Gene Ther Mol Biol Vol 13, 91-129, 2009

Genes and Happiness

Review Article

***Kenneth Blum[1, 4, 5,10], Amanda LC Chen[2], Thomas JH Chen**[2], Abdalla Bowirrat[3], B.William Downs[4], Roger L. Waite[4], Jeffrey Reinking[5], Mallory Kerner[6], Dasha Braverman[6], Nicholas DiNubile[7], Patrich Rhoades[8], Eric R. Braverman[5, 9], Stella M. Savarimuthu,[6] Seth H. Blum[10], Marlene Oscar-Berman[11], Tomas Palomo[12], Eric Stice[13], Mark Gold[14], David E. Comings[15]**

[1]Department Physiology & Pharmacology, Wake Forest University School of Medicine, Winston–Salem, North Carolina
[2]Chang Jung Christian University, Tainan, Taiwan
[3]Clinical Neuroscience & Population Genetics, Ministry of Science, Israel
[4]Department of Nutrigenomics, LifeGen Inc, San Diego, California
[5]Department of Rehabilitative Medicine, University of California Medical School, Davis, California
[6]Department of Clinical Neurology, PATH Research Foundation, New York, New York
[7]Department of Orthopedic Surgery, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania
[8]Department of Clinical Medicine, Modesto Pain Clinic, Modesto, California
[9]Department of Neurological Surgery, Weill Cornell Medical College, New York
[10]Department of Nutrional Genetics, Synaptamine, Inc., San Antonio, Texas
[11]Boston University School of Medicine and VA Healthcare System, Boston, Massachusetts
[12]Hospital Universitario 12 de Octubre, Madrid, Spain,
[13]Oregon Research Institute, Eugene, Or.
[14]Department of Psychiatry, University of Florida, Gainesville, Fl.
[15]Emeritus; Department of Medical Genetics, City of Hope Medical Center, Duarte, CA

***Correspondence: Kenneth Blum, Ph. D.** Department of Physiology & Pharmacology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, North Carolina 27157; Tel + 619-890-2167; Email: drd2gene@aol.com and **Thomas JH Chen Ph.D.,** Department of Engineering, Chang Jung Christian University, Tainan, Taiwan; Email: tjhchen@yahoo.com.tw.
Key words: Happiness, Genospirituality, Reward Deficiency Syndrome (RDS), Gene Map, Dopamine

Received: 22 May 2009; Revised: 25 May 2009;
Accepted: 31 May 2009; **electronically published: 4 June 2009**

Summary

Since the discovery of the double helix, the study of brain function, in terms of both physiology and behavioral traits, has resulted in a plethora of research linking these activities to the genetic basis of neurotransmitter function. Knowledge about how genes are expressed, as well as their potential impairment due to polygenic inheritance, can shed light on predispositions to addiction and self-destructive behaviors. Genetic information derived from scientific explorations of genetic traits may have important links to understanding the basis for feelings of well-being and potentially the phenomena associated with human happiness. While non-genetic oriented research of social, political, and biological studies have addressed the impact of social and institutional environments on mass political attitudes and behaviors, there is a paucity of solid research on the interrelation and influence of genetic and environmental factors on these parameters. The separate fields of psychology and molecular biology are subject to inherent limitations that may only be resolved through collaboration across disciplines. Certainly areas relating to spirituality ("Genospirituality") and political science are just two that are beginning to emerge as fruitful grounds for identification of specific polymorphic gene associations and may pave the way to advance a new science of human nature. We address the issue of *"Nature vs. Nurture"* as it relates to questions regarding the definition of happiness, its causes, and its promotion. These questions are central to understanding human nature and are emerging as an important target of research, especially in the area of nutrigenomics. The present commentary attempts to identify key "vector influences" that link genes, the brain, nutrition, and social behavior to a most desired, but misunderstood, and potentially fragile experience known as "happiness." Specifically, we propose that successful changes in body composition/body mass index (BMI)/ percentage of body fat will increase not only positive self-image, but overall wellness that produces a state of happiness. We provide preliminary evidence that utilization of a customized dopaminergic agonist LG839 DNA directed

nutraceutical, significantly increased happiness in obese subjects. We detail genotypes that may play a role in determining happiness, based on current knowledge.

I. Psychology of Happiness

For most of its history, psychology has concerned itself with all that ails the human mind: anxiety, depression, neurosis, obsessions, paranoia, delusions, etc., and the behaviors they produce. The goal of practitioners has been to bring patients from a negative ailing state to a neutral normal state. Or, as University of Pennsylvania psychologist Martin Seligman puts it, "from a minus five to a zero" (Seligman 2002).

In Seligman's' work he and his colleagues studied very happy people. In a sample of 222 undergraduates screened for high happiness, using multiple confirming assessment filters, they compared the upper 10% of consistently very happy people with average and very unhappy people. The very happy people were highly social, and had stronger romantic and other social relationships than less happy groups. They were more extraverted, more agreeable, and less neurotic, and scored lower on several psychopathology scales of the Minnesota Multiphasic Personality Inventory. Compared with the less happy groups, the happiest respondents did not exercise significantly more, participate in religious activities significantly more, or experience more objectively defined good events. No variable was sufficient for happiness, but good social relations were necessary. Members of the happiest group experienced positive, but not ecstatic, feelings most of the time, and they reported occasional negative moods. This suggests that very happy people do have a functioning emotion system that can react appropriately to life events (Diener and Seligman, 2002).

II. Happiness Characteristics

Over many decades, psychological researchers have begun to place more and more emphasis on understanding influences upon mental and emotional health and well-being. Some of Seligman's own research, for instance, had focused on optimism, a trait shown to be associated with good physical health, less depression and mental illness, longer life, and, yes, greater happiness. Perhaps the most eager explorer of this terrain was University of Illinois psychologist Edward Diener, a.k.a. Dr. Happiness. For more than two decades, Diener had been examining what does and does not make people feel satisfied with life. Seligman's goal was to shine a light on such work and encourage much, much more of it.

So, what has science learned about what makes the human heart sing? More than one thing you might imagine, along with some surprising things about what doesn't ring our inner chimes. Take wealth, for instance, and all the delightful things that money can buy. The age-old belief that people seek wealth to achieve power, which is then expected to produce pleasure and happiness, may be wrong. In agreement with Kahneman, research by Diener, among others, has shown that once your basic needs are met, additional income does little to raise your sense of satisfaction with life. How about a good education? Sorry Mom and Dad, neither education nor, for that matter, a high IQ paves the road to happiness. Youth? No, again. In fact, older people are more consistently satisfied with their lives than the young. And they're less prone to dark moods. A recent survey by the Centers for Disease Control and Prevention found that people ages 20 to 24 are sad for an average of 3.4 days a month, as opposed to just 2.3 days for people ages 65 to 74. The earlier notion – "where you live makes you happy", has recently been challenged by the work of North and others (North *et al. 2008)*. They suggest that happiness can change and underscore the importance of exploring more deeply the role that family relationships play in facilitating such change and this is not related to economic status (Wenz, 1977). Similarly, the idea that marriage increases happiness has been challenged by the evidence that married people may have been happier than single people because the former were happier to begin with. What about the relationship between sunny climate and happiness? Although evidence does not support this view, a 1998 study showed that Midwesterners think folks living in balmy California are happier, and that Californians incorrectly believe this about themselves too.

A. Genospirituality

On the positive side, there is "*genospirituality*," the coupling of genes and spirituality. That is, religious faith seems genuinely to lift the spirit, although it is difficult to determine whether it's the God part or the community aspect that does the heavy lifting. Charlton (2008) believes that it is possible that genospirituality could explain why some people are unable to have the kind of spiritual or religious experiences they want (or perhaps even need) in order to lead the kind of life to which they aspire. Further, according to Charlton (2008), "While greater religiousness may be associated with greater happiness, more altruistic behaviors and higher fertility (Stark, 2007), and these may turn-out to be significantly causal, it is possible that genetically-enhanced religiousness might lead to other problems. Perhaps churches would get too powerful and attempt to control science, technology, and the economy with disastrous effects. Or perhaps church members might become fanatically loyal and too easily manipulated into dangerous behaviors. On the other hand, it is also possible that highly moral, altruistic, peaceable, and principled behaviors might become more prevalent; and the energy and joyousness of the best churches might spread and be strengthened".

Moreover, Nilsson et al. (2007) found that among boys, self-transcendence and spiritual acceptance were negatively correlated with the short5-HTTLPR genotype and positively correlated with the short AP-2beta geotype.

Both among boys and girls, significant interactive effects were found between 5-HTTLPR and AP-2beta genotypes, with regard to Self-Transcendence and Spiritual acceptance. Boys and girls with the combination of presence of the short 5-HTTLPR, and homozygosity for the long AP-2beta genotype scored significantly lower on Self-Transcendence and Spiritual Acceptance. In this regard, Comings and associates have found gene polymorphic associations with spirituality (Comings *et al*. 2000). It is noteworthy that using a spiritual inventory as part of clinical history is important as an additional tool for medical treatment and diagnosis (Braverman, 1987). Although controversial, clinical studies are beginning to clarify how spirituality and religion can contribute to the coping strategies of many patients with severe, chronic, and terminal conditions (Post *et al*. 2000). One interesting notion has received considerable attention distinguishing religion from spirituality, especially in dying patients (Sulmasy, 2006). Twin studies of spirituality showed that genes accounted for 50 percent of the variance, the unique environment for 50 percent, and the common environment, including cultural influences, zero percent (Kirk et al. 1999). This suggests that spirituality may be an intrinsic biological trait. By contrast, common environment and cultural transmission accounted for a significant percent of the variance of church attendance suggesting that religion is transmitted, at least in part, by non-genetic transmission from generation to generation (called *meme*) (Kirk *et al*. 1999). There are certain advantages that favor spirituality in terms of achieving well-being for both genders and these include but are not limited to – *"spirituality alleviates man's fears of his own death and of mortality"; "Spirituality gives man control over a threatening world"; spirituality and near death experiences"; spirituality and optimism"; spirituality, religion and social cohesiveness"; "spirituality as a defense mechanism"; "inborn spirituality as a moral watchdog"; and "finding a spiritual mate"*.

The concept of spirituality having significant benefits for the human "psyche", potentially leading to both optimism and happiness may be independent of the existence or non-existence of God (Comings, 2008). Hamer in his popular book "*The God Gene"* suggested that the selection for dopaminergic spirituality genes was driven by their ability to produce an innate sense of "feel good" optimism. Accordingly, this would have selective value in the sense that optimism relates to the will to keep on living and procreating, despite the fact that death is inevitable (Comings, 2008). Moreover, studies have shown that optimism seems to promote better health and quicker recovery from disease, features that would have positive selective value. Newberg *et al* (2001) suggested a different kind of association of spirituality with a "feel good" sensation. They suggested, "the neurological machinery of spiritual transcendence may have arisen from neural circuitry [limbic system] that evolved for mating and sexual experience. We find this very interesting especially in light of work on dopaminergic genes and dopamine function suggesting that the substance dopamine is now considered to be both the *"pleasure and anti-stress molecule"* (Comings and Blum 2000).

Newberg and associates proclaimed, "It is no coincidence that mystics of all times and cultures have used the same expressive terms to describe their ineffable sexual experience: bliss, rapture, ecstasy and exaltation." They further suggested that the feel-good sensation was linked to the very neurological structures and pathways involved in transcendent experience-including the arousal, quiescent, and limbic systems –evolved primarily to link sexual pleasures to the powerful sensations of orgasm; the dopamine jackpot! Finally as Comings (2008) suggests, "Spirituality can be defined as a feeling of a connection with something greater than oneself including any form of social order.

Perhaps the greatest factor in the evolution of spirituality is that such a trait would maximize the development of man as a social animal". While the former concept is true, behavioral scientists suggest that the connection to "higher power" is morphed by man's greatest fear, which is death. In consideration of one's spirituality pondering the unattainable notion of our immortality and the doom of being a mortal man, ultimately leads to feelings of doom with no escape at hand. We have witnessed it in the form of comedy as viewed in the film ***"What About Bob?,*** **which explores** the subject of "death therapy" and the never-ending question of inescapable death as observed by a prepubescent child. In this regard Deepak Chopra in his New York Times best-selling book *"Life After Death"* (2006), clearly explains the many facets of peoples beliefs as they relate to the possibilities of life after death. He emphatically asserts, "Those who have the least freedom of choice are driven by obsessions, compulsions, addictions, and unconscious impulses. To the extent that you become free of these, you have more choice. The same is true of a soul contemplating its next physical incarnation". The thought and most of all, the belief that through a series of rules man will emerge into a higher plane never going back in terms of their spiritual wisdom (soul). According to Chopra, this is a very positive psyche attribute especially to those who actually believe that death is not just dissolution and the end. However, incontrast to this belief David E. Comings in his book *"Did Man Create God"* (2008) points out that if consciousness is a prerequisite for the soul, and consciousness is extinguished when brain damage causes the loss of core consciousness, it would also cause the loss of the soul. According to Comings, "While the concept of a soul representing the essence of an individual and living on after death is central to many religions, its existence is not supported by modern neuroscience which states that consciousness, the spirit and the soul are the product of neuronal activity and die when the person dies. This has major consequences for religion since without a soul there is no cosmic consciousness, no afterlife, no hell, no heaven and thus no reward in heaven for good behavior." It is not the intent of this scientific treatisee to address the existence or

non-existence of God. It is, however, important to realize that the quality of and dependence on the cognizant connection to such a belief system can be significantly influential in an individual's ability to achieve a state of peace and happiness.

