modify the association between the dopamine D2 receptor gene and alcohol dependence. *Journal of psychiatry & neuroscience*, 32(3), p.185.

Huppertz, C. et al., 2014. The dopaminergic reward system and leisure time exercise behavior: a candidate allele study. *BioMed research international*, 2014.

Huvenne, H., Dubern, B., Clément, K. and Poitou, C., 2016. Rare genetic forms of obesity: clinical approach and current treatments in 2016. *Obesity facts*, 9(3), pp.158-173.

Hruby, A. and Hu, F.B., 2015. The epidemiology of obesity: a big picture. *Pharmacoeconomics*, 33(7), pp.673-689.

Institute for Public Health, 2015. *National Health and Morbidity Survey 2015 VOLUME II: Non-Communicable Diseases, Risk Factors & Other Health Problems*. [pdf] Kuala Lumpur, Malaysia: IKU. Available at: http://iku.moh.gov.my/images/IKU/Document/REPORT/nhmsreport2015vol2.pdf [Accessed 1 October 2020].

Institute for Public Health, 2019. *National Health and Morbidity Survey 2019 VOLUME I: Non-Communicable Diseases, Risk Factors & Other Health Problems*. [pdf] Kuala Lumpur, Malaysia: IKU. Available at: http://www.iku.gov.my/images/IKU/Document/REPORT/NHMS2019/Report_NHMS2019-NCD_v2.pdf [Accessed 1 October 2020].

IPAQ Research Committee, 2005. Guidelines for data processing and analysis of the *International Physical Activity Questionnaire (IPAQ)-short and long forms*. Available at: http://www. ipaq. ki. se/scoring. pdf. [Accessed 12 October 2020].

Ishiguro, H. et al., 1998. Association study between the 441c ins/del and taqi a polymorphisms of the dopamine d2 receptor gene and alcoholism. *Alcoholism: Clinical and Experimental Research*, 22(4), pp.845-848.

Jáuregui-Lobera, I. and Montes-Martínez, M., 2020. Emotional eating and obesity. *In Psychosomatic Medicine*. IntechOpen.

Jetté, M., Sidney, K. and Blümchen, G., 1990. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. *Clinical cardiology*, 13(8), pp.555-565.

Jokela, M. et al., 2013. Association of personality with the development and persistence of obesity: a meta‐analysis based on individual‐participant data. *Obesity reviews*, 14(4), pp.315-323.

Jönsson, E.G. et al., 1999. Polymorphisms in the dopamine D2 receptor gene and their relationships to striatal dopamine receptor density of healthy volunteers. *Molecular psychiatry*, 4(3), p.290.

Jumbe, S., Bartlett, C., Jumbe, S.L. and Meyrick, J., 2016. The effectiveness of bariatric surgery on long term psychosocial quality of life–A systematic review. *Obesity research & clinical practice*, 10(3), pp.225-242.

Katz, D.A., McHorney, C.A. and Atkinson, R.L., 2000. Impact of obesity on health-related quality of life in patients with chronic illness. *Journal of general internal medicine*, 15(11), pp.789-796.

Kazantseva, A., Gaysina, D., Malykh, S. and Khusnutdinova, E., 2011. The role of dopamine transporter (SLC6A3) and dopamine D2 receptor/ankyrin repeat and kinase domain containing 1 (DRD2/ANKK1) gene polymorphisms in personality traits. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 35(4), pp.1033-1040.

Kirsch, P. et al., 2006. Imaging gene–substance interactions: the effect of the DRD2 TaqIA polymorphism and the dopamine agonist bromocriptine on the brain activation during the anticipation of reward. *Neuroscience letters*, 405(3), pp.196-201.

Keller, C. and Siegrist, M., 2015. Does personality influence eating styles and food choices? Direct and indirect effects. *Appetite*, 84, pp.128-138.

Kirac, D. et al., 2016. Effects of MC4R, FTO, and NMB gene variants to obesity, physical activity, and eating behavior phenotypes. *IUBMB life*, 68(10), pp.806-816.

Klein, C. et al., 1999. Association of a missense change in the D2 dopamine receptor with myoclonus dystonia. *Proceedings of the National Academy of Sciences*, 96(9), pp.5173-5176.

Kolotkin, R.L. and Andersen, J.R., 2017. A systematic review of reviews: exploring the relationship between obesity, weight loss and health‐related quality of life. *Clinical obesity*, 7(5), pp.273-289.

Korkiakangas, E.E., Alahuhta, M.A. and Laitinen, J.H., 2009. Barriers to regular exercise among adults at high risk or diagnosed with type 2 diabetes: a systematic review. *Health promotion international*, 24(4), pp.416-427.

Kroes, M., Osei-Assibey, G., Baker-Searle, R. and Huang, J., 2016. Impact of weight change on quality of life in adults with overweight/obesity in the United States: a systematic review. *Current medical research and opinion*, 32(3), pp.485-508.

Lahey, B.B., 2009. Public health significance of neuroticism. *American Psychologist*, 64(4), p.241.

Lazarevich, I., Camacho, M.E.I., del Consuelo Velázquez-Alva, M. and Zepeda, M.Z., 2016. Relationship among obesity, depression, and emotional eating in young adults. *Appetite*, 107, pp.639-644.

Lazarevich, I., Irigoyen-Camacho, M.E. and del Consuelo Velázquez-Alva, M., 2013. Obesity, eating behaviour and mental health among university students in Mexico City. *Nutricion hospitalaria*, 28(6), pp.1892-1899.

Lee-Winn, A.E., Townsend, L., Reinblatt, S.P. and Mendelson, T., 2016. Associations of neuroticism and impulsivity with binge eating in a nationally representative sample of adolescents in the United States. *Personality and individual differences*, 90, pp.66-72.

Leibowitz, S.F. and Alexander, J.T., 1998. Hypothalamic serotonin in control of eating behavior, meal size, and body weight. *Biological psychiatry*, 44(9), pp.851-864.

Lek, F.Y., Ong, H.H. and Say, Y.H., 2018. Association of dopamine receptor D2 gene (DRD2) Taq1 polymorphisms with eating behaviors and obesity among Chinese and Indian Malaysian university students. *Asia Pacific journal of clinical nutrition*, 27(3), p.707.

Lin, E. and Chen, P.S., 2009. Molecular genetics of human personality traits for psychiatric, behavioral, and substance-related disorders. *The Open Translational Medicine Journal*, 1(1).

Lin, S.C. et al., 2007. Specific personality traits and dopamine, serotonin genes in anxiety– depressive alcoholism among Han Chinese in Taiwan. Progress in Neuro- *Psychopharmacology and Biological Psychiatry*, 31(7), pp.1526-1534.

Lindekilde, N. et al., 2015. The impact of bariatric surgery on quality of life: a systematic review and meta‐analysis. *Obesity reviews*, 16(8), pp.639-651.

Liu, Y.J. et al., 2008. Genome-wide association scans identified CTNNBL1 as a novel gene for obesity. *Human molecular genetics*, 17(12), pp.1803-1813.

Loos, R.J. and Yeo, G.S., 2014. The bigger picture of FTO—the first GWAS-identified obesity gene. *Nature Reviews Endocrinology*, 10(1), pp.51-61.

Loos, R.J. and Janssens, A.C.J., 2017. Predicting polygenic obesity using genetic information. *Cell metabolism*, 25(3), pp.535-543.

Lucht, M. et al., 2010. Influence of DRD2 and ANKK1 genotypes on apomorphine- induced growth hormone (GH) response in alcohol-dependent patients. Progress in *Neuro-Psychopharmacology and Biological Psychiatry*, 34(1), pp.45-49.

Lydecker, J.A. and Grilo, C.M., 2016. Different yet similar: Examining race and ethnicity in treatment-seeking adults with binge eating disorder. *Journal of consulting and clinical psychology*, 84(1), p.88.

Ma, Y., Yuan, W., Jiang, X., Cui, W.Y. and Li, M.D., 2015. Updated findings of the association and functional studies of DRD2/ANKK1 variants with addictions. *Molecular neurobiology*, 51(1), pp.281-299.

Maes, H.H., Neale, M.C. and Eaves, L.J., 1997. Genetic and environmental factors in relative body weight and human adiposity. *Behavior genetics*, 27(4), pp.325-351.

Magallares, A. and Schomerus, G., 2015. Mental and physical health-related quality of life in obese patients before and after bariatric surgery: a meta-analysis. *Psychology, health & medicine*, 20(2), pp.165-176.

Manfredi, L., Accoto, A., Couyoumdjian, A. and Conversi, D., 2021. A Systematic Review of Genetic Polymorphisms Associated with Binge Eating Disorder. *Nutrients* 2021, 13, 848.

Marks, D.F., 2015. Homeostatic theory of obesity. *Health Psychology Open*, 2(1), p.2055102915590692.

Marques, A. et al., 2021. Bidirectional Association between Physical Activity and Dopamine Across Adulthood—A Systematic Review. *Brain Sciences*, 11(7), p.829.

Martins, L.C.G., Lopes, M.V.D.O., Diniz, C.M. and Guedes, N.G., 2021. The factors related to a sedentary lifestyle: A meta‐analysis review. *Journal of Advanced Nursing*, 77(3), pp.1188-1205.

McCrae, R.R. and Costa, P.T., 1987. Validation of the five-factor model of personality across instruments and observers. *Journal of personality and social* psychology, 52(1), p.81.

McCrae, R.R. and John, O.P., 1992. An introduction to the five‐factor model and its applications. *Journal of personality*, 60(2), pp.175-215.

Melchers, M.C. et al., 2016. Similar personality patterns are associated with empathy in four different countries. *Frontiers in psychology*, 7, p.290.

Micanti, F. et al., 2017. The relationship between emotional regulation and eating behaviour: a multidimensional analysis of obesity psychopathology. *Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity*, 22(1), pp.105-115.

Morris, M.J., Beilharz, J.E., Maniam, J., Reichelt, A.C. and Westbrook, R.F., 2015. Why is obesity such a problem in the 21st century? The intersection of palatable food, cues and reward pathways, stress, and cognition. *Neuroscience & Biobehavioral Reviews*, 58, pp.36-45.

Munafo, M.R., Matheson, I.J. and Flint, J., 2007. Association of the DRD2 gene Taq1A polymorphism and alcoholism: a meta-analysis of case–control studies and evidence of publication bias. *Molecular psychiatry*, 12(5), p.454.

Munafò, M.R., Timpson, N.J., David, S.P., Ebrahim, S. and Lawlor, D.A., 2009. Association of the DRD2 gene Taq1A polymorphism and smoking behavior: a meta-analysis and new data. *Nicotine and Tobacco Research*, 11(1), pp.64-76.

Nacak, M. et al., 2012. Analysis of dopamine D2 receptor (DRD2) gene polymorphisms in cannabinoid addicts. *Journal of forensic sciences*, 57(6), pp.1621-1624.

Napolitano, M.A. and Himes, S., 2011. Race, weight, and correlates of binge eating in female college students. *Eating behaviors*, 12(1), pp.29-36.

National Nutrition Surveillance Centre, 2009. *The interrelationship between obesity, physical activity, nutrition and other determinants*. [pdf] Dublin, Ireland: Health Service Executive (HSE): HSE Framework for Action on Obesity. Available at: https://www.ucd.ie/t4cms/nnsc_MHeinen_position%20paper%20series8.pdf [Accessed 3 October 2020]

Ndiaye, F.K. et al., 2019. The expression of genes in top obesity-associated loci is enriched in insula and substantia nigra brain regions involved in addiction and reward. *International Journal of Obesity*, pp.1-5.

Neville, M.J., Johnstone, E.C. and Walton, R.T., 2004. Identification and characterization of ANKK1: a novel kinase gene closely linked to DRD2 on chromosome band 11q23. 1. *Human mutation*, 23(6), pp.540-545.

Ng, B., 2018. The neuroscience of growth mindset and intrinsic motivation. *Brain sciences*, 8(2), p.20.

Ng, M. et al., 2014. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*, 384(9945), pp. 766-781.

Nicholls, W., Devonport, T.J. and Blake, M., 2016. The association between emotions and eating behaviour in an obese population with binge eating disorder. *Obesity reviews*, 17(1), pp.30-42.

Nolan, L.J., Halperin, L.B. and Geliebter, A., 2010. Emotional Appetite Questionnaire. Construct validity and relationship with BMI. *Appetite*, 54(2), pp.314-319.

Ntoumanis, N., 2001. Empirical links between achievement goal theory and self-determination theory in sport. *Journal of sports sciences*, 19(6), pp.397-409.

Okada, Y. et al., 2012. Common variants at CDKAL1 and KLF9 are associated with body mass index in east Asian populations. *Nature genetics*, 44(3), pp.302-306.

Oliveri, R.L. et al., 2000. The dopamine D2 receptor gene is a susceptibility locus for Parkinson's disease. Movement Disorders: *Official Journal of the Movement Disorder Society*, 15(1), pp.120-126.

Paik, S.H. et al., 2017. An association study of Taq1A ANKK1 and C957T and−141C DRD2 polymorphisms in adults with internet gaming disorder: a pilot study. *Annals of general psychiatry*, 16(1), p.45.

Pappas, S., 2017. *Personality Traits and Personality Types: What is Personality?* [Online]. Available at: https://www.livescience.com/41313-personality-traits.html [Accessed: 1 July 2021].

Pérusse, L. et al., 2005. The human obesity gene map: the 2004 update. *Obesity research*, 13(3), pp.381-490.

Pearson-Fuhrhop, K.M. et al., 2014. Dopamine genetic risk score predicts depressive symptoms in healthy adults and adults with depression. *PLoS One*, 9(5), p.e93772.

Provencher, V. et al., 2008. Personality traits in overweight and obese women: Associations with BMI and eating behaviors. *Eating behaviors*, 9(3), pp.294-302.

Psouni, S., Chasandra, M. and Theodorakis, Y., 2016. Patterns of eating and physical activity attitudes and behaviors in relation to body mass index. *Psychology*, 7.

Reshadat, S. et al., 2017. A Study of the Correlation of Personality Traits (Neuroticism and Psychoticism) and Self-efficacy in Weight Control with Unhealthy Eating Behaviors and Attitudes. Annals of Medical and Health Sciences Research. Reich, D.E. and Lander, E.S., 2001. On the allelic spectrum of human disease. *TRENDS in Genetics*, 17(9), pp.502-510.

Reynolds, G.P. et al., 1999. Brain neurotransmitter deficits in mice transgenic for the Huntington’s disease mutation. *Journal of neurochemistry*, 72(4), pp.1773-1776.

Rivera-Iñiguez, I., Panduro, A., Ramos-Lopez, O., Villaseñor-Bayardo, S.J. and Roman, S., 2019. DRD2/ANKK1 TaqI A1 polymorphism associates with

overconsumption of unhealthy foods and biochemical abnormalities in a Mexican population. *Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity*, 24(5), pp.835-844.

Rhodes, R.E. and Smith, N.E.I., 2006. Personality correlates of physical activity: a review and meta-analysis. *British journal of sports medicine*, 40(12), pp.958-965.

Richard, M., Christina, M.F., Deborah, L.S., Rubio, N. and Kennon, M.S., 1997. Intrinsic motivation and exercise adherence. *Int J Sport Psychol*, 28(4), pp.335-354.

Ritchie, H. and Roser, M., 2017, *Obesity* [Online]. Available at: https://ourworldindata.org/obesity [Accessed: 1 July 2021].

Ritchie, T. and Noble, E.P., 2003. Association of seven polymorphisms of the D2 dopamine receptor gene with brain receptor-binding characteristics. *Neurochemical research*, 28(1), pp.73-82.

Rhodes, R.E. and Smith, N.E.I., 2006. Personality correlates of physical activity: a review and meta-analysis. *British journal of sports medicine*, 40(12), pp.958-965.

Rhodes, R.E. and Boudreau, P., 2017. Physical activity and personality traits. *Oxford Research Encyclopedia of Psychology*, pp. 1-16.

Richter, A. et al., 2013. Motivational salience and genetic variability of dopamine D2 receptor expression interact in the modulation of interference processing. *Frontiers in human neuroscience*, 7, p.250.

Rosiek, A., Maciejewska, N.F., Leksowski, K., Rosiek-Kryszewska, A. and Leksowski, Ł., 2015. Effect of television on obesity and excess of weight and consequences of health. *International journal of environmental research and public health*, 12(8), pp.9408-9426.

Rosso, A.L. et al., 2018. Dopamine‐related genotypes and physical activity change during an intervention: the lifestyle interventions and independence for elders study. *Journal of the American Geriatrics Society*, 66(6), pp.1172-1179.
Ryan, R.M. and Patrick, H., 2009. Self-determination theory and physical. *Hellenic journal of psychology*, 6, pp.107-124.

Ryan, R.M. and Deci, E.L., 2000. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. *American psychologist*, 55(1), p.68.

Salamone, J.D., Correa, M., Mingote, S.M. and Weber, S.M., 2005. Beyond the reward hypothesis: alternative functions of nucleus accumbens dopamine. *Current opinion in pharmacology*, 5(1), pp.34-41.

Sallis, J.F. et al., 1985. Physical activity assessment methodology in the Five-City Project. *American journal of epidemiology*, 121(1), pp.91-106.

Sari, M. and Wijaya, D., 2017. Relationship between calorie intake, physical activity, and dopamine D2 receptor Taq1A gene polymorphism in normal-weight, overweight, and obese students of the faculty of medicine of university of Sumatera Utara. *Bali Medical Journal*, 6(1), pp.125-129.

Saunders, B.T. and Robinson, T.E., 2013. Individual variation in resisting temptation: implications for addiction. *Neuroscience & Biobehavioral Reviews*, 37(9), pp.1955-1975.

Schmitt, D.P., Allik, J., McCrae, R.R. and Benet-Martínez, V., 2007. The geographic distribution of Big Five personality traits: Patterns and profiles of human self-description across 56 nations. *Journal of cross-cultural psychology*, 38(2), pp.173-212.

Sendi, P., Brunotte, R., Potoczna, N., Branson, R. and Horber, F.F., 2005. Health-related quality of life in patients with class II and class III obesity. *Obesity surgery*, 15(7), pp.1070-1076.

Simonen, R.L. et al., 2003. A dopamine D2 receptor gene polymorphism and physical activity in two family studies. *Physiology & behavior*, 78(4-5), pp.751-757.

Sorisky, A., Magun, R. and Gagnon, A.M., 2000. Adipose cell apoptosis: death in the energy depot. *International Journal of Obesity*, 24(4), pp.S3-S7.

Spinosa, J., Christiansen, P., Dickson, J.M., Lorenzetti, V. and Hardman, C.A., 2019. From socioeconomic disadvantage to obesity: the mediating role of psychological distress and emotional eating. *Obesity*, 27(4), pp.559-564.

Steanovv, T.S., Vekova, A.M., Kurktschiev, D.P. and Temelkova-Kurktschiev, T.S., 2011. Relationship of physical activity and eating behaviour with obesity and type 2 diabetes mellitus: Sofia Lifestyle (SLS) study. *Folia Med (Plovdiv)*, 53(1), pp.11-18.

Stephan, Y., Sutin, A.R. and Terracciano, A., 2014. Physical activity and personality development across adulthood and old age: Evidence from two longitudinal studies. *Journal of Research in Personality*, 49, pp.1-7.

Stunkard, A.J., Harris, J.R., Pedersen, N.L. and McClearn, G.E., 1990. The body-mass index of twins who have been reared apart. *New England journal of medicine*, 322(21), pp.1483-1487.

Suriyaprom, K., Tungtrongchitr, R. and Harnroongroj, T., 2013. Impact of COMT Val 108/158 Met and DRD2 Taq1B gene polymorphisms on vulnerability to cigarette smoking of Thai males. *Journal of Molecular Neuroscience*, 49(3), pp.544-549.

Takeuchi, H. et al., 2015. The associations among the dopamine D2 receptor Taq1, emotional intelligence, creative potential measured by divergent thinking, and motivational state and these associations' sex differences. *Frontiers in psychology*, 6, p.912.

Thomas, G.N., Tomlinson, B. and Critchley, J.A., 2000. Modulation of blood pressure and obesity with the dopamine D2 receptor gene Taq I polymorphism. *Hypertension*, 36(2), pp.177-182.

Tolea, M.I. et al., 2012. Associations between personality traits, physical activity level, and muscle strength. *Journal of research in personality*, 46(3), pp.264- 270.

Traversy, G. and Chaput, J.P., 2015. Alcohol consumption and obesity: an update. *Current obesity reports*, 4(1), pp.122-130.

Ul‐Haq, Z., Mackay, D.F., Fenwick, E. and Pell, J.P., 2013. Meta‐analysis of the association between body mass index and health‐related quality of life among adults, assessed by the SF‐36. *Obesity*, 21(3), pp.E322-E327.

Vainik, U., García‐García, I. and Dagher, A., 2019. Uncontrolled eating: a unifying heritable trait linked with obesity, overeating, personality and the brain. *European Journal of Neuroscience*, 50(3), pp.2430-2445.

Vanhecke, T.E. et al., 2009. Cardiorespiratory fitness and sedentary lifestyle in the morbidly obese. Clinical Cardiology: *An International Indexed and Peer‐Reviewed Journal for Advances in the Treatment of Cardiovascular Disease*, 32(3), pp.121-124.

Van Nunen, A.M., Wouters, E.J., Vingerhoets, A.J., Hox, J.J. and Geenen, R., 2007. The health-related quality of life of obese persons seeking or not seeking surgical or non-surgical treatment: a meta-analysis. *Obesity surgery*, 17(10), p.1357.

Van Strien, T., 2018. Causes of emotional eating and matched treatment of obesity. *Current diabetes reports*, 18(6), pp.1-8.

Verdejo-Garcia, A. et al., 2015. Neural substrates of cognitive flexibility in cocaine and gambling addictions. *The British Journal of Psychiatry*, 207(2), pp.158-164.

Vijayan, N.N. et al., 2007. Association of dopamine receptor polymorphisms with schizophrenia and antipsychotic response in a South Indian population. *Behavioral and Brain Functions*, 3(1), p.34.

Volkow, N.D., Wang, G.J. and Baler, R.D., 2011. Reward, dopamine and the control of food intake: implications for obesity. Trends in cognitive sciences, 15(1), pp.37-46. Wacker, J. and Smillie, L.D., 2015. Trait extraversion and dopamine function. *Social and Personality Psychology Compass*, 9(6), pp.225-

238.

Walther, M. and Hilbert, A., 2015. Emotional Openness, problematic eating behaviours, and overweight in adolescents. *Eating behaviors*, 17, pp.111-114.

Wang, F., Simen, A., Arias, A., Lu, Q.W. and Zhang, H., 2013. A large-scale meta-analysis of the association between the ANKK1/DRD2 Taq1A polymorphism and alcohol dependence. *Human genetics*, 132(3), pp.347-358.

Wang, G.J. et al., 2001. Brain dopamine and obesity. *The Lancet*, 357(9253), pp.354-357.

Wang, G.J., Volkow, N.D., Thanos, P.K. and Fowler, J.S., 2004. Similarity between obesity and drug addiction as assessed by neurofunctional imaging: a concept review. *Journal of addictive diseases*, 23(3), pp.39-53.

Wang, T.J. et al., 2007. Possible interaction between MAOA and DRD2 genes associated with antisocial alcoholism among Han Chinese men in Taiwan. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 31(1), pp.108-114.

Wanat, M.J., Hopf, F.W., Stuber, G.D., Phillips, P.E.M. and Bonci, A., 2008. Corticotropin‐releasing factor increases mouse ventral tegmental area dopamine neuron firing through a protein kinase C‐dependent enhancement of Ih. *The Journal of physiology*, 586(8), pp.2157-2170.

Wardle, J., 2007. Eating behaviour and obesity. *Obesity reviews*, 8, pp.73-75.

Ware Jr, J.E., 2000. SF-36 health survey update. *Spine*, 25(24), pp.3130-3139.

Warkentin, L.M., Das, D., Majumdar, S.R., Johnson, J.A. and Padwal, R.S., 2014. The effect of weight loss on health‐related quality of life: systematic review and meta‐analysis of randomized trials. *Obesity Reviews*, 15(3), pp.169- 182.

WHOQOL Group, 1995. The World Health Organization quality of life assessment (WHOQOL): position paper from the World Health Organization. *Social science & medicine*, 41(10), pp.1403-1409.

Wiebe, D.J. and Smith, T.W., 1997. Personality and health: Progress and problems in psychosomatics. In: Hogan, R., Johnson, J., and Briggs, S.. Handbook of personality psychology. *Academic Press*., pp. 891-918.

Wilson, K.E. and Dishman, R.K., 2015. Personality and physical activity: A systematic review and meta-analysis. *Personality and Individual Differences*, 72, pp.230-242.

World Population Review, 2020. *Most Obese Countries 2020* [Online]. Available at: https://worldpopulationreview.com/country-rankings/most-obese-countries [Accessed: 9 October 2020].

World Health Organization 2018, *Physical activity* [Online]. Available at: https://www.who.int/news-room/fact-sheets/detail/physical-activity [Accessed: 8 November 2020].

World Health Organization 2020, *Obesity* [Online]. Available at: https://www.who.int/topics/obesity/en/ [Accessed: 20 September 2020].

World Health Organization 2020, *Obesity and overweight* [Online]. Available at: https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight [Accessed: 20 September 2020].

Wu, C.Y. et al., 2008. The association between DRD2/ANKK1, 5‐HTTLPR gene, and specific personality trait on antisocial alcoholism among Han Chinese in Taiwan. American Journal of Medical Genetics Part B: *Neuropsychiatric Genetics*, 147(4), pp.447-453.

World Health Organization, 2018. *Obesity and overweight fact sheet* [Online]. Available at: http://www.who.int/mediacentre/factsheets/fs311/en/ [Accessed: 20 September 2020].

Xia, Q. and Grant, S.F., 2013. The genetics of human obesity. *Annals of the New York Academy of Sciences*, 1281(1), p.178.

Yeh, J. et al., 2016. Food cravings, food addiction, and a dopamine-resistant (DRD2 A1) receptor polymorphism in Asian American college students. *Asia Pacific journal of clinical nutrition*, 25(2), p.424.

Zuo, Y. et al., 2009. DRD2-related TaqIA polymorphism modulates motivation to smoke. *Nicotine & Tobacco Research*, 11(11), pp.1321-1329.

Appendices

Appendix A

UNIVERSITI TUNKU ABDUL RAHMAN
Wholly Owned by UTAR Education Foundation (Company No. 578227-M)

Re: U/SERC/97/2018

13 August 2018

Dr Alia Azalea
Department of Psychology and Counselling
Faculty of Arts and Social Science
Universiti Tunku Abdul Rahman
Jalan Universiti, Bandar Baru Barat
31900 Kampar
Perak

Dear Dr Alia,

Ethical Approval For Research Project/Protocol

We refer to your application which was circulated for the consideration of the UTAR Scientific and Ethical Review Committee (SERC). We are pleased to inform that your application for ethical approval for your research project involving human subjects has been approved by SERC.

The details of the project are as follows:

Research Title	Personality Traits, Eating Behavior, Physical Activity and Genetic Correlates of Obesity Among UTAR Staff and Students
Investigator(s)	Dr Alia Azalea (PI) Dr Say Yee How Dr Chie Qiu Ting
Research Area	Social Science
Research Location	UTAR, Kampar Campus
No of Participants	300 participants (Age: 18 - 55)
Research Costs	UTAR Research Fund
Approval Validity	13 August 2018 - 12 August 2019

The conduct of this research is subject to the following:

(1) The participants' informed consent be obtained prior to the commencement of the research.

(2) Confidentiality of participants' personal data must be maintained; and

(3) Compliance with procedures set out in related policies of UTAR such as the UTAR Research Ethics and Code of Conduct, Code of Practice for Research Involving Humans and other related policies/guidelines.

Appendix B

Wholly owned by UTAR Education Foundation
(Co. No. 578227-M)

FACULTY OF ARTS AND SOCIAL SCIENCES

INFORMATION FOR PARTICIPANTS

for the study of

Personality traits, eating behavior, physical activity, genetics and quality of life

- We would like your permission to enroll you as a participant in a Master's degree research to explore how personality traits, eating behavior; physical activity and genetics associate with the quality of life.

- First, you will then have to answer a series of questions in a questionnaire to assess your personality traits, eating behavior; physical activity and quality of life.

- We will then take your body measurements, which include your height, weight, waist and hip circumferences. You will then be asked to step on a scale which will measure your Body Mass Index, Body Fat Percentage, Subcutaneous Fat Percentage, Visceral Fat Percentage, Resting Metabolism Rate and Skeletal Muscle Percentage. After you have rested for 5 minutes, we will then take your blood pressure. Please make an appointment with us if this part could not be completed at the time of answering the questionnaire.

- Finally, you will be asked to rinse your mouth with water. Then, pour the 5 ml sugar solution given to you into your mouth, rinse, rub your cheeks with your tongue for 1 minute and spit it back into a test tube. This study involves the detection of genetic variants using the DNA extracted from your mouthwash sample.

- You will receive a small token as an appreciation for your time and effort. Thank you.

CONSENT FORM

I, _____

volunteer to participate in the study of

Personality traits, eating behavior, physical activity, genetics and quality of life

I am willing to donate my mouthwash sample for this study. I also understand that I have to answer a series of questions in a questionnaire as honest as possible.

I have also been informed that all the information provided by me and all the results obtained will be kept in strict confidence by the researchers, and all the data and samples from this research project will be destroyed after the end of it.

Hereby, I give my consent to participate in this above study.

Respondent	**Interviewer**
Date : _____	Date : _____
Signature: _____	Signature: _____
Name : _____	Name : _____
Contact number: _____	
Email: _____	

Personal Data Protection Statement

Please be informed that in accordance with Personal Data Protection Act 2010 ("PDPA") which came into force on 15 November 2013, Universiti Tunku Abdul Rahman ("UTAR") is hereby bound to make notice and require consent in relation to collection, recording, storage, usage and retention of personal information.

Notice:

1. The purposes for which your personal data may be used are inclusive but not limited to:-
   - For assessment of any application to UTAR
   - For processing any benefits and services
   - For communication purposes
   - For advertorial and news
   - For general administration and record purposes
   - For enhancing the value of education
   - For educational and related purposes consequential to UTAR
   - For the purpose of our corporate governance
   - For consideration as a guarantor for UTAR staff/ student applying for his/her scholarship/ study loan

2. Your personal data may be transferred and/or disclosed to third party and/or UTAR collaborative partners including but not limited to the respective and appointed outsourcing agents for purpose of fulfilling our obligations to you in respect of the purposes and all such other purposes that are related to the purposes and also in providing integrated services, maintaining and storing records. Your data may be shared when required by laws and when disclosure is necessary to comply with applicable laws.

3. Any personal information retained by UTAR shall be destroyed and/or deleted in accordance with our retention policy applicable for us in the event such information is no longer required.

4. UTAR is committed in ensuring the confidentiality, protection, security and accuracy of your personal information made available to us and it has been our ongoing strict policy to ensure that your personal information is accurate, complete, not misleading and updated. UTAR would also ensure that your personal data shall not be used for political and commercial purposes.

Consent:

1. By submitting this form you hereby authorise and consent to us processing (including disclosing) your personal data and any updates of your information, for the purposes and/or for any other purposes related to the purpose.

2. If you do not consent or subsequently withdraw your consent to the processing and disclosure of your personal data, UTAR will not be able to fulfill our obligations or to contact you or to assist you in respect of the purposes and/or for any other purposes related to the purpose.

3. You may access and update your personal data by writing to us at dhr@utar.edu.my.

Acknowledgment of Notice (Please tick)

☐ I have been notified by you and that I hereby understood, consented and agreed per UTAR above notice.

☐ I disagree, my personal data will not be processed.

Appendix C

Respondent No:

PART A: Demographics
Instruction: Please complete this part. Fill in the particulars or circle only one most relevant answer.

1. **Age** : _____
2. **Sex** : [1] Male [2] Female
3. **Circle ONE ethnicity and its subgroup that would best describe yourself as:**

[1] Bumiputra [A] Malay [B] Orang Asli, Peninsular [C] Orang Asli, East Malaysia

[2] Han Chinese [A] Hokkien [B] Hakka [C] Cantonese [D] Teochew [E] Mandarin [F] Hainanese [G] Fuchow [H] Straits Chinese [I] Others _____

[3] Indian [A] Tamil [B] Telegu [C] Malayalam [D] Punjabi [E] Ceylonese [F] Others

[4] Others

PART B: Big-Five Personality Traits
Instruction: How much do you agree with each statement about you as you generally are now, not as you wish to be in the future?

