Genetics of human obesity

Ahtesham Hanifi
School of life sciences, department of Life Sciences, Central University of Tamil Nadu, Thiruvarur, Tamil Nadu, India

***Abstract*— It has been found that there is a genetic component behind obesity. Genome wide associated studies successfully revealed that there is a variety of gene locus associated with more common form of obesity. New approaches for data analyses and advances in technology will be required to uncover the elusive missing heritability and to aid in the identification of the key causative genetic of obesity.**

***Index Terms:* Obesity, Body mass index, BDNF, Proopiomelanocortin (POMC), Melanocortin-4 receptor (MC4R), Chromosomal inversion, Leptin**

INTRODUCTION

Excessive accumulation of fat in the body that impairs human health is known as obesity. Fat performs many advantageous function in our body such as: stores food, provides warmth, good for vitamins (fat soluble vitamins- vitamin A,D,E &K), protects body from mechanical injuries etc but level of fat is above the required, it impairs our health.

Required fat percentage for healthy lifestyle is:
For man = it should be 2% to 4% , above 25% it is considered as obesity.
For woman= it should be 10% to 13%, above 32% it is considered as obesity. Most common methodology used to measure the fat content of body is body mass index [B.M.I]. It is a ratio of body weight (kg) to the square of height of person (m^2).
B.M.I = weight of person (kg) / square of height of person (m^2).
Unit = kg /m^2.
BMI is a comparative index, it doesn't provide accurate information regarding fat content but it gives comparative information between overweight and obesity. An adult with BMI ranges between 25 to 30 is considered as overweight while BMI equals to or greater than 30 is considered as obese. Ancient Greek physician Hippocrates was first that recognised the obesity as disease and stated that sudden death is more common in those who are naturally fat than in the lean. Nowadays, phenotype of obesity is increasing rapidly and becoming serious health issue globally, because of high calorific food intake and relatively sedentary lifestyle of modern times. This phenotype is seen more common in industrialised countries. United States of America ranked top in most obese nation. Many serious medical condition such as type-2 diabetes (NIDDM= Non Insulin Dependent Diabetes Mellitus), hypertension, cardiovascular disease, stroke and physical disabilities are related with obesity.
Evidences for genetic component of obesity
According to twin study it is found that there is much greater resemblance in degree of obesity between genetically identical monozygotic twins. This is much used model to study genetic component of obesity. As we know monozygotic twins are genetically identical hence genetic material shared between them is above 90% while sharing of genetic material between non-identical dizygotic twin is 50%. Hence, content of fat mass in monozygotic twins ranges from 70% to 90% while in dizygotic twins the range is in between 35% to 45%. Another model used for study is adoption study. According to this, adopted children have been shown to have weight much more similar to the weight of their biological parents than those parents who adopted that child.
From above mentioned findings, it is concluded that in determination of BMI, genes play major role.

Monogenic obesity model
Model based on single gene disorder that exhibit the feature of obesity, it is known as monogenic obesity model. This model is useful in various study regarding obesity in rodents as well as humans. In 1950s ob/obmutant strain of mice was described having excess adipocytes and weight is three times more than normal mice along with impaired

reproductive behaviour. A gene 16-kDa is known which code for leptin Called leptin gene (lep gene), was found in this mutated mice. Normally leptin suppresses hunger but this mutated lep gene increases food intake and organism become obese. This lep gene is also present in humans. Homozygous reading frame shift, series of missense mutation and number of polymorphisms are included under leptin mutation.

Homozygous reading frame shift mutation causes skipping of exon 16, which produces truncated protein due to this it lacks transmembrane and interacellular domain so secretion of impaired growth hormone takes place which causes early onset of morbid obesity and pubertal development failure, while polymorphism mutation causes obesity in caucasians. Proopiomelanocortin (POMC) produced by hypothalamus and plays role in feeding behaviour. Leptin positively regulates the expression of POMC. An early onset of obesity is caused by frame shift mutation in POMC gene.Proteolytic cleavage site present in between beta- MSH and beta-endorphin, distrupts by R236G mutation in POMC gene. It causes production ofabberant fusion protein which has lower binding capacity to Melanocortin-4 receptor (MC4R) hence severe and early onset of obesity produced, because MC4R plays an important role in controlling of effects of leptin. There is a brain-derived neurotrophic factor (BDNF) and its receptor tyrosine receptor kinase B (encoded by NTRK2) used to regulate eating behaviour and energy balance. Mice develop obesity and hyperactivity due to conditional knockout of BDNF. According to study, it is revealed that chromosomal inversion leads to loss of one functional copy of BDNF which results into increased food intake capacity and hence severe early onset of obesity takes place.

CONCLUSION

From the above study, it is concluded that genetics plays a very important role in obesity. Earlier it is known that obesity is only caused by intake of high calorific junk food but now it is changed. How leptin and its mutation puts the effect of it on our health also revealed. Especially the monogenic obesity model clearly tells us that there is a different types of gene and mutation that changes the nature of leptin and person becomes obese.

REFERENCE

[1] Chadwick, JMW Medical works of Hippocrates. Blackwell scientific publication. Boston, MA.

[2] Reaven, G.M 1998. Banting lecture 1998. Role of insulin resistance in human disease. Diabetes 37: 1595-1607.

[3] DeFronzo, R.A& E. Ferrannini. 1991. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity,hypertension, dyslipidemia and atherosclerotic cardiovascular disease. Diabetes Care 14: 173-194.

[4] Haslam, D.W& W.P James. 2005. Obesity. Lancet 366: 1197-1209.

[5] Must, A. 2003. Does overweight in childhood have an impact on adult health? Nutrition reviews.61: 139-142.

[6] Seeley, R.J. et al.1997. Melanocortin receptors in leptin effects. Nature 390:349.

[7] Houseknecht, K.L et al. 1998. The biology of leptin: a review. J .Anim. Sci. 76:1405-1420.

[8] Halaas, J.L. et al. 1995. Weight- reducing effect of plasma protein encoded by the obese gene. Science 269: 543-546.

[9] Chua, S.C., Jr. et al. 1996. Phenotype of mouse diabetes and rat fatty due to mutations in the OB(leptin) receptor. Science 271:994-996.