Other points of view may have this to say about this conjecture and it is these two independent views that have significant impact on ones happiness. According to one of us (BWD) it is not the existence or non-existence of God that is at issue in this matter. It is an individual's state of mind that dictates their 'synaptic' reality. It has been pointed out that this philosophical terrain is based on excessive psycho-religious speculation and psycho-neuro-genomic conjecture to explain how we created God. This is similar to determining whether other dimensions exist based on the mental competence of people. It exists or it doesn't exist. Whether or not we grasp it is irrelevant. We believe the key points can be made about the psycho-genomic mechanisms of how "we" connect to the concept of God and an afterlife without delving into atheistic hyperbole. The existence or non-existence of God is an entirely different issue than that of whether we do or do not have a conscious connection to a God-presence. To base the existence of God on a healthy state of brain chemistry is a very sophomoric premise, and dangerously eclipsing the boundaries and capabilities of science.

In terms of a few specific genes, Comings and associates (2001) were the first group to identify the role of a specific gene in spirituality. The gene was the dopamine D_4 receptor gene *(DRD4)* gene, which was found to play a role in *novelty seeking*, one of the personality traits in Cloninger's Temperament and Character Inventory (Cloninger *et al*. 1993*)*, and has been associated with compromised dopamine signaling in an in vitro study (Asghari et al., 1995).

Comings and associates did identify genetic correlates of self-transcendence, but the association of this gene and novelty seeking linked to dopaminergic circuits did not emerge in a sample of substance abusers (Cohen *et al*. 2009). Specifically, there was a borderline association with a self-forgetful sub-score but a strong association with spiritual acceptance. Other genes included the dopamine vesicular transporter gene *(VMAT2),* which was reported to be associated with spirituality. The fact that two different genes, DRD4 and VMAT2 have been found to associate with spirituality, and the fact that dopamine is the "feel good" neuro-chemical, may help explain why spirituality plays a powerful role in the human condition and why the majority of people derive great comfort and happiness from a belief in a God. It is of further interest that in the Comings et al study (2001), those individuals that scored high on self-transcendence are less likely to abuse alcohol or drugs. Accordingly, this may be because individuals whose reward pathways, and possibly other interacting pathways (serotonergic) activated by spirituality, would have less need to artificially activate their reward circuitry with foreign molecules like ethanol and cocaine. This is, indeed, the central pillar of Alcoholics Anonymous 12 Steps (Gold & Dackis, 1984). Moreover, Borg and associates at the Karolinska Institute in Sweden found that the binding of ethanol was lowest in those with the highest scores for self-transcendence, suggesting, "Such individuals had higher levels of brain serotonin". They showed that the *HTRIA* gene [serotonin1A receptor gene] was significantly associated with the self-transcendence scale and with the substance of spiritual acceptance. It is noteworthy that the lysergic moiety as in LSD is similar structurally to serotonin having modifying effects through psychedelic spiritual experiences. Finally, many different plants around the world contain a range of psychedelic drugs (serotonergic, opioid and catecholaminergic), which are capable of strongly enhancing man's spirituality and/or spiritual awareness. It is suggested that this is accomplished by providing a "powerful feeling of communication with a supernatural power" (Shultes et al. 1998). Comings (2008) further points out that these entheogens (good-producing substances) played a profound and critical role in facilitating human's early belief in a god or gods and in the development of religion.

B. Friends, Love Partners and Mariage: Birds of a Feather Flock Together

A 2002 study conducted at the University of Illinois by Diener and Seligman found that the most salient characteristics shared by the 10% of students with the highest levels of happiness and the fewest signs of depression were their strong ties to friends and family and commitment to spending time with them. "Word needs to be spread," concludes Diener. "It is important to work on social skills, close interpersonal ties and social support in order to be happy." (Diener et al. 2006).

More recently our laboratory found evidence for family members carrying multiple Reward Deficiency Syndrome (RDS) types of behaviors (i.e. drug and alchol addiction, smokinging, sex addiction, pathological gambling, violence behavior, juvenile delinquency, criminal behavior, ADHD, etc.) to marry other individuals possessing the A1 allele of the DRD2 gene 100% of the time. This lends further support to the old folk concept especially observed in addiction rehab clinics and Psych hospitals that many individuals hook up with other drug addicted persons. This has been referred to as **"Birds of a Feather Flock Together".** Have we found the genetic basis for this behavior?

Of course, happiness is not a static state. Even the happiest of people--the cheeriest 10%--feel blue at times. And even the bluest still has their moments of joy (Bruijnzeel, Repetto, & Gold, 2004). That has presented a challenge to social scientists trying to measure happiness. That, along with the simple fact that happiness is inherently subjective makes the challenge even more difficult. In a questionnaire detailing everything they did on the previous day, and whom they were with at the time, and rating a range of feelings during each episode (happy, impatient, depressed, worried, tired, etc.), on a seven-point scale a

group of 900 women in Texas was tested with some surprising results. It turned out that the five most pleasurable and rewarding (positive) activities for these women were (in descending order) sex, socializing, relaxing, praying or meditating, and eating. Exercising and watching TV were not far behind. But way down the list was "taking care of my children," which ranked below cooking and only slightly above housework. The results of this rating should not be interpreted as meaning these activities were viewed as the most beneficial, productive or important; just activities associated with greatest *feelings* of pleasure. Our overall happiness is not merely the sum of our happy moments minus the sum of our angry or sad ones. In other work, Kahneman proposed that the belief that high income is associated with good mood is widespread but mostly illusory. People with above-average income are relatively satisfied with their lives but are barely happier than others in moment-to-moment experience, tend to be tenser, and do not spend more time in particularly enjoyable activities. Moreover, the effect of income on life satisfaction seems to be transient. It has been argued that people exaggerate the contribution of income to happiness because they focus, in part, on conventional achievements when evaluating their life or the lives of others (Kahneman *et al*. 2006)

Happiness goes deeper than that, Kahneman argues in his 2002 book "***Authentic Happiness***". As a result of his research, he finds three components of happiness: pleasure ("the smiley-face piece"), engagement (the depth of involvement with one's family, work, romance and hobbies) and meaning (using personal strengths to serve some larger end). Of those three roads to a happy satisfied life, pleasure is the least consequential. He insists, "This is newsworthy because so many Americans build their lives around pursuing pleasure. It turns out that engagement and meaning are much more important." However if one would ask the "man on the street" a different response may turn up. One of us (KB) decided to test this notion and found that the response was not surprising. One such respondent was a bus operator from Sydney Australia, Mr. William A. C. Fraser who when asked about what made him happy stated *"While we need a balance in our life, I am always seeking for love not just sex. But if it was only sex, what a way to go!"*

III. Biology, Politics, and Human Nature

One of the biggest issues in happiness research is the question of how much our happiness is under our control. In 1996, University of Minnesota researcher David Lykken published a paper looking at the role of genes in determining one's sense of satisfaction in life. Lykken, now over 76, gathered information on 4,000 sets of twins born in Minnesota from 1936 through 1955. After comparing happiness data on identical vs. fraternal twins, he came to the conclusion that about 50% of one's satisfaction with life comes from genetic programming (genes influence such traits as having a sunny, easygoing personality; dealing well with stress; and feeling low levels of anxiety and depression). Lykken found that circumstantial factors like income, marital status, religion and education contribute only about 8% to one's overall well being. He attributes the remaining percentage to "life's slings and arrows."

Because of the large influence of our genes, Lykken proposed the idea that each of us has a happiness set point much like our set point for body weight. No matter what happens in our life--good, bad, spectacular, horrific--we tend to return in short order to our set range. According to Lykken "It may be that trying to be happier is as futile as trying to be taller" (Lykken 2007).

Seligman in a New York Times article on the Psychology of Happiness (1997) argues, "but the cerebral virtues--curiosity, love of learning--are less strongly tied to happiness than interpersonal virtues like kindness, gratitude and capacity for love."

The real question we must ask: Can a dyed-in-the-wool pessimist learn to see the glass as half full? The answer to some degree may reside in simple molecular rearrangement of certain genes called polymorphisms and the interaction of these polymorphic genes with environmental elements like love. There is evidence mounting that genes may play a role in everything from spirituality to politics and even to love styles. In terms of politics, our understanding of bridging of scientists and public policy together has its beginnings under the Third Reich in Nazi Germany. During the Nazi period, the symbiotic relationship between human genetics and politics served to radicalize both. The dynamic between the science of human heredity and Nazi politics changed the research practice of some of the biomedical sciences housed at the Kaiser Wilhelm Institute for Anthropology, Human Heredity and Eugenics (KWIA). It also simultaneously made it easier for the Nazi state to carry out its barbaric racial program leading, finally, to the extermination of millions of so-called racial undesirables.

IV. Can't Get No Satisfaction: "Missing the Dopamine Jackpot"

When we talk about politics and social behaviors we must reflect on the song "Can't get no satisfaction". What do Janis Joplin, Charlie Parker (the "Bird"), Billy Holiday, and Jimmy Hendrix have in common? If you want to find examples of people whose brain reward circuits have gone haywire, the world of jazz and rock stars is probably a good place to look. Earlier work supporting the "dopamine hypothesis" related to craving behavior (Davis and Walsh, 1970; Blum et al. 1973) came as a result of work with progessional athletes, rock n' roll musicians, and other celebrities (Gold & Dackis, 1984; Dackis & Gold, 1985). Our first paper on the identification of polymorphisms of the dopamine D2 receptor gene and severe alcoholism led the way for the understanding of deficiencies in brain dopamine and sensation seeking (Blum *et al*.1990). Thus, the A1 allele yields receptors that don't work as well, and that translates into less dopamine firing up the reward circuits, which can

lead to a tendency to abuse drugs and engage in impulsive, sensation–seeking or anti-social behavior. This includes problems forming relationships leading to low neuroticism and high extroversion (Ozkaragoz and Noble EP 2000; Weiss *et al*. 2008).

Eisenberg and associates (2007) found that carriers of the A1 allele of the dopamine D2 receptor gene were more likely to engage in early sexual activity but were less inclined to develop steady relations. This is further explained by additional work on the relationship of the DRD2 A1 allele and love styles. Others have shown that statistical analysis revealed a significant association between the DRD2 TaqI A genotypes and "Eros" (a loving style characterized by a tendency to develop intense emotional experiences based on the physical attraction to the partner), as well as between the C516T 5HT2A polymorphism and "Mania" (a possessive and dependent romantic attachment, characterized by self-defeating emotions) (Emanuele et al. 2007).

This putative role in attachment has attracted the attention of political scientists. Fowlers group recently published on the association of the dopamine DRD2 gene polymorphisms and the tendency to affiliate with a political party (Dawes and Fowler 2009). They hypothesized that people with more effective DRD2 receptors — that is, with one or more A2 alleles would be more trusting and therefore more likely to join a political party. Utilizing information from the National Longitudinal Study of Adolescent Health (NLSAH), they reported that indeed, people with two A2 alleles (and no A1 allele) were 8% mote more likely to form political attachments. In his landmark paper Fowler called it "the first gene ever associated with partisan attachment".

Guo et al (2007) looked for a link between social behavior (morality) and the dopamine D2 receptor gene by assessing delinquency rates in teenagers. The study was based on a cohort of more than 2,500 adolescents and young adults in the National Longitudinal Study of Adolescent Health in the United States. For DRD2, the trajectory of serious delinquency for the heterozygotes (A1/A2) is about 20% higher than the A2/A2 genotype and about twice as high as the A1/A1 genotype, a phenomenon sometimes described as heterosis (LR test, P = 0.005, 2 df). The findings on violent delinquency closely resemble those on serious delinquency and depression (Haeffel *et al*.2008).

While we are cognizant of free will, we must not be so naive that we underestimate the relationship between our basic social behaviors including political persuasion and biology. The study of genes potentially promises a better understanding of the constraints imposed on basic political behavior (See Aristotle 1996). Thus, we agree with Fowler and associates and also argue that biologists and political scientists must work together to advance a new science of human nature (Fowler and Schreiber, 2008).

In simple terms, can we as scientists reduce the state of happiness to molecular rearrangements leading to gene polymorphisms? If this was that simple, then why not consider the following: Love relationships relate to polymorphisms of the DRD2 gene whereby carriers of A1 alleles lead to an inability to form lasting relationships involving only EROS kind of love. However carriers with the appropriate serotonin polymorphism would be potentially happier because they can form lasting relationships having romantic love styles. If that isn't enough, consider the fact that DRD2 A2 carriers are more likely to have social attachments compared to A1 carriers. This is further supported by earlier work from our lab showing the significant association of schizoid/avoidant behaviors in A1 carriers compared to A2 carriers (Blum *et al* 1997). It is well established that schizoid/avoidant behavior occurs in people that are less passionate and cannot form meaningful relationships or attachment. Couple this with genospirituality and the probability, albeit small, of genospirituality engineering, and other as yet unidentified gene polymorphisms, and what emerges is a complex map of human nature tied to the unconscious state of happiness. There are multiplegenes involved in the state of happiness that are interactive and thus affect reward type of behaviors (see **Figures 2,3**).

V. Body Size and Happiness

Certainly in Western society *"thin is in"* and this concept more than many other more important meaningful health orientated doctrines drives the western world thoughts about self-image especially in females. The scientific support relating to nutraceuticals, dopamine gene polymorphisms, obesity and aberrant craving behavior is well established (Althaus *et al*. 2009, Stice *et al*, 2008, Blum *et al*. 2007, Rothman *et al*. 2008, Chen *et al*. *2007a,b)*. With this in mind our laboratory embarked on a series of studies to determine a potential link of body image and wellness, specifically happiness, by administering a customized DNA directed nutraceutical designed to reduce weight and increase well being (Blum *et al 2008a,* Blum *et.al*. *2008b,* Blum et al. 2008c)

One study systematically assessed the weight management effects of a novel experimental DNA-customized nutraceutical, LG839 (LifeGen, Inc., San Diego, CA, USA). A total of 1058 subjects who participated in the overall D.I.E.T. study were genotyped and administered an LG839 variant based on polymorphic outcomes. A subset of 27 self-identified obese subjects of Dutch descent, having the same DNA pattern of four out of the five candidate genes tested (chi-square analysis) as the entire data set, was subsequently evaluated. Simple t-tests comparing a more systemic range of physical, biochemical, emotional and behavioral parameters related to weight management, before and after 80 days of treatment with LG839, were performed. Statistically significant results were observed for weight loss, sugar craving reduction, appetite suppression, snack reduction, reduction of late night eating, increased perception of overeating, enhanced quality of sleep, increased happiness, and increased energy. Polymorphic correlates were obtained for a number of genes (LEP, PPAR-gamma2, MTHFR, 5-HT2A, and DRD2 genes) with

positive clinical parameters tested in this study. Of all the outcomes and gene polymorphisms, only the DRD2 gene polymorphism (A1 allele) had a significant Pearson correlation with days on treatment (r=0.42, P=0.045). If these results are confirmed in additional rigorous, controlled studies, we carefully suggest that DNA-directed targeting of certain regulator genes, along with customized nutraceutical intervention, provides a unique framework and strategic modality to not only combat obesity but induce a state of happiness in the individual (Blum *et al. 2008c;* Blum et al 2008d).