No.	In general, I...	Strongly disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Strongly agree
		1	2	3	4	5
1.	Am the life of the party.					
2.	Sympathize with others' feelings.					
3.	Get chores done right away.					
4.	Have frequent mood swings.					
5.	Have a vivid imagination.					
6.	Don't talk a lot.					
7.	Am not interested in other people's problems.					
8.	Often forget to put things back in their proper place.					
9.	Am relaxed most of the time.					
10.	Am not interested in abstract ideas.					
11.	Talk to a lot of different people at parties.					
12.	Feel others' emotions					
13.	Like order.					
14.	Get upset easily.					
15.	Have difficulty understanding abstract ideas.					
16.	Keep in the background.					
17.	Am not really interested in others.					
18.	Make a mess of things.					
19.	Seldom feel blue.					
20.	Do not have a good imagination.					

PART C: Eating Behaviour
Instruction: Please tick ONE most relevant answer for the questions below. Thank you.

	Question	Definitely true	Mostly true	Mostly false	Definitely false
1.	When I smell a sizzling steak or juicy piece of meat, I find it very difficult to keep from eating, even if I have just finished a meal.				
2.	I deliberately take small helpings as a means of controlling my weight.				
3.	When I feel anxious, I find myself eating.				
4.	Sometimes when I start eating, I just can't seem to stop.				
5.	Being with someone who is eating often makes me hungry enough to eat also.				
6.	When I feel blue, I often overeat.				
7.	When I see a real delicacy, I often get so hungry that I have to eat right away.				
8.	I get so hungry that my stomach often seems like a bottomless pit.				
9.	I am always hungry so it is hard for me to stop eating before I finish the food on my plate.				
10.	When I feel lonely, I console myself by eating.				
11.	I consciously hold back at meals in order not to weight gain.				
12.	I do not eat some foods because they make me fat.				
13.	I am always hungry enough to eat at any time.				
	Question	**Only at meal times**	**Sometimes between meals**	**Often between meals**	**Almost always**
14.	How often do you feel hungry?				
	Question	**Almost never**	**Seldom**	**Usually**	**Almost always**
15.	How frequently do you avoid "stocking up" on tempting foods?				
	Question	**Unlikely**	**Slightly likely**	**Moderately likely**	**Very likely**
16.	How likely are you to consciously eat less than you want?				
	Question	**Never**	**Rarely**	**Sometimes**	**At least once a week**
17.	Do you go on eating binges though you are not hungry?				

18. On a scale of 1 to 8, where 1 means no restraint in eating (eating whatever you want, whenever you want it) and 8 means total restraint (constantly limiting food intake and never "giving in"), what number would you give yourself?

_____

PART D: International Physical Activity Questionnaire
Instruction: We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the last 7 days. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?
   _____ days per week

   ☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

____ hours per day

____ minutes per day

☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

____ days per week

☐ No moderate physical activities → ***Skip to question 5***

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

____ hours per day

____ minutes per day

☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

5. During the last 7 days, on how many days did you walk for at least 10 minutes at a time?

____ days per week

☐ No walking → ***Skip to question 7***

6. How much time did you usually spend walking on one of those days?

____ hours per day

____ minutes per day

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the last 7 days, how much time did you spend sitting on a week day?

____ hours per day

____ minutes per day

☐ Don't know/Not sure

PART E: Motives for Physical Activities Measure

Instruction: The following is a list of reasons why people engage in physical activities, sports and exercise. Keeping in mind your primary physical activity/sport, respond to each question (using the scale given), on the basis of how true that response is for you.

		1 Not at all true for me	2	3	4	5	6	7 Very true for me
1.	Because I want to be physically fit.							
2.	Because it's fun.							
3.	Because I like engaging in activities which physically challenge me.							
4.	Because I want to obtain new skills.							
5.	Because I want to look or maintain weight so I look better.							
6.	Because I want to be with my friends.							
7.	Because I like to do this activity.							
8.	Because I want to improve existing skills.							
9.	Because I like the challenge.							
10.	Because I want to define my muscles so I look better.							
11.	Because it makes me happy.							
12.	Because I want to keep up my current skill level.							
13.	Because I want to have more energy							
14.	Because I like activities which are physically challenging.							
15.	Because I like to be with others who are interested in this activity.							
16.	Because I want to improve my cardiovascular fitness.							
17.	Because I want to improve my appearance.							
18.	Because I think it's interesting.							
19.	Because I want to maintain my physical strength to live a healthy life.							
20.	Because I want to be attractive to others.							
21.	Because I want to meet new people.							
22.	Because I enjoy this activity.							
23.	Because I want to maintain my physical health and well-being.							
24.	Because I want to improve my body shape.							
25.	Because I want to get better at my activity.							
26.	Because I find this activity stimulating.							
27.	Because I will feel physically unattractive if I don't.							
28.	Because my friends want me to.							
29.	Because I like the excitement of participation.							
30.	Because I enjoy spending time with others doing this activity.							

PART F: Quality of life
Instruction: Please complete this part. Fill in the particulars or circle only one most relevant answer.

1. In general, would you say your health is: [1] Excellent [2] Very good [3] Good [4] Fair [5] Poor

2. **Compared to one year ago**, how would you rate your health in general **now**?
   [1] Much better now than one year ago
   [2] Somewhat better now than one year ago
   [3] About the same
   [4] Somewhat worse now than one year ago
   [5] Much worse now than one year ago

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?		**Yes, limited a lot**	**Yes, limited a little**	**No, not limited at all**
		1	**2**	**3**
3.	**Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports			
4.	**Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf			
5.	Lifting or carrying groceries			
6.	Climbing **several** flights of stairs			
7.	Climbing **one** flight of stairs			
8.	Bending, kneeling, or stooping			
9.	Walking **more than a mile**			
10.	Walking **several blocks**			
11.	Walking **one block**			
12.	Bathing or dressing yourself			

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

13. Cut down the **amount of time** you spent on work or other activities [1] Yes [2] No

14. **Accomplished less** than you would like [1] Yes [2] No

15. Were limited in the **kind** of work or other activities [1] Yes [2] No

16. Had **difficulty** performing the work or other activities (for example, it took extra effort) [1] Yes [2] No

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

17. Cut down the **amount of time** you spent on work or other activities [1] Yes [2] No

18. **Accomplished less** than you would like [1] Yes [2] No

19. Didn't do work or other activities as **carefully** as usual [1] Yes [2] No

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?
    [1] Not at all [2] Slightly [3] Moderately [4] Quite a bit [5] Extremely

21. How much **bodily** pain have you had during the **past 4 weeks**?
    [1] None [2] Very mild [3] Mild [4] Moderate [5] Severe [6] Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?
    [1] Not at all [2] A little bit [3] Moderately [4] Quite a bit [5] Extremely

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks...		All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
		1	2	3	4	5	6
23.	Did you feel full of pep?						
24.	Have you been a very nervous person?						
25.	Have you felt so down in the dumps that nothing could cheer you up?						
26.	Have you felt calm and peaceful?						
27.	Did you have a lot of energy?						
28.	Have you felt downhearted and blue?						
29.	Did you feel worn out?						
30.	Have you been a happy person?						
31.	Did you feel tired?						

32. During the **past 4 weeks**, how much of the time has **your physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

[1] All of the time [2] Most of the time [3] Some of the time [4] A little of the time [5] None of the time

How TRUE or FALSE is **each** of the following statements for you.

		Definitely true	Mostly true	Don't know	Mostly false	Definitely false
		1	2	3	4	5
33.	I seem to get sick a little easier than other people					
34.	I am as healthy as anybody I know					
35.	I expect my health to get worse					
36.	My health is excellent					

PART G: Anthropometric measurements

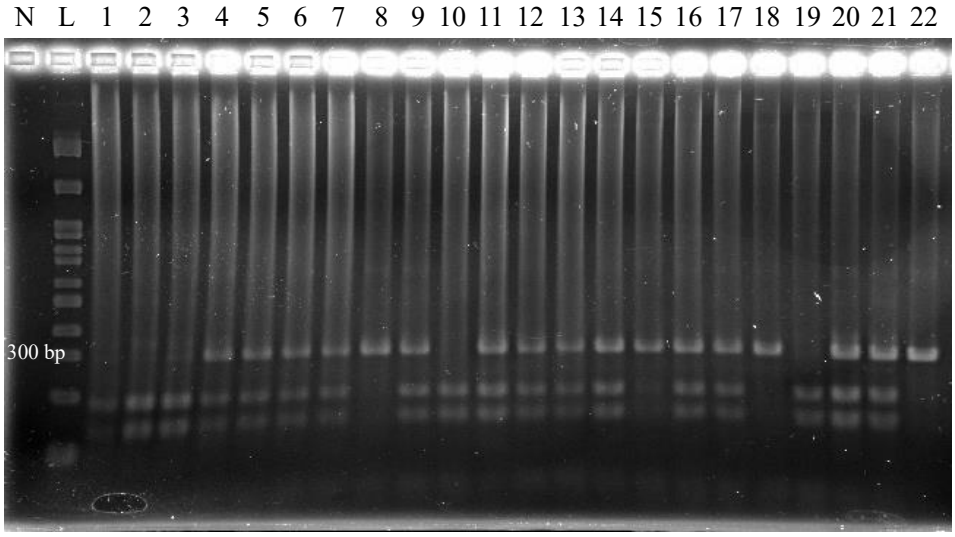
Instruction: The anthropometric measurements will be performed for you. Please make an appointment with us if this part could not be completed at the time of answering the questionnaire.

Measurement	1st reading	2nd reading	Measurement	1st reading	2nd reading
SBP (mmHg)			Weight (kg)		
DBP (mmHg)			BMI (kg/m^2)		
Pulse rate (bpm)			TBF (%)		
Waist circumference (cm)			SF (%)		
Hip circumference (cm)			VFL (%)		
Height (cm)			SM (%)		
			RM (kcal)		

- End of questionnaire-

Appendix D

Representative gel image for genotyping of *DRD2 Taq1A* (rs1800497)



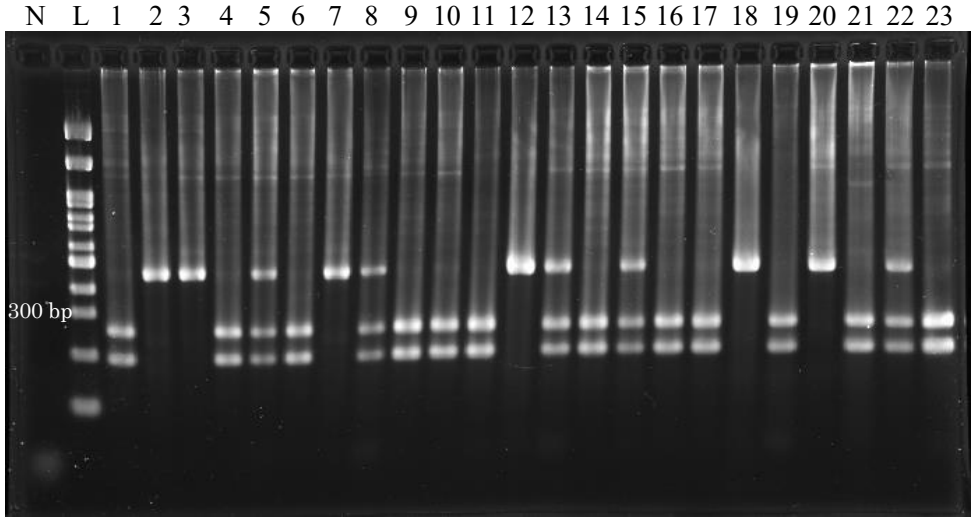
The 100 bp DNA ladder was loaded onto lane L. The negative control was loaded on lane N. The genotypes of each sample is as followed:

Lane	Genotype
1	GG
2	GG
3	GG
4	GA
5	GA
6	GA
7	GA
8	AA
9	GA
10	GG
11	GA
12	GA
13	GA
14	GA
15	AA
16	GA
17	GA
18	AA
19	GG
20	GA
21	GA
22	AA

*GG: Homozygous wildtype; GA: Heterozygous; AA: Homozygous mutant

Representative gel image for genotyping of *DRD2 Taq1B* (rs1079597)

The 100 bp DNA ladder was loaded onto lane L. The negative control was

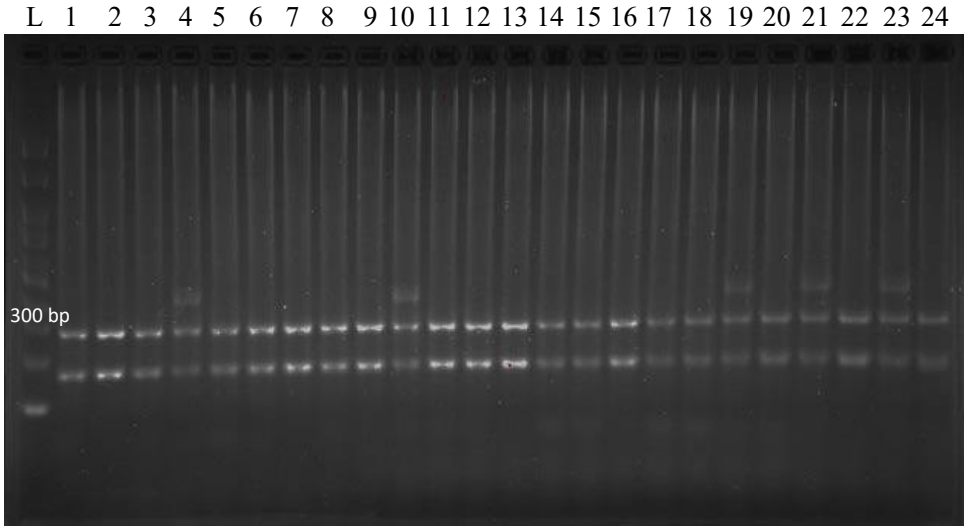


loaded on lane N. The genotypes of each sample is as followed:

Lane	Genotype
1	GG
2	AA
3	AA
4	GG
5	GA
6	GG
7	AA
8	GA
9	GG
10	GG
11	GG
12	AA
13	GA
14	GG
15	GA
16	GG
17	GG
18	AA
19	GG
20	AA
21	GG
22	GA
23	GG

*GG: Homozygous wildtype; GA: Heterozygous; AA: Homozygous mutant

Representative gel image for genotyping of *DRD2 Taq1D* (rs1800498)
The 100 bp DNA ladder was loaded onto lane L. The genotypes of each sample



is as followed:

Lane	Genotype
1	GG
2	GG
3	GG
4	GA
5	GG
6	GG
7	GG
8	GG
9	GG
10	GA
11	GG
12	GG
13	GG
14	GG
15	GG
16	GG
17	GG
18	GG
19	GA
20	GG
21	GA
22	GG
23	GA
24	GG

*GG: Homozygous wildtype; GA: Heterozygous; AA: Homozygous mutant

Appendix E

Subject	Genotype

	DRD2 Taq1A	*DRD2 Taq1B*	*DRD2 Taq1D*
1	AA	AA	GG
3	GA	GA	GG
5	GA	GA	GG
6	GG	GG	GG
8	GG	GG	GG
9	GG	GG	GG
11	GG	GG	GG
12	GA	GA	GG
13	GA	GA	GA
15	GG	GG	GG
16	GA	GA	GG
17	GA	GG	GG
18	GG	GG	GG
20	GA	GG	GG
21	GG	GG	AA
24	GA	GA	GG
25	GA	GA	GA
26	AA	AA	GG
27	GA	GA	GA
28	GA	GA	GG
29	GG	GG	GG
30	GG	GG	GG
51	GG	GG	GG
52	GA	AA	GG
53	GG	AA	GG
54	GA	GG	GA
55	GG	GA	GG
56	GG	GG	GG
58	GA	GA	GG
59	GG	GG	GA
60	GG	GG	GG
61	GG	GG	GG
62	AA	AA	GG
63	GG	GA	GG
64	GG	GG	GG
65	GA	GA	GG
66	GG	GG	GA
67	GG	GG	GG
68	AA	AA	GG
69	GG	GG	GG
70	AA	AA	GG
71	GG	GG	GA
72	GA	GA	GG

73	GG	GG	GG
74	GA	GA	GG
75	GA	GA	GG
76	GG	GG	GA
77	GG	GA	GA
78	GA	AA	GG
79	GA	GA	GG
80	GA	GG	GG
81	GA	GG	GG
82	GG	GG	GG
83	GG	GG	GG
84	GA	GA	GG
85	GA	GA	GA
86	GG	GG	GG
87	GG	GG	GG
88	AA	GA	GG
89	GA	GA	GG
90	GG	GG	GA
91	GG	GG	GG
92	AA	AA	GG
93	AA	AA	GG
94	GG	GG	GG
95	GG	GG	GG
96	GG	GG	GG
97	GG	GG	GG
98	GG	GG	GG
99	GG	GG	GG
101	GA	GA	GG
102	GA	GA	GG
103	GA	GA	GA
104	GA	GA	GG
105	GG	GG	GG
106	GG	GG	GA
107	GA	GG	GG
108	GG	GG	GA
109	GA	GA	GG
110	GA	AA	GG
111	GG	GG	GA
112	GA	GA	GG
114	AA	AA	GG
115	GA	GA	GA
116	AA	GA	GA
118	GG	GG	GG
119	GA	GA	GG

120	GG	GG	GG
121	GA	GA	GA
122	GG	GG	GG
123	GA	GA	GG
124	AA	AA	GG
125	GG	GG	GG
126	GG	GG	GG
128	GG	GA	GG
129	GA	GA	GG
130	GG	GG	GG
131	AA	AA	GG
132	GA	GA	GG
133	GA	GA	GG
134	GG	GA	GG
135	GG	GG	GG
136	GA	GA	GG
137	GA	GA	GG
138	GG	GG	GG
139	GG	GG	GA
140	GG	GG	GG
141	GG	GG	GG
142	GA	GA	GG
143	GA	GA	GG
144	GA	GA	GG
145	GA	GA	GG
146	AA	AA	GG
147	GA	GA	GA
148	GG	GG	GG
149	GA	GG	AA
150	GA	GA	GG
152	GA	GA	GG
154	GA	GA	GG
155	AA	AA	GG
156	GA	GA	GG
157	GA	GG	AA
158	AA	AA	GG
159	GG	GG	GG
160	GA	GA	GG
161	GA	GA	GG
200	AA	AA	GG
201	GG	GG	GG
202	GA	GA	GG
204	AA	AA	GG
205	GA	GA	GA

206	GA	AA	GG
208	GA	GA	GG
209	GA	GA	GG
210	GG	GG	GG
211	AA	AA	GG
212	GA	GA	GG
213	GA	GA	GA
214	GA	AA	GG
215	GA	GA	GG
216	GA	GA	GG
217	GA	GA	GG
218	AA	AA	GG
219	GA	GA	GG
220	GG	GG	GA
221	AA	AA	GG
223	GA	GA	GG
224	AA	AA	GG
225	GA	GA	GG
226	GG	GG	GA
227	GG	GG	GA
228	AA	AA	GG
229	GA	GA	GG
230	GA	GA	GG
231	GG	GG	GG
232	AA	AA	GG
233	GA	GA	GG
234	GA	GA	GG
235	GA	GA	GG
236	GA	GA	GG
237	GA	AA	GG
238	AA	AA	GG
239	GA	GA	GG
240	GA	GG	GG
242	GG	GA	GA
243	GA	GA	GG
244	GA	AA	GG
245	GG	GG	GG
246	GA	GA	GG
247	GA	GA	GG
248	GG	GG	GG
249	AA	AA	GG
250	GG	GG	GA
251	GG	GG	GG
252	GG	GG	GA

253	GG	GG	GG
254	AA	AA	GG
255	GG	GG	GG
256	GA	GA	GG
257	GA	GG	GG
258	AA	AA	GG
259	GG	GG	GG
260	GG	GG	GG
261	GA	GA	GG
262	GA	GA	GG
263	AA	AA	GG
264	AA	AA	GG
265	GG	GG	GG
266	GG	GG	GA
267	GG	GG	AA
268	GA	GA	GG
269	AA	GA	GG
270	GA	GG	GG
271	GA	GG	GG
272	AA	AA	GG
273	GA	GG	GG
274	GG	GG	GG
275	GG	GG	GG
276	AA	AA	GG
278	AA	AA	GG
279	GG	GG	GG
280	AA	AA	GG
281	GA	GA	GG
282	GG	GG	GG
283	GA	GA	GG
284	GA	GA	GG
285	GA	AA	GG
286	GA	GA	GG
287	GG	GG	GG
288	GA	GA	GG
289	AA	AA	GG
290	GA	GA	GG
291	GA	AA	GG
292	GA	GA	GG
293	AA	AA	GG
294	GA	GA	GG
295	GG	GG	GG
296	GG	GA	GG
297	AA	AA	GG

298	GG	GG	GG
299	GG	GG	GG
300	GA	AA	GG
301	GG	GG	GA
302	GG	GG	GG
303	GG	GG	GA
304	GA	GA	GG
305	GA	GA	GG
306	GA	GA	GG
307	GA	GA	GG
308	GG	GG	GG
309	AA	AA	GG
310	AA	GA	GG
311	GA	GA	GG
312	GA	GA	GG
314	GG	GG	GG
315	GA	GA	GG
316	GG	GG	GG
318	GA	GA	GG
319	AA	AA	GG
320	GG	GG	GG
321	GA	GG	GG
322	GA	GA	GG
323	GA	GA	GG
324	GG	GG	GA
325	GA	GA	GG
326	GA	GA	GG
327	GA	GA	GG
328	GG	GG	GG
329	GA	AA	GG
330	GA	GA	GA
331	AA	AA	GG
332	GG	GG	GG
333	GG	GG	GA
334	GA	GA	GG
335	GA	GA	GG
336	GG	GG	GG
337	GA	GA	GG
338	GA	GA	GG
339	GA	GA	GG
340	GG	GG	GA
341	GG	GG	GG
342	AA	GA	GG
343	GG	GG	GG

344	GA	GA	GG
345	GA	GA	GG
346	AA	AA	GG
347	GA	GA	GG
348	GG	GG	GG
349	GA	GA	GA
350	GG	GG	GG
351	GG	GG	GA
352	GG	GG	GG
353	GG	GG	GG
354	GA	GA	GG
355	GG	GG	GG
356	GG	GG	GG
357	GA	GG	GG
358	GG	GA	GG
359	AA	AA	GG
360	GA	GA	GG
361	GA	GA	GG
362	GA	GA	GG
363	GA	GA	GG
364	GA	GA	GG
365	GA	GA	GG
367	GA	GA	GG
368	AA	AA	GG
370	AA	AA	GG
372	GG	GG	GG
373	AA	AA	GG
374	GA	GA	GG
375	GA	GA	GG
376	GA	GA	GG
377	GG	GG	GG
378	GG	GA	GG
379	GA	GA	GG
380	GG	GG	GA
381	GA	GA	GG
382	GG	GG	GA
383	GG	GG	GG
384	GA	GA	GG
385	GA	GA	GG
386	GG	GG	GG
387	GA	GA	GG
388	AA	AA	GG
389	GA	GA	GA
390	GG	GG	GG

391	GA	GA	GG
392	GG	GG	GG
393	GG	GG	GG
394	GA	GA	GG
395	GA	GA	GG
396	GG	GG	GG
397	AA	AA	GG
398	GA	GA	GG
399	GA	AA	GG
400	GA	GA	GG
401	GG	GG	GG
402	GG	GG	GG
403	GA	GA	GG
404	GG	GG	GG
405	GA	GA	GG
406	GG	GG	GG
407	GG	GG	GG
408	GG	GA	GG
409	GG	GG	GA
410	GA	GA	GG
411	GG	GA	GA
412	GA	GA	GG
414	GG	AA	GG
415	GG	GG	GG
417	GG	GG	GA
418	GG	GG	GG
419	AA	AA	GG
420	GG	GG	GG
421	GA	GA	GG
422	GA	GA	GG
423	AA	AA	GG
424	GA	GA	GG
425	GA	GA	GG
426	GA	GA	GG
427	GA	GA	GG
428	GA	GA	GG
429	GG	GG	GG
430	GG	GG	GG
431	GA	GA	GG
432	GA	GA	GG
433	GA	AA	GG
434	GA	AA	GG
435	AA	AA	GG
436	GG	GG	GG

437	GG	GG	GA
439	GA	GA	GG
440	GG	GG	GG
441	GG	GG	GG
442	AA	AA	GG
443	GA	GA	GG
444	GA	GA	GA
445	GA	GA	GG
446	GG	GG	GG
447	GA	GA	GG
448	GA	GA	GG
449	GA	GA	GG
450	GG	GG	GG
451	GG	GG	GG
452	GA	GA	GG
453	GA	GA	GA
454	GA	GA	GG
455	GA	GA	GA
456	GA	GA	GG
458	GG	GG	GA
459	GG	GG	GG
460	GG	GG	GA
461	GA	GA	GA
462	AA	AA	GG
463	GG	GG	GG
464	GA	GA	GG
465	GG	GG	GG
466	GG	GG	GG
467	GG	GG	GG
468	AA	AA	GA
469	GA	GA	GG
470	GA	GA	GG
471	GG	GG	GG
472	AA	AA	GG
473	GG	GG	GG
474	GG	GG	GG
475	GG	GG	GA
476	GG	GG	AA
477	GA	GA	GG
478	GA	GA	GG
479	AA	AA	GG
480	GG	GG	GG
483	GA	GA	GG

*GG: Homozygous wildtype; GA: Heterozygous; AA: Homozygous mutant

Appendix F

5’ to 3’ homo sapiens dopamine receptor D2 gene on chromosome 11

ANKK1/DRD2 Taq1A (rs1800497)
5’-CACAGCCATCCTCAAAGTGCTGGTC[G/A]AGGCAGGCGCCCAGCTGGACGTCCA -3'

5’-
ATAGAGCGCAGCCCAGGAAGGGAGTCCCCTGCAGACAGGAGCCCAGCCTCCCCCGCAACT
CTGTCCCTGCTGACCCCTCCTTGGTAACCTATAGCACACCAAGGCTGGCTAACAAACAAA
CAAACAAAACCCCAACAAGAACAAAGGAAACATGAAACCAGTCAGACCAACAGATTCAGA
CCAGAAAATCCCCATTAAAATTGTTTGAGCCCCATACTTGCTGGATAGGGGCAGGGGTCC
AGGCCTGAATCCTTCATAAACCATAAAACCTTGAATGCACTGAAGGAATGCATAAACCGA
TTTCACTTAGCGCTGGGCCTAAATAAACTGGATCCAACTTCTCAGGCTGGACTTCTTCCA
GCTTCGGGACACCTTCTCCCAGCATCCCTCCCTAGGGGGAACTGGGGAAAATCAAAGGCT
GAGACAGGGGAAATGCGAGGGCTTCGGAGGGACATACCCTCTTCCCCAGGCCCAGGTCGC
TCCATCCCTGCTGGGGCCTCAGGGCTCATGTCTGGGATTTCCCCACCTTTGCGGGGCAGG
AGCGGCTCCTCTTGGGCGGGGAAGGAGGCAGGGCCGGCTCGTCTCCCCATTCCCCTCTCC
CGGACCCGAGGAGCAGGAAGCGGCGGCTCCTTCGGCCACCCAGGCAGCAGCCACAGCGGG
GAGTGCGCGGCGCGGGGACAGGAAGAGAGGGGCAATGGCTGCCGACCCCACCGAGCTGCG
GCTGGGCAGCCTCCCCGTCTTCACCCGCGACGACTTCGAGGGCGACTGGCGCCTAGTGGC
CAGCGGCGGCTTCAGCCAGGTGTTCCAGGCGCGGCACAGGCGCTGGCGGACGGAGTACGC
CATCAAGTGCGCCCCCTGCCTTCCACCCGACGCCGCCAGGTACTGCCAGCCTCGCCCTCC
CCTTTCTCGGAGGAGAAACTGAGGCCCGGCAAGCTTTGGGCCCAGGGAGCTTGCGAGGAA
GGAGTGGGCTGAGTTTGGGGCTGAGGACTGTCCCCCGCGGTATTTCTGAATTCCACCCAG
TAGCCTGAGCCTCCCAGGCACACCCATACCTGTCTCCCTAACCAAAATAGAGTTGGCACA
TAATACCTGTTTGTAGACTCAACAGAGGTCAAAGGCAAGCGGGAACTACCTACCAAAGAC
GCCTTTATCCCATCTGACCTTCCGAACTTGTCCTGCCTGCTTCCATCCTTCTCTCCAGCG
CCTTCTTCCCCCGGTGTCCTGTGGCAATAACTGCTCTTGACCGCTCTCTGCCATCCTCCT
ACCCACCCCAGCTCTCAGGGCAGGGCTGAGCATCCTGGGAGGCTGTGGCACTTTGCTCAG
ATCTGCAGGGAATCATGTTCTCTCTTCCCACGGTGGCGGGAGGGAGGAGGCCCCTCCCAA
TCAGTGCAGGCTGAGGAGGTCAGGGGATGGAGACTGCCCGGCCTGATGGCCTGTCCAGGC
CCTTGGAGGGTCAAGTCTGGAGTTCTCTCATCTCTGTTTTTGTTTTTGTCCCTTGCTGTC
ATGCGCACTACAGCGACGCCTTGACATGCCCCTATTTTTCTCTTCCTACCTCTTTCCTAC
GTTTCCATTATTCTCTGTCTTCCCACTGATTTGGAATCCAGTCTCATTCCCACTGGAGTT
GCATATACTAGCTGTGTGCTTGCACCTTGCAGCCATGAAGAAGACACTCGGGATGTTAAA
CCTGAGCATGATAACCATGTCCTCCTCCCAAGGCTCTGGGACATCAATTAGAGAGTCCGG
GACGGGGGTCTCTCTGACTGGCATCTGGCTTGGATGCTATCTGTGGTTCTCTAGGATTAC
CATGCAAACTCTTAAGATACAGCCTCAGGTGCCACACACTCAGTTCCCAGGCCTTCCCCC
ACCTTATGAGGAGAGGAAAAATAAGATCGCCTAAGGCCCACTCACCTTCCTCCCTCAACA
TCTGCCTGTTGGTTTTGGAGGAGGGTCAGAGTATGCTAGGATTTGTCTAAATCATTTATA
GCCTTTTGAATATAGAACGAAAGGAAACAGATGGCAGTGACATGATTACACTGTGAGACA
TTGATGCTAACTCCTGCCACTTTCCCTTCCCAAGTTCTGGGAATTCCCTGGGTGGAGGGG
GTAAGATAATTAATGGTAATTAAGACTTAGTATGTATGGATTACTATACTAGGAGCTTTA
CGTGCATTACTTTACTAGATCCTCTTTCCAGCTATTCATTCATTCATCCACTTGACAAAT
GCTTACTGCTCTTCTACTATGTGTCAGGCACTGTTCTACACCCTGGGATTAACGATGAAT
GCAACAGATGTGTCCTTTCTCTCCGGGAGATTGCAGCCTAGGGGGAGGAAGACATTAACC
AGATAACCCCACATGTAAATGTAAATGTGCTACTGTGAGAAGCTTAAGAAGGGGAGATTT
GTGGCTCTAGGAGAGCTCATTAACAGAAAGTTTGACTGATATCAGAAAAGGCTTCCTTGA
AGAAGTTACACTACAGCTGAAATGTGAAGAATGAGTATAAGTTAAGTAGGTGAGGAGGAG
AAAGTTTTCCAAGAACAGACAACAGAGTGTGCAAAGAATCTGTGGCAAGAGGGGCATGGT