Comparisons between obese patients and drug-addicted patients have been made for decades. More recently, scientific progress (i.e., better imaging technology) has allowed direct comparisons and evidence points to hedonic-eating resembling drug-taking in many ways from both neurological and psychosocial perspectives (Volkow & Wise, 2005) (Joranby, Frost-Pineda & Gold, 2005). In a recent article involving brain dopaminergic pathways and implications for understanding obesity, Wang and co-workers provided a succinct and compelling argument for the role of the dopamine D2 receptor and obesity. Brain imagining studies in humans implicate the involvement of dopamine (DA) modulated circuits in pathologic eating behaviors(s). Food cues increase striatal extracellular DA, providing evidence for the involvement of DA in the nonhedonistic motivational properties of food. Similar to drug–addicted subjects, striatal DA D2 receptor availability is reduced in obese individuals, which predispose obese subjects to seek food as a means to temporarily compensate for understimulated reward circuits. Obese subjects have increased metabolism in the somatosensory cortex, which suggests an augmented sensitivity to the sensory properties of food. The reduction in DA D2 receptors in obese subjects coupled with the enhanced sensitivity to food palatability could make food their most "salient" reinforcer putting them at risk for compulsive eating and obesity. Moreover, in addition to amplifying the consequences of the dopaminergic genetic predisposition, the authors hypothesize that the development of dopamine resistance, possibly due to lost dopamine sensitivity in a similar manner as insulin, leptin and other endocrine hormones, plays a role in catalyzing the excessive drive to stimulate dopamine-based reward sensations. To date much research has been accomplished concerning the potential of sugar solutions on the neurogenetics and neurochemistry of brain as it relates to its addiction liability. The consensus of this research is that glucose, fructose and sucrose may act differently in the brain but are all addicting substances (Davis et al. 2008; Rada et al. 2005; Chang et al. 2008; Blass, 2003; Hodgekins et al. 2004; Grimm et al.2008; Serre et al. 2007; Gearhardt et al. 2009).

The identification of a specific gene that imparts risk leads to information about the method of causation of any disease. Being cognizant about the role of polygenic inheritance in complex diseases such as obesity, it is necessary to make note of certain singular discoveries. For example, the FTO gene (discovered by a genome–wide association study using the HapMap) is unquestionably important in relation to inheritance of BMI (Scuteri et al. 2007) and could be targeted by administering omega 3 fatty acid. It is this type of information that holds promise for future research and potential gene guided nutritional targets that provide information to develop scientifically sound nutrigenomic solutions (Blum *et al*. 2009*)*. The results from these studies suggest that multiple but similar circuits are disrupted (genetically) in obesity and drug addiction (under the rubric of RDS) and further suggest that strategies aimed at improving DA function (Stice et al 2008) might not only be beneficial in the treatment of and prevention of obesity but also improve one's mood and thus their state of happiness (Wang *et al*. 2009).

VI. The Pleasure Brain

A major question associated with Deepak Chopra's view that humans lose free will because of the frailty of becoming obsessed or addicted to some substance and/or behavior, is why humans are so susceptible to becoming addicted to tobacco, alcohol, drugs, sex and gambling. There are at least three major motivations in life "hunger, thirst and sex." If we want to keep from starving, we have to eat. To ensure that we do, the brain sets up a mechanism whereby we feel hunger, thus signaling the time to eat. Moreover, if we want our species to survive, we must reproduce, to ensure that happens, the process has also been made pleasurable. Certainly eating, sex and love are called natural rewards and are critical to the survival of the species. It is further understood that neuronal pathways are rich in dopamine. Thus the reason we become easily addicted to drugs, alcohol, gambling, sex and other activities is that these substances and activities also commonly stimulate the same pleasure-producing dopamine reward pathways.

While the fact that drugs of abuse such as alcohol, cocaine, speed and nicotine stimulate the release of dopamine explains part of the question of why humans become addicted to things, this does not explain why some people have serious problems with addictions. While environmental factors play a role, there is a significant variation in addictive potential among individuals exposed to the same environment or even substances (Hoebel, Avena, Borcarsly, & Rada, 2009, Avena, Rada & Hoebel, 2009). Genetic factors may also contribute to the drug abuse-derived pleasureform; in one genomic study on rats exposed to chronic methamphetamine abuse, the SLC6A gene and its variants were shown to be altered upon exposure to methamphetamine (Kobeissy, et al., 2008)(Gold, et al., 2009). The SLC6A gene is involved in cocaine abuse, alcohol dependence, smoking behavior, juvenile delinquency, pathological aggression, bipolar disorder, schizophrenia, ADHD, impulsive aggression, cognitive impulsity and is a major component in the happiness gene map (see **Figure 4** and **Table 2**). In 1995 one of us (KB) coined the term "RDS (Blum et al. 1996; Comings et al 2000; Blum et al. 2000). This disorder is due to genetic

defects in the dopamine reward pathways. As a result of such defects the natural rewards are no longer sufficient to improve mood and provide pleasure, and affected individuals pursue an excessive amount of "unnatural rewards" such as from alcohol, nicotine, drugs, gambling, sex and risk taking in the form of dangerous sports, such bungie and base jumping, sky diving, extreme skiing, race car driving, video gaming and others to stimulate their reward pathways

A test of this hypothesis has been successfully carried out by others in two strains of rodents. One strain liked drinking alcohol more than drinking water; the other strain did not. If the preference for alcohol was due to a defect in the dopamine D2 receptor, then increasing the level of D2 receptor in the reward pathways should eliminate the alcohol preference. This was accomplished by injecting copies of the D2 receptor gene directly in the nucleus accumbens. This resulted in a temporary over expression of the D2 receptors that lasted several days. The over expression of the D2 receptor gene reduces alcohol intake demonstrating that high levels of the D2 receptor gene are protective against alcohol abuse (Thanos et al 2001).

VII. The Happiness Brain

There are many theories as to what constitutes the state of happiness in humans, as we have discussed earlier. We believe that Richard Bolstad (2006) best summed it up –" *Success means getting what you want: happiness means wanting what you get* "

Over the past 10,000 years *Homo sapiens* have evolved as much as 100 times faster than at any other time. Human beings have evolved an emotional system that leads them to be generally happy, to think positively, and to quickly adjust to both positive and negative events. A strong and supportive social network of friends, family, and helping others are among the greatest contributors to happiness. Helping others may provide a significant contribution to the positive effects of religion on longevity and health. In fact, Christian, Jewish, Buddhist, Islamic, and Native American spiritual traditions all emphasize the happiness benefits of helping people.

Post (2005) suggests that altruism and volunteerism are associated with happiness, improved mood, enhanced self-esteem, and better mental and physical health; and that helping others, per se, may be a major part of the increased longevity seen in religious versus non-religious individuals. However others have rejected the idea that religion was a key factor. They concluded in their studies of over 8,832 subjects that volunteering, rather than its religious context, explained the beneficial effects and happiness (Musick *et al.* 1999*)*. These findings are not so simple and cannot be taken without understanding that we really cannot determine whether a confound drives an observed correlation. That is, that correlational data is always vulnerable to potential third-variable confounds.

Another facet of certain environmental elements that may affect one's happiness and ultimately longevity is "being in control". Langer (1989) carried out a landmark study that suggested that "being in control" resulted in greater longevity. In his study performed in a nursing home for the elderly, one group of subjects was given a plant and told to look after it, they were responsible for the plant's health. Another group was also given a plant but told that the staff would look over the plant. Over the next 18 months twice as many of those who were not "in control" of their plants died compared to those "in control" of their plants.

As we stated earlier, wealth does not necessarily correlate with happiness. In fact, as pointed out in Comings book *"Did Man Create God,"* a major reason for the lack of correlation between Gross National Product (GNP) and happiness is that people quickly adapt to a wide range of circumstances. He stated, "Someone inheriting or winning a great deal of money may be temporarily be happier, but they soon settle back to their previous innate level of happiness. The same holds for those with progressively increasing yearly incomes."

In support of this notion Allen Parducci (1995) suggested that after each raise, people adapt and return to a previous level of happiness (a set point genetically programmed), a phenomena he termed *"hedonic treadmill."*

VIII. Proposed Happiness Gene Map

In this commentary we have taken the opportunity to at least propose a schematic of a number of potential genes (a sampling) and their polymorphisms including SNPs to encourage others to investigate this very intriguing and important area of neuroscience. The genes listed have not all been tied to happiness per se. But, we believe that because of the effects these gene polymorphisms have on both the Central Nervous System (CNS) and peripheral systems, targeting these loci will have profound influence on health and wellness for the organism (See **Figure 1**) This will ulitamately impact the happiness experience (**Table 1**). Our view is that since many of aberrant behaviors are a consequence of and fall under RDS, one initial goal in the scientific pursuit of happiness in the human would be to first identify those gene polymorphisms associated with RDS and then utilize genomic principles to develop novel tailored made pro-happiness agonists utilizing immunological compatible ('body friendly') natural substances (Blum et al. 1996; Blum et al.2009). It is important to realize that everything that our brain does is ultimately the result of an interaction between our genes and our environment. For some traits, our genes play a major role, for some others environment is a primary factor, and for most it is a combination of the two. On average, depending upon the trait, the genetic contribution accounts for 40 to 90 percent of a trait. In the latter case it is a combination of many genes, referred to as "polygenic inheritance" (Stern 1973). To reiterate, it is well established that "polygenic inheritance" is due to the additive and epistatic interaction of many genes, each accounting for only a small percent of the total trait and interacting with the environment (Comings 2003).

Table 1: Proposed Happiness Gene Map with gene denoted, the SNPs involved and references.

Gene	SNP	Reference
DRD2	CTGGACGTCCAGCTGGGCGCCTGCCT[C/T]GACCAGCACTTTGAGGATGGCTGTG	Van der Zwaluw CS, Engels RC, Vermulst AA, Franke B, Buitelaar J, Verkes RJ, Scholte RH **(2009)** Interactions between dopamine D2 receptor genotype and parental rule-setting in adolescent alcohol use: evidence for a gene-parenting interaction. **Mol Psychiatry**. Feb 24 Ikeda M, Yamanouchi Y, Kinoshita Y, Kitajima T, Yoshimura R, Hashimoto S, O'Donovan MC, Nakamura J, Ozaki N, Iwata N. **(2008)** Variants of dopamine and serotonin candidate genes as predictors of response to reseridone treatment in first-episode schizophrenia. **Pharamcogenomics** 9(10), 1437-43 Huang W, Payne TJ, Ma JZ, Beuten J, Dupont RT, Inohara N, Li MD. **(2009)** Significant association of ANKK1 and detection of a functional polymorphism with nicotine dependence in an African-American sample. **Neuropsychopharmacology** 34(2), 319-30 Ballon N, Leroy S, Roy C, Bourdel MC, Olie JP, Charles-Nicolas A, Krebs MO, Poirier MF. **(2007)** Polymorphisms TaqI A of the DRD2, Ball of the DRD3, exon III, repeat of the DRD4, and 3' UTR VNTR of the DAT: association with childhood ADHD in male African-Caribbean cocaine dependents? **Am J Med Genet B Neuropsychiatr Genet.** 144B(8), 1034-41
	AGGAACTCCTTGGCCTAGCCCACCCT[G/T]CTGCCTTCTGACGGCCCTGCAATGT	Huang W, Payne TJ, Ma JZ, Beuten J, Dupont RT, Inohara N, Li MD. **(2009)** Significant association of ANKK1 and detection of a functional polymorphism with nicotine dependence in an African-American sample **Neuropsychopharmacology.** 34(2), 319-30
	CTGCTTCCCACCTCCCTGCCCAGGCC[A/G]GCCAGCCTCACCCTTGCGAACCGTG	Lucht M, Barnow S, Schroeder W, Grabe HJ, Rosskopf D, Brummer C, John U, Freyberger HJ, Hermann FH. **(2007)** Alcohol consumption is associated with an interaction between DRD2 exon 8 A/A genotype and self-directedness in males **Neuropsychobiology** 56(1), 24-31
	GTCACTATTATGGTTTTTATTACTAT[G/T]GCTCTTTTTGAGGAATTGGGAAATT	Preuss UW, Zill P, Koller G Bondy B, Sokya M. **(2007)** D2 dopamine receptor gene haplotypes and their influence on alcohol and tobacco consumption magnitude in alcohol-dependent individuals **Alcohol Alcohol**. 42(3), 258-66
	CTGACTCTCCCCGACCCGTCCCACCA[C/T]GGTCTCCACAGCACTCCCGACAGCC	Wu SN, Gao R, Xing QH, Li HF, Shen YF, Gu NF, eng GY, He L **(2006)** Association of DRD2 polymorphisms and chlorpromazine-induced extrapyramidal syndrome in Chinese schizophrenic patients **Acta Pharmacol Sin**. 27(8), 966-70 Monakhov MV, Golimbet VE, Chubabriia KV, Zykov VV, Kovtun AL, Karpov VL. **(2007).** The association study of the DRD2 gene C939T polymorphism and schizophrenia **Zh Nevrol Psikhiatr Im S S Korsakova** 107 (10),58-60
	CCACCAGCTGACTCTCCCCGACCCGT[C/G]CCACCACGGTCTCCACAGCACTCCC	Shi J, Gershon ES, Liu C. **(2008)** Genetic associations with schizophrenia: Meta-analysis of 12 candidate genes **Schizophr Res** 104(1-3), 96-107
	ACCCATCTCACTGGCCCCTCCCTTTC[A/C]CCCTCTGAAGACTCCTGCAAACACC	Sasabe T, Furukawa A, Matsusita S, Higuchi S, Ishiura S. (**2007)** Association analysis of the dopamine receptor D2 (DRD2) SNP rs1076560 in alcoholic patients **Neurosci Lett.** 412(2), 139-42 Bertolino A, Fazio L, Caforio G, Blasi G, Rampino A, Romano R, DiGiorgio A, Taurisano P, Papp A, Pinsonneault J, Want D, Nardini M, Popolizio T, Sadee W. **(2009)** Functional variants of the dopamine receptor D2 gene modulate prefronto-striatal phenotypes in schizophrenia **Brain** 132(Pt 2), 417-25
	TTTTGCTGAGTGACCTTAGGCAAGTT[G/T]CTTACCTTCTATGAGCCTGTTTCCT	Glatt SJ, Faraone SV, Lasky-Su JA, Kanazawa T, Hwu HG, Tsuang MT. (**2008**) Family-based association testing strongly implicates DRD2 as a risk gene for schizophrenia in Han Chinese from Taiwan **Mol Psychiatry** *(in press)*