AAGTACAAAGATGGGAAAAGGCCATGATGGCTGGAGTTGGGAGAGTAAAAGAGCAGTGGA
AAACCACTGAGCATTTACAACCAGGTAGCGGTGGTGACCATGGGAGGGATTAATCAGAAT
TGCAGTATGGAGAATGCATTGGGAGGGGTAGAGTGGATTCTGGTTAAGTTAGGAGATTGT
TATCTTCATTCTGATGAGAGACGGATAATAGGGGCTAGAGTGGAGTGTTGGTAGTGGAGA
TAGGAAAGGAATGGGTCAAGCCATATTTAGAAGGTAAAAATCCACCCGACTTGGTGCTGG
ATTAGTCATGGGGAGGATCACGATGAGGAAGAGGGGTATTAAAGCTAACTTGATGTCTGG
CTTGCCCAAAGGAATGGAGGATCCACTAAAATGTCCACTCCATGAGAGTGTCTGTTTTGG
TCACAGCTCTGTCTCCTGTGCCTGGCACAGAGTTGGTGTTCAATAAATATTTATTGAATG
GCAGTGTTGACAATTAATGGAGAGACTATGAAAAGAGGCCTAGACTTGGAGAGGAAGATC
ATGAGTTCAGCTTTGTACCTGTTGAGTTTCAGATGCCTTTAAACAACCAAGAAGAGTTGT
CATGGACATCAGAGTAAAGGTTGGTGCTAACAATATTAAAACTTGGGAGTCATTTGTTAT
AAGTGGTCATTAAAACTAGGGCATCAGGCTGGGCCTGGTGGCTCACGCTTGTAATCCCAG
CACTTTGAGAGGCCAAGGCTGGTGGATCACCTGAGGTCAGGCAAGACCAGCCTGACCAAT
ATGGTGAAACTCCATCTCTACTAAAAATACATAAATTAGCTGGGCGTGGTGGTGGGCACC
TGTAGTCCCAGCTACTCAGGAGGTTGAGATAGGAGAATTGCTTGAACCCAGGAGGCAGAG
GTTGCAGTGAGCCAAGATCATGCCATTGCACTCCAGCCTGGGCAACAAAAGTGAGACTTG
GTCTCAAAAAAAAAAAAAAACAAAGCAAAAAAAAGGCATGGAGGAGATGCATTCATTCCA
AGCACTACGTGAAAAAAACAAAGTCCTTGCCCTCATGAAGCTTATAGTCTAAAGGAGGAA
GACAAAATAAATAGCAAATGAATAATAAACTTTTTAGCTATAGCACTCATGACCACCTGA
CAGTTCTTGATTAAAATATCTAAGAAGGGTTGAGAAGTCTGATTTTCCAAGAAATGGGTT
GGTCTAAAAATATTAATGCCAGGGCCCTCTGTGTATGGGGAATATAAGAGTTGGAATGGG
GTTGCTTTTTTATGTAGACTTCTCTGTGAAATCCATACTAATTAGGTACCATTTGAGTAG
AGATTTGAAGGAAATGAAGGGGTAATCCATGTGGCTCTGTTAGGGAGGAGTGTTCTAGGC
AGAGAGAACAACAGGTGCAAAGGTCCTGAGGTGGGACCACACTGGGCATGGTGGAGGAAC
AGTGGGAAGCCCGTGTGCCAGGGGCACAATGAGAGGAGGGTGATTAGGAAAGGAGGTCAG
CAAGCTATGCCTGGCATTGGGGACAAATCTTGTAGGACTTTCTCAGCCATGAAAGAACTT
TGGCTTTTACTGTGAATGAGGAGAGCCATTGGAGAAGGGCAGTGACATGTTGTGACTTAG
ATTTTAAAATATGACTTTGGCTGCTGGGTTGAGAATAGATTGTGGAGAGGAAGCGGGAGA
AACAGAGTCCAATTAGGAGGCTTGGGCTGAGATGCACCTTGGGGGAGAGGTGGTGAGAAG
TGGTCAGCTTGTTGCTCGACAGTATTTTGAAGGTGGTGCTGGCAGGATTTGCGAAGACTT
GGCTGTGGGAAGTGAGAGGAAGAAAGGAGTCGAAGATGACACCAGGGTCCTATTCTGAGG
ACTAGAAGGACAGAGGCCCCATTCACTGAAATGATGAAAACTAAAGGAAGAGCAGGTTTC
AGGGGAAAATCAGGAGGTTAGCTTCAGACACATTTGGTATTGAATATCCAATTGGAGATG
ATGAGGTTGACTATAGAAAGATTATAGAGGGAGAAGAGCAGAGAAGAAGGGCTTGGACTA
AGCCCCGTGGTCAAGTAACAGGATATGAGCCTGCAAAGAAAACAGAGAGGAAGTGACCAG
ACAAGTAGGAGAAAAGCAGGAGAATGTTGACACGTGGCTCAAGTAACGAAGTTTCAAGAA
AAAGAGTCAGAGATCTGAACTATACACTGAGAACTGAAAATTATTGGTTAGATATAGCAA
CATAGAGGCTGTTGGTGACCTTAGCCACAGGTGTTCAGGGGAGTGCAGGTACCAGAAACT
AGACAAAAGTGGGTGCAGCAAGATGATGAAGAGGAGAGACAGCAGTAAATGCTCTCAAGA
CTTCTGGGTAGGAAGCTATGAAAGAACTGTGCAAGGTAGTTACAATTATTCCCAGTTTTT
AGTTTAGAAACTGAGGCCCAGAGGATTCCCTTGCCCAAGGTCATACAGATAATAACGGGT
GAAACTGGGATTTGAAATCAGGGCAGTGTGATTCCCACATCCCATGCTTTTTTCCATGCC
ATGGCAGATGTCATTGGTTCCTGTGAACCCAAGAGGATGAGAGAAGACAGATTAAAAATA
TCACAGAGGTGGAGAAGGGATCTCTGGCACAAGTGAACAAGAATAGGAGAAACCTACACT
AGCCAACATGTCCAGATGCCAGGAAGAGCATGTGGTTTTTCCTGAAGGTTGGGGCTCTCC
AGCTGGCTTCCCAGGGAGACCCCGGGAGCACATTGCCAGCAGTCTCTGACTACAGCACCA
TCACAGTTTTGCAAATACTGTGCTCTCAAATATGTCATTTCTCCTTAATCCCCATCCCTG
CAATCCCAAAATAATCTATAACAATTTTCATATTTACTGTTCTGTGGGCACATACAGTGA
AATGAGCAACAGGGTTTGCAAATGCTTATTTTGTAAGGCCTTCCCTTAAGTTTCGACTTC
TGTTCCAATTCAACAAAGATGTATTGTGCAATGCATGGCAATGCACTTTGGGAATTATAG
AGATGAATAATTACAGTTCATCCATAAAATGGAATAGTGTGCAGCCACTAAAGATCATGC
TTTGGAAGAACAGCAGTGTGGGGAAGTGCTCGTGCTCCACATACTATGTGATCCAAAAGG
AGAGAGCAGAAAGAAGGAGTGAAAGAGAGGGAGAAAGGGAAAGAGATACCTTGAAGGTGG
ATAGTAAAAGGATATACTAAAATATCAACAGAGGCTAGCTCTGGAAGGTTGCATCCCTGG
TAACTTATTTTTCTTTTATATAGCTCTCTATATTCCCTATGTTTCCTACAAGGTATATGT
ATTACTTCCATAATTTAAATGGTAATAAATGATGTTTTGAAGCAGAAGCATGAGGCATCA
TGTTGGTCCTCTGGGGGCTCAAAATCTACTAGGGGAGATAAACATAGAAACAAGCAACTA
GAATAAAGGGCAAACTGTGATACCTGCTTTTTTGTGGCCACCTTTGCAGAATGGACTGGC

TCCTAAACCTGCAAACTCCTTTACTTCCTGCCTTGTTGCTGCTGTACTGAAATCTAAGCG
GCCTGCTAAGTATTGCTTCATGTCTCTCTTTCCTCTTCCACTACCTTGCAAGCTCCTGAG
GCTTCTGTGGGTCCCCACAGTCTGGCATCATGGCTAGTTTATGTGTTCAGCTGGTTGCTG
TAGTAATGAATGGGTCACCCCCTTCCATATCTTGCTCCCCCTCTCCATAGCTCTGATGTG
AATTACCTCATTGAAGAAGCTGCCAAAATGAAGAAGATCAAGTTTCAGCACATCGTGTCT
ATCTACGGGGTGTGCAAGCAGCCCCTGGGTATTGTGATGGAGTTTATGGCCAACGGCTCC
CTGGAGAAGGTGCTGTCCACCCACAGCCTCTGCTGGAAGCTCAGGTTCCGCATCATCCAT
GAGACCAGCTTGGCCATGAACTTCCTGCACAGCATTAAGCCGCCTCTGCTCCACCTGGAC
CTCAAGCCGGGCAACATACTCCTGGACAGCAACATGCATGTCAAAGTAAGGGCTCTGGCC
AATCCTCCGCTCCCTTTCACTTGAGGGTTGCCTCCAGGTGAGCAGAATTATCCACCTGCC
TGACCGGCCTGTCAAGGGTTTTAAGCAGTTCCCTTCATGGACAAATTCTAAAGGCAGGGA
TCACACTGCAATAGAGATGGCTAAGCAGTGAAATTTGGGGCATAAGGCTGGGTATCAGGA
TGCCTATAATAACCCTCTTTGGACTCAGTTTCCCATTTCTAAATTGGATAGAATAATCTC
TATTTCCCTGCACTTTCTTTTATTTGGATGGAGACGTGTGTAAATGAGACAATCCCTAAG
AAAGGTTGTAATGGACATTCTTTCACTTCCTAAAACTCTTTTTTGCCCCAGGACCTTTGC
AGCTTCTGTTTCCCCACTCCCCTCTATTTACCTAGCGAAGGTCTACTCACTATTCAGCTT
AACCATCACCTCCTCAGGGAGCTCTTCCCTGATCTACTCCAGTAGGTCCCCATTATATGC
CTTCACTGTACCTCTGATTCTCCATATTACTAACCCCAACATAGGTATATAATCATTAGT
GAAACACTTTCATTAATGACTGGACCCCCTATTTGAATAAGTATTTACGAGGATATGGAG
TGTGTGTGTTGGCAGGGGGTGTCTCATTTTTCTTATCTGCTGCCCAGTCCTTGGTCCACA
GCCTTCCTGGCCCTCAATGCATGGCCAACTTGACAAGTGAATGACTCAGTGGATGGGAGC
AAAGGGAAGATAAATGTCCATGGTGTGTTTCAGGGCCCCCGGAGGTGCAATGAATAGCTT
ACCGAAGGTGGCAACTTCATTCATAGTCTCTGGATAATAACACCTACCACATCCTAACTA
CATGCCAGGCACTGTTTAAGTGCTTTTTGCATGGCACCTCATTTAGTGCTCACAATAGCA
CTGTGAGTTAAATGGTCATATTACTTCTACTTTACAGGTGAAGAAACTGAGGCTCTGAGA
AGATAAGTAATTTGGCCAAGACCATCCAGATAGTAAGTGGTAGTGCTAGGAGGGAGTGTC
ATAGAAAACCACTACTCTACCCTGGAACAGGCAGATAGCAGGAGGGGTGAGAAGCCATAG
CCGTTTTCTGGTCATGAGGCTCTATCACGGCTTTATCTCTGCCCCTGCCTTCTCCCAGATT
TTCAGACTTCGGCCTGTCCAAGTGGATGGAACAGTCCACCCGGATGCAGTACATCGAGAG
GTCGGCTCTGCGGGGCATGCTCAGCTACATCCCCCCTGAGATGTTCCTGGAGAGTAACAA
GGCCCCAGGACCTAAATATGATGTGTACAGGTGAGAAGGAGGCCTGGCGTGATGCCACAC
ACCCAGCAGGCAGTTTGCTGCCACCACCCTGCCTGGCCTCTATGGCCCAAAGGGCAGGGC
AGTGCGGGCATGAGGTCTGGCCCAAGGCGGAGGACTCTGGCTGGAGAGGCAGAGGGCTGG
GGAGTACTTTGGCCGGTGAGGCTTGCCTGGGACTGTGTGAACTGTAGCCCCCCGACCCTG
CCACCCCGGGCTGGGGTGATCTTGGATGTTCAACTAAGTCATTCAGAAAGGGTTCTCTGC
ATCCACAGCTTTGCAATTGTCATCTGGGAGCTACTCACTCAGAAGAAACCATACTCAGGT
AAGCAGGCGGCTGTGGCTCTGTGTTGGGGGCAGGAGGACCCCTGGGATGGGCTCCTGGAA
GGGGCTGTGGGAGGACTGAGGGTTGGGGGGGGTCAAGTTGCAGGTTTGTGTGGAACTGTA
TTCTCTTCAGGGATTCCTCTCCTCACCCTCCTTCCTTCCTGCCTCTATTTCTAGAGCTCA
CGTCACAGCTAAAGGAAAGGAAAGGTCAGCCCAGCCCCCAGCCCATGCTTGGTGGCTCTA
ACTTCCTTGCTTCTAAAGTGCCCTTTCTGCCTTCTCACACCCCTGCCCCCTGCCACCTAG
ATGCCAGGTAAAGAGACTGCAGGAAACTTGGGCAACCTTGCAACCTTGAGAGTCAGAGCC
TTTACCTAGGCCTGCCCATCAGCTGCCTGTCCTGCTGCCTTTGGACAGCACAGACCTGCA
ATGTGGGGTCATGTCTAGTCTTGACCTGGGAGGCAGCTGGAGCCAGACCAGAGAGACTTG
GCTGCTCAACACAGAACCTCAAGTTGGTTGAAAGTCTAGCTGTTTACTCACCAAGCATTT
GTGGAGCCCCCACTGCGTGCATGCCCTGTTGGGATCCTCAGAGCCCCCGCCTTCCTCCCC
AGCTCCCCTCCAGCCCTACCTCTCAGCACCCACATAGCCTGAGCCTCCCTTTGCAGGGTT
CAACATGATGATGATTATTATCCGAGTGGCGGCAGGCATGCGGCCCTCCCTACAGCCTGT
CTCTGACCAATGGCCAAGCGAGGCCCAGCAGATGGTGGACCTGATGAAACGCTGCTGGGA
CCAGGACCCCAAGAAGAGGCCATGCTTTCTAGGTGCTTATCCAGTGCCCCCTACCCAGGG
ACTGGGAGCTGGGTGGGGCCGGGAGGGGAGATGACTGGGCACTCCTGGGAGCTATGCAGA
GAGACACTTTTGGTACTACGGCCTAGAAGGACTTTTTTTTTTTTTTTTCAGAGACACGG
TCTCTCTGGTCCAGGCTGGAGTGTGGTGGTGTGATCATACTTCACCATAAGCTCAAACTC
CTGGGCTCAAGATATCCTCCCGCCTCAGCCTCCTGAGTAGCCAGAACAACAAGCACACCA
CCATGCCTGGCTAATTTTTAGATTTTTTTTAAGAGATGGGGGTCTCGCTATGTTATTCAG
GCTGTTCTCAAACTCCTGGCCTCAAGTGATCCTCCAGCCTCATCCTCCCAAAGTGCTGGG
ATTACAGGTATGAACCACTGTACCTGGCCTAGAAGGACTTTTTGAGGCAGGATCTGCATC
ACGGGGCTGGGAAGGCAGCACTGGGAGCCAGGAGTAGCTGAGGATGGGGTCTGGGCTCTG

TGTGTGTTAATGCATGTCCCTGTGGGAGGTGGAGTAGAAAACCCTCGGTGCCAAAAGGCA
GAAGCCACAGCATCTGGGCCTGGCCCTGTCACCAAGCTCTCCAGCCAGCCTTGAGTCCTT
TCAGAGCTACTGTTTCCTCATTTGTAAAATGTTTCCAGGCCATGAGATCACAGGCTGAGG
ATGGCCCATGAGCTCATCCAGTCCTTTGGGGACTGTGAAAATGCACCTGTGTGTAAGTGT
GAGCATCTTAGAGATTGCCTGAACTTGCCCCCTCATTCTGTGGGAAAGGACCCTGATAAC
TCAGAGGGTCAGTGACTTGCTGAAGGTGCCCCACCATGACCCAGGTTTCCTGCCTTCTCG
TGCATTTATATGAACATATGTGAGCCCAGGAATGGATTTTGGGAGACAGGAATGTTAGGG
TATCTAAAACAGGGAGGGTACTGTGGGCCAGCCCGTTGCTTCCTTTCCTGTCTTTCTCCC
ACTCATGGAGCAGACATTACCATCGAGACAGACATACTGCTGTCACTGCTGCAGAGTCGT
GTGGCAGTCCCAGAGAGCAAGGCCCTGGCCAGGAAGGTGTCCTGCAAGCTGTCGCTGCGC
CAGCCCGGGGAGGTGAGTGTGTGGGCTGGGCAGTCCTTATGGTCATGCTAAGCTGGAGCC
CGCTGTGTGGACTGTTGTGATCTCTGGCCAGACACTGAGCACTCATGCACAGCCCAGCTT
GGGGCCACCTCCATCCAGAGGGGACACATTTCCCTAATTTGCATGAAGGTACTCCAAGGG
ATAGTGGTGGCTAGAGCACAGGGCCCCTGGGAAGGATATACCTTCTCTCTCATGTTTGGG
ACCAAACTGACTCCTGTCCTGCAGAGGAAGGCCCGGCTCTCCCAAGCTTTCATGCTGTGG
GTGTCAACATCATCCCCCTGCTCTTCTGTCCCTATTCTTAACACGGGAACCAGCCATGAG
TTAACATGGGGCTCCCCCAGCTGAACTCACAGATCCACCCTGAAGTTCACATGGCCCAAG
GGGAAGGCAAGGCCCTGAGCTGCCTCTTTCTGGAGGGTTTCTCCAGCTCAGTGTTTTCCT
CTAGACAGCTGGGGATAGTCATGGCAAAGGATAAAGGTTTCCCAGGATAGGGTGGGATGT
GAGTCCTGACAGTGACCGGGAAGGTTGGAGAGAGGGAAGGAGGGGAGGAGGGCACAGGCT
AGAACTGCGCCACTGATCTCCACCCTGCCTGCTGGTTATGCCTCCCCAGGTTAATGAGGA
CATCAGCCAGGAACTGATGGACAGTGGTGAGTCTGGGTGCCACGGGCGGGACCAGAGAAC
TCACAGCAGAGAAAATGGAGTCAAACCACACCCTTTCCCCATCCCCCTGGCCTCCCCCTC
ATCCCCAGGCCTATCACACATCCAGGGTTTAGGTGCCCTTTTCCAGCACCCAGCTGCATG
TTCAGAAAGCACATGCCCTCAGGGAGCCTGGCTGCCTCCCTTTCAAGTCTGTGTCCTTGC
AAGACGGAATTTTCCCTTTCCTGACCTGAAAGGTGGAGCATTGGTTCTCAAGGCTGGCTG
CATGTTAGAATTGCTCGGGAAATTAAAAAAAAAAAAAAAAAAAAGCTTTGCCTTGGGCAC
ACCCTAGACTAATTAAACCAGAATCTGTGAGGGTTAGGCCTGGGTAGTGATCATTTTTGT
CATTTTAATTCTCATACTCCACTGGGTAGAGCAGAAGGATGTTGATCCTTAAGACCTCAG
AGGGGAGTTTAGATCATAGAACTCCAACCACAAGTTTATTTCCAACTTAGAATTGCTTAC
TTTCCCTCAGGTCCTCCACTGAAAGTTTTTACCTATATAATTTGTCCTTCCAATGGTAGA
ATGAACTGATCATTGTTTGTCCCCTCTTCCATATCTGATCCAGATATGGAAGCTCAAAGA
GGCAGTGAATTGGCTAAGGTCGGGGGATGCTGAGGAGTGAAATCAGGATTTGCACTCGGG
CCTCCTGAGCCCACTGCTCTTTCTGCCTCACCTGTGAGGAAAGGACTGCAGGACTCAGCT
CTCCAGGACGACCGAGCCTGAACTTGAATAGTAACATTTATGGCTGTGTAGAGAGCCATG
CTTAGGAAAGGCATTGCCCTTACTGCTCTAGCCTCTGTTCCTGGATGGTACTTCCAGGAG
GCAGGGGGATGGCCATGATGACCTCTGGACGGGTCACAGGTCTTTTTTTTCAACCCCATC
TTTCTCCCAGCAGACTCAGGAAACTACCTGAAGCGGGCCCTTCAGCTCTCCGACCGTAAG
AATTTGGTCCCGAGAGATGAGGAACTGTGTATCTATGAGAACAAGGTCACCCCCCTCCAC
TTCCTGGTGGCCCAGGGCAGTGTGGAGCAGGTGAGGTTGCTGCTGGCCCACGAGGTAGAC
GTGGACTGCCAGACGGCCTCTGGATACACGCCCCTCCTGATCGCCGCCCAGGACCAGCAA
CCCGACCTCTGTGCCCTGCTTTTGGCACATGGTGCTGATGCCAACCGAGTGGATGAGGAT
GGCTGGGCCCCACTGCACTTTGCAGCCCAGAATGGGGATGACGGCACTGCGCGCCTGCTC
CTGGACCACGGGGCCTGTGTGGATGCCCAGGAACGTGAAGGGTGGACCCCTCTTCACCTG
GCTGCACAGAATAACTTTGAGAATGTGGCACGGCTTCTGGTCTCCCGTCAGGCTGACCCC
AACCTGCATGAGGCTGAGGGCAAGACCCCCCTCCATGTGGCCGCCTACTTTGGCCATGTT
AGCCTGGTCAAGCTGCTGACCAGCCAGGGGGCTGAGTTGGATGCTCAGCAGAGAAACCTG
AGAACACCACTGCACCTGGCAGTAGAGCGGGGCAAAGTGAGGGCCATCCAACACCTGCTG
AAGAGTGGAGCGGTCCCTGATGCCCTTGACCAGAGCGGCTACGGCCCACTGCACACTGCA
GCTGCCAGGGGCAAATACCTGATCTGCAAGATGCTGCTCAGGTACGGAGCCAGCCTTGAG
CTGCCCACCCACCAGGGCTGGACACCCCTGCATCTAGCAGCCTACAAGGGCCACCTGGAG
ATCATCCATCTGCTGGCAGAGAGCCACGCAAACATGGGTGCTCTTGGAGCTGTGAACTGG
ACTCCCCTGCACCTAGCTGCACGCCACGGGGAGGAGGCGGTGGTGTCAGCACTGCTGCAG
TGTGGGGCTGACCCCAATGCTGCAGAGCAGTCAGGCTGGACACCCCTCCACCTGGCGGTC
CAGAGGAGCACCTTCCTGAGTGTCATCAACCTCCTAGAACATCACGCAAATGTCCACGCC
CGCAACAAGGTGGGCTGGACACCCGCCCACCTGGCCGCCCTCAAGGGCAACACAGCCATC
CTCAAAGTGCTGGTC^GAGGCAGGCGCCCAGCTGGACGTCCAGGATGGAGTGAGCTGCAC
ACCCCTGCAACTGGCCCTCCGCAGCCGAAAGCAGGGCATCATGTCCTTCCTAGAGGGCAA

GGAGCCGTCAGTGGCCACTCTGGGTGGTTCTAAGCCAGGAGCCGAGATGGAAATTTAGAC
AACTTGGCCAGCCGTGGTGGCTCACGTCTGTAATCCCAGCACTTTGGGAGGCTGAGGCAG
GCAGATCACCTGATATCAAGAGTTTGAGGCCAGCCTGGCCAACATGGCAAAACCCTGTCT
CTGCTAAAAATACAAAATTTAGCTGGGTATGGTGGCACGTGCCTGTAATCCCAACTACCA
GGGAGGCTGAGGCAGGAGAATTCCTTGAACCCAGGAGGCAGAGGTTGCAGTGAGCCGAGA
TCGCACCACTGCACTCCAGCCTGGGCAACAGAGCGAGACTCCATATAAAAAAGAAAGAAA
GAAAGAAATTTAGACTACTTGGGGCCTCTCGCCTGGATGGAGTAGGAACTGGTGAAAGTG
CAGCTGGGCTTCTGGCAGGGCATCTTCCCTGTCTGCAGTCTTCACCTGCCCCTTCCACCT
TGAGAGGAGACAGGAACCTGGGTGATGGGGGCATGGGGAGAGGTATCACTGTGGCTGTAG
CTGAGGAAGGGGCTCTGGCTTGGAGAGCTGCCTTCAACACATCCTCCAGTCACTTCCAAC
AGACCCCAGGCCTCCTCCTCCTCCTTTATGGGGATGCAAGCTCCCCAAATGAATACCCTC
TCCAATCCAAGACACCTACCACCTTTTGCCACTCGCTTCTGAGTTCACAGGGGCCCTTGC
ATCCTAGCAGACCCCCTCTGGAGATGGAGGGAGGCACAGCGGTGAGGGAAGCAGGATCCT
CCCATCTCACGTCTTGGGCTCTTGGCTCC -3′

Key:

: Exon : Primer amplification region

: rs1800497 : nitrogenous base mutation

5’ to 3’ homo sapiens dopamine receptor D2 gene on chromosome 11

DRD2 Taq1B (rs1079597)
5’-ACAGTGCTGTCAGAATCACCTATTC[A/G]AAAGGCGAATCTGATCATGTGGTTC-3’

DRD2 Taq1D (rs1800498)
5’-GGTGTGAAGAAAAGAGCCTTGGGTT[C/T]GACTAGGGAACCTGGGGCCACTCCT-3’

5’-
GTGCGGGATCAGGGGCCTGGTTTTCTTTCTGTGTGTGACTTCTGAATCTGACACAGAATC
TGGCAAACTGAGGACAGTTGGTAACTAATTGCTGCAGAAGAAAGAAAAGAAAGAGAAAGA
AAGAAAAAGAAAGGAAGGAAGAAAGAAAGAAAGAAAGGAAAGAAAGAAAGAGAAAGAAAG
AAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAAGAAAAGAAAAGA
AAGAAAAGGAGAGAGGAAGAAAAGGGGAGAAGAACGAGGTTCCTCTGCAGCCCAAATGAC
AGTGGGCAGGGTAGCAGCGGAACACCCTTCACCACTCTATCTCTTTCTCCCTCTCCCCAC
TCCCTGCCTCACACACCTCAGTTTGGAGTCAAGGGTGAGCTGGAACCCCTGAGGCCTCCT
TTTGCATTTCCATGTCAGGTCAACTCCAAACAGGCTTTTTCCTTTGGATGAGTCCAGCAA
TAGAACTGACTACATAGATTCCAAGACCTGAAGTCAGAAAACGGATGCGGACCTCTTCCA
ACACCTCCTCTCCTTGCCTGACTTGCTGGATGGGTGGTGCCTCCCGCAACCCTTGGCTTC
TGAGTCCTCAAAGGAGAAGACTGGCGAGCAGACGGTGAGGACCCAGCCTGCAATCACAGC
TTATTACTCTGGGTGTGGGTGGGAGCGCAGTGGGCGGTCGAGGGTTGCGTTCCCGCCTCA
AAACAAGGGATGGCGGAATCCCCCAACCCCTCCTACCCGTTCAGGCCGGGGATCGCCGAG
GAGGTACAGCTCCTTTGGTGGGGGGCGGGGGCGGGGCCTGTCTCAGGGGCGGGGACCGGG
GCACCTCCCTCCCGCGCTCCCCGCGCTCGGGCGCCGCAGAGCTGTCCAGCTTCAGTGCCG
AACCGGCAGCCTCACGCGCGCACCGCGCCGCCTCCGCCCCGTCCCCGCGCTCCCTCCTGC
CCGCCCGCCCCGCGCCCGGCCCCGCCCCGCCCCGCCCCGCCGCGGCCCGTCCACTGCTCC
CCGCGGGCCAGAGCCGGCCGAGCTGCTGCCCGCCGGGGCTCTGAACGGCGCGGCGGGGCC
GGGAGCCAGGGACCGGCCGAGGAGAGTGGCGGCCCCGGACGGCTGCCGGAGGGGCGGCCG
CGCGTGGATGCGGCGGGAGCTGGAAGCCTCAAGCAGCCGGCGCCGTCTCTGCCCCCGGGC
GCCCTATGGCTTGAAGGTAAGCACCGGCCGGATGGAGCGGCGGGCGACTCAGTGTCACGG
GGAGAGGAGGAGGGACCTCCAAGGGGAGCGAGGCCAGGACCAGAAGTTTGTGCGGCCACT
CCTGGCCGCCTGCTCGGGAGCGCCCGCCTGGGATCCGGCTCTGCATGGGCTCCCCGTCGG
GCGGGGGCAGAGGGCGTCTGGAGCCCGCGGCTGCTATCCCCTCTCCCTCCTTCTCAGTAG
CCTCCTCGCCACTTAGAAGGGAATCCTCTCCCCGAGCACGAGCGGGCGCAGCTGGGGCAG
CCTCCCCGCGGGGCGCCCAGGGCAGCACGGCGGAGCCGCGGCATCGGAGGGCGGGAGGGA
GGCCGCTCCCCACAATCTCGGGAGGGCACTTCCCCCAGCACCCAAGCGCGAGACCCGGGG
CTCGCGGCCAGAGTTTCCGACTTCTTCCGGAGGAAGAAGGGCTGTTTTTGGCAACTCTGT
GTTGGTGCGACCTGACCCTTTTCAGTTTCTAAGGCAGAAGCTAAGGATGGGGGAGAGGCA
GATTCTGGCTGGATTCTCCCGCTCCCACGGTTGCCGCTGTCCTTGGTCCTGAACTTTCGT
TCTCCTTCGCCTTCTCTTGGGTTGACACCTAGTCGGGGAGGGAGGCTTGGGTGCCAGACC
CGTTTCTACCCGGCAGTGCAGGCGACGGTGGCGGCAGTAGCGGAGGGTGACCGCCCGGCT
CTCGGCCCGGCTCTATGATGGACCGAGAGCCCCTCTAGGGTGGTATGCGGAGACAAGAGA
CACCTCTAAGCACCAGACAGAGCGCTTCCCTATCCCTGTCTGAGGCGGGCAGCCCTTGAG
TGCTTCCTCTTGAAGAGCAGAGGTAAGAGGGTGCGTGTGCGTCTACATAACAGGCTTCAC
CATGGACACAAGTCACAGCAGTGCAGCTCCGTGGGGACAGGCGCTTGCTCTCAGCCACAA
GGAAGCTGTCTGAGCAAGTCACTGTTGCCCCACCTGACACCCCACTACTTTTTTTTCGGT
GGCTCTTGAGGTTGGGTGAGGGGGTGAGGGAGTGAGGTGCAAGGCACTTTGTGGATCCCA
CTCCAGATCCTTCTGCAGATCCAAGCCTTTCTGTATTTTGACCAGGCTACAAACCTTTTA
GGCCAATCCTTGCTCCTCCTTAGGGAGCTAGATGTTCAACGATTCTCCCCACTCCCACCC
TGCTTCAAATGCAAATATGCATGCTTATCTCTGATTCATCCTGCAGCATTAGGACCACTT
GAAAAAGAAATCATGCTTATCGTCTTTCCCTCATGCAGCTGTTTGATGAGGGTGGCCAGA
TAGAGAGACTGTGGTCAGCATGACCAGTTTCAAGAAAATCAGCAAGCTGCTTTCCTGGGT
TTCAGTCCCTGCCTTGGACTTCCCTCCTTAGTGTTCAAAATTCCTGGATTATTTGTTGCA
GGGGGTTTTGATGCCATCTCTGAATGCAGACATCTGACAAGGAAGTGGTTTGGGAGGGTT
AGACCTAGAACCAAATGAGGGCCAGGGTAGTCCCAGCTCTTAAAGATCATTGAGTTCCTT

CTACCTTCCCTGCACAGCCTGAGGTGCCCAGAAAGTGGAGAGGTTCTGATTTGTTGTAGA
AGTCCGGGCAGCATTTCTCTAAGGGTTTTTTTCTTTTTAATGAATTCCCTGAGAAGCTGG
TTAAAAATGCGTATTTTTGCTTCTTCCTTGAAAAACTGCTGAATGAGAATCTCAAGCGGA
GGCCCAGGAAATTTATATTTTAACAATGTTTCTGAGTGATTCATGTGTACACTGAATTAG
CAAATTACCTCCCAAAAAGTTGAGACTCCTTAGAGAGTCTGTATACATTTATTTTATTTT
GAAAATGGAAATCAAGTTTATTTTACATAAAATTGGTAGCAGGTATTCTATCTGAGAAAA
TCCCTTGAAGATATAAAAATGCATTTCTAAGAGTTAAAAGAATCATGTACCTTGGCAACC
ATTTGCTGATATCTTAAATATTCCTAAATTTCATACATTTGAAATTTATAAAATTAAGGT
ATTTAATCTCACCCTTTGTCTCCTGCTGTTATACCTGTTAAATTCTTCAAGTGTGAGACT
CTTGGTAGAAAGACCATCCCCCTGATTAAATCTTTGCTGAAATTAAGGATGCAATCCAAT
CTCCTCTCCCCCAGGATCTTCCTGGGCTTTTCTTCTTTCTAAAATTTTTGGCCCTTTTAA
GGAATCACCAATATGGCTTCAGGTTGACTTATGTAAATACTAACTGTCCCTCTATGGGGG
TCAACTCAGTGTTTCCCTCCTGCCCTCCCCTCTGGGTGAGTTATTGTCTTTCATTATGCA
TGTGCTGTGATCTGTTAACCTAAGTGCTCCTGAAATGCCAAGGAGTGATTAGTTCAGCCT
AGTAGCACGTCATGCTCCCCAAGGCTGGTAGCCACTCATGCCCTGCTGGAAGTGACATAT
TGACTGTATTGATTTGGTTCTTTTGTTCCATAAGCAAGGAGGCTTGTAGGGGTAAAAAGG
CTAGTAATGATGCTTGTGGGCTAGTTAGTCTTGTACCTTCACCTACAAAGGTGGATTATT
TCTGTCTAGAAAATGCAATTATCTTGAGAATGATATAGGAGAATCTGAAATTGAGACAAA
CGCTTCTGTTCTTTCTTTGATACTATGGGAAACAAATGGGAACTTAGGGTCATTAGAAAT
ATGGCCTCACATACTCCTGAGATTGTCTTGCTGAAGCCGGACTGGTCTGGGGTCACCATT
CTCTGAATAAACAAGTATAAGGGGAAAGACGTGGGGACTCTGCCTGGAGAGAATGGTTTC
CATCTCCCCTGCAAGTAAAAGTTACATTTTAGTGTTAACAAAAAAGTGTGGCTGTGAAGA
TAGCACTGTGTGTATGTGTATGTGTTTGTGTGTGTTTGCATACACGTGCATGCACACATA
TGAGCACATCGCCCAGGAGAGACAGATATGATGAGACTTCCTTGAGCCAATCCTGTGTTG
GCACCCACCACTTCTCCCCGCTTTGTGGCTTAATACCTATGAATCTCCAACAGTGAAGGT
GCCTCAACACCTAGGAAGAGAGAAGAATCAAGTTGAGGTTTTATAATGCCAGAACCCTAA
GTCATATTTGTAATATCTCCCAGAATCAAGTTATATATCAGCAGGCTACAGTTACCTAAG
AGTTGAGGTCTTGAAAATAGCTTAGAACAGCAGCCCAGTCATTTGCATTTTCCTGGGATA
TAGTTTATAGGACTTTAGATTCTTAGGTTATCTTCTTGGGCTCCTCAGAGGTCATGCCAG
ATGCCCCTGACTCCAAACAGGGAAGCTGTTTCCTTAGTCCAGAAATACAATGGTCTTTCT
TCTTTTATTAAAGTTCTCCTAAACAGAACTTTTTCCAATGAATTTTCCAGTTTCTGAACA
CCAGGACTGGACTCAGCAACTGGAGCTTCTCCATCCTACCAGGTACTCTGCTTAGCAGAG
GAGCATCCTGCATATAGGAAACACTCGGAAACCATGGGCAGCAGAAAGGACACAGGTTGA
TTCAACTTCTCAGCAGGCACCCTCCTTTGTAGGTAGCCTCTTACTTAGCTGAACCCCAGC
ACCATTTTCCCTCTTCTCACCTCCAGTAAGGCATTTTGTGGCCTTGGAAGGACCTTGGGA
TTAGGTATAAGCCCTTCTGCTCTCCAGAATATACCATGGAGCCACTAAGGATGCACAAAT
TGCTTATTTACCAATTTGAGCAGTAGACTAATGTTATCTCTGGCCTTTTAAATTACTCTA
ATGGTGTTGGAATCTAATATTAATATACTTTTGCCTCTCACCTGTTCCCATGACCAATGT
AATTGGAGATTTCTTTCCTCTGTACTTAAATGGATGCAAAACTTTCTTATTTTTTGACAA
TAGAATCATATTATCTAAATGTACAGGCCTGGAAAATAGCTTGATTATAGTGTCAGCACA
TGGGGATGGAGGAGTAATAAAACTATAAGACTCAGCCACTTGGTTTTCTTTGATTTGGGT
CCAGAGAAAGGAGAGAAATTTGCCCTCAGAATTGCAGATTTTTCTTTTCTTTTTCCTTTC
ACCTTAATCTGGTAAATGGGTTAAATCAATACCCTTGGCAGCTGGGATGCCCTTGGAAGG
CACAGCCTCTTCTCTCCCTAGGATACATGAGAGTGTTTCACTGCAGAGGGGCCAAGGACC
CTGGTGGCTCTAGTGTATAGGGAGGAGTCAGAGATGACACACTGGGGTCTGAGGCCTCCC
TCTTCCCCTGGATAGAAGAAACTGTGCTGCTGCAGTGCTTTGAACTCAGAAGCCTGGAAA
CTCCTAGGGGCATTTGGGAGAGTATGGGACAGTGTACAGAGGTGAGAGCAGAGGAGAAGT
AGACTCTTAGGAGGCCCTGAAAGAGGCTGATGTTAAATATGCATTGAATATAGGTATCAG
CTTAGTGTAGTTTGGGCAATTTTGTCATAATCTGATGTCACCTGTAAGGATTTTTACTTT
TTCCAGTAGGAGATGAGGGAATTCTTTGCTGTCTGAAGGGACAGGGAGGGGAAGGAGGGA
AAACCTCTGGTTTCCCCTGCAGCCCTCTGGGTAATGTCAGCTTGCTTCCAGACAGAGGGC
GGTAAGGGAAGTCAGGCAGACCTGGCTCCCAGGAGCTCCATCAATAGGCCTGCAGTTAGC
CTGGGCAGTCCTGCCTTCCAGGAAGCTGTCGCTCAGCACAGAACTGCAGCTGTGGCCCCA
ACGATAATCCCCTGCAGATGTCTGGGAGCCAAAGGGAGTCCTGGCGCCTGTTCATTTGTT
ATTGGTCTCCTTCAGAACGTGCCTGCCCTTCTCATTTCCACCCCCTCCTTGTTGTTATTG
TTTGGGTTCTAAGTGGCCCAGCAGGAGAAAGACATTAGAAATGAAATTATTTTTGTTACA
TGCTACATCATTGCCTCCTCTCCTACCTGCTACCCCAGGCAGCACCATCACTAGCAACTC
CCAGGAACTCTTGATATGGGAAAGTGGCTTAGTACCAGGCTTCCCTAGAATGAGAAGTGG

TCCTGTTCACCAGACCCTCCTTTGCTGGCCTCATCATCATAACGGCCAGCATTTATTGTG
CACTTACTGTGTGCAGGGCGCTGTGCTCAGCACTTGACATAGGTTCTTCATTTAAACTCC
CAATCCTGCAACAACTCTGTGAAATAGGAACCCTTGTTTTTACATTTTTTGTTTGTTTAT
TATTTATTTATTTATTTATTATTTTCATTTTTAGAGAGAGGTCTTGCTCTGTCACCCAGG
CTGGAGTGCAGTGGTGCAATCATAGCTCACAGCAGCCTTGAACTCCTGGGCTCAAGTGAT
CCTCCTGCTTCAGCCACCCGAGCAGCTGGGAGTACAGGTGCATGCCAGCATGCCCAACTA
ATTTTTTAAAGAATTTTTTGTAGATATAGGGCCTTGCTTTGTTGTCCAGTCTGGTCTTGA
ACTCCTGGCTTCAAACGATCCTCCTGCCTCAGAGTAACCCTTATTATTCCATTTTGCAGA
GGAAGAAGCATAGGCTTAGAAAGGTAAGTGGTTTGCACAAGGTCACACGTTTCATGTGTG
AGACAAAGATTCAAAACCAGACTGTTTAAGGCTAAAGCAATAGCCCTCTCTGATACGTAA
GTGGCATAAAGAACAAGAAAAGGAGGAGAATAGGGATAAGAAGATAATTCTTTAGTGAAT
GAAAGGGCAGTAATCTTTGTGTATGATACCAGGAAAGTGAAGAGGGAGACAGCAGATGGA
GAAGGATGAATAAAATAACTCCTTGGGATTCTTAAATTTGAGAACCAGCGAGGAAGTGTT
CTGTACCTGGATCTGGGTCCCTTTGGATGAAATGCACTGGGCGTAAACCTCAGCAAGCAG
TGGGAGCAGGAGGGAGGGCGGCAGGAGCAGGAGGGAGGCAGGGTCAACTAAGCCTTCCAA
CCTGGGGGAGGAGCTGGGAGGAGGTGTAGACGGATGTTTTGTCAAGCTCTTCTGGAACTG
TGATGACATTACCTTCTGTCCCACATCTCTTTGAGGTGAACTGAACTGTCCAAAGGATGA
AAGCCAGACTTCTGCCAACAATTAGGTCTTTGGGTTTGCTTTCTTATTACCATAGAAGGA
AAACTTGTTATATCTCCAAGACTAAGCTTCCACATTTTACAGAAATGTGAGGGCGGGATG
GCCTGGGATCCTGGACAGACACAGGAGTGACTCATGAGAGCTGCCTTTAAAAAATGAGCT
GATTAGCCAGACGCGGTGGCTCACGCCTGTAATCCCATCCCTTTGGGAGGCTGAGGTGGG
CAGATTGCTTGAACTCAGGAGTTCACAACCAGCCTGGGCAACACAGTGAAACCCCATCTC
TACTAAAAACACACAAAAAAATTAGGATCTGGCAGCATGCACCTGTGGTCTCAGCTACTCA
GGAGGCTGAGGCAGGAAAATTGCTTGAACCTGGGAGGTAGAGGTTGCAGTGAGCCAGTAT
CGTGCCACTGCACTCCAACCTGGGTGGCAGAACGAGACTCCATCTCAAAAAACAAACAAA
CAAACAAACAAAAAACAAAAAAAACCCTGATCAATGCTTTTCTGATAGACAGAGGCAGGT
GAGGCCTGGATGTCCCTGGGCAGGGCACTTAACCTGCTCATCAGTTATTTCAGGCACAAA
TAAGGGACTGTAATAATCGTGTTCACCTCATAATAAGTGAGAAGACTCCTCTGTTGTTGA
GCCTCACCATGAGTTTTATGAATGACATATATCAATATTTAGTCACCTATTTAAACCCTT
TAAAAACAACACCATATGGTAGTTAAACCTGTGGGCTCTGGAATTAGACTTCCAGGATTT
GAATCCTGACTCTAACACTTACTAGCTATGTGACCATGAGCAAGTTAATTAACCTCTATC
ACCTGGGGGTTCTCACCTGTAAGTGGATGTTAATACCAACATAATTGGGTCACAGTAATT
AATTAAGGTAATAGAGACAAGACATTTGAAAGAGTCCCTGGGAAAAGTGAGTACTCTTTA
AATGTTAACTGTAATGATTGTTATTGTTATTATTAAGATGCTTAAGTAAGAAACAACACT
TTGAGCTGTTGTCCTTTTGCAGTAATTCAGCACCTGATTTTACATTTCTGAAATCATGTT
TCTAAAACGTTCACAAAATTCAAGGATATACTTCTTTCTTACACTCTCCACTTATCTGCA
CCAAAATTCTTTGGCTTTCACCTGTCAGCAGCTCTTGCTCATTTTGAGCGAGATAGGGGT
TTGAATTGCTTGTCATCCCTTTGATTTAGGTGCAGCTGAATTCATTTCCATCTTACACCA
CATGAGCTAGGAAGAGGCATAAGTTATCCTGGTGATAGCTTTTCATGGCCTAATTTTTCT
TCCTGGTTTCCTGGGCTCTGTGTCTGCTACCTCATGGTTGGAGCCTCCCTGATTGGCAGT
GTCACATGGTATGTTGCTCTGGCACAGGCCAGTTTTTATTAAAAACAAAAAACAAGGAGA
ATGTACTGGTGTACAAGGACAAGGTGACTTTTTTTCTTTTCCCAGATTGAAAGGGCCAAA
GAACTTCACATGAGCAGACCCCCAAAGCTGGCAGAAATATGTGTTCTGCAGCTTCTGGAG
TCATTCTTGGCAGGAGCAAATGCTATCATGTTTTTAGGTGAAGTATGGTCCTGCCTGAGA
AAGGAGGATGGAAACAGTAGCTTCTGGTCCTGAGATTCCCCAGTGCATAAAGATAATCCC
TCTTGTTGGCCTTTTTCTTGGTCTATGAATCCCTTCTTGGGGAGGACTCTCTTGTAATTG
ATGTGCATCTATTTCTGGCCAGCTACAAATGCTCACCATTTAGCTATGGTAGAATATTTC
AGAAGGCACTGTAGGTATTCTGTTCCTGGGTCATCTTCCTTGGTTCATCCTTTTTTGGAC
TCAGCCCTTTCAACTCTTTCACTCATTTATGGCAGGGTCAATAAGAGACATGTGTTGACA
AGCAGAAACTAACTTCCAGGGTCCCAGGCAGAGGATGTCAGCACCGCCTCCCACCGCCTG
CCCCCGCACCACGGTGGATCCATGTTTCCACACACTATTTTTCTTTAGTAGTATGTGTAG
TTGAAGGTCTGGGATCACTCTAGAGTCACATTGTGACTAATGACACAAAATCTCCCTTGT
GGCCTGTCTTCTGTGAGGAGCCAACTTAATGCTTAATGCTAATCTCTCAATTGTGCATTT
CTTGTCTTCTCCACCAGACCATGAGCTCCTTGAAGCAGAGAATTTGTCTCATGCTTCTCT
AAAATCTATTATAACCTAAAATGGTGCTAGGCACTTGGTAGTTACTTAAATTGTTGAGTG
AGAGTGGGTGAGTGGATAAGTGATGGGTAGGTGAGAGACAGCTTACTTCCCCATAGCGAC
ACTCTCCCTCTACTTTACTTGCAGCTTAACAAGAGTGGCAGTGTCTGAGGCATCCCCCAC
TAGAGGTATCTCATAGGTCAGCAACATACTTCATGCCTTCTCTCTTTCATCCCTAACCTG

CACTATCTGGCCACCCTCAGCCATGAAGACATTATAGGTTGGATGGAAATTTTTCGCAGT
TGTCACAGGGCATGGAAGTTGGGGAATATTGAATGGTTGGAACCTACTTCAATCAGACAC
ACTCATGGAGAAAATGCACTGGGGGGGCTGTTGAGGAAACATACACAGGTGTGTTTGTTC
AGGTCAGCCTGGGGACCTGAAGACAAAAGAGCTGTTATTGAGGGATGCCATTAGTGCTTT
GGTGATTTCTGTGTTTAGACTTTGGGGAATTGGACTAGTCCTTACTTTAAAAGGTACAGA
TAAGCATGATTATACCCAAGACCCTCCAAACGCAGTAACAGTTTGAACCTATCTTTCCAC
AAAGCACTTTTAAGAAGTGGGCTATGCATCCCCTGTCCCTCTAGTTATTTAGTTAAACAA
AGTGGTTCAGAGCACTCAAAAACCAGGCTAATGCAGGATCAGATCTTTGTTCTATCGGTC
ATGAGCTATGTGACCTCTATCAAGTTACTATCACCCCTTTGAGATGCAGTTCTTTATCCC
TTCATAAAACAGGATGACTATATACTTACCTGATTGGGTTTTGTGCAAAGGAAATGAGTC
ACGCACATAAAGTGCTTGTCTCAGTACCTGATGCATGGTAAGCTCTCAGCAAACATTCAC
TATCATTATCCTTATCGTAATTATCAGTGGGCAGAGAAGTGTCCACAGAACCCTTCCCAA
CCTGTGCTCCAAATTTTATATTCTCTCTTCTGGAGGGAAGAAAGACACCATTGCAGATGA
AGACATTAGACCAGGTATGAATTGGCATAGAGTGTTATACTTGAAAGAACCCAATGTTAC
ACAGCAGAGAAGTAGGAGAGCTGGACTAGAACTCACTTCTGCCCAGGGTTTTTCCTCCAC
ACCTGGCTCAGGTTAGACCATGGAGTTTTGAAGAAACTCAGTGGCTAATGAATGGGATTT
GAAGTGAAGATGGTACAAGGTAAGGCCAAAGGCTTAGGCAGGGGCCTGACTATGAACCTT
GAAGTCTTATGTAGGAGACTGGATTCCATCCTGAGGGAAAAAAGAAGCCAACTTGAAGGA
TTGGGTTTTAAGCACAGGGACAACTCCAGTGATTCAATTTGCAGTAAAACAAACAAACAA
ACAAACAAACAAACAAACAACAACAACAACAAAAACTGGCCAGGCATGGTGGCTCATGCC
TGTAATCCCAGCATTTTGGGAGGCCAAGACAGGCAGATCACTTGAGGCCAGGAGTTTGAG
ACTAGCCTGGCCAACATGGCAAAAGCTCATCTCTACTACAAAACTTAGCCGGATGTGGTG
GCTCACACCTGTAATCCCAGCTACTGGGGTGGCTGAGGCACGGGAATTACCTGAACCCAG
GAAGCAGATGGTGCAGTGAGATCAGGCCACTGCACTCCAGCCTAGGCAACATAGTGAGAC
TGTCTCAAAAAAAAAAAAAAATCACAGAGGCTGCTATGTGGGGGAACTGATTATAGAAGAT
TCAAGACTGGAGGCAGAGTACCTAGGAGAGTTTGCAGTTGTTCAGGACAGCAATGCTGGC
AGCCTGATCTAGGGAGGGGCAGTGGAGGTAGGAAGGCTTGAAAGACCTGAAAAGATATCT
TAAATTCGCCAGAACTCAGTGATTGATGGGCTATGGAGGATGAGGGGAAGAGAGAAGCCA
AGGATGATTTAAGAACAATGAAGCAAGGGAATTAAGGATATCGGTAAAAGTGTATGCATA
TTGGGCCAGAAACCTAAGCTGGATTGAAAGGGAAGGGAAGATAGGCTGATAGAATCGGTG
GACTGATGGTGTTGATGAAATCAGAGAACTGGTATACTTGGAATCACTGAGCACTTGAAC
TGGGCTGCAGAGGCAATTGTGGTCACACAGTGGAGTAACTAAATTTGTAACCTCAGAGAG
GAACACCCCTGGCGATGTCAGTGCTCAGAATGCACTCATAGGAGCAGGTGACTAATGTGA
AGGGTGTGCTTGGGGAGTAGGAGGCCAGGCATCAAGAGGCCAAGCTGTTGGAAGTTGATT
TCACCTGAGTTCATGGCACAACTTGGGCTGGAGTTGAAGACAGTGAGCTAGTGCCAAAGA
CAGTGAGGGAGGGGAAGTGACCAGGAATGTATGGATGGCAGTGACAAAGAGAGATAGAGT
GGGCATAAATGGTTGGTGGGCACCTGAAAGGAACAGAGTCTTTATGAGAGGGTAGGGGAG
GTGGTAATGAGGCACAGGGATGTGGGGCTGAGCACTTTCCTGGAAGGGCCGCAGCGGAAG
TGGTGCCCTCAGTTGAGGCTGGGAGGGGAGGGGCTGCTGCCGCCATGCAGTACACACCTC
CAGTGTAGGTCTTCTCATCCTGCTTTTCTCTTCCGCTCCCTCCGTGGCTCATGGAACCCA
TTCCTCTCCATAGCTACAGAGAATGGAAGAAAAACAGAAGAAAGGTGAAGACAGGGTGGC
AAGTGGGTATAAAGATGTGGATGAGAGAGCTGAAATAGGTGGAAGTTACAGGGAATAGGA
AAGAAAATGGATCTGTGGACATCCATTGTTCCTCTGCACCCAGTGTGCCACCTGTAACCT
TCTAACATGTTGTGTTGTTTTCTCTGCCAGAATGCTCCAGCCCTTAACTTATAAGGTTAA
CTCCTACTCAGCTTTTAAAACAGAGCCCAGGTATCACCTCTTCCAGGGAGGCTTCCCCAA
TTTTCCTTCCTACACTCTTTCACCTACCTGGGCCAAGGGCCTCTCTTCTGTATTTCTCTA
GCATACAGTATTGAGTTATGTTGTCATTGCTTATTTACTGGTCTGTTTCCTTCCCTAGAT
GGTAAATTCCTCAAAGGCTGGAATGGAGCCCTTACCTCTCTAGCTCCAGGTGCCTGCCTG
CTGCACTGCACAAAGTGGGACTGTCATTGAGCCCCGCCCCCGCAAACACGCATGCACACC
ATAATAAGACAGCAGCAGGCACTGTCCTCTGCTCATCCCTGAAGTCCTCCACATTATTAA
GGCAGGCTGGAATGCTCCTCCAGCAAGTGATTCAGACGAGACATTCCAGATTGTCAAGGC
TGTAAAGAAAGGGACCTACACTAACTCTACACATGAATGAGAAAATTGTACTTGGAGAGG
GAAGTAACGTGTTCAGGGTCTCATGGCTGCTTGGAAGCAGACCAGTCCCAGATCTGGGAC
CCGTCCCTGACACGGCCCACTTCCTACCATGCCAAACCCCGTGCCCAATGGCCACAGATG
GTGTGCACCACACTGTGGCTGCAGGTAGCCACATTAAAAGTTTCCCCAATTTAACCAGCT
CCAAAAATCATCCTCTTGTCCTTTCTTCTCATTTCTGGGTTCAAAATTGCTGATTTGGTG
AGCCTTATTATTCAGCTATACTCCACTGCCTGGGAAATAGAGATAAGTGAAATGTAAAAG
TAGGACCAAAATACTTATGTATTTTGAGGGGTTCACTTTATGTGATGGGGCTACAGCACC

ACCAACATTCCCGTTTTCTCACAGGGAAGCAGATTAGGCAAGTCAGTGCTCAGCGTATCA
CGTGACGTGCATATGCTCCTTGAATGCTGTGCTATTGTCTTTAATAATACTAACCACCTA
AGGTCCACTGATTACTCCTACATCATCAGTCATATCTTAGGAACTGGGCAGAAGGGAGGG
GGCAGGAGAAGGGGGAGTTTCTGGGTGTTCCATCTAGCACATGCGTGGGAAGTAGTAGGA
TGCCAATAAATACTTGTTGCATAGATGAAGGAGTGAATGAGTGAATATTTTCCTCTTGCA
GAGCAGGCTGAGATTTGCTCAGAAGCATGTAGAGCAGATTGGCTGCCCACCTGTGTGGGC
TCCCTGAGACCCAGGGCATCCAGAAAGTCTCCAGAGGGAGAGGGAAGGTGGGAGAACCTC
TGTAGAGCTCACAGCCACATGCCTTAAACACTGCTCCTGCATGGAGCATGATACCTGTTC
CTGCATGGCCATGCTTCCTCTAAAGCCTGCAGGGGAGGATACTGTCTTGTCTCTTCCAGC
TCCCCATGGCTCCTGGCGCTCCTTGGCATGTGGCAGCATCACCCCAATCTCTGCCTCTGT
CTTCACATGATTGTCTCTCCCCCATGGCTCTCTGTCTCCTCTCTGCTTCTTATAAGGGTA
CACCAGGTGTTGATTTAGGGTCCACTGTAATCCAGAATGAACCTATCTTATCCTTAACTA
ATAATGTCTGCAAAGACCACTTCCAAATGAGGTCACCTTCTGAGCTTCCGGGTGGACATG
AATTGGTGGATGTTGGGGGCTTGGGGGTCGGAGGGGAACACTCTTTACTCCTGTAAGGGA
GCTTCCTGCCTTGGTGGATCCTGTTCCTTATAGACATCTTTTGTTTCCTCCAGAGTAGGA
CTGTTTTCCTTCCTAGTCACCTGTTTGGGAATAGCTGCCCACTTATCTAATTGAAGCCTC
ATCTCCTGAGTTAGAAGGCAAATGAGGACAAGAAAGAAAGCAATTAGTACAACTGGGAGT
TCAGGATTAAAAAGGATTCACTGACCTGCTGGCACAATGGTTGGTAAGGGGGGAAAGTAA
AGGGAGTTTGGAGGAAGAGAGGGGAAGGAAGGGGGTCCCTTGAATGTTCCAGCAAGGGAA
GGCCCATGGGAACCTGGATTTCTGGGGCACTTGGGCACAGGCCCTGTGAGGGTGGTGATT
GGGCGTGCATGTTAAATGCCTTTTATAGTCATAAGAAACTCAGGAATTGCTCCCCGTGAG
GGCAGCTGGATGTGCATATTAAGTGCTTTATATAGTCATAAGGAACTCAGGGATTTGAAG
TTGTTTACTCAATGTTCATTCTACAAGCATTTATTAAATGCCTCCTATACACCAGGATCT
CAGACTAATGCTCTAATTTCACAGATGAGCACACTGAACTCCGGTAGGCCAAGTGAATTA
CCCAGGATCTTTTGGGGGCAGAGTCAGGACTAAAATCCTAGTCTTTAACTCTCACCATGC
CTCACACAAAGCAATGTTCTTCTCTTATATACTCCAGTCTGCCTTGGGGGATCCCTCATC
TCCACCAGGTAATAGTAATAATAGTAACAACCCCTGCTTGACTGTGCCCAGGGTGTGTTT
CCAGAAGTCATTTTACTGCTGCTCCCTGATGTGTGGGGTGGAGGCAGGGGTAAGGAGGGC
TTCCTGACTCCTGCCATTGAGTTCAGCTTTGCTGGGGGTGGTGGATGGGAGGCCTGGGAC
CTGTACTCTCCATAGAGAAGAAGATCAAGGACCTCTTAGACAAAACTAGCGGGACTCACT
CTCTGAAACTGGGAGCCCCATCATTAAGTTTGCCCAGCTGGCCAGTCTGTAAGGACATAG
GGGATGCTGATGGTGCTAGCAAGGTGTTCTGGGCCCCTGTAAATGAGGATCCTGTGGCCT
CGCAGATTCATCTTCCAACAGGCCTGTCTTAGCACACAGGTGGCAACATTTGGTGCTGTC
TGTAATATCTCCCAGCAGGTCTGAGCCTTCAGAGCCTGCCCTCTTGGGCTTTCCAATCTG
GATGTCTCTGATGACCCGGTCCATAGCTTAGTAATTACTTGTTGAATGACTTGAGTAAGT
CTGGAGAAAAAGTTAACTCCTTCACTGTGATAGGTGAGGGAAGGTATCAGAGAAGGAGGT
ACAGGGGATTTCCAAGGAGCTGTTCTCAGGCCAGCTTTGGGACTTGAGGCCTTGGAGGCT
CCACCTGGGACTTGGCATTGGGCCTTCACTACCTCCCTGAGTGCACAGGATGCTGGAGCC
TCCCAGTTTCTCTGGCTTTCATCTCGTCTTCATCCCTGGGCAGCTCCCTGCCCTCTGCAG
CATCTCCCCACACCCTGTCTCCACGGTAACGTCACAGCCACAGGAGTCCATAATCCTGGT
GGGAGGAGAGGAGCAAAGGGCAGGGACAGGGGCACATGTGGCCAGCAGTGTCCATGTGCC
TCTGAGCAGCCAAGCTCCCACAGGCCAGGGAGGGTGCCTGCCCCAAAGCCTGGCAGCAAG
GAGGGGCCAGGGCAGAGGGCCCCCAGGCAGTGCCTCTGAACATTCTTCTGTCTAGAAAAG
GAGCCAGGGAGCTCTTAAGCAACAGGTGGAGCCTCTGACCCCAGGAAGCTTTTGGAGGCT
GGCAGCTCGAGTGTCTCCCTAGGTCAAGATCACAGCCAGTCCAGCTTGAGGCAGAACCCA
GATTCTCTGTGGCTCAGGAAAGTCTGCCCACCTGAGTATCCCCACGTCCTCCCTCCCTGT
CCTGCCCAGTCCCTGTTCCATCAGCCTGTGGCAGCACACAAGTGCTGCTGGGGCTGGGGG
TGACTGGGGAGGGCAGGGCACCAATGCCAGCCAGGAGAGGGCAGGGTCCACTGGCAGCTT
CGACCCTGGAGCAGCCCCACTGAGGGAACTGGAATAATGGTTGAAATGAGCAGCTTGTCT
GAAGACAGTCAATTTGATAGTGCCTCTAATCATAGCCGCTGAGTTTCTGTCTGCCAGACA
CAGAGATCCAGGAAAATGTAATAGAATGGACACAAAAAGCAAAGAAATGCAAAGTAGAGC
TGGAATCCCATAGATTTCTTTCTTCCCAGACCCACAGCACTATTCCTTGGGGCCCACTGC
CCAGTTTCTTTGAAGATTTGGCAATCTGCTAATTTGCTGATTAGCAGTACACACATAATA
GTTGTACATATTTTGGAGGTACATGTGACAATTTGATACGTGCATGCACTGTGTAATGAA
CAAATGAGGGAAACTGGGATATCTGTCACCTCAAACATTTATCTTTCCTTTATGTTGAGA
ATATTCCAATCTTCTCTTCTATCTATTTTTAATGATACAATATGTTATTGCTAATTAGTC
ACTGTACTATACTATTATTGGTAGATCTTATTCTGTCCATCTAACTGAATTTTTGTATCT
ATTAACCAACCTCTCTCCATCTCCCCCTCCCCTTCCCAGCCTCTGGTAACTACTACTATT