	TGTGATGAATGGGTGCCAAATACACA[A/G]ATACAGAATCTAAGAAAACACATGG	Glatt SJ, Faraone SV, Lasky-Su JA, Kanazawa T, Hwu HG, Tsuang MT **(2008)** Family-based association testing strongly implicates DRD2 as a risk gene for schizophrenia in Han Chinese from Taiwan **Mol Psychiatry** (in press)
	ctagaggaagtgatgttcaacagaca[A/G]acaactgaaggatgtgtaggaatta	Xing Q, Qian X, Li H, Wong S, Wu S, Feng G, Duan S, Xu M, Gao R, Qin W, Gao J, Meng J, He L. **(20070** The relationship between the therapeutic response to reisperidone and the dopamine D2 receptor polymorphism in Chinese schizophrenia patients **Int J Neuropsychopharmacol** 10(5),631-7
	TGGAAGTCATGTGCTTTGTATGAAAC[A/G]CCTTGGAATGCTGATAAGTTTAATT	Hwang R, Shinkai T, De Luca V, Muller DJ, Ni X, Macciardi F, Potkin S, Lieberman JA, Meltzer HY, Kennedy JL. **(2005)** Association study of 12 polymorphisms spanning the dopamine D (2) receptor gene and clozapine treatment response in two treatment refractory/intolerant populations **Psychopharmacology (Berl)** 181(1), 179-87
	GTCTAAAGCAAATGGAACCTTTAGGG[A/G]GAGAGATTTGTGTTTGCTGTGTCCC	Huang W, Payne TJ, Ma JZ, Beuten J, Dupont RT, Inohara N, Li MD. **(2009)** Significant association of ANKK1 and detection of a functional polymorphism with nicotine dependence in an African-American sample **Neuropsychopharmacology.** 34(2), 319-30
	GAGGGGACTGGGGTCAGGCCTCATTC[A/G]GGTTCCCTAGAGTGGAAAGGATTGG	Huang W, Payne TJ, Ma JZ, Beuten J, Dupont RT, Inohara N, Li MD. **(2009)** Significant association of ANKK1 and detection of a functional polymorphism with nicotine dependence in an African-American sample **Neuropsychopharmacology.** 34(2), 319-30
	GTATcagacagatctaggctcaaata[A/C]cagcttcagttctcaccacctgtgt	Huang W, Payne TJ, Ma JZ, Beuten J, Dupont RT, Inohara N, Li MD. **(2009)** Significant association of ANKK1 and detection of a functional polymorphism with nicotine dependence in an African-American sample **Neuropsychopharmacology.** 34(2), 319-30
	CCTGAGTGCACAGGATGCTGGAGCCT[C/T]CCAGTTTCTCTGGCTTTCATCTCCGT	Laucht M, Becker K, Frank J, Schmidt MH, Esser G, Treutlein J, Skowronek MH, Schumann G **Genetic variation in dopamine pathways differentially associated with smoking progression in adolescence.** *J Am Acad Child Adolesc Psychiatry* **2008** Jun; 47(6): 673-81
	AATCCCCCAACCCCTCCTACCCGTT[-/C]CAGGCCGGGGATCGCCCGAGGAGGTA	Shi J, Gershon ES, Liu C. **(2008)** Genetic associations with schizophrenia: Meta-analyses of 12 candidate genes. **Schizophr Res.** 104(1-3), 96-107. Ton TG, Rossing MA, Bowen DJ, Srinouanprachan S, Wicklund K, Farin FM. **(2007)** Genetic polymorphisms in dopamine-related genes and smoking c essation in women: a prospective cohort study. **Behav Brain Funct.** 28, 3:22 Parsons MJ, Mata I, Beperet M, Iribarren-Iriso F, Arroyo B, Sainz R, Arranz MJ, Kerwin R **A. (2007)** Dopamine D2 receptor gene-related polymorphism is associated with schizophrenia in a Spanish population isolate **Psychiatr Genet.** 17(3), 159-63
	GAGGACCCAGCCTGCAATCACAGCTT[A/G]TTACTCTGGGTGTGGGTGGGAGCGC	Ikeda M, Yamanouchi Y, Kinoshita Y, Kitajima T, Yoshimura R, Hashimoto S, O'Donovan MC, Nakamura J, Ozaki N, Iwata N. **(2008)** Variants of dopamine and serotonin candidate genes as predictors of response to reseridone treatment in first-episode schizophrenia **Pharmacogenomics** 9(10), 1437-43
5HT2A	GCTCAATGGTTGCTCTAGGAAAGCAG[C/T]ATTCTGAAGAGGCTTCTAAAGACAA	Hawi Z, Segurado R, Conroy J, Sheehan K, Lowe N, Kirley A, Shields D, Fitzgerald M, Gallagher L, Gill M. **(2009)** Preferential transmission of paternal alleles at risk genes in attention-deficit/hyperactivity disorder **Am J Human Genet**. 77(6), 958-65
	CTGTGAACTCAGGAGCAAGTGCACAC[A/G]TTGCTTATCACTTACCAGAAGCATT	Unschuld PG, Ising M, Erhardt A, Lucae S, Kloiber S, Kohli M, Salyakina D, Welt T, Kern N, Lieb R, Uhr M, Binder EB, Muller-Mysok B, Holsboer F, Keck ME. **(2007)** Polymorphisms in the serotonin receptor gene HT2RA are associated with quantitative traits in panic disorder **Am J Med Genet B Neuropsychiatr Genet**. 144B(4), 424-9
	CTCTGGTTTTAAGCAAGTCATTTAAT[-/C/T]GGAGTTTTTTTTCTCCCATAAAATG	Oades RD, Lasky-Su J, Christiansen H, Faragone SV, Sonuga-Barke EJ, Banaschewski T, Chen W, Anney RJ, Buitelaar JK, Ebstein RP, Franke B, Gill M, Miranda A, Roeyers H, Rothenberger A, Sergeant JA, Steinhausen HC, Taylor EA, Thompson M, Asherson P. **(2008)** The influence of serontonin- and other genes on impulsive behavioral aggression and cognitive impulsivity in children with attention-deficit/hyperactivity disorder (ADHD): Findings froma family-based association test (FBAT) analysis. **Behav Brain Funct.** 4, 48
	aaatggtcctaccatctatccagata[C/T]acagcttaaaaacttaggagtctct	Oades RD, Lasky-Su J, Christiansen H, Faragone SV, Sonuga-Barke EJ, Banaschewski T, Chen W, Anney RJ, Buitelaar JK, Ebstein RP, Franke B, Gill M, Miranda A, Roeyers H, Rothenberger A, Sergeant JA, Steinhausen HC, Taylor EA, Thompson M, Asherson P**. (2008)** The influence of serontonin- and other genes on impulsive behavioral aggression and cognitive impulsivity in children with attention-deficit/hyperactivity disorder (ADHD): Findings froma family-based association test

		(FBAT) analysis. **Behav Brain Funct.** 4,48
	TGCTATTTGTAATGCTG CTTATTAGA[G/T]ACATC GCTGATCCTCCTGTCAA CTC	Unschuld PG, Ising M, Erhardt A, Lucae S, Kloiber S, Kohli M, Salyakina D, Welt T, Kern N, Lieb R, Uhr M, Binder EB, Muller-Mysok B, Holsboer F, Keck ME. **(2007)** Polymorphisms in the serotonin receptor gene HT2RA are associated with quantitative traits in panic disorder **Am J Med Genet B Neuropsychiatr Genet.** 144B(4), 424-9
	ATGAACCAAATTGCATG AGCTCTATT[A/G]TGTGC CCCTCTTGTAATATAAA AAT	Giegling I, Hartmann AM, Moller RJ, Rujescu D **(2006)** Anger- and aggression-related traits are associated with polymorphisms in the 5-HT-2A gene **J Affect Disord**. 96(1-2), 75-81
	CAGGCAGAATTTCCACA AATGAAATG[C/G]AAAT TCAGATATATATCTCTT AATC	Unschuld PG, Ising M, Erhardt A, Lucae S, Kloiber S, Kohli M, Salyakina D, Welt T, Kern N, Lieb R, Uhr M, Binder EB, Muller-Mysok B, Holsboer F, Keck ME. **(2007)** Polymorphisms in the serotonin receptor gene HT2RA are associated with quantitative traits in panic disorder **Am J Med Genet B Neuropsychiatr Genet.** 144B(4), 424-9
	TCACTCATAACTGAAGA TCATTTCAC[C/T]TTTGA ATGAGAATTTGTCTCTG AAG	McMahon FJ, Buervenich S, Charney D, Lipsky R, Rush AJ, Wilson AF, Sorant AJ, Papanicolaou GJ, Laje G, Fava M, Trivedi MH, Wisniewski SR, Manji H. **(2006)** Variation in the gene encoding the serotonin 2A receptor is associated with outcome of antidepressant treatment **Am J Hum Genet** 78(5), 804-14
	TGGGCAGAGGAGGGGA AGGGTCACTG[C/T]ACTC AGGGACAAGAGAAGGG GTGGG	Unschuld PG, Ising M, Erhardt A, Lucae S, Kloiber S, Kohli M, Salyakina D, Welt T, Kern N, Lieb R, Uhr M, Binder EB, Muller-Mysok B, Holsboer F, Keck ME **Polymorphisms in the serotonin receptor gene HT2RA are associated with quantitative traits in panic disorder** *Am J Med Genet B Neuropsychiatr Genet*. 2007 Jun 5; 144B(4):424-9
	ATCAGTGTGGTCACTTC ACTGCTTGC[C/G]AAGG ATTCCATCTAATTCTGA GGAA	Giegling I, Hartmann AM, Moller RJ, Rujescu D.**(2006)** Anger- and aggression-related traits are associated with polymorphisms in the 5-HT-2A gene **J Affect Disord**. 96 (1-2), 75-81
	AGGCTCTACAGTAATGA CTTTAACTC[C/T]GGAGA AGCTAACACTTCTGATG CAT	Benedetti F, Barbini B, Bernasconi A, Fulgosi MC, Colombo C, Dallaspezia S, Gavinelli C, Marino E, Pirovano A, Radaelli D, Smeraldi E . **(2008)** Serotonin 5-HT2A receptor gene variants influence antidepressant response to repeated total sleep deprivation in bipolar disorder. **Prog Neuropsychopharmacol Biol Psychiatry**. 32(8),1863-6 Saiz PA, Garcia-Portilla MP, Paredes B, Arango C, Morales B, Alvarez V, Coto E, Bascaran MT, Bousono M, Bobes. J. **(2008)** Association between the A-1438G polymorphism of the serotonin 2A receptor gene and nonimpulsive suicide attempts **Psychiatr Genet** 18(5), 213-8 Tander B, Gunes S, Boke O, Alayli G, Kara N, Bagchi H, Canturk F. **(2008)** Polymorphisms of the serotonin-2A receptor and catechol-O-methyltransferase genes: a study on fibromyalgia susceptibility **Rheumatol Int** 28(7), 685-91 Saiz PA, Garcia-Portilla MP, Arango C, Morales B, Bascaran MT, Martinez-Barrondo S, Florez G, Sotomayor E, Paredes B, Alvarez C, San Narciso G, Carreno E, Bombin I, Alvarez V, Coto E, Fernandez JM, Bousono M, Bobes J. **(2008)** Association study between obsessive-compulsive disorder and serotonergic candidate genes **Prog Neuropsychopharmacol Biol Psychiatry**. 32(3), 7 65-70 Unschuld PG, Ising M, Erhardt A, Lucae S, Kloiber S, Kohli M, Salyakina D, Welt T, Kern N, Lieb R, Uhr M, Binder EB, Muller-Mysok B, Holsboer F, Keck ME. **(2007)** Polymorphisms in the serotonin receptor gene HT2RA are associated with quantitative traits in panic disorder **Am J Med Genet B Neuropsychiatr Gene***t*. 144B(4), 424-9 Ni X, Bismil R, Chan K, Sicard T, Bulgin N, McMain S, Kennedy JL. **(2006)** Serotonin 2A receptor gene is associated with personality traits, but not to disorder, in patients with borderline personality disorder **Neurosci Lett.** 408(3), 214-9 McMahon FJ, Buervenich S, Charney D, Lipsky R, Rush AJ, Wilson AF, Sorant AJ, Papanicolaou GJ, Laje G, Fava M, Trivedi MH, Wisniewski SR, Manji H. **(2006)** Variation in the gene encoding the serotonin 2A receptor is associated with outcome of antidepressant treatment **Am J Hum Genet** 78(5), 804-14 Huang S, Cook DG, Hinks LJ, Chen XH, Ye S, Gilg JA, Jarvis MJ, Whincup PH, Day IN. **(2005)** CYP2A6, MAOA, DBH, DRD4, and 5HT2A genotypes, smoking behaviour