CTCTGCCTCCAGGAGATCCACCTTTTTTAGTTCTCACTGCTCGGCTTTCTTTCTAAGGAA
AATGGACTCAGATGGGTCTTTATGGAGGTCTCTAGAATTAGGAGTCTTAGGTTCTAGTCT
CAGTTCTGTCATCTAACTGGCAGCTTAGGTATAGTTAACTTTTCTTGTCCTCTGATTTTT
TATTCTAAAATGATGGTATTGGATTGGATGAAGTCCCTTACAGACTATAACCAACAACAC
CCGCACTTTTCTGCCTTTGTCCATCCAGAGCTGCATTGGGGGTGACAAACCTTGCTTTAA
AACACATATTCTATTAAGGTGTTCATTTTTCAAGCAGATGCTTTCTTGCCCACAGTACAT
TCAATTTATCCAAGTGAATAATATCTACCACTTTCAAATACTGACTATATTATCTTCCTT
ATATGCATCAGCTTTAATCTCTGTGACAGCCATAAAAGATAGAAATTATTACTCCCATTT
TACAGAGGAGGAAACGGAGACTCAGAGATAGAAAGTAAAGTGTTAATCAAGGCCACACAG
GTGGTGAGAACTGAAGCTGTTATTTGAGCCTAGATCTGTCTGATACAATATTTCCATGCT
GCCCCAGATCATATTTTCTACATATGCTAGGTTTATCTTCTTCACTTTCATTATGATATA
TATCACAACATATGTGATGGCTTGCCTCTTATTTCCCCCTGCCCCATCGCTGCCCCCAGC
ATGTGAGGTCGATAATGACCTCACATAAGATCTTGCCCTTGGTGTTTAGTGCATAGTAGA
CCCTGAACATTTGTAAAGAGGATGTACAAATAAAGGAATGAATATATTCCAAAATTTTAG
AACTTGGGTAAGTTGGAGACTGCTTTTAAATATAGAAGTATAGTCCACAGTGCCAAAATA
GTGGGCATTCAATAAATCCTAATTTATATGCAAATGTGTACACACACACACATGCACACA
CACACAATAATCAAAGCTTGTTTGTGATGATATACACACAGCATAAGTTGTGGTGGACCA
GCATTTTTTCCCCCAGATCAAAACTGGTACATAGCCTTTCAAATAAATTAGTGCTTTAAT
CTTAGCTGATGCATTTGAAGGAAGGAGTATATCCACATGCCAGTGCCAGGGTGATCCTGT
GGCCTCTCCAACAGAAACCATAGAGGGCTGTGTTTTCAGAAAGAGTAAACACAACCTTTT
CTCTCATTTTTTTTTTTCTGGTGATATTTGTAGGCCCACACCTGGCATCCCATATCACCC
ATGTGGGTCAGAGATTACATATGCAATAAAAAAGGAAATCAAAGCACGAAATGAGGAAAT
TACTGATAACAGCATTTATCAAAAGGTGAGGGCAGAAAATCATTTTAAAATTTAAAAACA
AAAGCCCATACACTGTGTGTTACAGGGATGTGTGTGTTTATATATAAAAATTGCTAAATA
CCCAGGTTAGGCACCATTTAACCAGCAGAGCTGTTGCCTCAGGCAGTTGTTTTTCTAATT
GCAGGTCTCGGCTGTGTCACCAGCTAGCTGGGAGCCCAAGGGGAGCTAAGAAAGTCTTGT
TCTGTCCTTTGAATTCCTTTTCAACAGTCTGGCTTCCCTACCACCCAGGAGGGCACAGAT
CTTCCATGCCCCTCCCCAGCCCAGGCTGCTGCTGGCCTGCTGTGTCCCACCCACTGGGGA
ACAGCCCTTGGAACAAGAGGCTGCTGTTAGGTTCAGCTTCCAGGGCTGGGACATAATTGG
CCCTGGCTCTAATGAGCAGGGCTAAGGTGGCAGAGCCTATCGCTGATTGCAACTGCTACC
TGCAGAGGGACCAGGACAAGCATCAAGCTAACAGCTTGGAGAGCTGCCACTCGGACAGCC
CATAATTTCCAAATTAGATACTTCAGAGGTCTGGATTTTGCTGTGCGGACAGAGCTCAGG
GGCAGCTCTCGCAGAAGGTGGAGAACTTAGACAAATTTTCATTCATAGTCAACAGGGTCC
CAGGCTCCCCTTTCTTCGTTTTTCATTTACATGTAAATAGTGGGGGGTCGGGGGGGTGGT
AATGGAGAGGGGATTCTGGAGCTCAGTTCCTGGGGCAAGGGGTGGCAGGAGACCTTGAAG
CCAGTGAGGCCGGTTCTATTGCACTCTTTCAACTCGGTGGAAGCAGAAGTACTATAAACT
TTGTAGATTCATCCTTGAGGGCCCTGCCCAGAAATAGAACTGTACAGTCCACAAAGCAGC
ACTGAACAAGAGAACAGGGTCGCTTTGTATTGCTGAGATCTCCCCTTCTTGTTATTTACT
TGTAGCTTTCTGTAATTGGATGAGTGGATATTTACTGAGTAAAGTGACATCTGTACTAGG
CATATGTTCTTTAACTACCCAGACCCACTGGAGGGAGAGAGACCATCTGATGTGGCCACT
GCACCTCACAGAGGTTGAGTGACTCCTCTAGGGAAGCGGCACAGTCAGGATTCAAATGCA
GGTCTGTCTTCCCGGCCGCTACCTACGTACTGTCATCTGTCTCTCCCATTGCCTCCGGAG
CTGCTTGGGTCTCCTGGTGTCAGTCTCCCAGCCTGGTGGCTCCTATGGTGGTGGCTGCCT
CTCAAATGCTGCACATGGAGGCCCACGGTGAGCCCAGGGGTCCATTCATTCCTTTTTGCT
GCAGGTCGGATGTGTGCATGTGAATTCCATTGGGGATCACAGTTTATTTTCTTTTACTGT
GGTTAAAAAAATACATGATGTGAAATTTACCATCTTAATAATTTTGACGTGTACAGTTTG
ATAATGTTAAGAATATTTATGTTATTGTAAAATAGATCTCCAGAACTTTCTCGTCTTGAA
ACACTGAAGCTCTATACTCATTCAACACGAATTCTCCATGTTACTCTCTCTGCAGCCTCT
GGCCACCACCATTTTACCTTCTGTCTCTATGAATTTGACTCCTTTAGATACCTCACATAA
TGCAGTATTTGTCTTTTTCTGCCTGGCCTATTTCCCTTAGCATGCTGTCTTCAAGGTTCA
TCCATGTTGTAGCATGTGACAGGATTTTCTTCTTTTTTTAAAAAAAATTGTATTTTTATT
GAAAAATAATAATTGAATGTGTTTATAGGGTACAATGTAATGCTTCAATACATGTATGTA
TTGTGGAACGAGCAAATGAGGCTAATTAACGTACCCATCACCTCACATACTTATCATTTT
TTTGTGGTGAGAACATTCAAAATTCATTCTTTTAGCAATTTTGAAATAGACAACTTGTCA
TTACTAACTATAGTCATGTTGCAATGCAATGGATCACCAAAACTTATTCCTGTTGCCTAA
TTAAAACTTAGTCAACCCTCATTCTGCCAATAGGCTCTGGTAACCACCATTTTACCTTCT
ACTTCTATGAGTTCAAATTCGTAGATTCCACATATAAGCAAGATCATACAATGTCTTTCT
GTGCTTGGCTTATTTCATTTAGTGTAATGTCCCCTAGATTCACCCAAGTTGTCATAAATG

ACAGAATTTCATTCTTTGTAAAGGCTGGATTGTATTCCATTGTGGATATATAGATCACGT
TGTTTTTTTCAATCTTTATCTGTTGATGGGCACTTAGGTTGTTTCCAAATCTTGGCTATT
GTGAATAATGCCACCATAAACATGAGGATACAGATATCTCTTCAATGTGCTGATCTTAGT
TCCTTTGGAGACACACCCAGATGTAAGATTGCTGGATTATATGGTAATGCTATTTTTAGT
TTTTTGAGGAACCTGCATATTATTCTCCAAAATGGCTATGTTAATTTATATTTCCACCAA
CGGTTTATAAGTGTTCCCTTTTCTCTACATCCTTGTTACCATTTGTGGTCTACCATATTT
TTGATAATAGCCATTCTATCCAGCATGAGGTGACATCTCATTGTGGTTTTATTTTGCATC
TCCCTGACGAATAGTGATGTTGAGCATTTTTAAAAAATATATGTTGACCTTTTGCATGTC
TTTTTTTTGACAAATGCCTATTCAGGTCCTTTGCACATTCTTAAACAGGGTTATTTTTTG
TCTTGGTATTGAGTAGTTTGAGTTCCTTATATGTTTTGTATATGAGCTCCTTATCTGATG
TATGATTTGCAAATATTTTCTCTCAATTTATTGTTTCCTTCACTACGTAGAAACATTTTA
GTTTGATGTAATTCAGTTTGTTGATTTTTCTTTTGTAGACTGTGATTTTGGGGTCATATG
CAAAAAATAATTGCCAAATCGACATCTTTTTTATTTATTATTATTTTTTTGAGATGGAGT
CTTGCTCTGTCACCCAGGCTGGAGTGCTGTGGTGTGATCTCAGCTCACCGCAACCTCCAC
CTCCCAGGTTCAAGCAATTCTCTGCCTCAGCCTCCCAAGTAGCTGGGACTACAGGCGTCT
GCCACCACGCCTGGCTAATTTTTTGTATTATTTTATTTAATTTTTTTAGTAGAGACGGGG
TCTCACCATGTTGGCCAAGATGGTCTCGAACTCCTGACCTCGTGATCCATCCACTTCGGC
CTCCCAAAGTGCTGAGATTACATGCATGAGCCACCGTGCCCGGCCCAGATCAACATCTTA
TAGCTTTTCCCCTATATTTTCTTCTAGTAGTTTTACAGTTTCAAGTGTTACATTTAAGTA
TTTATTTTAAGTTGATTCTTTTATAAAGGGTGAGACAAGCGTACAATTTCATTCTTCAGC
ATGTGGACAGCCAGTTTTCCCAACACCTCTCATTGAAGAGACTGCCCTTTTCTCACTGTG
TGTTCTTGGCCTTTTTGTTGAGAATTGATTGACTATAGATGCATGGGTTTACTTCTTGGA
TCTCTATCTGATTCCATTAGGATTTCCTTCTCTTAAGGCTGAATAATATCCCATTGTATG
TGGATACCACGTTTTCTCTATCTACTCATCCATTAGTAGACACTTAGGTTGCTTCCACTT
CTGCTATTATGAATAATGCTGCAGTGAACATGGGTGTGCCTGGTCCAGGGAGCTCTGACT
TTTACAAGGAGACTGAGTAGAGAGTGAAGCTTTTCTGTTCTGCCCTTCAGCCAGGACGAA
GTACAGACAATGCACTAATCTGTTCCTGATCAAGCCCACTGGGACACAAGGGGGATGGGT
GGGTCACAAGTTACAGAGGGAAAAGCCAGGGCTTTGGAATCAGATGAGTTTAAGTCCCAA
GTCTGCCTTCTATGATCTGTGTGACCTGGAGCAAATTACTCAACCTCTCTGAATCCTAAT
TCATATATATATGTATATATATAATAATTATTATTTTTCCATGACGGAGTCTCACTCTAT
TGCCCAGGCTGGAGTGCAGTGGGGTGACCTCAGCTCACTGAAATCTCCACCTCCCAGGTT
CAAGCGTGAATCCTAATTCCTTCACCTGTAACTAGATTATTGCAAGAGGACCATATAGTG
TCCGCTGGTAAATATTTTAACAACTAGCTCTCCAAAAATAATAATGCTCTAATTTGAAGC
ATTTAATGATTTTATTGTGTAAAGACTCAAACTGTAGCTGATTTGAAGCCACCAACCTGC
CTTCTTTAAATGTAGAGTGAGGAAGAGTGAGCCACCCACCAGCCCCAGCACACCACTGTC
CATATATAAAATGTCTTTCCCAGTATTTGGGATGTGCCAGGTTCTCTGTTAATACTAGTT
TCCTTCCTAATATTAGTTCCATCCTCCCCCCAGCCCCCCATCAAAAGGACTCTGGGTAAC
CTAGATAATAAGAATGATTGCTCAATTCTACACATTTATTTGACTAATATACATTGACCT
TCTATCACATACAAAGCTCTGTCCTAGGAGTAGAGTAAAAGGTGCAGAGGAATAAGGAGG
GGACTTTTAAAAAATCATGTGACCCAGCCCTGTCTTTAGGGAGTCCAGCCTGGGGGGACA
ACCCCTTCCGTGTGCCGGCATCTCCGTCATGGAACGTGTTAATCATCTGTGGACTTGTTT
CTCTCCCTGCACTGTGGTCTCCTGGAAGATAATGACTCTATCTTGCTTATTTTGTTATCT
ACATTGCTTAGCATTTCTAAAGTATTCAATAAATAGTTGTCGAATTATTTTACGAACTTG
AAATCTACCTAAGAAGGCATAACTAACAAATCCAAGACAGAGAAGAATACAAGAAAACAG
GCAATCGTAATTCTAAAACTTCTCATTTGATAGGCATCTTACTACTTCAAAGCTTTCTCA
GTTAAAATAGTTAACACGGACTGAGTGCGTATGGTATACCAGGCATCAGTATCCTCACTC
AACATACATTATCTCATTGAAAATTTACAACAACTCAATCTGTACAACTACCCCAATGGG
GTAGATACTGTTATCATCACCCCCACTTCCTAGATGAATAAAATGAGCAGCAGCAGTTAA
GTGGGTTTTTCAGTATTTTTTGTTGTTGATATTGTATGCATGGAGCCAGGATGTGAACCT
AGGACTTGATGTTTACTGCCCCATGGAGTAGAGAAAGTAGGAAACTTTCTTACGTACTCA
TTTGATAGGTGATAAAACTGTGGCTTAGAGAGGGAGATGGAGATTAAGTAACTTGCCCAA
AGTCACTCAGCTAACAAGATGCAGAACCCCAGGACTAAAATACAGGCCTGCTAACTCCTA
ATAAAATAAAGAGCATAAAGTAAAGTATGGTGTGAAGTACTATAGGCAAAAAGGGATAGT
GGCTGGGCAGGGTGGCTCACACCTGAAATCCTAGCGCTTTGGGAGGCCGAGGCGGGTAGA
TCACCTGAGTTCAGGAGTTTGAGACCAGCCTGGCCAACATGGTGAAACCCCGTCTCTACT
AAAAAAAAATACAAAAATTAGCTGGACATGGTGGCAGAAACCTGTGATCCCAGCTACTCA
AGAGGCTGAGGCAGGAGAATTGCTTGAACCCAGGAGGAGGAGGTAGCAGTGAGCTGAGAT
TGCACCACTGCACTCCAGCCTGGATAACAAAGCAAGACCTTATCTCAGAAAAAAAAAAAA

AAAAGATGGGGACTGGTTCAGAGAAGGGCCATACTACTGGGATATCCAGTGGTCAGTGGT
CAGTGGTCAGGGAAGAATTCCAGAAGATGTGTGGTTTGAGTAGGACCCTGGGGAGGTGAG
GGTGGATCTGAATCAGCAGTGTCTCATTTCCTGTCCCCCAATGTGCGCGCGCGCGCGCGC
GCACACACACACACACACACACACACACACACACACACGCATGCACACCAGTGGCCCTAGCC
CTTGCTCCTCAACATGGAAAGCAAGGGCTAAACTTCAGACAAGCTTTCCCCATCTTCTGG
AAACCACAGCTTCACAGTTGCTGCTTTTCTTGTGTATTTATTTTTCAAGTTATTTACATA
AAGGATCCACCGGCCCCTTGGCTGTCAGACAACATTGCCCTTTCTCCTGGCTTTTATCTG
ACTCCTGGAGAGGTTGTCATGCTCTCAATTACCTGAAACATGCCTGTGTCCCAATATGAT
TTGGGGTCAGCCACCTCTTACTTTGCAAGCAGTAAGTACTACAACCACAACGGCCGAACT
TGACGCACAGATCCCCATTAAAAGAAGAAGCGTGCAGGCTTTCCTGCAGGCCTCTTGGGC
TGCTGGCAGGCAGGCTGGGGTGTGAGTTGAATGTGTTGGGCTGGAGGGGGCCAGAGGAGG
GGAGAAGAAATGGGACAATGGAGCTCACTCAGCTTCCTAATCCATCCCAGCTATGGAATT
TTCCTGTGAATGTTTATTTTTTTGAGTCATGTACACTGTTAAAGTAATATTTTTCAAAAG
ATTAAAAATCTGTTTCTCAAACAATTACATGTCAAAGATTCATTTAACTCATGAATGAGA
CAACTAGCAGAATGACAAAGCTGGGTTTAAGAGAGGATACAGGCCTATAATCCCAGCACT
TTGGGAGGCTGAGGCCAGTGGATCACTTAAGGTCAGGAGTTTGAGACCAGCCTGGCCGAC
ATGGTAAAACCCCATCTCTACTAAAAATACAAAATTAGCCGGGCGTGGTAGCAGGTGCCT
GTAATCCCAGTTACTTGGGAGGCTGAGGCAGGAGAATCACTTGAACCCGGAAGCAGAGGT
AGCAGTGAGCCAAGATTGTGCCACTGCACTCCAGCCTGGGTGACAGAGCAAGATTCCATC
TCAAAATAAATAAATAAATAATAAATAAAAGAGGATACAGGAAAAATTATATATATACAT
ATATACGTGGAAGAAATCTGGAATAAGATTGCTAAATTAGATGCAAAACTTAATGTCTCA
CAGGGCAACAAAATCATAAGGCTTTGGACAATCTTCTCTACTGGATGGAAATCACTCACA
TGTTACCATCTTTTCTAACTGTTAGCATCTATCTCATAGGTTTAGGCCCTTTGTGGATGG
TAAATAGTAAACAAACAAAACAGATTCTCCTGGAGAATCAAAGCCTGAGGTGGGCTTGCT
GCCTTATTAACAAGTTTTGGATACATATTCTTAACAGCTTAAAAGAATCTAGCCAGTCCT
GTGCAGTGGCGATTCTGCAAGTTGCTGAATATGCCTATTCCAATTATGTGTTCTGGAACC
AGAGAGGTAACTACAGGGTGGGTTCACAGACCCACTGGACCCACTGTGAGAAGGAACTGA
GCTAAATCTCCATTGATTGCCTGACCTCCAGAAGTCCCACCTTTGACTGGGGGCTACAGT
GATGTTTTGGGTCTCCAGGAATTAGTGTCATTAGAGCCTGGTCAGAGCCCTCACCTAATC
TAGTAATCCTCCAAAAGTCTATTTTATTTTCCCAATGCATAGTTACCCTGGTAAGGAGTG
GTCCGTTTGGAGAAAGCTGGGAGAAATATTAACAATGTAAATTTTTGGCAGGGGTCTTCC
TCAAGAGGACCAAATCTCTCCTTCATTTACGGGTTCTGCATCTGTCAATTGGCTCAAATC
TGGGAATTAATCAGGGGCCATAACTCTCTGTTTTGGTGAAGAAAGTTAGACTTCTGATCA
CTTGATATAGAACTCTTCTACTTAAAGAGATTGAGTGAGAATGTAGTAGACTGCCTATCT
ATTTCTCTGCTAAGGATACCATGATCACCTAGCCAACACTGTTGGTCTCAGACTATTTTA
TTAACTGCTTTGGCTCTGCTGTCCATTAGGCTGTGGAGACAAGGTGGGGTTTGGGAGAGG
AGCCTTTGAGGCAGAATGTTGAGATGTGAGTTCTGATCCTGCCTTTGCTACTAACTAGCT
GAGTAATCTTGTGCAAATAGAGAAGCCTCTCTGGGCCAGCTTCTTCAACTCCTAAAGAGG
GAGTAATAACCCTGCCCTGCTTGGTCAGAGGGCTGTTTCGAGGCCTTCAAAAAGCACAAC
AATGTTGTTAGCTCTGGTTGCTTGTTTGGCATTGGTGTTTTAGATGGTGTGAGTAGAGGA
TGCAAGCTGGAAGTGCTTTGGCTCAGCTAGTGTGATGAGTTAGTTGCCGGGATTTCATGA
TAGGGAGATTTCAAATAAAAGTTCCAATTTCTGTCTTCTTTTGAAATATTGTTTCCATTC
TCAAATGGCAACAATAGACTAAGGATCCCATTCTCTCCAGTTTACCAGCCACCTCCCACT
ACTTCACTTGTGAACATTGCATTCGTGGAGGGTGGCAGGTGCAGCTCTGGATGCTGGGAA
TAAGTGCATACAAAATGGAAGAGATATGAACTGCACAGCGAGACAAGTGGAACAGCAGGG
CTGGTGCTAATCTGAACGGTAGCTCAGGGAGCAATCAGTTCTACCCACAACTGCTCACTA
AACACCGCCCCCTGATTTCTTTCTTGGCTCTCAGCCATTTTGCTCTGACTTTGGGGTGAA
TTTTCGCTTCTCTGGTAGTCTCTCTCTGGCTCCAATTCTTGGAAGACCCATCCGGCTTGT
CTGAGTATATCCACTTGCTAGGTATTCAGACCATTTCTGCACTCTCTTCAACTGTTACTC
CAGCTTAAAATCACAGCTTAACTGGCTAACAGTCCTCCCATGGCTGACACCGTCTTGGTG
GGAGCAGCTCCGTGTTATGGCCGTCACTCTGCTAGCCCAGCATTTATTCATCTAGAAGTT
TTACTGTGCACCTATGATGGCATGTGCTCAGGGGGAAGCAGCATTATGCTTTTCCAAGCC
TGCCCTTGGCTCACATGATCTGCTCATGTTGGAAGGACGCCTACAGTTCCCAACTCACTT
GTGTAGCACAGGTGCTTGACATGTCCAAACGTCATGAATGCCAAGGCCTTCCTGTCTCAC
CTGCCCAATTTCCCAGGGCATCTCAGTTTCCCTCCTCCCCCAGGGGTCTGGGACATGCCT
CAACTTTACAATATTACCTTGGCAGAGCCTCCCATATCAGACTCTATGGGAGCACAGCAG
GAAGAAGTCTTGATGAGCTCAGAGGGTTCAGGGAAGGCTATTCTAGGAGGTGGGCTTTTC
CCTTTGAAGAGTTGGAAGGATTTGGACAGTTGGGAATGGGGAGGCAGGTGGAGAAATGGC

AGCATTCAAAGGAGGATGAGGGGAAGCGAGGGGTACAAAAGTCACAGACTAGATCAACGC
CAGCTGCAGTCTAGCCTGTCCACAGGAGGGGCCAGCAGGTAATGTGGGAAGATCAAAGAC
AGAGAGCTAAAGAATCTGGACTTTTCCCTTCAGGGGAGTCATAGAAGATATTTTGAGCGA
GGCGGTGACATGAGCCTGAAGCCATGGCTTTGGGAGGTGGACTTGGTGGGCATGTGCAGG
ATGGTCAGGAAGGCAGGCTAAAGGTAGGGTTGAGAAGAAACTCTTGAATTTGGCCCCCTG
CTGACCCCTCCCATCTCCTCCATCCTGCCTGGGTCTGTGGGCCTGGTCTCCTCTTCGCAG
GCCCAGTGTGGTGCAGCTCCTTTAGAGGTGGCCAAGGAGAGCTACCCAGCTCCTTACCAA
TCCTTTCCACTCTAGGGAACCCGAATGAGGCCTGACCCCAGTCCCCTCTCGGAAGTGACA
ATGAGCTTGAGGAAGAGACAGAATAGACTGCTGTACCCGTGCCCTTGGATGAGGACAGTG
AACAACACCAGGCCCTCTGGCTCTGTCTTCCTCCTGTTCCTCTCTCATGGCTGGGGCTGA
GATGAAGACAGGTGATTAATACTGCTGTCAAGAGAGCATCACGTTGCAATTACTGAGATG
CCACCTCCTTCAGAAGGAAAAATATTGTAGCAGTGACTCCTGGGCTTTTTAGAGTGGGGA
GCAGCTCTGACAGGGAGCCAGGAGTCTCTGTGTTTCCAAGAATAGCCAGGGAGTTCCCCC
GGAGCTTGAGGCGTGGTTTTCAGCCACCGTGCATCTGGGCTGGGCTGGGATGCTGGAATC
ACAGTTGCTGCCTGGTTCCTTCCAAGGAGCGGCTGCCCCAGGTTGAAGTCAGACCCCCTT
ACCCATTGCTCTGGGCTTGGGTGCTCTACTGGCCTATGGACAAGAGATCTCATCAGGACA
GGAAAAGAACGTCATTAGACTCCTGCATCTTCCTGCCTCGGAGCTCATTATCTCTGGTGA
CTCACTCACTCCCTGTTTCGTGGTTCCATCTCGCAGAGTGATGATGACTTCCTAGCCTGA
AGGTCCTCTGACTACATTCTCTGCTGCCAGACACCATCTAGAGCCCCCTCAGTATCCCTT
TGTGGGATCTTACCTTCATCATGGCCTCAGACACCTGCTTTAACCACAATAGACAGTTGT
CCCCAGACTGACAAGCAGGGAGGGCCTGGGCACCCTGAGCTCCCTCCTTCAGCTACTGGC
CCCTCAACATGGACAAGGCTGGAGATCGCATCATGGCAGATTAGAATCTTAGGACTGGTG
GGAGGAAGCCTTGTGTGTCCTCTGATGTGGCCACACATGTTTGTTACAAAAGGACATCCA
GGGCCAGAAGAGGGAAGCCACTTGCTTGAGGTCACATGGTTGGAAATGTGGGGCAGAGCA
GGGGCCAGAAGCCAGATGCTGACTGCCTGTCAGAATTCAGTCCCTACACACCCCGCCCCA
TGTCTGTCTGTCTTGCTTCATGGACCACTCACACCCCAGAGTTCCGCCTGCCTTCTCTGT
TGCCCACCAAACCCGTGTGTGTTTGTTCGTTCATATGCAAGGTGAGTAGTGAATTTGCTG
GCTGGCTCGCATCCTCTGCAGGTGCTGGAACAAGCAGCACTTTCTTTTCTTTCTTTCTCT
CCTTTTTTTTTTTTTTTCAGAGGGTGGTATGGAAGCCTTGAATCCTGTCAAAGTTTCCTT
GTTTTGATTCTCATGGGCACTTCCATCTGCCCATACCAAGCATTCTGTGTAACAGGGGTG
TGCCAGAAACTGCAAATTCAATTAAAAGCCCGAGAGAGCTCCCCCAGGAAAGGCACAGGA
GCGGGGAGAGGATTTTATGATTTAAAGAACAACATCACGGAGCCTGAGCAATTCCAGGGC
AGCAGCAGCAGGGACAGACATGGGCACAACAGAACAGAGTGTGGCCGTGCAGCCCAGCGG
GCCTCCCGACTTTACCCCAGGCCCCGGGGAGGGTGGGGCTGCTGTCTTTGGAGGCTGGAG
CAGAAGTGGGCAGGTTTGGACTTGCAAGGGCTATGACATGCTAGAGGATCCCAAGTTCCC
TGAGGGCATCTACACAGATCTGAGTTTGTTCAGCATTTGTGCAGCCCTCTTCTTGTCTGG
TGTGAGTGCTGCTTAGGAGTCAAGACTGCAGATGAAGCCCACAGCAGCAAGTTAGGAATT
CTGTCCTATCAGCCATCAGCTCCTGTGGCAATGGTGTGATGGTTCCTTGAAGACCCCTCC
CACTTTGGAAACACAGGGAATATGCCTTACTGTCAGTGTTGGCCTCATCCTCACTCGCCA
CCAACACTGAGTTCCTAAATGGTGCTCTTACAGCCACGTGCCTCCACAGGACTTCTCTCT
GTTTCTCATTTTCACAACTACTTGCATCAATGTGTACTGTACAGTGGGGACATGGGATTG
AATTTACAGGATTATTATGAGGCTTAGCAGCAACATGGGTAAACTATTTCCAAATATCCC
ATCTTGCATTTGCAGTATGTTAATGTTAGTAGGGGGTGCCTCATTGCCACTGTGGAAACA
GAGGTTTTGCAACTAGACAAACCCAGTCTTCCATCCTCCACTGCCACTTCCTAGTTGACA
TAGGTTATTAAAGGAACTCCCTTGGCCCCATTGGCATTATCTGTGAAAAAGGATTAGTAA
TGTTTCCCTTTTAAGGTTGCTTTTAGAATTAGGACAAAGGTGTGTACAGTGTGCAAGACA
GTGTCCAGTATACGGTGAACAGTCAATAAACAGGAGCTACCGTTACTATGACTGCTGTGT
TTTCTCCAGTTCTGACAGCAACTCTGTGTCTGACTCAGCGCCGGGGGTAGAAACTGGTCT
TTTCAGCAGACGTGACTCTAAGGAGTTTGGATGAAGAGAGTGCCTGGGGAACTAGGGTGG
GATCCATGGAGGTGGGGTGACTGTATCAGATCTGTCATCAGGGCTTCTGGAAAGGGGCGA
GTGGGAAGGGGGAGCTGAAGACCCTCCATGTACTTCCCATGCATGAAGTGGGGTCCATGT
GTCCCAGGAGGAGTGAAACATGCCGCTGAGGTCTGGCAGGAAGCAAGGGGACAATTGCAG
GTCAGACACAGAGAAAAACTTACTGGGCCAGGACAACAGGCAACTCACTGGAACTCACGG
ACCCAGGCCCCTGGAAATGCTCCAGAACAGGCTGGAAAATGCCTCCAAGGCCAGGCCACC
CCCAGCATCTCTGTAGCCAGCAGTGGCTCTGGAGACAGGCTGAGCTTGTTAGAGTCCTGC
CTCTATCACCTAGCAGCTAGAACTGTGGATAAATTTTTGAAGTTCTCTGGGCTTCCGTCT
CCTGGGAAATGGAGACGTGATGAGGATTCATGGAGAGCACATGTATAAGGAGGGTTGCTA
TGCCTGGAACACAGTAGGTGCTTAAAATGATGGCTACGAAAAATGGATCAATTGACAGAT

ATTAATTCCCCTCTCCTCCTTTTCTGCTTCTCTGCCTCCTGCCCCTTGCATGCGCAGTCA
GCACCATGTGGGACAGATACTTGATATTTGCTCCATCCAAGGGTGAAGGAGAAGAGGACC
CTCCCCTTTGCCTGGAAAAAGTTTCTGCATCCTTGCCTGCAGGTGGGAGGAGGATACGAT
GCCTCAGGAAGGCCTGGACAGCCCCTTCACACAGATACCTGGGTATCGGAGGTGCCTGTG
TGAATGCCTGTTTTCCATTCGAGATAATTTTAGACTTGCAGAAGAGTAGCAAAGTAGTGC
AGAGAGTTCCCCTATACCCTTCACTCAGCTTCCCCTAAAGTGAACGTTTTATATAACCAC
AGAGTGATGATCAAAACTAAGAAAATAACATTGGCTCAATATTATTAACTAAATGACAGA
TTTTATTTGCATTTTGCCAGTTTTTCCACTAATGTCCTTTTCCTGGCCCAGGATCGAATC
CAGGATCCCACATGGTTTGGTTGTCACATCTGAGTCTCCTGTAATCTGTGACAGCTCCTC
AGTCTTTCCTTGTCTTTCATGACCTTGAGATTTTTGAAGAGTGCTGGTCAGGTGTTTTCA
GAATGTGGAGCTATTTTCACACTTGTGATGGAGTGTGCAGCACTGAGTTTTGCAGTCTTG
CTTTAATATTTTTCTGCTGTCTTATTTTTGCTAGACTCCCAGAGCCTTTGCTTCTGCCAA
AAATCTGTCCCGTGCAGTGAAAGATCCCATGCAGCTACAAAAGTGGCAGGAAGTTCATCT
GTTTAGTGTGTGACATTAGCCACGTTACCCTCTCTGCAAAATGTGCACCCTCTTTCCTAC
TCACTGGTCTGGCTTGTGCTCATATCAGAGCCCCAGCTGTCGAGCTAGTACCTCTATCCA
GATGGTGGCCTCCGTGAGGACAATGGAGCTTGCCTCTCTTGTTCAACGTTGTACCCTTAG
TCCCTAATCAGCACTGCATATAATAGGGGCTCAGCAAATGTGTGGTGAATAAAGGAGCAA
TCACCGTCATCATCAGCCACCATTTATAGATGGCCCATGGAGTGTAAAAGACAGTCATTC
AGGTTGTGGATGTGTAAGCCATGTAATTTCCTCAAGGAACATACAGCCCCGTTAGAGACT
GAACATAGATAGAAAAAGCTGATATGCTGGCCAGTCAGTACAGCAGAAGCCCTCATATTC
AGTATGGTGGATTGACTGATTTCAAAAGTTCTTTAAACAGGGAATTCATTTAAAAATGAT
ACTCCAATCATTTCATTTTACCTTAGGGCATTCATGTACATTCATTTACCAAACGTTCTG
TTCATATCTTGGGTCATTTCTTTGAGTACAAATACACCAGCTGGGTGTGGCTCATGCCTA
TACTCCCAGCACTTTGGGAGGCTGAGGCACGCAGATCACTGGAGGTCAGGAGTTTGAGAC
CAGCCTGGTCAACATGGTGAAACCCTGTCTCTACTAAAAAACATAAAAATTAGTTGGGTG
TGGTGGTGCATGCCTGTGATCTCAGCTATTCTGGAGGCTGAGGCAGTAGAATCGCTTGAA
CCCGGGAGGCGGAGGTTGCAGTCAGCCGAAATTGTGCCACTGCACTCCAGCCTGGGCCAC
AGAGTGAGAAAGAAAAACAAAAACACAAACAACAACAACAACAAAAACAAATTCATCAAC
TGGAGTCTTGCCTCACCCTATTTGCTTAAGTGTGCCCATAGTACTTTACTTACAGCTTCC
AGTTTTTTTTAGTTTTATTTTTTAAAGCACAGCAAAGACTTAAACTTACAAAATGATATA
GTGTAGACGCTTAGATTTTAAGAATTTTCAGTTATCTCATTTGCATATTAGATAACTAGT
TAGGTTTTTTGTTTGTTTGTTTTTAGCAATTTTTCTTTATCAAAATTTTTCCCAATGCAT
TCCACTTAGTTTTCATGGATCAATATTTTGACTTGGCATCCATATTTCATTGTTTATGAA
ATAGTGAGCTAAACTAATGACAATGACAAGAACTGGTGTACACAGGTTTGGCAGAGGACT
AACTGCCTGGCGAGCTGACAGCTCTCCTGGTATGCTAGGAGGACAGATAGAGCACAGGGT
CCTGGAAGGGAACATATGGTGTGCGGTGCACATCCGTCAGCGTCCTTTCCCAAAACAGTG
ATTGGAGAGCGATGGTTAATCCAATCTGCCCAAAACTTGGAGGTCACTAGAGAGCTTCTA
ATATGTATCTTTCCTCTCAAGTTAGTTGTCCTTGCTGAGCGCCACACTGTGCTAAAATGC
GCTGGATACCCCAGGAGCAAAAGATGAATAAGATACAAGCCTTGTTCTTAAAGAGCATAG
GAGAGGAGAGAGACAGACTTGCAGATTTTGGTACCACAAGTGCCAAGAAGAGCCAATAGT
GTACTATGAAATTGAAGAGGAATAAATAATTTGCCCAAAAATAGATCACAGAAGGCTTCT
CGGAGGAGGTGGCCTCAGATGAGCAATAGAGGCCATGGTGAGAAAGGAATTTGCAAGAGG
CTGAGACCACTGAGCCTCATCATCTCAAACAACCCAAGCATACAAATAAGCCTGGTAACA
GAGATGCTGGTGTTTTCTGAAATAGAAGTTGAAAGGACCAGTAGCAGCTGGATCCACTTG
TTCACTGTCATCAGCATTGGTCGTGAAGGGGACCAGAATCCTCCTCTCCCCCATCACGCA
AACCCTAGCATATTTGTTAGGCTTACAGATAAGAAAAGAGGGGGACAGAACCAGCCTTCC
CTCGGGGAGCCCAGCACTGCATGGAGGAAAAAAGGCACAAAGGTAATGGGCAGGCCCCTC
TCCCAGGTCACCAGCAGCCCTGCCTATCAAGCTGATGCATGCGGTAGAGTCCAGACCTCG
ATTTGCCTCATGCCAGGAAGATGGAATGTTTTGTTTCAATCTGTGACACGCACCTCAGTT
GCTGAAGAGATTAGCGCTTCCTGGGCTGCAAAGGTAATTAGATGATCAATCGTAGAAAGT
CTAAAGCAAATGGAACCTTTAGGGAGAGAGATTTGTGTTTGCTGTGTCCCATGGAATATC
AGCAGGGAAGAAAAGGAACCTAAAGGAGCTGTGTTTCTGAAGAAACAGGGGCCTCCAGAC
ACAGGGCTGAAGTCTCCAGGCAGGGCTGGGGAGGTGAGAAAATCAACACTTTGCTCAAAA
GCCACCAGTGTTGCCTCAAGCCTCCTTAGCCTCAAGAGTGCTCCTCCTCCTGCCGCTACC
CCTTGATGGGGAGGATTAGGTGAGAGGATCTGAGAGCATCATTCAGACACAGCCTTTGTA
GCTCAGCAACATAATAGCAACTCAGTTACCCCTGCTAACTATTATAAAACACGGGGCACA
AACTTAGATACATTCTGGGACCTGGTAGTTAATGTAAACTGAGTGAAACCAGCTGGGTGC
AGGGCTGTAAGGATGGCTGGGGATTGTGGTAAACTTGAGAGCATGTGTGGAACTGGACAT