		and cotinine levels in 1518 UK adolescents **Pharmacogenet Genomics** 15(12), 839-50 Wei J, Hemmings GP.**(2005)** The KPNA3 gene may be a susceptibility candidate for schizophrenia **Neurosci Res** 52(4),342-6
	TATGTCCTCGGAGTGCTGTGAGTGTC[C/T]GGCACTTCCATCCAAAGCCAACAGT	Saiz PA, Garcia-Portilla MP, Paredes B, Arango C, Morales B, Alvarez V, Coto E, Bascaran MT, Bousono M, Bobes J. **(2008)** Association between the A-1438G polymorphism of the serotonin 2A receptor gene and nonimpulsive suicide attempts **Psychiatr Genet** 18(5), 213-8
ANKK1	GGAGGGGGGTCTTGCCCTCAGCCTCA[C/T]GCAGGTTGGGGTCAGCCTGACGGGA	Huang W, Payne TJ, Ma JZ, Beuten J, Dupont RT, Inohara N, Li MD. **(2009)** Significant association of ANKK1 and detection of a functional polymorphism with nicotine dependence in an African-American sample **Neuropsychopharmacology.** 34(2), 319-30
	GGAGGGGGGTCTTGCCCTCAGCCTCA[C/T]GCAGGTTGGGGTCAGCCTGACGGGA	Van der Zwaluw CS, Engels RC, Vermulst AA, Franke B, Buitelaar J, Verkes RJ, Scholte RH. **(2009)** Interactions between dopamine D2 receptor genotype and parental rule-setting in adolescent alcohol use: evidence for a gene-parenting interaction. **Mol Psychiatry** (in press) Ikeda M, Yamanouchi Y, Kinoshita Y, Kitajima T, Yoshimura R, Hashimoto S, O'Donovan MC, Nakamura J, Ozaki N, Iwata N. **(2008)** Variants of dopamine and serotonin candidate genes as predictors of response to reseridone treatment in first-episode schizophrenia. **Pharamcogenomics** 9(10), 1437-43 Huang W, Payne TJ, Ma JZ, Beuten J, Dupont RT, Inohara N, Li MD. **(2009)** Significant association of ANKK1 and detection of a functional polymorphism with nicotine dependence in an African-American sample**. Neuropsychopharmacology.** 34(2), 319-30 Shi J, Gershon ES, Liu C. **(2008**) Genetic associations with schizophrenia: Meta-analyses of 12 candidate genes **Schizophr Res**. 104(1-3), 96-107 Neville MJ, Johnstone EC, Walton RT. **(2004)** Identification and characterization of ANKK1: a novel kinase gene closely linked to DRD2 on chromosome band 11q23.1 **Hum Mutat**. 23(6), 540-5.
	CCTGCAAGCTGTCGCTGCGCCAGCCC[A/G]GGGAGGTGAGTGTGTGGGCTGGGCA	McAllister TW, Flashman LA, Harker Rhodes C, Tyler AL, Moore JH, Saykin AJ, McDonald BC, Tosteson TD, Tsongalis GJ. **(2008**) Single nucleotide polymorphisms in ANKK1 and the dopamine D2 receptor gene affect cognitive outcome shortly after traumatic brain injury: a replication and extension study. **Brain Inj.** 22(9), 705-14
	ACTTTGCAGCCCAGAATGGGGATGAC[C/G]GCACTGCGCGCCTGCTCCTGGACCA	McAllister TW, Flashman LA, Harker Rhodes C, Tyler AL, Moore JH, Saykin AJ, McDonald BC, Tosteson TD, Tsongalis GJ. **(2008**) Single nucleotide polymorphisms in ANKK1 and the dopamine D2 receptor gene affect cognitive outcome shortly after traumatic brain injury: a replication and extension study. **Brain Inj.** 22(9), 705-14
OPRK1	AATTTCCCAAAAACTACAGTTTTTTT[-/T]TCTTAGCATGCTATTCAGGTAAACA	Edenberg HJ, Wang J, Tian H, Pochareddy S, Xuei X, Wetherill L, Goate A, Hinrichs T, Kuperman S, Nurnberger JI Jr, Schukit M, Tischfield JA, Foroud T. **(2008)** A regulatory variation in OPRK1, the gene encoding the kappa-opioid receptor, is associated with alcohol dependence. **Hum Mol Genet**. 17(12), 1273-9
	TTTGCTAGGTAAGGTTCAGCACCCAT[C/T]TGCTGTGGCCTTCCTATGAAACGTA	Edenberg HJ, Wang J, Tian H, Pochareddy S, Xuei X, Wetherill L, Goate A, Hinrichs T, Kuperman S, Nurnberger JI Jr, Schukit M, Tischfield JA, Foroud T. **(2008)** A regulatory variation in OPRK1, the gene encoding the kappa-opioid receptor, is associated with alcohol dependence. **Hum Mol Genet**. 17(12), 1273-9
	ATGACTAGTCGTGGAGATGTCTTCGT[A/C]CAGTTCTTCGGGAAGAGAGGAGTTC	Edenberg HJ, Wang J, Tian H, Pochareddy S, Xuei X, Wetherill L, Goate A, Hinrichs T, Kuperman S, Nurnberger JI Jr, Schukit M, Tischfield JA, Foroud T. **(2008)** A regulatory variation in OPRK1, the gene encoding the kappa-opioid receptor, is associated with alcohol dependence. **Hum Mol Genet**. 17(12), 1273-9
	GAAAACACAAGTGTGATCAAATGCCA[C/T]GGACCCACAGGAAGCTGGTGGCTCT	Levran O, Londono D, O'Hara K, Nielsen DA, Peles E, Rotrosen J, Casadonte P, Linzy S, Randesi M, Ott J, Adelson M, Kreek MJ. **(2008)** Genetic susceptibility to heroin addiction: a candidate gene association study. **Genes Brain Behav** 7(7), 729-9
OPRM1	TATATGGCATTTCACATTCACATGTA[A/G]TATTTGAATATACACATCAACA	Sherva R, Wilhelmsen K, Pomerleau CS, Chasse SA, Rice JP, Snedecor SM, Bierut LJ, Neuman RJ, Pomerleau OF. **(2008)** Association of a single nucleotide polymorphism in neuronal acetylcholine receptor subunit alpha 5 (CHRNA5) with smoking status and

	CCA	with 'pleasurable buzz' during early experimentation with smoking **Addiction** 103(9), 1544-52 Levran O, Londono D, O'Hara K, Nielsen DA, Peles E, Rotrosen J, Casadonte P, Linzy S, Randesi M, Ott J, Adelson M, Kreek MJ. **(2008)** Genetic susceptibility to heroin addiction: a candidate gene association study. **Genes Brain Behav** 7(7), 729-9 Saccone SF, Hinrichs AL, Saccone NL, Chase GA, Konvicka K, Madden PA, Breslau N, Johnson EO, Hatsukami D, Pomerleau O, Swan GE, Goate AM, Rutter J, Bertelsen S, Fox L, Fugman D, Martin NG, Montgomery GW, Wang JC, Ballinger DG, Rice JP, Bierut LJ. **(2007)** Cholinergic nicotinic receptor genes implicated in a nicotine dependence association study targeting 348 candidate genes with 3713 SNPs **Hum Mol Genet.** 16(1), 36-49
	CTAATTAGGATATTTTG TGGGTTTTA[A/G]AAAA GTGAATTTTATTAATAT TTGA	Ehlers CL, Lind PA, Wilhelmsen KC . **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians. **BMC Med Genet**. 9, 35
	acaccacacctggcagttcagAGC AC[A/G]CTCACTCTTTCT CCCTTTGACAGAA	Xu L, Zhang F, Zhang DD, Chen XD, Lu M, Lin RY, Wen H, Jin L, Wang XF. **(2009)** OPRM1 gene is associated with BMI in Uyghur population **Obesity (Silver Spring** 17(1), 121-5
	ATCAGGTTGGCCTAATT TACGTAAAC[A/G]TTAA TTTAAATCACACTAATG GTTT	Ehlers CL, Lind PA, Wilhelmsen KC. **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35
		Ehlers CL, Lind PA, Wilhelmsen KC. **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35 Zhang D, Shao C, Shao M, Yan P, Wang Y, Liu Y, Liu W, Xie Y, Zhao Y, Lu D, Li Y, Jin L. **(2007**) Effect of mu-opioid receptor gene polymorphisms on heroin-induced subjective responses in a Chinese population **Biol Psychiatry** 61(11), 1244-51
		Zhang D, Shao C, Shao M, Yan P, Wang Y, Liu Y, Liu W, Xie Y, Zhao Y, Lu D, Li Y, Jin L. **(2007**) Effect of mu-opioid receptor gene polymorphisms on heroin-induced subjective responses in a Chinese population **Biol Psychiatry** 61(11), 1244-51
	AAGAAATTGTCTGCATA TAAACAAAT[A/G]CATC ACATTTCCACAAAAGAC TTTG	Zhang L, Kendler KS, Chen X**. (2006)** The mu-opioid receptor gene and smoking initiation and nicotine dependence **Behav Brain Funct** 2,28
	TGAGAGCTAATGTTTCA AAGAAACTT[G/T]AAAT TCCCAAGATTAAAATTA TTGT	Ehlers CL, Lind PA, Wilhelmsen KC . **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35
	CCCAGTAAGTGAATTAA ATACTTTCA[C/T]AGACA CTCTCCATCTAGTAGAA CAA	Xu L, Zhang F, Zhang DD, Chen XD, Lu M, Lin RY, Wen H, Jin L, Wang XF. **(2009)** OPRM1 gene is associated with BMI in Uyghur population **Obesity (Silver Spring** 17(1), 121-5
	TGATAGGCACTGGTTCT ACAGTGAGA[C/T]ATAT CTCTCCTAAGTCTGGTG ACAA	Zhang L, Kendler KS, Chen X**.(2006)** The mu-opioid receptor gene and smoking initiation and nicotine dependence **Behav Brain Funct** 2,28 Max MB, Wu T, Atlas SJ, Edwards RR, Haythornthwaite JA, Bollettino AF, Hipp HS, McKnight CD, Osman IA, Crawford EN, Pao M, Nejm J, Kingman A, Aisen DC, Scully MA, Keller RB, Goldman D, Belfer I. **(2006)** A clinical genetic method to identify mechanisms by which pain causes depression and anxiety**. Mol Pain**. 19,2:14
	acagtggcacgatctcggctcactgc[A/C]acctccacctcccgggtttaagt ga	Ehlers CL, Lind PA, Wilhelmsen KC . **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35
	ttacctggctaacagttttctatctc[C/T]cacacgagcctggtgggaggcagtg	Ehlers CL, Lind PA, Wilhelmsen KC. **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35
	AGCTCTTGTTATCTTAC	Zhang L, Kendler KS, Chen X**.(2006)** The mu-opioid receptor gene and smoking

	CATTCCCAC[A/G]TTGATTCTCATTTTTATCCCTCTCC	initiation and nicotine dependence **Behav Brain Funct** 2,28
	TCAAGATAGCTAATTGAGAACAAGCA[C/T]GAGACTCCACTCCTGGTCCCCAAGC	Levran O, Londono D, O'Hara K, Nielsen DA, Peles E, Rotrosen J, Casadonte P, Linzy S, Randesi M, Ott J, Adelson M, Kreek MJ. **(2008)** Genetic susceptibility to heroin addiction: a candidate gene association study. **Genes Brain Behav** 7(7), 729-9 Zhang D, Shao C, Shao M, Yan P, Wang Y, Liu Y, Liu W, Xie Y, Zhao Y, Lu D, Li Y, Jin L. **(2007**) Effect of mu-opioid receptor gene polymorphisms on heroin-induced subjective responses in a Chinese population **Biol Psychiatry** 61(11), 1244-51
	CCATTTTCTTTTCTTCTTTGCTTGTC[G/T]Tttttttctgtttgtttttctttttc	Ehlers CL, Lind PA, Wilhelmsen KC. **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35
	AGAAAATAACTTTTGCTAGATTCACC[A/G]TTGGTTATAGACCTGCATGATCTAA	Ehlers CL, Lind PA, Wilhelmsen KC. **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35
	GTGATGTTACCAGCCTGAGGGAAGGA[A/G]GGTTCACAGCCTGATATGTTGGTGA	Zhang L, Kendler KS, Chen X**. (2006)** The mu-opioid receptor gene and smoking initiation and nicotine dependence **Behav Brain Funct** 2,28
	AGTTAGCTCTGGTCAAGGCTAAAAAT[C/G]AATGAGCAAAATGGCAGTATTAACA	Ehlers CL, Lind PA, Wilhelmsen KC . **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35 Zhang L, Kendler KS, Chen X**. (2006)** The mu-opioid receptor gene and smoking initiation and nicotine dependence **Behav Brain Funct** 2,28
	AATTTTATTAGATTAAACAATTTTTA[A/G]CAGACCTCATGCTTGTTGGAGATAA	Zhang L, Kendler KS, Chen X**. (2006)** The mu-opioid receptor gene and smoking initiation and nicotine dependence **Behav Brain Funct** 2,28
	GGTCCAGGGTACACAACCAAGCAGCC[A/T]TGCTCTAGAGCCCAGCAAGACAGGG	Smith RJ, Doyle GA, Han AM, Crowley JJ, Oslin DW, Patkar AA, Mannelli P, Demaria PA Jr, O'brien CP, Berrettini WH. **(2005)** Novel exonic mu-opioid receptor gene (OPRM1) polymorphisms not associated with opioid dependence. **Am J Med Genet B Neuropsychiatr Genet.** 133B(1), 105-9
	ACTGAAGAATAATCATGCTTAACTCA[A/G]GAGAAATGCTCCACCAGACGGGCTG	Smith RJ, Doyle GA, Han AM, Crowley JJ, Oslin DW, Patkar AA, Mannelli P, Demaria PA Jr, O'brien CP, Berrettini WH. **(2005)** Novel exonic mu-opioid receptor gene (OPRM1) polymorphisms not associated with opioid dependence. **Am J Med Genet B Neuropsychiatr Genet.** 133B(1), 105-9
	GCACATTTACTGTTTTGTCTAACCTG[C/T]CTAGCCATTTCAGTCAAGCTGATTG	Ehlers CL, Lind PA, Wilhelmsen KC . **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35
	GCAATCAGAAAGAAATTCAGTTATTA[C/T]AGTATATGCAAGTCACACTGCAAGC	Ehlers CL, Lind PA, Wilhelmsen KC . **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35 Gallagher CJ, Gordon CJ, Langefeld CD, Mychaleckyi JC, Freedman BI, Rich SS, Bowden DW, Sale MM. **(2006)** Association of the mu-opioid receptor gene with type 2 diabetes mellitus in an African American population **Mol Genet Metab.** 87(1), 54-60
	AATGAAACACAAATCATAATCTCTGA[A/G]GCAAATAAGAATGGAAGGACTCCTG	Zhang L, Kendler KS, Chen X**. (2006)** The mu-opioid receptor gene and smoking initiation and nicotine dependence **Behav Brain Funct** 2,28
	tttagggcaagtcagaaagtccaaaa[A/G]tgcctcagatattctgtgtgagtga	Ehlers CL, Lind PA, Wilhelmsen KC . **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35
	AAAAACTGGGCCTGAGCTCAGATGAA[C/T]TGGAGAACTGAACTTTGGCTTAGAA	Zhang L, Kendler KS, Chen X**. (2006)** The mu-opioid receptor gene and smoking initiation and nicotine dependence **Behav Brain Funct** 2,28

	GAGTCATCAGCTCCCAAGGTTTTCTG[C/T]ATGGCTCTGTTTTTATGATTTCTGT	Ehlers CL, Lind PA, Wilhelmsen KC . **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35
	gtgtgtactgcagtctggtcccatcg[C/T]attgccttgtgggatttgggagtag	Ehlers CL, Lind PA, Wilhelmsen KC . **(2008)** Association between single nucleotide polymorphisms in the mu opioid receptor gene (OPRM1) and self-reported response to alcohol in American Indians**. BMC Med Genet**. 9, 35 Zhang L, Kendler KS, Chen X**. (2006)** The mu-opioid receptor gene and smoking initiation and nicotine dependence **Behav Brain Funct** 2,28
COMT	GCTCCTACGGTCCCTCAGGCTTGGAG[A/G]GTCACTTTAAACAATAAAAAGCAAC	Funke BH, Lencz T, Finn CT, DeRosse P, Poznik GD, Plocik AM, Kane J, Rogus J, Malhotra AK, Kucherlapati R.**(2007)** Analysis of TBX1 variation in patients with psychotic and affective disorders. **Mol Med.** 13(7-8), 407-14
	TGTGGTTACTTTCTGGAGAGAGCATG[C/T]GGCATGCAGGAGCTGGAGGGGGGGT	Beuten J, Payne TJ, Ma JZ, Li MD. **(2006)** Significant association of catechol-O-methyltransferase (COMT) haplotypes with nicotine dependence in male and female smokers of two ethnic populations. **Neuropsychopharmacology.** 31(3), 675-84
	aaaagttacgcttaataatgaatgtt[G/T]cagcactttcttctcttcaggtatt	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak assocation with post-surgical pain in humans. **Mol Pain.** 2,24
	CTGTGAGGCACTGAGGATGCCCTCAC[A/G]CGTGCATCTGCATGTGGCGTGCATG	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak assocation with post-surgical pain in humans. **Mol Pain.** 2,24 Beuten J, Payne TJ, Ma JZ, Li MD. **(2006)** Significant association of catechol-O-methyltransferase (COMT) haplotypes with nicotine dependence in male and female smokers of two ethnic populations. **Neuropsychopharmacology.** 31(3), 675-84
	CTGGTTTGTGTATGTTCTTGGTAAAC[C/T]AGCCCTTGGTCTTACACATCATTTC	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak assocation with post-surgical pain in humans. **Mol Pain.** 2,24
	GCTTCCCTGTTCTCTTCTGCTCTGTC[C/T]TCTGGTGCCCTGAGGCTGGCCTCCA	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak assocation with post-surgical pain in humans. **Mol Pain.** 2,24
	GGCATTTCTGAACCTTGCCCCTCTGC[A/G]AACACAAGGGGGCGATGGTGGCACT	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak assocation with post-surgical pain in humans. **Mol Pain.** 2,24 Vargas-Alarcon G, Fragoso JM, Cruz-Robles D, Vargas A, Vargas A, Lao-Villadoniga JI, Garcia-Fructuoso F, Ramos-Kuri M, Hernandez F, Springall R, Bojalil R, Vallejo M, Martinez-Lavin M. **(2007)** Catechol-O-methyltransferase gene haplotypes in Mexican and Spanish patients with fibromyalgia **Arthritis Res Ther**. 9(5), R110 Bialecka M, Kurzawski M, Klodowska-Duda G, Opala G, Tan EK, Drozdzik M. **(2008)** The association of functional catechol-O-methyltransferase haplotypes with risk of Parkinson's disease, levodopa treatment response, and complications**. Pharmacogenet Genomics.** 18(9), 815-21 Halleland H, Lundervold AJ, Halmoy A, Haavik J, Johansson S. **(2009)** Associatoin between Catechol-O-methyltransferase (COMT) haplotypes and severity of hyperactivity symptoms in Adults **Am J Med Genet B Neuropsychiatr Genet**.150B (3), 403-10.
	ATAAGTAACTGTCGAGAAGATTCTCA[C/T]AGGAGACCACGTGGGTTGCCTGAAG	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak assocation with post-surgical pain in humans. **Mol Pain.** 2,24 Beuten J, Payne TJ, Ma JZ, Li MD. **(2006)** Significant association of catechol-O-

		methyltransferase (COMT) haplotypes with nicotine dependence in male and female smokers of two ethnic populations. **Neuropsychopharmacology.** 31(3), 675-84
SLC6A3	AATGTCCTCAGCTGGTTCTTCCCCCA[A/G]TGCCCTGATCCTGGGCTCACATGTG	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak assocation with post-surgical pain in humans. **Mol Pain.** 2,24
	GAGACGAAGACCCCAGGAAGTCATCC[C/T]GCAATGGGAGAGACACGAACAAACC	Guindalini C, Howard M, Haddley K, Laranjeira R, Collier D, Ammar N, Craig I, O'Gara C, Bubb VJ, Greenwood T, Kelsoe J, Asherson P, Murray RM, Castelo A, Quinn JP, Vallada H, Breen G. **(2006)** A dopamine transporter gene functional variant associated with cocaine abuse in a Brazilian sample **Proc Natl Acad Sci U S A.** 103(12), 4552-7
	AAAATCAAGTAATGATTGATTTGTAG[A/G]AGTTTGAGTGAGGCATCGGATCCCC	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak assocation with post-surgical pain in humans. **Mol Pain.** 2,24 Preuss UW, Zill P, Koller G, Bondy B, Sokya M. **(2007)** D2 dopamine receptor gene haplotypes and their influence on alcohol and tobacco consumption magnitude in alcohol-dependent individuals **Alcohol Alcohol**. 42(3), 258-66 Haeffel GJ, Getchell M, Koposov RA, Yrigollen CM, Deyoung CG, Klinteberg BA, Oreland L, Ruchkin VV, Grigorenko EL. (**2008)** Association between polymorphisms in the dopamine transporter gene and depression: evidence for a gene-environment interaction in a sample of juvenile detainees. **Psychol Sci**. 19(1), 62-9 Mick E, Kim JW, Biederman J, Wozniak J, Wilens T, Spencer T, Smoller JW, Faraone SV. **(2008)** Family based associaton study of pediatric bipolar disorder and the dopamine transporger gene (SLC6A3) **Am J Med Genet B Neuropsychiatr Genet**. 147 B (7), 1182-5
	ACCGTGCCCAGCCCTGTGTGGGCATC[A/G]GAGGTGGTTCCCTCTGGTCCTGTCG	Guindalini C, Howard M, Haddley K, Laranjeira R, Collier D, Ammar N, Craig I, O'Gara C, Bubb VJ, Greenwood T, Kelsoe J, Asherson P, Murray RM, Castelo A, Quinn JP, Vallada H, Breen G. **(2006)** A dopamine transporter gene functional variant associated with cocaine abuse in a Brazilian sample **Proc Natl Acad Sci U S A.** 103(12), 4552-7
	GTCCAGGCCCCAGGAGCTGCCGCAGC[A/G]GGCAGTGGAAGGAAGGCACGTTCAG	Mick E, Kim JW, Biederman J, Wozniak J, Wilens T, Spencer T, Smoller JW, Faraone SV. **(2008)** Family based associaton study of pediatric bipolar disorder and the dopamine transporger gene (SLC6A3) **Am J Med Genet B Neuropsychiatr Genet**. 147 B (7), 1182-5
	CAGCTTCCCCTCCCAACACAGAGGCG[A/C]GGCCCAAGTGCAGGACTCACAACGG	Guindalini C, Howard M, Haddley K, Laranjeira R, Collier D, Ammar N, Craig I, O'Gara C, Bubb VJ, Greenwood T, Kelsoe J, Asherson P, Murray RM, Castelo A, Quinn JP, Vallada H, Breen G. **(2006)** A dopamine transporter gene functional variant associated with cocaine abuse in a Brazilian sample **Proc Natl Acad Sci U S A.** 103(12), 4552-7
	AAGACACAGTGACGGTATACTCATGA[C/T]GGAATATGATTCGGCCTTAAAACAA	Mick E, Kim JW, Biederman J, Wozniak J, Wilens T, Spencer T, Smoller JW, Faraone SV. **(2008)** Family based associaton study of pediatric bipolar disorder and the dopamine transporger gene (SLC6A3) **Am J Med Genet B Neuropsychiatr Genet**. 147 B (7), 1182-5
	AAGGCGAAGCCGGCGATGGTACGTAC[A/G]TTGGTGACGCAGAACAGGGACAGGA	Talkowski ME, Bamne M, Mansour H, Nimgaonkar VL. **(2007)** Dopamine genes and schizophrenia: case closed or evidence pending? **Schizophr Bull.** 33(5), 1071-81
	GCCATCGCCACGCTCCCTCTGTCCTC[A/G]GCCTGGGCCGTGGTCTTCTTCATCA	Guindalini C, Howard M, Haddley K, Laranjeira R, Collier D, Ammar N, Craig I, O'Gara C, Bubb VJ, Greenwood T, Kelsoe J, Asherson P, Murray RM, Castelo A, Quinn JP, Vallada H, Breen G. **(2006)** A dopamine transporter gene functional variant associated with cocaine abuse in a Brazilian sample **Proc Natl Acad Sci U S A.** 103(12), 4552-7
	TGCTTCCTGCTACCAGCAGGCAGACT[C/T]GGATGGAGGTGGAGGGGACGAGAGT	Guindalini C, Howard M, Haddley K, Laranjeira R, Collier D, Ammar N, Craig I, O'Gara C, Bubb VJ, Greenwood T, Kelsoe J, Asherson P, Murray RM, Castelo A, Quinn JP, Vallada H, Breen G. **(2006)** A dopamine transporter gene functional variant associated with cocaine abuse in a Brazilian sample **Proc Natl Acad Sci U S A.**