AATGACTGGAGGGAGGGATCTCTGCCTTGGCTTCTGCCAAAGCCTTGGGGTCTGGCCACT
TCCAAGCTAAGGCAATTATGGCCAATTTTCTTTCATCTATGCCCCTACACCCATGCTGTT
TTCATATAATTCCCAGATAGCATATAATTTCATCTGTAAATATTTCAGTGCGTTATCTTT
AAAGGATAAGGACTCTGAAAAAATTCACCATATACGGGGGATGTGGGGAACAAGCGTGGA
GGTGTAGCTTTTTTTTTTTTTTTGGAGACAGAGTCTCACTCTGTCACCCAGCCTGGAGTG
CAGTGGTGCGATCTCAGCTCACTGCAACCTCCACCGCCCTGGTTCAAGTGATTATCTTGC
CTCAGCCTCCAGGGTAATTTTTTATATTTTTAGTAGAGATGGGGTTTCACTGTGTTAGCC
AGGATGGTCTTGATCTCCTGACCTTGTGATCCTTCCACCTCGGCCTCCTGAAGTACTGGG
ATCACAGGCGTGAGCCACCAAGGTGTAGCTTCTTTTTCCATCCTTGGAGTGTGGAGACAG
TCCATTCCTCATGAGCCGGGCTGTCCTCTGCTTTCTTCAATCGGTGTGTGCCTTGTATAA
AGGGGACTATCTGGACGACCCCAGCTTGTTGTTGCCATGCAAGAATGCTGACCCAGTGTT
TCCAAGATTTTATGATTCTTCTTGTAAAAGAAGCTAGATATCTGTATTTTAATGTGAAAT
GTCCAATTGTAAATATTGGCAATAAAATGCCAGTTTTTCAACAATGCTATGTGAGCCCAA
CAAATCCTGTATGCAAGCTAAATGTGGTCCATAGGCTACCAGTTTGCAGTCCCTGGGCAT
GAAGGAGATTAGCTAACCAGTACCAACTCTCCATTGCTGGGCTGTTGGAGACTAGCTGTG
TAGTAGGCAGCCTTGCAAAGGAAAAAGGTTTTAGCAGGCTGCCATTGCCAGCCTCCATTT
CCCACATAACAGAATGGGTTGATTCCATGTTATGGTCTGCCCATAAGTTGGGGCTTATGG
CATGTGGCTCATTGTAGGAAGACAGCAAACATCTGGTTCTCAGATGACTTCAGCATCCAT
TGGAGGGTTATTTGCACAAACTTGGCAGCTTGAACTGATCCCTGAGAAGAGCTTCTCCTC
CTTCTTGCCACAGCCATCAAAGCTCTCTCTGTCAACCTGTGCCTCAGGGAGCTGTCACAG
CCTCATTACTGCTAATTCATCTTCACTTAGTGCATCAAAAGGCTGATTTATCAAATTGGG
TGGGCGCACAGGAAGTTTGATTAGCAACATTATGTTGTTTGCCATGACAGGCTCAGAAAA
CTTAGCTCATCTGTGTCCCAGGAGCCCCAAGGTAAGACCGAAGTGTTTATATTCTGCCTC
TGAAATTCTCAAGATCAGAAACCAGCATGGTGGCTCTAGTCTGGGGTGTTCCCAATGGGG
TGCCCTCTCCATTTCTCTCCTTTCTGCCCCCTCATAAGTGGATCTCTGGAGTAAAATATC
TCGATTTCTTATCCAAAGAGGTACTGGTGTGAGCAGGGTCCCTGGTTGCATCCCATCATC
CTGGGTGGCAGAGTAGCTCTCATGCCTGGGAATGCCCTTTCATCTTCATATCTAATGAAG
CACTTGGGATTTGCATTATTTGCCTCTGCCATTATCCCCATCATGGCCCATGTCAAGCTG
CTGAGCAAAACATCCAAAGGCGCAGCCTTTTTCCCAGGCTCCTGGGACAGAATGGGACAG
AAAACCTCCCAAAGAAATAGTTTCAAGAAGTAGCATTTCGCAGAGAAACCTAACAGGCCC
CATGGCCCTGAGCTTCTCCCTGAAAGTCTGGGGGGGAATCATCTTTGAGCACATTCCTGTA
AGTGCATGCCTTTATCAATATCCAGAGGACAGAAAGAGAGGGAGTGCTTGGAAAACAGCC
CTTGCAAAGAAAGGTTAAAAGAAAAGTTTATGGCCTGGAAAAGAACTGGCTAGGTGGGAC
TTTCTATGTATGCATTGTTCCTGAGTGCCACTTGAGCCTGTCTCTGCTGAGGATAGGTAT
CTGGGCGAGGCGAGCATACACAGAAGTTGCATAAAGGTAAGTTGGACTCAGGAGAGGCAC
TCATGGAGGCTCCAGAATTACTCTCCTTAAGTTCATTTCCTTGAAGATGCAGATGATGAT
GATCCTACAGTGACCAGGATGGTAGTGACAAGGATTGAGCCCTTTCCAGGAGTCAGAGAG
CCCTGTAGGATAAAGCAGGGGACCTGTCTAGAGACCTTAATTGCAATCCTGGTTCTGAAA
GCAATAGGCTCTATGAACCTGGGTGAGTCATTTCACTTTCCTGGTCTTACTCTTAGCTTT
TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGAGACAGAGCCTCCCTCTGTCACCCAG
GCTGGAGTGCAGTGGTGTGATCTGGGCTCACTGCAACCTCTACCTTCCGGGTTCAGGCGA
TTCTCCTACCTCAGCCTCCTGAATAGCTGGGATTACAGGTGCCCACCTCCACCCAGGCTA
ATTTTTGTATTTTTAGTAGAGATGGGGCTTCACCATGTTGGCCAGGCTGGTCTCGAACTC
CTGACCTCAAGTGATCTAGCTGCCTCAGCCTCTCGAAGTGCTGGGATTACAGGTGTGAGC
TACCATGCCCAGCCCTGGTCTTAGTTTTTTAATCTGTAAAATGAAGAGATTAGATTAAAT
ATTCTCTAAGGCTTCTTCCAGCAGTAAAAGTCAATATTCTATATTTTTCCAGGTTAGCTA
CCATTAAAATAGGAACAACTGAGTGCCTTCTCTCTCTCAGAGACTGTGCTAGTGGCTTGA
TGTGTCTTGTTTAATCTTTATGATAACCCCACGAAGAAGGGAGTCTCGTCCTGTTTTAGG
CTGTTCAAAGGAGCACCGTCACTGTCAGCTTCCTCCAGCATAACAAACATCCAGGAAGCA
CTTACAAAACTGGTAGCCTTCCTAGGAGATGCTAAAGATACACATAGGTTTAAGACAAAC
TCTGCCCATTAAGGCTCACAGATGCATCAGACAGAAAGGACAGATGCAGAGCAATGTAGG
TACCGAAGAACCTGTGCATGGCAAAGAAATACCACCAACTACATGCTCCTGAGTGAGACG
ATAATAATACACTACATTCACATTTTTATGGGACTTTAGAGTTTGCAAGACACTTTGGAA
TATATCATTTTACTTGATTCATCTATCACTCTCTGAAATTAGGTCTGACAGCTCTCATCA
TTAAATTATTAACTATTAAGTTGAGAATTAGAGAAGTGGCTCATCCAAGGGAACTGGATT
TTCCTTCTGCATGTCAGACATCCACACAGTGAGACAATAATAATGCAGTGCTGATGATTG
CATGATACCTGATAGAGTCTGCCAAGCCTTATCACATCTCATGCTGGTCCTACTTCTGTC
CTGAGTAGCAGAGATGTCTCATAGCTGTTGCATCCTTAGATTTACCAGGAAGGTTACAGG

CCAGGTAGGACTTCTTTTTTCTCAAAGATTTAGAGGGAAGGCTCAGGGTTGTTGCAAATC
TGCATGACACACCCCAAAAGGACTTTAACCAAGGTCACCTGCCAGGTGCCCTGATATTTT
AGGGCTTTTAGTTCAGGGGTGAGTAGTGGGAACAACATGGTAGGCATGGCTGGAATCTCT
CTGAAGCATGCAGAAAATTGGGGGTCACAGAGAAATGGGGAGTTTCTTTCCCTTGGGCCC
CTCATTCCAGCTTGAGTCTTTTGCCTGTGACCCTCACACAGCTCAGCTCCTTTCCGGCAG
CTGTTGCAACCTTGTAATGACATTAGCTGCCACTTATTGGGCACCTACCACTTACTGGCC
CCTTTATTCACATTTTCTAAGTCAATTTTGCAACCACTCCCATGAGGAGGATGTTATTGC
CCCCATGTTACAGATGAGAAGACTGAGGCCCAGAACAATTTCATTGTCAAGGCCATACTG
CTACCAAGTGGGACTGGAACCCAGATCTAGCTGTTGTCTGTCTGATTAAAAAAAAAACAA
TAAAAATAGGACGCATTGACACACCTTCTTCAATTCCAGGGACAGAGGAAGTGACTCCTC
TGTATCCTGGGCATCACTGCTTAGGAAGGCCTCAATGTTGGCCCCAGGATGTGGAGTGGT
ATGCAGCAGCAGTGGGTGCACAGCCTGTTTTCAGGATGGTGCCCAGCACTGTGGCTGCTC
TTCCAACCTGCTTCCATCAACTGGGAGAGGCAGCTGGGGGCTCCTCTGCACCCCCCAGTC
TGTTGTCGGGATGAGGAGACTGCCTCTCTGCTCTCTTCCCTGTTGTGCCCATGTTGCCCC
TCCTCTGAGGGAGGTAGCAGAAGACCAGGCAAAGCAAGATGCCCAGACCTACAGTGCCAC
CCTTGGTGGTGGACGCACACCCTGTGGAATGAAAGGGAGCATTGGGGAGGAGCCTGGCCT
GCCAGATGGACCCAGAGGCAGCCCCAGGAGCTGAGAGAGGATGAGGGACCCCAGCTCTTG
CCCACACTCCTCGGCTCCACCCAGACTCGAGCATGCCCTGTGCTCCTTGGCTCCACCTGG
ACTCCAGCGTGCCCTGTGCTCCTCGGAGCTCCCTTGTCAGAGTAGCCCCATGTCCTGGAG
ACACTAAGAGTGTCATTTCTGGAAAACATGAGGTTGCCTAAGTCACTTAGAATTCTGAGG
AAACTTGGCTATGGCCTGGACCTCAACTTCCCTCTTTATAAGGCTCATATAATTCTTCCC
TCATATAATTATATGAGAAGTTCCTTTGGGGGCTCTGTGGACACCAGTCTGACACCTACC
AGCCTGGAGGGGTGAGACCCTGCCCATCCCCATGAAGGAACCGTGTAGATGTGCCTCGGA
CACAGGACTGTGAAAACCTTACTTCTTCGTACCCTAGATCCATACTCAACTCCTGGTGTA
AGGAAGAGTCTGGGTTCTGCAGGCAGATCCACTGATGTTCACAACCCACTGCCTGTTTCT
TTGTCTGTAGCATGGGGATCATATCTAATCTCACAGGGCTGCTATGCGGAGTAAATGAAA
TAGTAGGTGCCCAGCACTTCACGTGGTGCCTGGCCTGCAATAGGTGCTCAGTAGCTGTTC
TATTTGTCATTAAAGTGGGCTTTACCCTCCCACCTCCATCCCTACCAGCTGAGCCGCCAC
CTGCTGTGAAAGAGAGGACATGACTTATTAGGCCAAAGCTGTTATGTCATGAGAAAGGAT
CCCAGGCCATAGAAAGGGTTGCCAGGGCTCGTCCCCAGGGCTCCATCTGTCCTGGACAGG
GCAATGGAGTGATCAAAACAGAGGGAGAGTCTGGCAGCCAGACTGGCAGAAAAGGAAGCC
AGTGTTCATAATAAGAGAACTTGATCAGAAAGATACCTTGAAGCCTGGCTTGCACCCATC
TGTTTTCTTAGGGATGGGCGCTGGGGTGAGGGTTAAGGAGCAGATTAGATATTTTAAAAC
ATTTTGTTATAGAAAATTTCAAACATATACAAAATTAAAAAGAATAGCGTCATGAACCTC
AATGTATCTATCACCCACCTTTAACCACGATCAAATTATGGCCAATTTTCTTCCATCTAT
GCTTCTACCCCTATGCTATTTTCATATAATTCCCAGACAGCATATAATTTCATCTGTAAA
TATTTCAGTGTGTATCTCTAAAGGATAAGGACTCTAAAAAAATTCACCAGAATGCCATAA
TATCAATAATTCTGAATATCATAAAAAATCTACTGTTTAGATTTTCAATTGTCCCCTAAA
TTTCAGGGATTTTAAAAAATTGGTTTCTTTGAATCAGCATCCAACTAAGGCCCACACATT
GCAATTGGTGAAGATGGCTTTAAAGTTTATTTTATTCTAGAGGCTCTCCCCACTCCATCT
CTCTTTTTTTTCTTTGCAATTTATTTTTGGAAGAAACTGGGTCATTTGTCCTATTGTATT
TTCTGCAATCTGGATTTTACTGATTGCATTCCTGTGGTGAAATTTTACCTTCAATTCGTC
TTTGAGGTCTTGACACCAAAACAGTATTTGTGTGGGAGTCCTCAAGTCCCATCTTGCCTG
CCCACCCCTCCATTGCAAGAAGGCCTCCCATCGCCTTTGCCAAATGGGAAAGAAAGGTCC
CCGGTGTCAGCCTGCTGGAGCCGAAGGATGAGAAACGTGGGGACAAGGGCTTCCGGAGGT
TTCCAGCAGTGTGATCGTGGGTTGTGCTATTATTTGGACTGGGCCTTCTCTCTGTTTTTA
TGAACAGGAATGTCTTTTAATAAAGAAGAACAATTTTCTGCCAAATAGGCAGGATTGTTT
TTCCTCCATCTGGAGCAATAAGGTTCAGGATTTGTCTCCCAATTGACTTTCAAGAGCATG
TTTTCTCAATTCTTTCCTGAAATTAAAGTAAAGGTCAAGGAGGCTGGTCTAAGACCCAGC
CCTTCCTCCTCTCTGGGCTCTGGCTGGCAGGAGTTTGGTAGCTAAGTATGTCCTTGGCTC
AGGTGACCCTGTGTAGCCCCTGGGGCAAACCAAGCTCAACTTCCCAGATTTTTTTCTTTG
TGGGGGCAAATTGAGGAGGAAGGGAAAGTGGGGGGGCGGGGGGAGGAATACAGTGCCAGT
CTGTGGGCTCCATTCTGAATTTAGATCTCCTGGGCAATTTCTAGAGGCTTCATTCTCCCC
ACTGTGTTCCCTTCTCAGGGAGGGGGCCCCAGCCCCACACCTCCACCTGCCTCCCACCCA
CCAGTCTTCTGCAGTGCACGTGAGCTGCCCCAGGGATCTGCCCCTTCCCTCACACAGTAT
CGGAGCGGTGAGGATTTTTAATCAAAAGGCAGCACACGCAGAGAACAGCACCGCCACCAC
CCCGCTCAGCATCACTGAGCCATTCTCCCCCACCCCCCCCCACACTGAGTCACTCTAGCT
AACAGTTAATTAATTTGTGACACTTTGACAGTTTATGAGGAGACATTTTTACGGAGCCAT

CAAAATCTGCAGGGATGGGGCTGTCAGGCAGACACCCCTTCCTGCATTCACTGCATCTCC
CAGACCCTGCCTCACCCCGCTGCAGACCCTGGAGGCCTGCAACAAGGTAAGGCTGGGAAG
ACTCAAATTCTGCTGCTGCTCAGGCCTCTCAGAGATGCCACACTCCCAGGGACACCTGAG
CAGGCCCAGGGCCACCTGGCCACCTTGGGAAGAAGCAGAGAGCGGGGTTGTCTGGGATGA
GAGCCCTGGAGAAGGGGAGGCCTGGTCATGCTCAGCTGTGGTCTCCTCTGCTCCTAGACA
AAGTCTCACACAGGGGCCCTTTCGATAGCTGGGCAAGGAACTGTGCGTGCTCCAGCCTCC
CCCTGGGGACACCCCCACCCCACCCTTGTGCTCCATAGAGAACTGAGTCTCAGCTGCACT
CAGCTCACTCACTGTGGATGCTTGGTAGTCTCTGGCTGGTGCTGATGGGGGGGGGATGGCT
CCCTTGGCCTGCTGTGACTTCCCTCCCACAGGGTGCTGCCAACCTGGACACTCTGAAGCC
CTGGGCCTTCCAGAAGCCCAGAAGCCATCTCTACCAGCTCTGTGCTTTTCTTTCCACAGA
CTGTGTGTTGGCTATGACCTCTCCCCACCTCCCCACATCCCCACACTCACTTTCATCTGT
GTGCCTCTTCTTCTTTTTCCAATGCCTTATAACACCTTTGTGCCACAGTGATGCCCACCT
GGGAAACACCCTGCAAGGACCCGAACCAGCTGGGCACCCAACCCCAGCTACCACTGTGAC
TGGGACCCAGAGGGTCAACAGGAGATCTCAGAAGAGGCTATTGTACCCTTCACGAAGGAT
CTGGGAGGAGAAATGACTGCAGGGTAGGAAAAGACCTAGGGACTGGCCCCTTCACCCTTG
AATGAGATGCTATCTCCATGGACGTCTCTCAAACGTGTGGAGCATGTGCTATTGCCAAGG
CTGTGCTGGGGAGGGAGAAGACCAGGAGAGACAAGACACATGTGAGCCTTGCACACAGTT
TAGCAAGAAGAACAGACATCAAACAAATCTCTAGACAAATACTGACTTCATTACACCTGT
GCTGGGTGTCACCGAGGAGCACACGTGTTGTGAAAGCATTAAGTGAGAAGACGGGCTCTG
AGCTGGAGTGGCAGGAAGGCTTCCTTGGAGAAGGGGCTGGAAAGATAGTCCTGAAGGGTG
AGAAGGAGGAGGAGGCCAGCCAGGGTGTGCTATGCTGAGCCCAAGTGGCAGGAAGGGGCT
TAGGGTTAGGAGTTGGGACTCAAGGAGGGTGCATGTGGCTGCCTGTGCCTGTAAGTTTAT
GGATTTGGTGACAGGAAATTGAGAAAGTGCCGAAGGCTAGCTTCTATTTTTACTGTGAGG
TGGGAGGTAAGACTGGGAACTGCTGGCCAGGTTTAATTCCAGGGAGCAGGGGGAGAAGCT
TGGAGCAGGCGACCCGGGTTGCCAACCTCAAGCTGGGCCACAGAAGGCCCTCGAGATTGT
AGCCACTCTCTGGCTCCAGCTGCATAGGGCCAGACACAGCCAGAGACCACCAGTGGAGAG
ATTCATCCAGGCTGTTCCACGCCTTCTAAAGAAACCTAGACAATGTTCCCTGCAGATAAC
ATAGCCAAGAGCTGCTGCGCGGTCCCTGAGCTCTGCTGCCTCGCTGCCTCTGAAGAACTC
CAGGTTCCAGGGAGGCTCCCCATGCCGGGGGAGAAGGGGCAAATGGGGTATTAGTGTGTG
GCCTCCCCCTGTCTCCCACAGCAGCCTCTGCCACCCCCAAATGGTAGTCCAGGCCACTCC
CTGGGCTTCCACTAACGGGTATCCCCCAGCCTAGGTCTCTAGTCCAGACCTGTTCCCCCA
CAGTAGTGCTGAGGCTGTGGTTTGTGGGGGAGTCCAGGGGCTCAAGAAGGAGGAGCCCTT
CCCCTTAACAGGGAAAGAGCAATCTGCATTTCTTCCCTCAGGAGTGACTGCTGACACCGG
GGCCAGACCCACAGCCTCACACCCCACTCCCCTGTGCACTCGGGCCTGGGATGCAGGAAA
AACCGTTCCCAGTGAGCCCAGGAGGTTGCCATCGTCCATTGCTCCAGGTTCCTCTTTGTC
CCCACAGTCCTTTCTGTTTCTCCTCCCCCTCCTTTTTTTCCTCGCCACAGACCCTCCACA
CCCCAGCTCCAGGGCTTAGAGGCTTTGCCCTCCAGACAGTGACTGTGCCTGTCCATCTAC
CCACTCCCACCCTCGGCAACCCAAGGTCTGCAGCCGCCTGGCCTAGGGCTTTGGGAATGA
GGTCTCCATTTCCTCTGCCATCTGCTGAGGTTGCCTCCTCGGCCAGAGAACATAAAAGTG
TTATTCAGTAACTCTCTCCTTTTCCCTTGGATGTGGGAAGGAACGGGCGCACCACCTTTC
CTCCCTCTTCCATTTCCATGCTGCCTTTTTGAAGTTGCAAGAGATGCTAAAAGAAGGTCC
AACCCCAAGTGAGAGCCTGGCCTTTGCCTGGAGGGGTAGGGGCAGGTGGCCTATATCGCC
AGGGTCCTGGAAAGGAACCTCTTACCCACTCACTCCCAATTCCTATCCAACTCAAGTCAC
TCCAGTAGGCTGCTTTTGAGATGCAAATACAAAATGCTTTCTTCTCCCCCTCTACTTTTT
CATTGAAATGCTTTGCATCTCAGAAAAGAGGAAAAAATGATGTGTTTAAGACAGGAGTGT
CTCACCCGCCATCAAGCCTGATAAGGAATTGTTAAATTTTAATTAGACAATTTGATTCCT
TCAAGTGCCGAACTTTCAGGGAAGGCAGCACCAAGACTTAAGCTGAGACGGAAGCATAGG
AAACACGTTGCTGGGGTTTATGCTGCATCCAGGGCTTCTGTCCCCCACCTTTCTAGCTCT
GTGCCCCAGATGAAATAGAAATGAGGTGGTGGGGATAGAGGGAGGGAGAGAGAGAGAGAG
AGAGAGAGAGAGAGAGAGAGAGAAAGAGAGGATCAGAGAAAATCCTCTCTGTTCTCCCAG
GACCTGCCAGCTTTCTTCCTGGATCCCAGGCTGTCCTAACAGATTGACCCTTTTCACCCC
ACTCCATCAGCCTGGGGACTAAGTGTTGCTACACCTTCCAAGTTTCTCCTGAGAGAAAAT
GTCAGGTTTGGGTGTCAGCCTCAAACTGCTGAGCCTTAAAGGAGCTTTTTTCCCTTCCAA
TACACTTTATAGGTTGGGGCGCCTGCCAGTTTTGGGGCGTGACTGGGAAAGCAGCCCCTT
CCATACCTCATCTATACCCCAGAAGGCCTGCCCACTCCCTGTCCCCTCCTCTACTCCTGG
GGGGCAGTGCAGTGGGTGGCCTGAGCAGGGTGGCCTGCCTGGGGCAGCCTGGGTGGGCTA
GCTTAGCCCCGGGTATCTGGGCTCTTCCAGTACTTCTCAACTTGAGAGCTAGCTAATTTC
CAAATTAGGGCACGCACAGAAAATAGTAGCATTTGTAAGGCATATAGGGTGAATAGCAGA

AGCTGCTGAGGTTGGAAGTGCCTGCCTCTACATCCCAACTGACCTAATATTTCTATGCAC
CTTGATGCATTCTAGACCTCTGATTGGGGAAGTTCCACTCTGAAGCTTCTGAAGAGAGCC
ACTATTATAGAAGGCTGGAGTTAGGCTAGATGTTAGGAAGAACTTGACAGGCAGGGGTCC
TGAGCACTAGAATGGATGACTCTGAAAGATATTTCTGTAGATCTTTGCCCTTCTGAGCTA
GGGCAGAGCAAAGAGTCCTGGAGACAGATGAGGAGATCTTTGGCTCTTTGATGACCAGTA
GCTTGCAGGTCACCACACAAATGCAGTCTTCTCTTTCTCCTGGCTTCCACCAGGGCAGCT
GAGAAAGAAAAGCCTAGGAGGCCTCAGAGGACCCATGGAACCTTGTCTGCAAGCATCTGC
ATGGTGAGGGTGGAATGAGGAGCAGCAATTACCCCCACTTTCCTGCACAGAAAGGTGCCT
TAGGGGAGAGGCAGCCACCCCTGGAGTGAGGCCTGGCAGCTACAGGATTAGATTGTTCAT
CCTCCACCCAGGAAACACTGTCAAGTAGCTCAACCTGTAACAGCTGGAAAATAACAGTGT
CCATGCATGTATTTGGTGCTCACTAAGTTCTTGTTGACTGGGGATTGTGATTTGGAGTTT
TGTAAGCTTTTATGCATGCCCAGGGGCCACCTGGGAGAAAGATGGAGATGACATTTGGAG
GGTGGTGAGCAAGTTGATCATATTTTCACAATCAAAAATCAAAATGCTTGTTTTGATAAC
AATAGATTTTTAAATATACTGTGCCACTTTATTTGTCTCAAAAAAATTTCTCATGTAAGA
ATAATGCACCTTGGGTTATATATTTAGCCAATCTCCATTTTAAAAAAAGAACAAGAAATT
GGGACCATCATGGCAAATACAAGGTGCCATGTGTTATGTGGCTTTGCATTTTCCCTCAAC
AAGCTCCAGAGTGGACAAAGAACTCACCAGGCTTCTTTGGAGCCAGAACCAGCCCAGCGT
AACTGGAGCAGCACTGAGAACCTTTCCTCACTCCGCTACCATGAACACAAGCTCCAGCCA
GGATGGAGAAGCTACTCACTTGTGTATTCTTTTGGGATGCCCCTTGGAGCCCAACAATCT
GTGCAGCCCGGAGACAGAAGGACAAAAGGGAGGGATGGGCTGGAGCTGCAGCAGGGAAGC
CTGGGGACCAGCAGGTTTTCTCAGGCCCCTTGAGAAAATACCAGCTTAGAAATGCTGGGA
AGGCCCTGTATTGCTATCCACTCTACAATGCACTTCCCCCTGCCCCCACCATTTTAATGT
CTCTGAAATCAGAATGCATTTTACAATGGATGACATCTTGGAGCTCTACTGGGGTTGGAT
GGCATTTTTTTCTTTCCTAGTGATATATAAAATAGTGGTGCATCTTCATTCGATTTTGTC
TTAGAGTCTATGAAATGTGGTGATTAGTATGACAGTCATCGGCTATAGCAGCTGGGCTGG
GAGAGCTGTATCTTCCAGGCCAGCTGCTACCTCATCTCAAGGGTCACTTGAGTTTGTCCT
ACAGCCAGGGCCCAGGGACAGGCTTTGTCTTTTCCTTCCTTTACTTCCTCCCAAGGAGTT
GGTGGCTGCATCTTGAAATCCATCTCCCTTCATCTAGCCACCTATTTTTCAGGATGGGCC
ATAGGAGGCAGTGGGCCCAGGAGGACCTCAGACCCTAGTGAGCTGCATTTGAACAGCAAC
AGTCACTTCATCTTGCTGAGCCGTTGGCTTGTGGTCTGATTGCTTGTTTCATTTCATTCT
TTTGCTTGGTTTGATTTTTAAAGTTGACATTCTCAAGGGCTTACCTGTGCCTGGCACATG
GCCATGAGTCATCTTACTTAATACTCACAATTGTTGTTATCTCTATTTTGTGTATGGGAA
AACTGGGCTCAGGAAAGCCAAATAATCTGGCTGAGGCCCCAAAGTTAGTAAATGGTAGAG
TTGGGACTTGAACCCAGGTTTTTTAGTCCTCAACTCGAATGTTATACTAGCACCTCTCAG
GCTAGAGTACCTTCTCTGTGGCAGTGGATTTGCTGATGTCTGAATTCCTGCTCAGCTTGA
TGTTTACATGGTGAGAGCCAGCTAGGCTGCCCCTGCTTGTGAGAGGTGAAAGCCCCAAGT
AGATAAGGTGCTGAAGACACGATAGAAACCAGGACTGACACCAGGTGTTAAAAGATAGCC
CTGTACTGGCCGGGTGCGGTGGCTCACGCCTGTAATCCCAGCACTCTGGGAGGCCGAGGC
AGGCAGATAATGAGGTCAGGAGATCGAGACCATCCTGACTAACACGGTGAAACCCCGTCT
CTACTAAAAATACAAAAAAATTAGCTGGACATGGTGGCGGGCACCTGTAGTCCTGGCTAC
TCGGGAGGCTGAGGCAGGAGAATGGCGTGAATCCAGGAGGCGGAGCTTGCAGTGAGCCGA
GATAGCCCCACTGCACTCCAGCCCGGGTGACAGAGCAAGACTCCATCTCAATAACAAAAA
AACCCCCAAACAAGCAAACAGACAAAAAGATAGCCCTGTACCAAGGTACTTATAGGGGTT
ACAGGTATTTAGGCATTTGCCATGTTTTCCCTTTTTTTTCCTATGGTGTAAATATACTAC
GTTTGTATTAGCAACAAAAAGCAACGAGAACAACCAATAATAAATAATAGATTAGAAAAT
CAAATGTGTGAGGCCTTTCTCAGAACTTGGGTACAGGGACTCTCCCTTACCCTGCAGAAG
TAACCAGCACTCCAGAGAATGAATGCTCACCCTCAACCCCACCTGACCTGCAGTGCTCAC
ATTTGCCATCTACATTGTACTCATAATTTTAAATCCTAGACTAGTGCCTGTAATCCCAGC
ACTTTGGGAGGCCAAGGCAGGAGTATCTCTTGAGGCCAGGAGTGTGAGACCAGCCTGGGC
AACATAGTGAGACCCCCATCTCTACAAAACATTTTTAAAAATTAGCCAGGCATGGTGGCA
CATGCCTGTATTTCCAGCTACTCAGGAGGCTGAGGTGGTAGGATCACTTGAGGCCAGGAG
TTGAGGCTGCAGTGAGCTATGATTGTGCCACTGCACTCCAGCCTGGGTGGCAAAGTGGGA
TTCTGTCTCTATTAAAAAAAAATTAAATCCCAGTTTACATCCTCCCTCCTCCAGGAAGTT
CTCCACAAACGCCCCAGCCACACACATGTGCATATGCTCCTGAACATCAACTGTAGTGGA
CACGGTGGAGTGCCACCCAGATCCCCCTGCAGGACCACAGCCCTCATCCCCATCTACTGG
GAGTGTTGGCAACTGACAGTTTTTGGCAATTGCCCACTGCTGAGGAGAGATGCCTCTTTC
AAGGCCTCGCTGCTTTCCCTGGGACAGCCAGAAGCTGTGACATCTATGAGAGGGGATTAA
AGGCCCTACCCTGTTGCCCTCATTTAGGCAACTGGCAGGGTGCCCTGTGGGGTCACCTGA