		103(12), 4552-7 Le Strat Y, Ramoz N, Pickering P, Burger V, Boni C, Aubin HJ, Ades J, Batel P, Gorwood P. **(2008)** The 3' part of the dopamine transporter gene DAT1/SLC6A3 is associated with withdrawal seizures in patients with alcohol dependence. **Alcohol Clin Exp Res**. 32(1), 27-35
	CACGGTAAAAATACAA GGACAGTGTG[A/T]GCA GCAGAATGGCCAGGCA GACCAC	Preuss UW, Zill P, Koller G, Bondy B, Sokya M. **(2007)** D2 dopamine receptor gene haplotypes and their influence on alcohol and tobacco consumption magnitude in alcohol-dependent individuals **Alcohol Alcohol**. 42(3), 258-66 Shi J, Badner JA, Hattori E, Potash JB, Willour VL, McMahon FJ, Gershon ES, Liu C. **(2008)** Neurotransmission and bipolar disorder: a systematic family-based association study. **Am J Med Genet B Neuropsychiatr Genet.** 147B(7), 1270-7
	AGGGTTATTAGGATGCT GTGGTCATG[C/T]CGTGT GTGGATGAGTCCATGCT GTT	Shi J, Badner JA, Hattori E, Potash JB, Willour VL, McMahon FJ, Gershon ES, Liu C. **(2008)** Neurotransmission and bipolar disorder: a systematic family-based association study. **Am J Med Genet B Neuropsychiatr Genet.** 147B(7), 1270-7
	GCCAGGCAGGGGCTGG TGGAGGTGCA[C/G]GGC CTGGAGGAACACAGAG CCCAGC	Mick E, Kim JW, Biederman J, Wozniak J, Wilens T, Spencer T, Smoller JW, Faraone SV. **(2008)** Family based associaton study of pediatric bipolar disorder and the dopamine transporger gene (SLC6A3) **Am J Med Genet B Neuropsychiatr Genet**. 147 B (7), 1182-5
	AGGAGAGGACGTTTGC GCGATTCTCC[C/G]CAG ATCCAGTGTTTCCCGTC AGCCA	Friedel S, Saar K, Sauer S, Dempfle A, Walitza S, Renner T, Romanos M, Freitag C, Seitz C, Palmason H, Scherag A, Windemuth-Kieselbach C, Schimmelmann BG, Wewetzer C, Meyer J, Warnke A, Lesch KP, Reinhardt R, Herpertz-Dahlmann B, Linder M, Hinney A, Remschmidt H, Schafer H, Konrad K, Hubner N, Hebebrand J. **(2007)** Association and linkage of allelic variants of the dopamine transporter gene in ADHD **Mol Psychiatry** 12(10), 923-33
	GGCTCGTGGCCCTGCGG GCGGATCTT[G/T]GGAA GAGCTTGTTCACACTCA CCTA	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak assocation with post-surgical pain in humans. **Mol Pain.** 2,24
	TCGAGGCAGGGCCACC GGGGACGTCC[A/G]AGA ACATTGGTGATCCCTTC CCAGG	Preuss UW, Zill P, Koller G, Bondy B, Sokya M. **(2007)** D2 dopamine receptor gene haplotypes and their influence on alcohol and tobacco consumption magnitude in alcohol-dependent individuals **Alcohol Alcohol**. 42(3), 258-66
	AATGCAGGCGTGGGAC AAGGCAGCTC[C/T]GAG TCCTGCTCAATGGTTTT GTGAC	Oades RD, Lasky-Su J, Christiansen H, Faraone SV, Sonuga-Barke EJ, Banaschewski T, Chen W, Anney RJ, Buitelaar JK, Ebstein RP, Franke B, Gill M, Miranda A, Roeyers H, Rothenberger A, Sergeant JA, Steinhausen HC, Taylor EA, Thompson M, Asherson P. **(2008)** The influence of serotonin- and other genes on impulsive behavioral aggression and cognitive impulsivity in children with attendiotn-deficity/hyperactivity disorder (ADHD): Findings from a family-based association test (FBAT) analysis **Behav Brain Funct**.4,48
	GAGCTCATCCTTGTCAA GGAGCAGAA[C/T]GGAG TGCAGCTCACCAGCTCC ACCC	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak assocation with post-surgical pain in humans. **Mol Pain.** 2,24
	GTGGGGAGGGGTGCAG GGGAAGGAGG[A/G]GCA AACCAGAGTGTCTGTCT TGAGG	Genro JP, Polanczyk GV, Zeni C, Oliveira AS, Roman T, Rohde LA, Hutz MH. **(2008)** A common haplotype at the dopamine transporter gene 5' region is associated with attention-deficit/hyperactivity disorder. **Am J Med Genet B Neuropsychiatr Gene**. 147B(8), 1568-75
	AAACACGCTGCTGCTGG ATCCAAATG[A/C]CAGA AGTCGCCCTGGCTGGGG CGGT	Guindalini C, Howard M, Haddley K, Laranjeira R, Collier D, Ammar N, Craig I, O'Gara C, Bubb VJ, Greenwood T, Kelsoe J, Asherson P, Murray RM, Castelo A, Quinn JP, Vallada H, Breen G. **(2006)** A dopamine transporter gene functional variant associated with cocaine abuse in a Brazilian sample **Proc Natl Acad Sci U S A.** 103(12), 4552-7

	CTGCGCGCTGGTGCTCT GGGCAGGGC[G/T]GGGA GGCCGGGCGAGGACTC GCCAG	Guindalini C, Howard M, Haddley K, Laranjeira R, Collier D, Ammar N, Craig I, O'Gara C, Bubb VJ, Greenwood T, Kelsoe J, Asherson P, Murray RM, Castelo A, Quinn JP, Vallada H, Breen G. **(2006)** A dopamine transporter gene functional variant associated with cocaine abuse in a Brazilian sample **Proc Natl Acad Sci U S A.** 103(12), 4552-7
	GGAGCCAGGACGCGAG GGCGACCCCG[A/T]CGG CGGGAGGGCGGGGCGG GGCGGA	'Talkowski ME, Bamne M, Mansour H, Nimgaonkar VL. **(2007)** Dopamine genes and schizophrenia: case closed or evidence pending? **Schizophr Bull.** 33(5), 1071-81
HTR3B	CCTTTACAGCCTTTACC TAAGGCAGT[A/G]CTCTT GCTGACATTCAGGACAC TAA	Levran O, Londono D, O'Hara K, Nielsen DA, Peles E, Rotrosen J, Casadonte P, Linzy S, Randesi M, Ott J, Adelson M, Kreek MJ. **(2008)** Genetic susceptibility to heroin addiction: a candidate gene association study. **Genes Brain Behav** 7(7), 729-9
	TTTGGCCTTCTCTCTTGG GCCAAGGA[A/G]TTTCT GCTCTATTGCATGTTCT CAT	Ruano G, Thompson PD, Windemuth A, Seip RL, Dande A, Sorokin A, Kocheria M, Smith A, Holford TR, Wu AH. **(2007)** Physiogenomic association of statin-related myalgia to serotonin receptors. **Muscle Nerve** 36(3), 329-35
	GAGAGCTCCTTGGAGAT GGAATAGGC[C/T]CCAA GGTTAGCCTGTAATTGC CTCC	Ducci F, Enoch MA, Yuan Q, Shen PH, White KV, Hodgkinson C, Albaugh B, Virkkunen M, Goldman D. **(2009)** HTR3B is associated with alcoholism with antisocial behavior and alpha EEG power—an intermediate phenotype for alcoholism and co-morbid behaviors**. Alcohol.** 43(1), 73-84 Oades RD, Lasky-Su J, Christiansen H, Faraone SV, Sonuga-Barke EJ, Banaschewski T, Chen W, Anney RJ, Buitelaar JK, Ebstein RP, Franke B, Gill M, Miranda A, Roeyers H, Rothenberger A, Sergeant JA, Steinhausen HC, Taylor EA, Thompson M, Asherson P. **(2008)** The influence of serotonin- and other genes on impulsive behavioral aggression and cognitive impulsivity in children with attendiotn-deficity/hyperactivity disorder (ADHD): Findings from a family-based association test (FBAT) analysis **Behav Brain Funct**.4,48
	CCTTAGCACCTGTGTGT CTATCATtc[C/T]gggcagga aaacttgcacaattaaa	Oades RD, Lasky-Su J, Christiansen H, Faraone SV, Sonuga-Barke EJ, Banaschewski T, Chen W, Anney RJ, Buitelaar JK, Ebstein RP, Franke B, Gill M, Miranda A, Roeyers H, Rothenberger A, Sergeant JA, Steinhausen HC, Taylor EA, Thompson M, Asherson P. **(2008)** The influence of serotonin- and other genes on impulsive behavioral aggression and cognitive impulsivity in children with attendiotn-deficity/hyperactivity disorder (ADHD): Findings from a family-based association test (FBAT) analysis **Behav Brain Funct**.4,48
NOS3	CTTCATCCGGGGGTAAG TGAGATGGA[A/G]GACT TGGTGGGGAGCTGCCCA GGGT ACTATAGCTCCCAGAGC CAGAGCTGG[G/T]ATCA AACCGGCTGGCCCTGTG GCTT ACCAGGGCATCAAGCTC TTCCCTGGC[C/T]GGCTG ACCCTGCCTCAGCCCTA GTC AGGGTGGGGGTGGAGG CACTGGAAGG[C/T]AGC TTCCTGCTCTTTTGTGTC CCCC	Kullo IJ, Greene MT, Boerwinkle E, Chu J, Turner ST, Kardia SL. **(2008)** Association of polymorphisms in NOS3 with the ankle-brachial index in hypertensive adults **Atherosclerosis.** 196(2), 905-12

	GACTCCCTTCAGGCAGT CCTTTAGTC[A/C]CCAGC CTCACCTTTGCTCTCAA TGT	
PPARG	AAACTCTGGGAGATTCT CCTATTGAC[C/G]CAGA AAGCGATTCCTTCACTG ATAC	Sanghera DK, Ortega L, Han S, Singh J, Ralhan SK, Wander GS, Mehra NK, Mulvihill JJ, Ferrell RE, Nath SK, Kamboth MI. **(2008)** Impact of nine common type 2 diabetes risk polymorphisms in Asian Indian Sikhs: PPARG2 (Pro12AIa), IGF2BP2, TCF7L2, and FTO variants confer a significant risk. **BMC Med Genet.** 9,59
	AGGATTTTCTTACATTT AAAGCAGAA[C/T]GACA CTACTGATACACAAAAG TAAA GAGAAATCTTCGGAGG GCTCACCAGC[A/G]TCA CAAGTAGGTAGACCAG AAGAGG	Chen L, Velasco Mondragon HE, Lazcano-Ponce E, Collins A, Shugart YY. **(2006)** Effect of the peroxisome proliferators-activated receptor (PPAR) gamma 3 gene on BMI in 1,210 school students from Morelos, Mexico. **Pac Symp Biocomput.** 467-77
	GTTTACAGACCTTGTCA GAGTTGGTA[C/G]TAATT CCAGAATATAATCATTT CAA	Kilpelainen TO, Lakka TA, Laakasonen DE, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiukaanniemi S, Lindi V, Tuomilehto J, Uusitupa M, Laakso M. **(2008)** SNPs in PPARG associate with type 2 diabets and interact with physical activity. **Med Sci Sports Exerc** 40 (1), 25-33
	TGGTTGACACAGAGATG CCATTCTGG[C/G]CCACC AACTTTGGGATCAGCTC CGT	Hancock AM, Witonsky DB, Gordon AS, Eshel G, Pritchard JK, Coop G, Di Rienzo A. **(2008)** Adaptations to climate in candidate genes for common metabolic disorders. **PLoS Genet**. 4(2), e32
	GATTTATTTAAATCATC TCTAATTCT[C/T]ACAAC TCCGAAAAGATAAGAA AACA	Gallicchio L, Chang H, Christo DK, Thuita L, Huang HY, Strickland P, Ruczinski I, Hoffman SC, Helzlsouer KJ. **(2008)** Single nucleotide polymorphisms in inflammation-related genes and mortality in a community-based cohort in Washingtom County, Maryland **Am J Epidemiol**. 167(7), 807-13
	AGGATTTTCTTACATTT AAAGCAGAA[C/T]GACA CTACTGATACACAAAAG TAAA	Saez ME, Grilo A, Moron FJ, Manzano L, Martinez-Larrad MT, Gonzalez-Perez A, Serrano-Hernando J, Ruiz A, Ramirez-Lorca R, Serrano-Rios M. **(2008)** Interaction between Calpain 5, Peroxisome proliferator-activated receptor-delta genes: a polygenic approach to obesity **Cardiovasc Diabetol.** 7,23 Fox CS, Heard-Costa N, Cupples LA, Dupuis J, Vasan RS, Atwood LD. **(2007)** Genome-wide association to body mass index and waist circumference: the Framingham Heart Study 100K project **BMC Med Genet.**8, Suppl 1:S18. Kiel DP, Demissie S, Dupuis J, Lunetta KL, Murabito JM, Karasik D. **(2007)** Genome-wide association with body mass and geometry in the Framingham Heart Study **BMC Med Genet**. 8, Suppl 1:S14 Chen L, Velasco Mondragon HE, Lazcano-Ponce E, Collins A, Shugart YY. **(2006)** Effect of the peroxisome proliferators-activated receptor (PPAR) gamma 3 gene on BMI in 1,210 school students from Morelos, Mexico. **Pac Symp Biocomput.** 467-77
	GTTGGGGATCCAGTTGG CCTCATTCT[A/G]AGCTG GCTGTGGATTCACAGAA GAA	Fox CS, Heard-Costa N, Cupples LA, Dupuis J, Vasan RS, Atwood LD. **(2007)** Genome-wide association to body mass index and waist circumference: the Framingham Heart Study 100K project **BMC Med Genet.**8, Suppl 1:S18.
	AAGATACGGGGGAGGA AATTCACTGG[A/G]TTTT ACAATATATTTTTCAAG GCAA	Gallicchio L, Chang H, Christo DK, Thuita L, Huang HY, Strickland P, Ruczinski I, Hoffman SC, Helzlsouer KJ. **(2008)** Single nucleotide polymorphisms in inflammation-related genes and mortality in a community-based cohort in Washingtom County, Maryland **Am J Epidemiol**. 167(7), 807-13 Huang HY, Thuita L, Strickland P, Hoffman SC, Comstock GW, Helzlsouer KJ. **(2006)** Frequencies of single nucleotide polymorphisms in genes regulating inflammatory responses in a community-based population **BMC Med Genet.** 8,7
	GAGAAATCTTCGGAGG GCTCACCAGC[A/G]TCA CAAGTAGGTAGACCAG AAGAGG	Chen L, Velasco Mondragon HE, Lazcano-Ponce E, Collins A, Shugart YY. **(2006)** Effect of the peroxisome proliferators-activated receptor (PPAR) gamma 3 gene on BMI in 1,210 school students from Morelos, Mexico. **Pac Symp Biocomput.** 467-77
ChREBP	GACAAAAAGCAATTGA	Kooner JS, Chambers JC, Aguilar-Salinas CA, Hinds DA, Hyde CL, Warnes GR,