TGCCTTTCTTGTGACTTCTCCCTCTGGCCTGTCCTGCTTCCTCACTTCTTTGCACATCTT
GATCCTGAGAGCATTCCCCTGTACATTTCCTGCAGGCTGATTTCCTCTTCAGAGTCTACT
TCTAGGGACCTGTATTAGTCTGCTCTGGCTGCTATGACAAAATTCCACAGATTGGGTGGA
TTGAACAACAGAAATCTGTTTCCTCATAGTTCTGGAGGCTGGGACGTCCCAGATCAAGGT
GTCAACAGGGCTGATTTTGCTTAAGGCCTCTCTCCATGGCTAGCAGATGGCCGCCTTCTT
GCTGCATTCCCACTTGGTCTCTCCTCTGTGCGCGCATCCCTGATGTCTCTTTTTATGTCC
AAAGCTCCTCTTATAAGGACTCCAGTCAGATTGGGTTAGGGCCCACCCTAAGCGTCTCAT
TTTAACATAATCAACTCTTTAAAGGCCCTGTATCCTAATACAGTCACATTCTGAGGTACT
GGGGGTTAGGACTTCAACATATACATTTTGTGGGTTGGGGGAAGAGCATAGTGCAGACTG
TAACAGGACCCAACATGCAGCACCTATGGCACCCTTGGGGTGCCTTACTTTTTCATCACT
TGTTAATCTGGTAGCCTATGTTAGCAGGTGCCTTTCAAGTGGGAAGGGGTTTTCTTCCCA
GTTGCACTAACAGAGCCTTTGATTCAGTTCAGCAAACATCTGTTGAATACGTACTGCCCA
CAAACCAGAGTCAAGAGTTGGGAAAGAACAAGATAGTATGGTTTTTATTTGTTCATTCCA
AGAACAAGAGGAGGAATGAGCAAGACATGTTGTAACTCTTGTGATGTCTACACCCCAGTG
AAAAAAAGAGACTCCTAAACAGGTGTCTCCTGCAGCACTGGGGTGTGTTTCAGTGCTGCA
GGACCCTGAGGAGGGTGGGTGATGGCTCAGGCAGGAGGATATGGGTGGATTCTAAGACAG
GAGGATTCTAGGCAAGACTCACTTTGAAGGATGCATAGGGACTGGAAAAGCAGAGGGAAG
GGAAGTGAACAGAAGAGTTTTCCAAATCCCTTTCTTATTAAAGTAGGGATAATAATTAGA
CAAGATCAAGCATGTTCCAGGTAGTATGGCCATAGACAGGGATAATAATTAAAAGCCTCC
GAGGGTTGTTTTGAGGATAAATGAGACAGTATATCCAAAAAACTTAGCAAACTATCAAAC
CCTTTACAAGTATATGATGCTATCATCAGCAGCAGGGAGTGGGGGGAGAAGAAGAGAGCG
ATGGTCAGGATGGGGGCAGTAAGTGTGCCTCACACGCCTCAGGCCCCTGACACTGCTTTG
CACAGTGCTTTATGCCCAGCAGGTTCAATAAATGCCGATTGAGTAAATGAATGTCAGAAG
CAGCCCCAGGCACCTGATCAATACATACATGCAGGCCTCCCGCTGTGGGCTCCAAATGGG
AAGAGGGCTCAGTTGGTTTTGCAGAATACAGCATCAATATGACATATGCTTCATTACCTT
AGAACAGGAAGATTTGCTGCGTGGTGGCATTCCATGTCACCCCACATGGAATTAGGCACT
TTGCTTTTCCCCGAGGCTCCAGAGTGATGGTGGTTGGTAGGACATGATCCATATTCTTCT
ACTAAAGCTGGAAGAGTGGGTGTGTCAGACAGGGATGAGAGTGTGGAGATTGGGCAGACC
CTCTTCCACCATCCTCTCTGACCCATTGCTGGAGGTGTGCCCTGTTCATTGATTGGACAT
GGCACCACATTCATCCCAAATGGCATCAATTGGTGGTTTTCAATTTGCAGTAGCAAAGTA
CCTGGAAGTCATGTGCTTTGTATGAAACACCTTGGAATGCTGATAAGTTTAATTCTATTC
TGTAAAAGAGGAAGACTTTTGTTAGCTGAAAAGCCAACTATATTATCCATGCATTATGCT
TCAGTCACAACCAAAACTCCGGCTGTCAAGTTCATCAACTCCTGATGCCTCCCAAGTCTG
CTCCTGAGCCCCTCTGGTCCCTTTTCTCTGTGAATATGCGACACCAGCCTCCCAGAGCCC
CACGCAGAAATCCTAGCATTACCCTCAACTCCTTATCTCCCTGCTTGTCCCATACCCACT
TTTGCCCCACACCTATCCAAGGACCAAGGACCATGAAATTGACTTGCAGTTTAGCTCCTA
ATTCTGAACAGGTCTCTCCATCCTCGTTTCCACTATCTTCGTTCAGATGACCACAATTTC
TAACCTAAATTACAGCCAAAACATCACTCTCCTCTGAGCTCTCTTCTACACCATACACTT
TCTAGAACACCAGTCCAATAGGGTCATGTCTCTGGGCCCAACCTCTCAGGGACTCTCCAG
CTGACAAGACACAATCTGGCCTGTAAATGTCCCTGCAGTTTAATTATCCTCAACGTTACT
GCCATACCCTACATTTTTGGCCAAACAGAATTGTTTGCTGTTTGATGATTTGATACCATG
TCATATTGTCTGTCTGGAACATCCCCCCACCCCTCTCATTTAGCAGGCTAAGTCCTCCTT
CTACTTCATCCCAGATGATACCCACTTCAGGAAGTCTTTCCCTTCTGTGGGATGAGATGC
CCATTCTGCAGGGCTTTCACTCCCTGCATCCTGCCAAACCTCATCATCTCTTACCTGGAT
TCCTGCTACAGCCTCCCAGTTGGTGTCCCGCTTCCACTCTGGGCCCCTCCTCTCCGTTCT
CCACAGTGCTGTCAGAATCACCTATT^CGAAAGGCGAATCTGATCATGTGGTTCCTGCTG
CCCTTAGGATCATGTATAAACTCCTAGCATGACTTTTAAGGCCCTCTATGATCTTGCCTA
TTGCAACCTCCCCAGACTCAACCCTTGCCAGGTCCCTCTGCATCAGCTATCCAGAATCTC
TTTGAGGCCCTCCACCTGCTGTCTACCTCTCTACCTCTGTGCTTTGCATATACTGCTTCC
AATGTCTAGACCTTCTGCTGACTCCTAGTTCTTTACCTGGCTAATTCCTACACATCCTTC
AGTTGTTTGTCTGTTGAACATCACTTCCTCTAGAAAGCCTTCCCTGAATACCTGAACTAG
GTTATGTATCTCTCTCCCTGTTCCATTTCCTACTCCCTATCACCCTTAGATGTAATTGCT
TGATTAATTGGCTGTTGTTTCTCCTAGAATGTGAGCTACAGAACCATGTATATTTTGTTC
CTGCCTATATTTCTAGAACTATATAGAACAATGCTTAATAAATATTTATAGAATCAAGAA
TGAATGAATACCCATTTCTGTTTCGATGACTAGAAGGTAGCAAGCCTGGTTAACTGAAGT
GTGTGGTGCATGGGTCGTGCTTAAGAAGTGTTTGTTGAATGAATAAATAAATGATGGATC
AGCTCTGTTCAAGCTCATCTTATTATGCATTTTTAAAAAATTGTGTTTGCTCATTTGTCC
TACCAGCTGTAAAAACTTGCTAGCAAAAGAGTGGCAGAAGGCCCAACATTTTTAGAAAAT

TCTTAGCCGTAAACCTTAAAATCCCGAGTTGGAAAATTCTCATTATTAAATGCCAGGAGT
TGGTCTTCTTCCTGGAGACCTCTGCAAGAGGCCCTCTCACTGACACCTTGTGTCCATTTT
TCCTGGCCAGAGCCTGGCCACCCAGTGGCTCCACCGCCCTGATGGATCCACTGAATCTGT
CCTGGTATGATGATGATCTGGAGAGGCAGAACTGGAGCCGGCCCTTCAACGGGTCAGACG
GGAAGGCGGACAGACCCCACTACAACTACTATGCCACACTGCTCACCCTGCTCATCGCTG
TCATCGTCTTCGGCAACGTGCTGGTGTGCATGGCTGTGTCCCGCGAGAAGGCGCTGCAGA
CCACCACCAACTACCTGATCGTCAGCCTCGCAGTGGCCGACCTCCTCGTCGCCACACTGG
TCATGCCCTGGGTTGTCTACCTGGAGGTAGGTGGGCCCCCTGCTTGCTCCAGCACTTTCT
CCAGCAGGGCCCTGCACTGGACACTGGGGACTCTAGCTCCCCACTGGCTTTTACCAATGA
GTTTCCTGGTGCTTCCCCAGGTGGTTTTTCCTTCACTCTGGGCTTACTTTTTCTCCTTAC
GAAATGGGTAGATTGTTTCCTTAATAATCCCAACTACCATTTGTAAAGTGCTTACTAAGT
GCTGGGCCTCACGTAGGGACTTTAAATATAGCATTTTCCTATATAACCCTCACAGCAGCT
TAGAGGCTGGCATTATTGCCACCATTTTGCAGTTGATAAACCAGGTGGTCAGAGATGTTA
AGTAACTGCTGCAGCATCACACGGCTGGCAAGTCCAAGCTGGAATTCTGGCCTCAGAGTT
AGTTCCTTAGGTCATATTGGAAATAGGAGTAACCGGCAAGGATCCCCAAGGAGGGGCATG
TTTATGCTCCCAGGCCCCTGAAACCTTCACTCCCATCTCCCCACTTCAGAAATGGGTCTG
CTGCTTTATGCTCCCCATATCCCCTCTCCTTCCCACAGCTTATCCTGGGGCCCTGTCCAG
GACCTGCAGGTAGAGGCTGCCATGGACTGTGCTGTAGCCCTTTTGTTAGGAAGAATTGTG
TAGTCACTCATTTCTTGGCCCAGCTCTGCACCTCAAAATGGGGAGTAGGCAGCACAGTCT
AGACACTGTGCCTGGTGCATTGCTGACACAGACCCAGTGAATACTCTTGGTAACCCTGGG
AGTCCATGCTACTCTTCTCACTTTACAAAATAGGAAACAGGCCGAGCACGGTGGCTCACG
CCTGTAATCCTAGCACTTTGGGAGGCCGAGGCAGGCAGATCACGAGGCCAGGAGTTCAAG
ACCAGCCTGGCCAACATGGTGAAACCCCATCTCTACTAAAAATGCAACAATTAGCCAGGT
GTGGTGGCATATGCCTGTAATCCCAGATACTTGGGAGGCTGAGGCAGGAGAATTGCTTGA
ATCTGGGAGGCAGAGGTTGCAGTGAGCTGAGATCATACCATTGCACTCCAGCCTGGGCGA
CAGAGCAAGACTCTGTCTCAAAAAAAAAATAAAATTAAATTAAAACAAAAACAAAATAGG
AAATAGAAGCTTTGGAGAAGTTGCCTTTCTTCACCCAGGTCACAGGGAGAAATGCTGATG
GAGAAATCCCAAAGCAGATATTATTCTCCAGGAAGACACCTTCAGAGCCAGCGAGCAGAT
GTGGGAGCATTTAGGGATCATCGGTGGGCACAAGCTGGATCCTGCCCCTTTCTCTGCCCA
GCTTTCTAGGATGGCATGTCCAGGACTCAAGCAATCTGGGAGTCTAGGTGCATGGGAAGG
CATGGGATCAGGCATTTAGGAAAGTGCCGGTGCTCTGCCCACTGAACCGTTACCTTCCTT
CCCTGAGCAGGAGAGGAATTGACCAGTGCCTCTGAGGCCATCCCTGCCTGAGAGGGAAGG
GGTTGTTGAAAGAAAATGAGAAAGCTTTGTAGGTTTAAACAGGGGAGAAATCTAGATGAG
GACGCTCAGGTGAGGAGGCGAGACTGGTGGAAAGTGGCACACCTCCCTGTCCCTGGGCCC
CCAAGGGGCTCGTGCGCTTACTGTTCTCACCACCACCCCGGGCCCAAGGGAGCTCTGATC
CATCACCCCTTGGCTTCCTTTACTACAGCCAATGCAGGCTGCAACTTCCAAAATGACCTG
ACTGGATATTAAGGAAGAACCAAAAGGAAACACAAATACAAAACCACATAAAAATATTCA
GTTGACACAGGCCAGGAGTCCAATTCCCCCTGGATCCATGTTTATGAGGGCCCCTAGACT
CTGTCCATGCCTTCTTAATTCTTACGCTTGATCCCCTCCTTCTTCCCTCTTCCAAAGGAG
GGTCCTAGGTCTCAGACCATAGGGAAAAATGGTAGAGCAAACAAACTCTCTGTGCCTCAG
TTTCCTCATCTGGAAAATGCAGATAATAATAGTATCATACATCATAGCATTGTTGAGGAT
CGAATTAGTTGATGTATGAAAAGTGATTAGAATGATACATGGCTCACAGTGAGCACTGTG
TAAATGTCAGCCATGGCGATGATGATAAAGATGAAGATGACAATAGACATCCAGCACTGC
TCCACATAGGGAGGACTCTGTCTTTCCTATTCACCGCCCCCTTGGGATAAAGAGGAAGGA
GAGAGTACTCCCTATGTTCGCCCCAGGCAAGTAGGTACCCTCTTCCCAGAGGAACGTGTG
TTCTACCCAGGGCTCTGGGCATGGCTTCTGTTAGCTTCCAGACCCCCTGTCCCTACCCAG
GCACTTGGGTAGGGACAAATCCATACATGGGCTATAGGGGGTTCCCAGGAATCTGTAAGT
CTTTCGAACAGATCCTTTAAACATGCTTGTTCACCTTATTTTAAAGGTGAAGCTGAGTGT
GTCAGGGGAGGAGGGTGCAGAAGCCATTCTCAGAGGGCAGGGCTCAGACTTCCCCACAGC
ATCTCATCAAACTAGAGCTGGGCACTGAGCCTTGTTTAATGGACATTATCTCAGCGATTT
GTTGTCCCTAGAGAACGTCCCAGGTGACGTCTCACCCTGCCCTGATGTCCTATCAGCGCA
CCCTCACAACCACGCACTGTCCCCTCTCTAATACATGCTCTTGTCATCCAGATTTTTTCC
TCCTGTTCCATTTCCAGCAATGCCATGCCAACATCTGTCTGGCTTAGGACTAAGTGTGCG
TTATTTATCTTGCTAAGTGTATGAAAAGCACGCTGGTTTTGGAGTGAGAGGACCAGGTTC
AATTCCCAGCTCCATTCCTTTCCATCTAGATGCTATTGGAAGAGTTCCTGATGTCCACAT
GTGCCATTCCATGTCAGCCTCACAACCCTTTAAGGAGCGGCTTCCTGTGTGCATTTATTT
TCTAGATGAGGAGATTGAGAAGATGAACAAATATCTCAGAGTTATTCATTCACTCAGTCA
GCACTGACTGAGCACTCCGAGGTCTTACCCCAATCCTTGTGCAATGGGCTAAGGCACTGA

CCTGCTGGGGATGCAGAGGTTGACAGGGCCCCTACAGTGCAGTCTGCTGCCGGTGACAGT
GGAGCAGTCCCCATAGGAGGTGTGGGGCATAAGGCCCAGCATGAGGGTGTCAGGGAAGAC
TTTCAGGGAGAAATGATGCTTTCGGAAAAATTATGCAGGAGAGGGAGGGAGACACTTGCA
TTCTCAAGAAAGCCACCCAGCAGGGAGAGGGAGTAGCTGGCTGGAGGTATGGAGGAGAGG
TGGTTATGTCATTTGCCTCTGAGGCTTACTGTCTGCATTCTAAGATATAAGCATCAAGTG
TTTGGAACAGTGCCTGACACATGGTAAGTCCTTAGTATTATTACAGTTATTAGGACTTAG
CTGAGCCAGCTCAGGGCCTGTACTGCAGGTCTCAGCTTTATGTGAGCAAGAGCATTAAGG
AATGATGCCTGGATGCCTGGGGGTGTGAAGAAAAGAGCCTTGGGTT^CGACTAGGGAACC
TGGGGCCACTCCTTCCTCTGCTACTAAATCACCAAGTGATCTTGTTCTGTTTTCTTCTCT
GACCCTCCCTAGTTTTGTCCACCCTTGAAATAATCATCTTTCCTTTTCACATTTCATGCT
TACCAAGTACTTGTCACCTAATTATCTCCTCTCTTGATAAGCTAGATGGTCCCTTCCAGG
GCAGCTTAGTAGAGAGCATGGGATGTGATGTTTCAGATTCCAGCTCTGCTGCACACCTGC
CAGGTGAACTTGGCCACGTTACATGGCCTCTCTGGGCTTCAGTTCCCTCACCTATGAGTG
GGATAAGCAAGCCCTTCTTGTAAAAGTTTTAAGAACGATACATGAGATAAAGTGCAATGC
CCACAGTAGATGTCTTATGGACAGTGGCCACCAATGCATTTTCTTGAGTCTTTAAGTTAG
CAGCCCTAACTACTCTCCAAGGCAGCTTCCCCTGGGACCACAGAGGAAATCTCTTTGTTA
TTCTGGGCTCCAGATAGGCCAGTGCAAGGAGAGATTTAAGATGTCCATGAAGGCAGGACT
GTGTCTGAATTGCTCACAACTGTGTCCAGGAGCCTAGGATAGAGGCTGGAACACAGTAAT
TTGCTCAATAAGTGTTTGTAGGAAAGAAGGGATGGCAGAAAGGAGGGAAGGAGAGGAGGA
AGACAGGGAGGAAGGCCCTGATATCTCAACCTAGATCCCCAGTGGCTCCCAAGTACTGGT
CCCAGGAGGGGCTTCAAAGTGGGATGTAAATCAGGTAGTGCTGGTTTTCTGCCCAGTGGT
ACCCTAAAGGCACACTCTGTTTATGCCAGGAAAGCCCTTTACGTACCCTCCTGCCTCCAC
CCGCAAAATGGGCATCCAGCTGTTAGCTCCTGCCAAACTGGTCAGCGCAGCAGCACAGGG
AGCTGGGAGAGAGGCCCTGGTACGGGGCCCCCATGTGAGCTCCCAGGAAGACAGTGCCGC
ATGAGAGGCTTGCTGTGTTCTGGGGCAAGCTGCTGTTTCTGCCACACAGGATGACAGCAG
CTGCATTGCCCATCATTGAGCTTAAATGCCAGCATTTGGTTGGATGCCTAGGAGCAGAAG
AGAGGGCAGTGATCAGAATGAGCAAGGTTATAATTAGCCCTGCTGCCAAGCTACACGGTG
ACACGAAGTCTGCCCTACTCCGGGTTGCGGGAGGGGGCTTTCACGCTCCTCTCTGCTCCT
ATTGGTAGAAGCCAAAGGTGCATCTCCCTGTCCTGACTCCATCCTCAGGGAACTGGGGCT
GCTCCAAGCTTCCAGAGCGCTAGGGACAGCTGCCGTGAGTGTGTGCCTGCGTAATCTGCC
ATGAGTGTGTGCCTGTGTGTGAATGGGTGTTACGTGGGGAGGGGGGAGGGCGGTGCGTTC
ATGTGTGTGTGTGTGTGTGTGTGTGCCTGTGTGCATGTGTGTATGAGAAACGTGCTCC
TGCCAGGAGCTAGACTCTTCATTTCCCATCCTACCAAGGACACAGCTCATCACAGCAACC
CCTCCGCCTACCCCAGCCCACTCGGGTGTTCCTCGAGCACTAGCCCAGATCTGCCTTCTT
TCGTTCTCTGGGTATAAGAAGGAGCAGAAATTTCTTCTCTGTTTCATGGCGAGTCTTCAT
CTTCACCATTATTCTTAACAGATCATTTTGGGGCCCCGACTCTGCCATGTACTGGGCCAA
CCACTGAAGGGCTTGCCTGGCTCAGCCAGAGCCTGGGCCAGAGCAGGACTAGGAACTGAG
CCCACAGGCCTTGGGGAAATCACTGCACTTTTTGGAGGCTTGGTTTCCTCATTGGTTCTC
AGTTTCCTCACGGGCATTCTAAAATTTTACCTGGAATCTAATTTACAGAGGTATGGCTGA
GTGATAACACAGGGAAGCCAGTGCCATTGGGAAGAGTTTAACGTGATACACAATGTCCCT
AGAAACCAGATGCTCAGCCCGCCATGTGGGGTGCAGGGGGAAGCAGCAGGCTTGGGTCAA
GAGTCAGAATCAGGGGTGAGGGAAAGCCCAGGCTACAGCCCTGTTGGGGCTCCCACAGGA
AGTGCAAGGCAGGGCAGATTAAGCAACCTAGGGTTGGCTAGTCTCAACATCCTGGCAGGC
TTTGGGCTACAGGGGTGATCTCTAGTTGTCTCTCTGGTACCTGAGATAATTTGGGACAGG
GGAAATATTGTCTTGGTGTGTGTGTGAATTAGAGAAACGGGGTGGCTGGCTTGCATTTGA
GAGGCATCCTTCCAAGTCAGTCATTTTCTGTCTTCAGGAATTAACTAGCTCTGGGACAGT
AAGTCTCTCTCTGGGTCTGTGAGGCTCCCAAGTGCCAGAATATCAGGATCAGAGAAGATA
GAAAAATATAGTCAATATAGGTGTCTCTGTGATGAATGGGTGCCAAATACACAAATACAG
AATCTAAGAAAACACATGGGGTTAACAAAGGTTGCAGAGATTAAGGTTTAAAGTTGAGGC
CCTCCGTATAAGTTGGCTGTCTTTCTTCTAGCACAGTAATTGGCAATAAGTGGTCTTATG
TATCTGGGAGAAGATAAGCGAGGGGCAAGGGCCTCAGACACCCATGGGCATCACTCCCCA
CACCCCAGCTGGATGCCCACAAGACTTGCAGCTGCCTCCTGAGTCTGTGGCCTCATCGGC
TCCAGGAGTACCAGGCTACAGGACCTAAGCTAATCTCCCACTCCTGCTGTCCATCCATTA
TGTTGCTTTGTCCCCAGGTGGTAGGTGAGTGGAAATTCAGCAGGATTCACTGTGACATCT
TCGTCACTCTGGACGTCATGATGTGCACGGCGAGCATCCTGAACTTGTGTGCCATCAGCA
TCGACAGGTGAGCCCAGCCAGGGTGGAAGAGGTTGCTCTGGCCACTCACCATTCTGGCTG
CCCCAGCTTTTCTCAAAGCCAGGCTGTGTCTCGTGTCTGTGATGCTGTGCAGCTGGCTGT
GTGCATGGGGGTCCATGTGTTTGTGTGTATGGGTGTGCATGTGTGTATGTTTGGCTAGGA

GAGCACACACTCCCTAAAGAGAAGCCATCTATGGACAGTGATGCTGCCAAGCATACTCAG
ACAGTGACTGGTACAAAAGGGGAAAGATTGTGATTCTGACGGAAGCCCTAGCTCTAGCAC
ATCTTACTCATGTGACCTTGGGCAGATGATGGACGTTTTCAGAGCTCTCAGTTTCATTTT
CTAGAAACCTACATTGATGACACCTGTGGCCTGGAGCTGCAGTATCTGGTTATGCATTTT
ATGTCCTTGGCACATGGCCAAGGGTCCCAGGCCATGCACACCTTGCTAAGCTGCATCCTT
GGAGCCTTCCACTAATTTGCACAGATATGACCCTACCTCCCTCACACCATTCTTGGAAGA
TGAAATAAGTTAATGAATGAGAAGGGCTGGGTAAAAAAAAAAATGTGATGAAGGATTGTA
GACAATTGCCATTGTTATTTCCTGCTAACTAAGGCTTAAATCTTGCTCTGAGGGGCCTGG
CTAACAATTTATCAACAAACATTTCCACCTTATGGGCTCAACACAAGTGCAGTGGGTACA
GTTTCAAAAGTGCAAAGATGCAGGCCATGGTTCTTCGAAAAGCCTGAAATCCAGGTGGGG
CCGGTTAGAATAATAGATATGAGCTAAGAGTAAACAATAGCTCACCAGTGATTAAGTGTT
TGGGCTTTGCCAACTGTCCTCGCCATCTGAGTTTGGGGACAGGAGGGAGGGTTGAGTTAG
CATCTCAGGCAAGCTTCATAGAGGTGTGTCAACTGTTTAGCCCCAAGGAGTGAGGGTGTC
TCTGGTGTGTGCATATTGTGGAGTGAGGGGTCCCTGGGCCTGCACCCCAGATTCAGGGTC
CCCCGCCCTTGCAGGTACACAGCTGTGGCCATGCCCATGCTGTACAATACGCGCTACAGC
TCCAAGCGCCGGGTCACCGTCATGATCTCCATCGTCTGGGTCCTGTCCTTCACCATCTCC
TGCCCACTCCTCTTCGGACTCAATAACGCAGGTACATTCTGCTTTTGTTTGCCTGAGGCT
CAGCTGGCCCTGGGCCCCTGCTCCCTCGAAGGGCCCTGAGGGAGCAGAGTCCCTGGCACA
GATATGGGTGGAGGCCCAATGGAGGCCTATCACTACCCTGGACTGAGTCCAGGCTACGTG
TCCTGGGCCAAGCCCCACTCAAGAGTTGTTCTAGGTTGGCAGAGAGGAAACAGTGGCCCA
GGACACAACGGAGTTGGATGAGGAGTGGGGATAATGGTTCAGGGGTATGTCTGGGAATTT
TCAACTTTGGTTATTAAGTTGAAGAGGCAAGACGTGCTTCACAAACTGCATGTGTGTATA
TGTGCACATGAACATGGGATGGCGGAGGCTACTGGGCTTCCATCCACTCCTGACAATAGT
ATTTTTGTAATGAAGCTGCAGCCCTCAGGGCCTGCTAAACCCAGGTCAGGCCTTAGCCAC
CTGGAGCAGGAAAGCTAGAAGTGAATAGGAGGTAAGCTGACCACATGCCCATTTCTGTGG
GAGGCAGAGTCAGGAGTGTCTCAGACAGAGGCAACACAAAGCCCCCGCCAGCGTGGAACT
TCCTCTCATCAGGGAGGCAAGAGCGATGGCAGGTGTGCACCTCTGGAGATCGTAACAACA
AAAGATACAGTGAAGCCTTGAAAATGTGTGGTTCGGTATCTATTATAAGCATCACAGGAA
TTCTAAGTGGGAATAACACTAAACATACTTGGATTAATGCACAAGGCCCTGAGATAGAGG
ACAGGCGTCTGGTAGACCTAGAAGGGCACGCAAACATATGAAACACATAGGAACACAAGT
GAGTTCAACAGACAGAGCCAAGTTATCTTGCTGCAAACATTAAAAGGTGGCCAACCTCTC
CCAATACACAGGTCAGACTAAAAAGATGGTTTACTCTTTTAAAAGTTTTCTTGTGTCATT
CTTTCTGGATACATCGGCTTCACTTGTTATGCCCAGACATGGCAAAACTAATGACCAAGT
AATGAGGGAATAGTAATGGAAAGACTTGGGAGCAGTCCATCATCACAGCTTAACTTTTTG
CTCACAACCGTGTTTTTAATACTCTGGTATCTGCTGTGCGTTTGTGTATATCTAAGATGA
CCAGGCAGCCTTAAACATCTAGTTGCGTTCATATTCTCTGTAAAATCGCTCCTTGTTCCT
GGAAGGACATGAATGGGCTCTTGTGGAATTATGGCCGGTGGGCCCGCTGACTCCCTGCCT
GCCCGGGCTCTCCCTCCCCCAGACCAGAACGAGTGCATCATTGCCAACCCGGCCTTCGTG
GTCTACTCCTCCATCGTCTCCTTCTACGTGCCCTTCATTGTCACCCTGCTGGTCTACATC
AAGATCTACATTGTCCTCCGCAGACGCCGCAAGCGAGTCAACACCAAACGCAGCAGCCGA
GCTTTCAGGGCCCACCTGAGGGCTCCACTAAAGGTCTCAAGACACCCCCCAACCAACTCC
AAGGGTCCCCACCTAACCATTACCAAGAGGGCTCATCTTATGCTCAGGTGGGGGCTTGGG
AAACCTCAGCAAGGGTTAGGTCTAGGCTAAAGGAATTCCCAGGAGCCGGGCAAGGGCAGA
TTTTGAAGGCATGGACCTCAGTGGAGCAATCTGAGTCTCCAGGAGAGGGAGGCAGGGTCC
ATGACACTAAATAACAAGGGGAAGTCTTTGCTTGGAGATCTTTGTGACTGAAGGCGGCAA
CTCTTGCTTGGTACCCCCGTGGGCTCCTCTCTTCCTCTTTTCTGGTTTCTCTGTCTCACT
TTAGCTCCCTCTGACTCCTCCATCCTCTTTCCTTTACCTTCCGTACTCTCTGTCCTCCCC
TCCAAACACACATCACTTTTCCTGACTTCCTCTCCACTATGTCTCTCCTGTGCTTCTCTT
TCATTTCCCCCCTGATGTCTTGTGAATTCTCCCCTTCACTCAGTCCTTCACAAGGAAGAC
AGTGTGTGGGCACAGAAGGAACAAGAGCTCTTGGGCTAGACGCATCAGGTTCAGATCCTG
TCACTGACACTTTTTTTGCTGAGTGACCTTAGGCAAGTTGCTTACCTTCTATGAGCCTGT
TTCCTCATCTGTTAAATGGGAATCAAAATACCAGCCTCACAGGGTGGTCTTGAGGATTCC
ACGTGAGAAGGGACGTGAGTGTGCCTAGCACAGTGCCAGGCCCTTAGCAGGTGCTCCATA
AAAAACCAGGTCCTTGTGTTCCTCGTCATACCCACCACTTTTTGTCTCATTCCAGCCTTC
CCCCTTGCCCCAACTGCCTCCTCTGGCCCCCACCCTCCTGATCTCTGAGCCCTTCTGCCC
AGTCTGAGTTCCATGGACTGCTGCACTTTGGGTTTCTGTCCCCCCTCCATCCCCACCACT
TTGTGTGACCCATGTGCTGGCTCACTCCACAGGGCAACTGTACTCACCCCGAGGACATGA
AACTCTGCACCGTTATCATGAAGTCTAATGGGAGTTTCCCAGTGAACAGGCGGAGAGTGG

TAAGTGCTCAGGCCAGGGACCCAGAGCCAGGTCTTTCTGCCCCTAGGGAAGCCCACTGGC
CATGGTTCTGAGACCTCAGAAGCTGGCCAATGGGAGAAGCACCCCAGAAACCCCCACCTT
GCCTCAGCTGAAGGCAGACTCACCGTGCACACCTCCAAGCAGGCATGAAGTGAGACACCT
CGGTTCTGCAAGGCATGGATGTGTACGAGAAAATGGTTGGCCATACCAACGTAATAAAAA
TGATAATAATGGCTATTCACATTTCTCAAACATCTACCATATCCCTATTATCTCATCAAA
TCCTCACCACGACCCCGGGAGGTAAGTCTCTTTGATCGAACCGATCTTCAGTTGACAGAA
GAGGAAACAGGCTCAGAAAGATTAGGCAACTCACCCGTCTCAAGAGTTGGTGACACTAAG
CCCAGACCTGTGTGACTCTGAAATCCACACCTGTGTTCTTTCCACTGACATGAGCTGCCT
TATGGATGGGCAGGTTCTGGGGTAGGACGCAGCAGAGCAGCTGCGGGGACTGGTGGCGGA
GCAGTTTGTGTACATAGAGCCCTCAGGTGCGGAAGCACAGCAGACCCCAGCCTCTGCCAG
GTGGTAGCTGTACCAACATGCAAGCAGCAGGCATTCCATCCTCCAGAGGGATGGAGAACA
GGGCCAGAGAACCCACAGAGGGCCGCATACAAAATCCAGGTCTGGTGTCCTGCCTTCACC
TGCACTGCAAGGGCAGGACTCTAAGAAGCTGTTTATGAGGCAGGTGCCAAAACAGAGCCT
CAGAGTCAGGGCCAAGGCAGCAGCCCAGTCATGCCACCTAGGCACATAGTGAGGCTGCAC
TTTAGAAGTTCAGACTAACACCTCCAAGGCCTCAAACAAGAGAACCTATGGAAGAACCCA
GGAGGCCATGAGTGGATCCATGCCAGGGCTCTCTAGGTCACCCCAGCAGGGAAGATGTGG
GGCCCCAGGGGTCAGCCTTTTGGCACCTAGATTAGTCTATCCAGGAGAATATGGAGCCCA
CGTGTGTACGCAGGTGCAGGTACCCATGAAGTGGGAGCACTGGGCCCCTTGTTTGACAGG
GAGAACAGGGGTGGGCACCCTCTTTGCAGTCGGAACATGAGTTTCTGGAGGCAGGGCCAA
ACATCATCAGCTCTTGACCCCAGCAGCCACTGTGGCACCTGGCACTTTGCTAACAGTAAG
TGTTGCTCAGGCCATGAGAGACAAGTCCCTGGTATTCAGCCCTGGCAGAACAGAAGTGGG
GTATTGAGGCTGCATGAGGATTGCCATGGGAAAAAGGACAGGGGCAATCCTGCAGGGGCT
GCCATGGGTCCTGGGTCCCATGCCTCAGTGACATCCTTGCCTCCCTGGCAGGGTGACCCT
GTGGTGTTTGCAGGAGTCTTCAGAGGGGGAAAGGGAGGGGCCAGTGAGATGGGTGGCTGA
TGCCTGGGAACTTGTCCGGCTTTACCCAGAGCCCTCTGCCTCTGGTGCAGGAGGCTGCCC
GGCGAGCCCAGGAGCTGGAGATGGAGATGCTCTCCAGCACCAGCCCACCCGAGAGGACCC
GGTACAGCCCCATCCCACCCAGCCACCACCAGCTGACTCTCCCCGACCCGTCCCACCATG
GTCTCCACAGCACTCCCGACAGCCCCGCCAAACCAGAGAAGAATGGGCATGCCAAAGACC
ACCCCAAGATTGCCAAGATCTTTGAGATCCAGACCATGCCCAATGGCAAAACCCGGACCT
CCCTCAAGACCATGAGCCGTAGGAAGCTCTCCCAGCAGAAGGAGAAGAAAGCCACTCAGA
TGCTCGCCATTGTTCTCGGTGAGTCGGCCCTGGCTGCTGGCCACAGCCCGGTCTGTGAAA
GGTCCCATTCCCTGCCATGTCCTTCCTAACCATGGCTGCAGGATCATGGGGCTAGCATTT
CCTCAGGCACAGGCCAAGCCCATTGACATACAGACAGCCCTATTAGGTAGATTCTGTAAT
TGTGCTCACTTTACAGATGGGCAAACAGAGTTTTAGAGTGGTTATAAAACCTGACCAAGA
GGACCCATGGTTTGAACTCAGGCAGTCTGACTCCAGAGTCTGGAAATTTGACTAGTCTAT
TATGCTGGCACCAGAACCTCATGGGCCTATGTGCCCAGGAAAGTCACTTTCTCTCTCTAG
GCTCCTCATCTGTAGAGTAGGTTACTTCTCAGGGCTGTCATGGCAATCAGTTGGTGAAAG
CATTTTCTAAACTACAAAGCACTATCCATATGTAAGTGTCACTATTATGGTTTTTATTAC
TATTGCTCTTTTTGAGGAATTGGGAAATTCAGTTCACTTGCACTCAAACAAGACTCCATG
GGACCAGAGCTGTGAAAAATAAATGAGATGTTGGGGAGTGGCCCCCAATCTAAATGAAAA
GCATCCCTGTCCATAAAGCAGGATTTTTCAATAGAAGTCTAGAAAACCACATAGTAAAGG
TCAAAACCCAAAAGGTGGACTGATATGGGTGGCTGGGAAAAGGAGGGTCCCCTGTGACTC
TGTCTTCCAGGAAGCACCTGAATCCCCTTTGACTGCCGGATGATCCTGGGGCGTGAGTGG
GGCAGCTGTTACCTCCCTTCTTTTATGAATGAGAGCACTTGATCCCATGGGACTACTCAC
GATCATGGGACTGGGATATGGTAGGCTAGGATTGGAGCCAGGCCCTCTGCTGCAGTCCAT
AGGGGCTCAGCTCTGTGGCCCTACTCTTCCCAGACACCATTCAGTCTCCAGGGATGCCTC
CTGTGCCTGTAGGGCATTCCATGTACACATTGCTTCCAGGATAAATATCACACCTGTGCA
GGAGGTCCTGGAAAAAGTGCACCTGAGTTAGGTGAGCAGAGCAGGTAGGTGGCTGCCCTG
GGTGAGAGGGCATGGTTCAAGGCAGGGACTAGCAAGGGTGTACCCACCAAGACTGGGGAA
ATTGGGGGAAGGCTAGAGCGAGATCATCTGGGGACCTGGATAGACCGGAGTTCAGCTCTC
AGCCTCGCTGCTCAAGAGTGAATGACCTTGGGTATATTGCAGAGCTGTTGTGAGTGTTTT
TCTTATGTACCTTATGAGGATGCTATAAGAACTAAGTGGCATGGGTCTATAGCCCTCAAA
GATGACCTGGAAGTAGAGTAGATATTTCCATTTCTACTGGCTAACCTGGGTCAGAATGGT
AACCTTTTGGATTTATTGTTAAACCATGTACCCTTTTCTAGGAGGTGGGAAAGGGACAAA
TGAGGGAAGTGAGGCTGAAGGAGCTGAAGGGATACTTCACTGCAAATGGGTGTCAGAGGC
AGGTCTAGGATCCAAGACCTGGACTCCTCCTACAGTGCTTCTGTGGCTACAGCCCACCGT
CTTGGCATACGAGCCAGGGCGCACTGGGTGTGGGTGTTCCCAGCCGTGCCTCCCCGGCTC
TGGGGACCAGCCTGACCATGCCCTCTCCCCCAGGCGTGTTCATCATCTGCTGGCTGCCCT

TCTTCATCACACACATCCTGAACATACACTGTGACTGCAACATCCCGCCTGTCCTGTACA
GCGCCTTCACGTGGCTGGGCTATGTCAACAGCGCCGTGAACCCCATCATCTACACCACCT
TCAACATTGAGTTCCGCAAGGCCTTCCTGAAGATCCTCCACTGCTGACTCTGCTGCCTGC
CCGCACAGCAGCCTGCTTCCCACCTCCCTGCCCAGGCCGGCCAGCCTCACCCTTGCGAAC
CGTGAGCAGGAAGGCCTGGGTGGATCGGCCTCCTCTTCACCCCGGCAGGCCCTGCAGTGT
TCGCTTGGCTCCATGCTCCTCACTGCCCGCACACCCTCACTCTGCCAGGGCAGTGCTAGT
GAGCTGGGCATGGTACCAGCCCTGGGGCTGGGCCCCCCAGCTCAGGGGCAGCTCATAGAG
TCCCCCCTCCCACCTCCAGTCCCCCTATCCTTGGCACCAAAGATGCAGCCGCCTTCCTTG
ACCTTCCTCTGGGGCTCTAGGGTTGCTGGAGCCTGAGTCAGGGCCCAGAGGCTGAGTTTT
CTCTTTGTGGGGCTTGGCGTGGAGCAGGCGGTGGGGAGAGATGGACAGTTCACACCCTGC
AAGGCCCACAGGAGGCAAGCAAGCTCTCTTGCCGAGGAGCCAGGCAACTTCAGTCCTGGG
AGACCCATGTAAATACCAGACTGCAGGTTGGACCCCAGAGATTCCCAAGCCAAAAACCTT
AGCTCCCTCCCGCACCCCGATGTGGACCTCTACTTTCCAGGCTAGTCCGGACCCACCTCA
CCCCGTTACAGCTCCCCAAGTGGTTTCCACATGCTCTGAGAAGAGGAGCCCTCATCTTGA
AGGGCCCAGGAGGGTCTATGGGGAGAGGAACTCCTTGGCCTAGCCCACCCTGCTGCCTTC
TGACGGCCCTGCAATGTATCCCTTCTCACAGCACATGCTGGCCAGCCTGGGGCCTGGCAG
GGAGGTCAGGCCCTGGAACTCTATCTGGGCCTGGGCTAGGGGACATCAGAGGTTCTTTGA
GGGACTGCCTCTGCCACACTCTGACGCAAAACCACTTTCCTTTTCTATTCCTTCTGGCCT
TTCCTCTCTCCTGTTTCCCTTCCCTTCCACTGCCTCTGCCTTAGAGGAGCCCACGGCTAA
GAGGCTGCTGAAAACCATCTGGCCTGGCCTGGCCCTGCCCTGAGGAAGGAGGGGAAGCTG
CAGCTTGGGAGAGCCCCTGGGGCCTAGACTCTGTAACATCACTATCCATGCACCAAACTA
ATAAAACTTTGACGAGTCACCTTCCAGGACCCCTGGGTAGAAGGCAGCAGTGCCACTTCT
GTGCTTGGCATTCAAGTATAGCAAGACCCCTGTGTCTGCAGGGTCTAACCCAAGGGAAGC
CAGGTTGCCCCCACTGCTCCACCTCCCCTGTTGCAGCTCCTGCTTCCTCTGAAGGACTCA
TCCTTTGCCCTCTTACCCACCAGGGCAGAGAAGGCTCTGTGGAAAAGGTGGCCTTGGATG
CACTGGCATTGCCTGTGTCTGCCTATGTCCCTTGCCCTGTCTTCTGTCCCATGTCAGGAT
CCCCTTCCTCTAGGGCAGGCTGGGAGAAGCAGGGAAGGCCCTGACCACTGCGGCCTGGAC
AGTTCTCCCTCCTCTCAGCTTCCAGGCCGGTCCCAAGCTCCAAGCCTTCCGGGGCAAAAA
CTTGGTACTGCCCCGACAACAGAAACTTGGCTTTCTACAAATGAAGCGTAAATCAACCCA
GTGAGGGAGGAATATTCTTACCACCTTGAGAATAACCGCAGTGATGACAAACAAGGTGCC
AGCACCCACGGGCTCAGGCGCTGGGGAGCTGTCAGGGCGTAATTTGCATGCTAAATACAA
TATTTTTAGCACCAAAGTT -3′

Key:

: Exon : Primer amplification region

: rs1800497 : nitrogenous base mutation

Appendix G

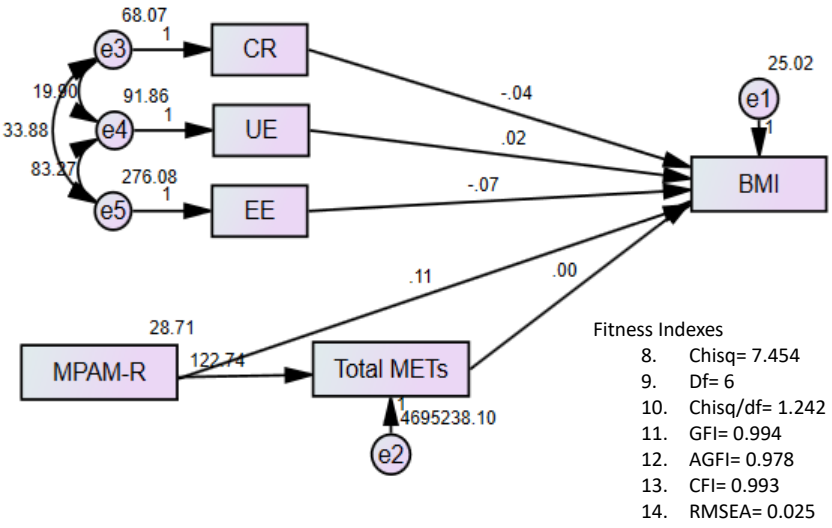


Figure: Path analysis study of eating behaviour, MPAM-R, Total Mets and BMI

Unstandardized Estimates for Taq1A Wildtype (A2/A2)

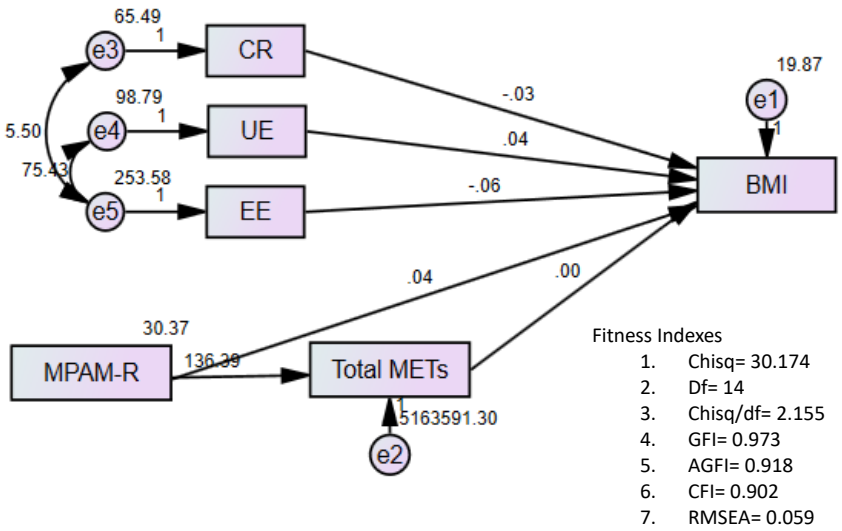


Figure: Moderated Mediation for *Taq1A* Wildtype (*A2/A2*)

Unstandardized Estimates for Taq1A Heterozygote (A2/A1)

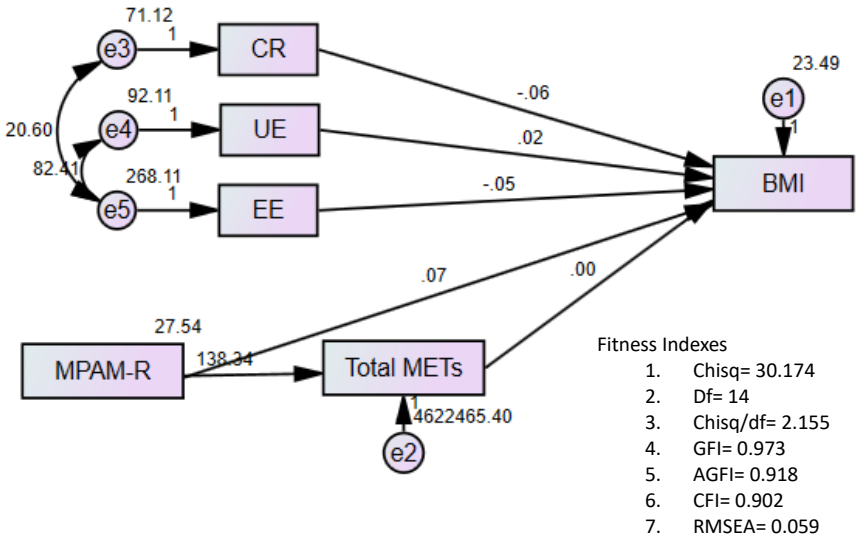


Figure: Moderated Mediation for *Taq1A* Heterozygote (*A2/A1*)

Unstandardized Estimates for Taq1A Homozygote (A1/A1)

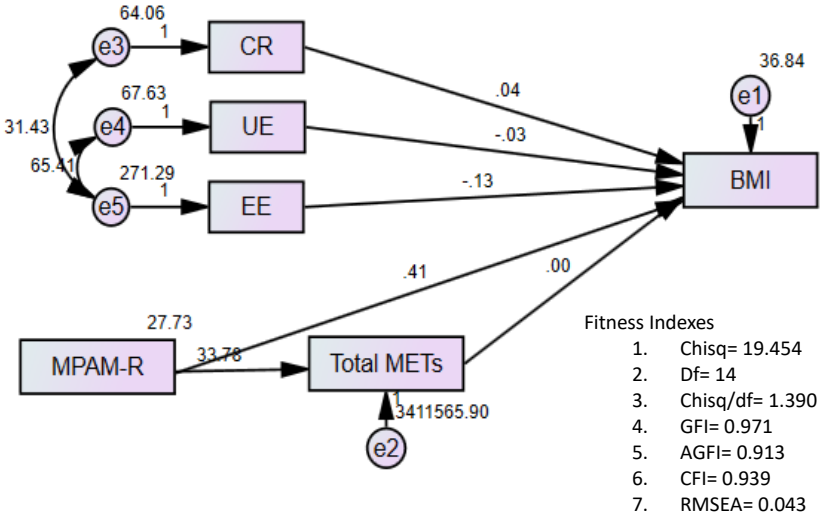


Figure: Moderated Mediation for *Taq1A* Homozygote (*A1/A1*)

Unstandardized Estimates for Taq1B Wildtype (B2/B2)

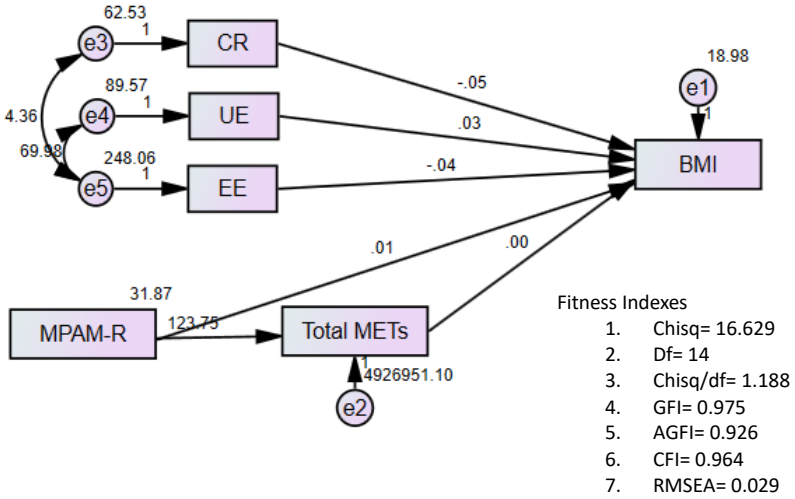


Figure: Moderated Mediation for *Taq1B* Wildtype (B2/B2)

Unstandardized Estimates for Taq1B Homozygote (B1/B1)

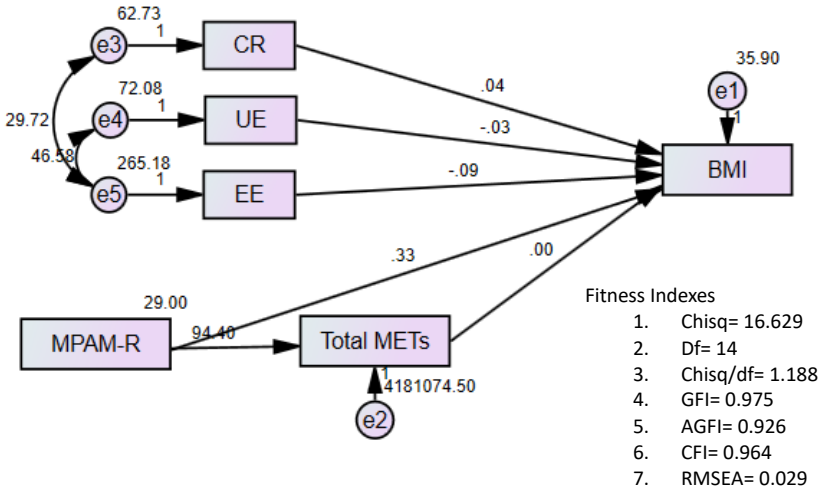


Figure: Moderated Mediation for *Taq1B* Homozygote (*B1/B1*)

Unstandardized Estimates for Taq1D Wildtype (D2/D2)

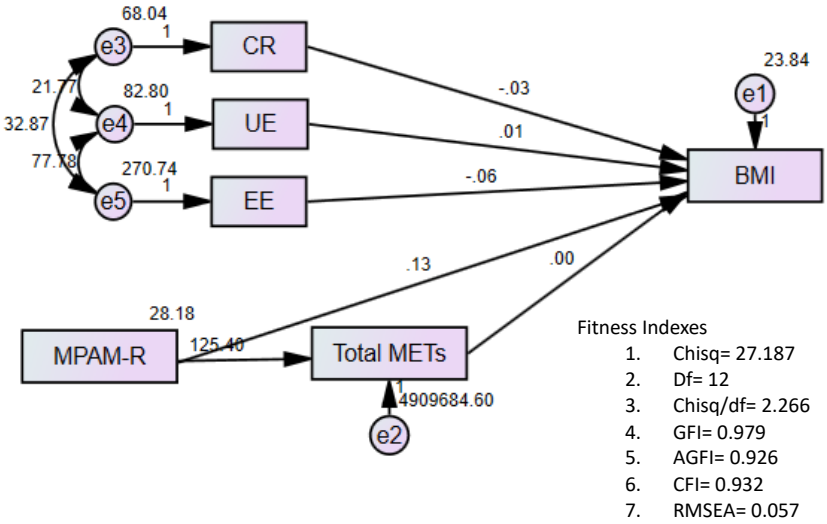


Figure: Moderated Mediation for *Taq1D* Wildtype (*D2/D2*)

Unstandardized Estimates for Taq1D Heterozygote (D2/D1)

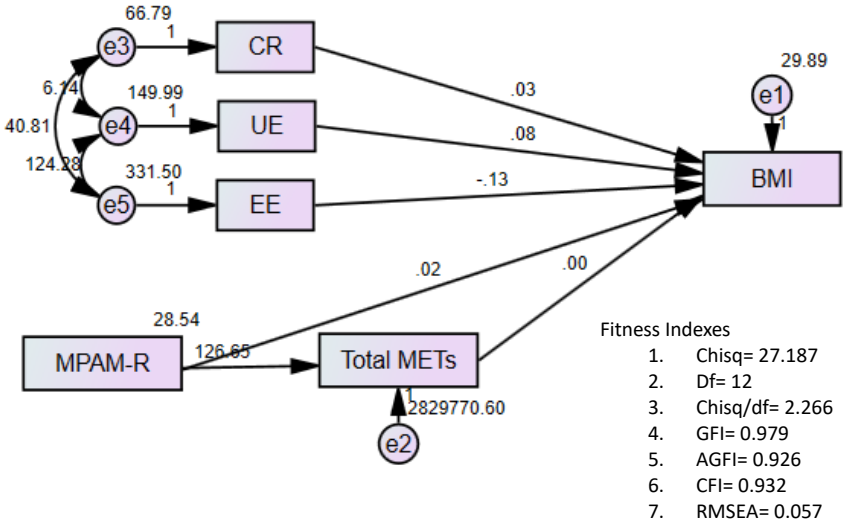


Figure: Moderated Mediation for *Taq1D* Heterozygote (*D2/D1*)

Unstandardized Estimates for Taq1A allele (A2)

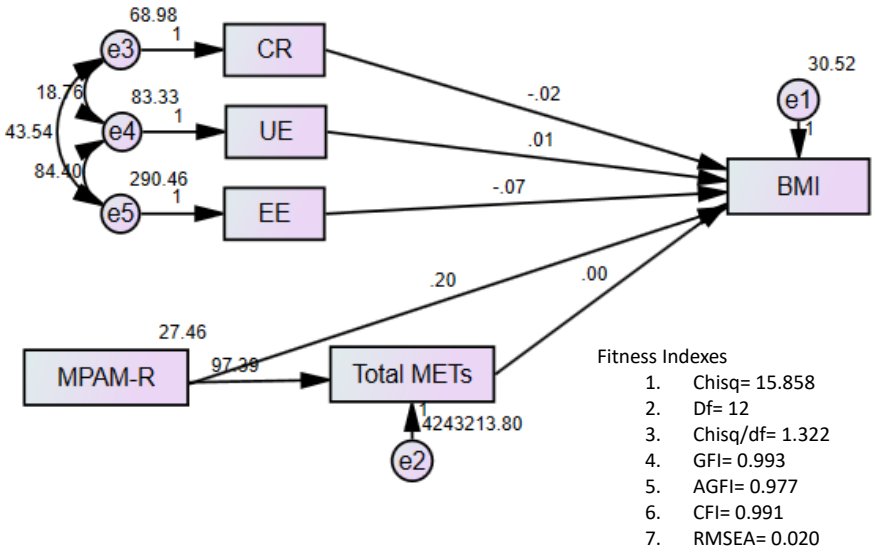


Figure: Moderated Mediation for *Taq1A* allele (*A2*)

Unstandardized Estimates for Taq1A allele (A1)

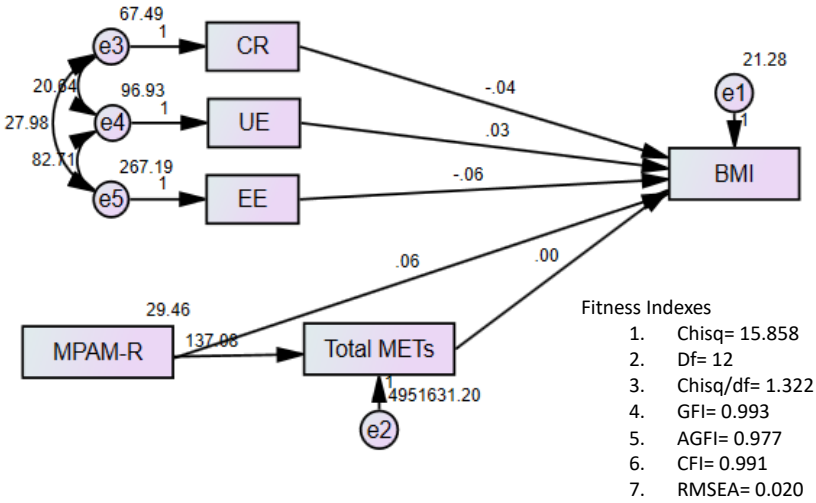


Figure: Moderated Mediation for *Taq1A* allele (*A1*)

Unstandardized Estimates for Taq1B allele (B2)

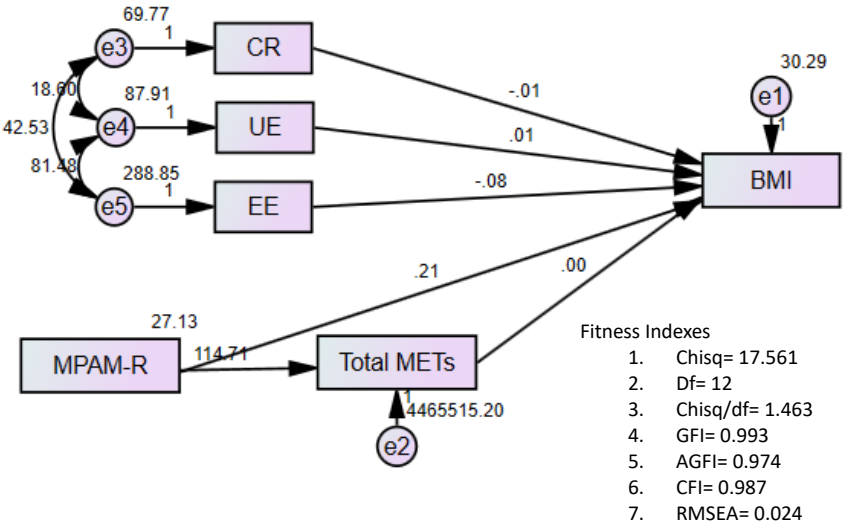


Figure: Moderated Mediation for *Taq1B* allele (B2)

Unstandardized Estimates for Taq1B allele (B1)

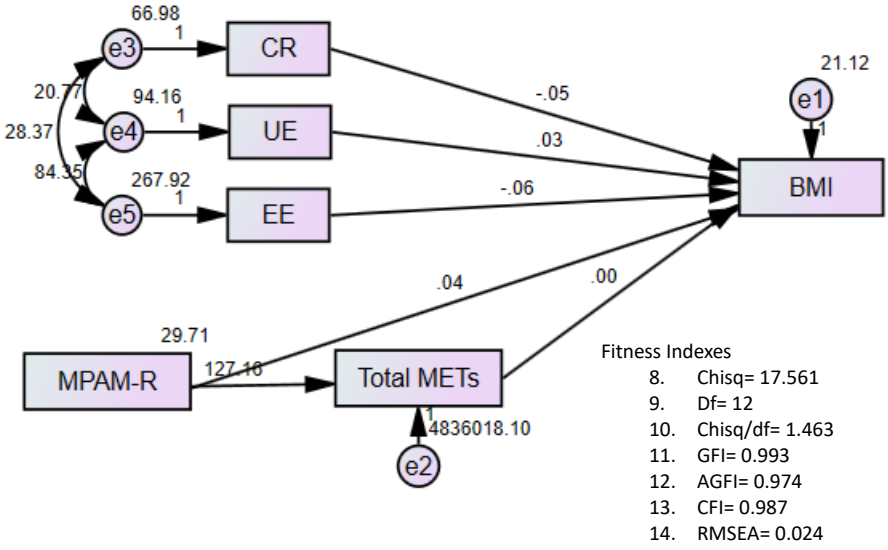


Figure: Moderated Mediation for *Taq1B* allele (*B1*)

Unstandardized Estimates for Taq1D allele (D2)

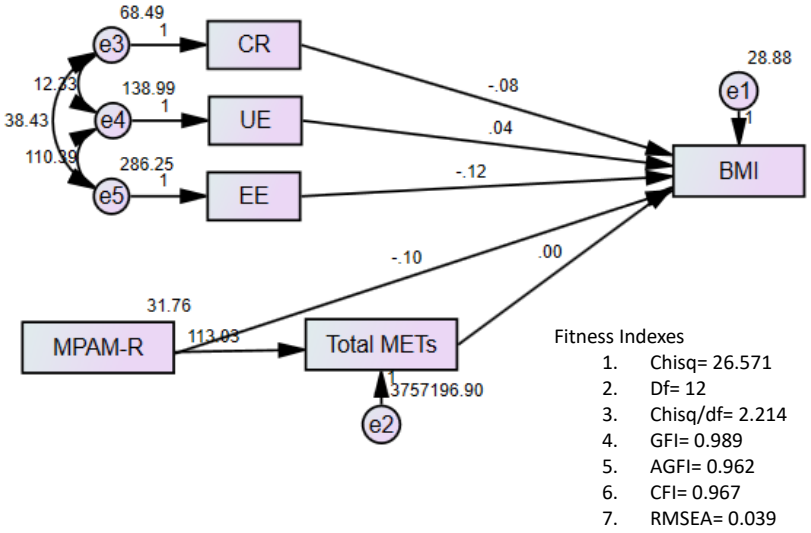


Figure: Moderated Mediation for *Taq1D* allele (*D2*)

Unstandardized Estimates for Taq1D allele (D1)

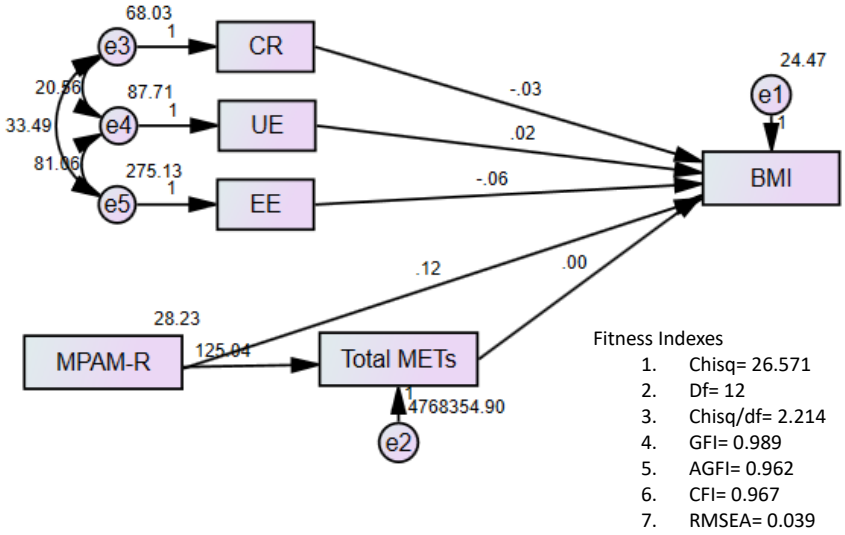


Figure: Moderated Mediation for *Taq1D* allele (*D1*)