	GGTCCAGGAG[C/G]TGCCGCCCACCCGGCTCCTCCTCTG	Gomez Perez FJ, Frazer KA, Elliott P, Scott J, Milos PM, Cox DR, Thompson JF **(2008)** Genome-wide scan identifies variation in MLXIPL associated with plasma triglycerides **Nat Genet** 40(2), 149-51 Vrablik M, Ceska R, Adamkova V, Peasey A, Pikhart H, Kubinova R, Marmot M, Bobak M, Hubacek JA. **(2008)** MLXIPL variant in individuals with low and high triglyceridemia in white population in Central Europe **Hum Genet.** 124(5), 553-5
FTO	GCTGTCAGCACCTGGTACAAATACCA[A/G]GATAGGGTTTTTGGGGCCACATTTT	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	GCATGCCAGTTGCCCACTGTGGCAAT[A/C]AATATCTGAGCCTGTGGTTTTTGCC	Haupt A, Thamer C, Staiger H, Tschritter O, Kirchhoff K, Machicao F, Haring HU, Stefan N, Fritsche A. **(2008**) Variation in the FTO Gene Influences Food Intake but not Energy Expenditure **Exp Clin Endocrinol Diabets (**in press). Song Y, You NC, Hsu YH, Howard BV, Langer RD, Manson JE, Nathan L, Niu T, F Tinker L, Liu S. **(2008)** FTO polymorphisms are associated with obesity but not diabetes risk in postmenopausal women **Obesity (Silver Spring)** 16(11), 2472-80 Kloting N, Schleinitz D, Ruschke K, Berndt J, Fasshauer M, Tonjes A, Schon MR, Kovacs P, Stumvoll M, Bluher M. **(2008)** Inverse relationship between obesity and FTO gene expression in visceral adipose tissue in humans **Diabetologia** 51(4), 641-7
	AGGTTCCTTGCGACTGCTGTGAATTT[A/T]GTGATGCACTTGGATAGTCTCTGTT	Hennig BJ, Fulford AJ, Sirugo G, Rayco-Solon P, Hattersley AT, Frayling TM, Prentice AM. **(2009)** FTO gene variation and measures of body mass in an African population **BMC Med Genet** 10(1), 21 Cecil JE, Tavendale R, Watt P, Hetherington MM, Palmer CN. **(2008)** An obesity-associated FTO gene variant and increased energy intake in children **N Engl J Med** 359(24), 2558-66 Fisher E, Schulze MB, Stefan N, Haring HU, Doring F, Joost HG, Al-Hasani H, Boeing H, Pischon T. **(2009)** Association of the FTO rs9939609 Single Nucleotide Polymorphism With C-reactive Protein Levels **Obesity (Silver Spring).** 17(2),330-4 Zabena C, Gonzalez-Sanchez JL, Martinez-Larrad MT, Torres-Garcia A, Alvarez-Fernandez-Represa J, Corbaton-Anchuelo A,Perez-Barba M, Serrano-Rios M. (**2009)** The FTO obesity gene. Genotyping and gene expressionanalysis in morbidly obese patients. **Obes Surg.** 19(1), 87-95
	GATGACAACATGCAAACTTTATGGCC[A/G]GAAACCAAAGAGTCAGGCAAAATAT	Rampersaud E, Mitchell BD, Pollin TI, Fu M, Shen H, O'Connell JR, Ducharme JL, Hines S, Sack P, Naglieri R, Shuldiner AR, Snitker S. **(2008)** Physical activity and the association of common FTO gene variants with body mass index and obesity. **Arch Intern Med**. 168(16), 1791-7
	aaaagaaaGTAAACATATTTAAGGTC[A/G]TAAATAAGGCCATGTCTAATAGTGA	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	aggaatgttctgatggcttggcccag[G/T]tggtgactgtgcagatagactgaag	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746
	tcagcacccaagggaccatcaaagag[A/G]ctgttgtggagagggaatccgaagg	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53 Hinney A, Nguyen TT, Scherag A, Friedel S, Bronner G, Muller TD, Grallert H, Illig

		T, Wichmann HE, Rief W, Schafer H, Hebebrand J. **(2007)** Genome wide association (GWA) study for early onset extreme obesity supports the role of fat mass and obesity associated gene (FTO) variants. **PLoS One**; 2(12), e1361
	TGGAGTGTTTTTCCTTC ACCTTTTCC[A/G]GTCTC TGGGTTGCATCGCCAGA CTG	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53 Hinney A, Nguyen TT, Scherag A, Friedel S, Bronner G, Muller TD, Grallert H, Illig T, Wichmann HE, Rief W, Schafer H, Hebebrand J. **(2007)** Genome wide association (GWA) study for early onset extreme obesity supports the role of fat mass and obesity associated gene (FTO) variants. **PLoS One**; 2(12), e1361
	TGTCTAGCCCTGTGGGT TTACATTAG[A/T]TAGGG TAGGTTATTGCTGCAAC GTA	Hinney A, Nguyen TT, Scherag A, Friedel S, Bronner G, Muller TD, Grallert H, Illig T, Wichmann HE, Rief W, Schafer H, Hebebrand J. **(2007)** Genome wide association (GWA) study for early onset extreme obesity supports the role of fat mass and obesity associated gene (FTO) variants. **PLoS One**; 2(12), e1361
	CTATCCAGGATGGCTCT AAAGGGACT[C/T]CGCT ATAGGTTGGGGCTATGA TAGA	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746
	GCTTATATTCAAAGCTC CAGGTAAAT[A/G]TAAG ATGTTGCTATAATTACC TAAG	Rampersaud E, Mitchell BD, Pollin TI, Fu M, Shen H, O'Connell JR, Ducharme JL, Hines S, Sack P, Naglieri R, Shuldiner AR, Snitker S. **(2008)** Physical activity and the association of common FTO gene variants with body mass index and obesity. **Arch Intern Med**. 168(16), 1791-7
	GGTAGGCAGGTGGATCT GAAATCTCA[C/T]ATAGT ACCAAGACACGTGACTA GGA	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53 Hinney A, Nguyen TT, Scherag A, Friedel S, Bronner G, Muller TD, Grallert H, Illig T, Wichmann HE, Rief W, Schafer H, Hebebrand J. **(2007)** Genome wide association (GWA) study for early onset extreme obesity supports the role of fat mass and obesity associated gene (FTO) variants. **PLoS One**; 2(12), e1361
	ttgattcttatacttttttgtttagt[C/T]g ttgaaatatgttgttttggttgaa	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53 Hinney A, Nguyen TT, Scherag A, Friedel S, Bronner G, Muller TD, Grallert H, Illig T, Wichmann HE, Rief W, Schafer H, Hebebrand J. **(2007)** Genome wide association (GWA) study for early onset extreme obesity supports the role of fat mass and obesity associated gene (FTO) variants. **PLoS One**;2(12), e1361 Berentzen T, Kring SI, Holst C, Zimmermann E, Jess T, Hansen T, Pedersen O, Toubro S, Astrup A, Sorensen TI. **(2008)** Lack of association of fatness-related FTO gene variants with energy expenditure or physical activity. **J Clin Endocrinol Metab** 93(7), 2904-8
	AATTAGGAAGATTTGAG TAGCTAAAA[A/G]TTCC AAGAGTGGAATAATAG TTTTA	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746
	TTTGGTGCACTCCCAAT TTACTCTAA[A/T]CTTCT ACGGGCTTCCTTGGAGA	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao

	AAC	K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	GACCTGAAAATAGGTG AGCTGTCAAG[G/T]TGTT GGCAGGGAGAGGCTCC TCTGG	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53 Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746 Scuteri A, Sanna S, Chen WM, Uda M, Albai G, Strait J, Najjar S, Nagaraja R, Orru M, Usala G, Dei M, Lai S, Maschio A, Busonero F, Mulas A, Ehret GB, Fink AA, Weder AB, Cooper RS, Galan P, Chakravarti A, Schlessinger D, Cao A, Lakkata E, Abecasis GR. **(2007)** Genome-wide association scan shows genetic variants in the FTO gene are associated with obesity-related traits **PLoS Genet.** 3(7), e115
	tggttcactgcatattcccagtaatt[C/G]gaacaatgcctgacatgaagtagac	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	TTAGAATGTCTGAATTA TTATTCTAG[A/G]TTCCT TGCGACTGCTGTGAATT TTG	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53 Scuteri A, Sanna S, Chen WM, Uda M, Albai G, Strait J, Najjar S, Nagaraja R, Orru M, Usala G, Dei M, Lai S, Maschio A, Busonero F, Mulas A, Ehret GB, Fink AA, Weder AB, Cooper RS, Galan P, Chakravarti A, Schlessinger D, Cao A, Lakkata E, Abecasis GR. **(2007)** Genome-wide association scan shows genetic variants in the FTO gene are associated with obesity-related traits **PLoS Genet.** 3(7), e115
	TTGATTTCGGTAGTCAT AACACCACC[C/T]TGGA AGGCACCCTAGATAGA GGTCA	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746
	TTCATTCTACCTGTCTTT AGTATCAT[A/G]GGGGT AGTTACCTCAGCGGGGG TAG	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	ttgctcaaggtcacacagtaaccta[A/G]gtaggcaggataagctctggttctg	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746
	TATGATGGTTAGGTTAG GTTGCAAGT[C/T]TTGGA ATATATGCAGAGGAATA ACT	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746

	TTATAAACCTCTAAAAT AGTTACTAA[A/G]TAAG TTATTCTTTTAGGTATTT TTC	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746
	TTTTATTTCCGCAATCA CTCCCTAAT[C/G]TTTAT TTCTTTTTTGCTTCGCAT CA	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	TAGCATTTTTCTGGAGC GTAATTTCA[C/T]AATGT GAATCAGAAGTCTTAAT AGT	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	GAGCACAGGTGGAGAG AAAGGGGAGT[A/G]AGA GAAGCAAAGAAGAAAA GCCTTT	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746
	TAGGGACACAAAAAGG GACATACTAC[A/G]TGA ATTACTaatatctaagaaaata	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	ATGAATTACTAATATCT AAGAAAATA[C/T]GATA Catttgagaacttagatgaag	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	GAAATGTGGTGTAGACG TGACCCAGG[A/G]GGAA ATGAGTTTTGTTGGACA GATT	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	CTACATCTCCTACTTAG CCGAGGTCT[C/T]TTCAC TCTCTGGGCAAGTCTCC TCA	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53
	ACACGGCTGAAGAGTC AGGAGTGGGA[C/T]GAA AAATACACTTCATTTGT AGGTG	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746
	GCACATTTATGCCTTTT ATATGCCAC[A/G]TACA CACGAAAACTccatatattct	Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, Yoneda M, Nakajima A, Miyazaki S, Tokunaga K, Kawamoto M, Funahashi T, Hamaguchi K, Yamada K, Hanafusa T, Oikawa S, Yoshimatsu H, Nakao K, Sakata T, Matsuzawa Y, Tanaka K, Kamatani N, Nakamura Y. **(2008)** Variations in the FTO gene are associated with severe obesity in the Japanese **J Hum Genet** 53(6), 546-53

	agagtgaataaaattatttctaaatt[C/T]atgcttcataccgtgtgtaatttag	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746
	tgttgcaacagagatgatggcagttt[C/T]ggccacggtgtaagaagcagaggtg	Grant SF, Li M, Bradfield JP, Kim SE, Annaiah K, Santa E, Glessner JT, Casalunovo T, Frackelton EC, Otieno FG, Shaner JL, Smith RM, Imielinski M, Eckert AW, Chiavacci RM, Berkowitz RI, Hakonarson H. **(2008)** Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP **PLoS ONE** 3(3), e1746
	ACATCTGCCTTCCCAGAGAAAGGAAA[A/G]TCAATGTTTAAAGTCTATTTAAAAA	Sherva R, Wilhelmsen K, Pomerleau CS, Chasse SA, Rice JP, Snedecor SM, Bierut LJ, Neuman RJ, Pomerleau OF. **(2008)** Association of a single nucleotide polymorphism in neuronal acetylcholine receptor subunit alpha 5 (CHRNA5) with smoking status and with 'pleasurable buzz' during early experimentation with smoking **Addiction** 103(9), 1544-52 Bierut LJ, Madden PA, Breslau N, Johnson EO, Hatsukami D, Pomerleau OF, Swan GE, Rutter J, Bertelsen S, Fox L, Fugman D, Goate AM, Hinrichs AL, Konvicka K, Martin NG, Montgomery GW, Saccone NL, Saccone SF, Wang JC, Chase GA, Rice JP, Ballinger DG. **(2007)** Novel genes identified in a high-density genome wide association study for nicotine dependence **Hum Mol Genet**. 16(1), 24-35
TNF Alpha	GGGAAGCAAAGGAGAAGCTGAGAAGA[C/T]GAAGGAAAAGTCAGGGTCTGGAGGG	Gallicchio L, Chang H, Christo DK, Thuita L, Huang HY, Strickland P, Ruczinski I, Hoffman SC, Helzlsouer KJ. **(2008)** Single nucleotide polymorphisms in inflammation-related genes and mortality in a community-based cohort in Washington County, Maryland. **Am J Epidemiol.** 167(7), 807-13
	GGAGGCAATAGGTTTTGAGGGGCATG[A/G]GGACGGGGTTCAGCCTCCAGGGTCC	Czerski PM, Rybabowski F, Kapelski P, Rybabowski JK, Dmitrzak-Weglarz M, Leszcynska-Rodziewicz A, Slopien A, Skibinska M, Kaczmarkiewicz-Fass M, Hauser J. **(2008)** Association of tumor necrosis factor -308G/A promoter polymorphism with schizophrenia and bipolar affective disorder in a Polish population **Neuropsychobiology** 57(1-2), 88-94 Wang SS, Cerhan JR, Hartge P, Davis S, Cozen W, Severson RK, Chatterjee N, Yeager M, Chanock SJ, Rothman N. **(2006)** Common genetic variants in proinflammatory and other immunoregulatory genes and risk for non-Hodgkin lymphoma **Cancer Res.** 66(19), 9771-80
	TGGCCCAGAAGACCCCCCTCGGAATC[A/G]GAGCAGGGAGGATGGGGAGTGTGAG	Loza MJ, McCall CE, Li L, Isaacs WB, Xu J, Chang BL. **(2007)** Assembly of inflammation-related genes for pathway-focused genetic analysis **PLoS ONE**. 2(10), e1035 Podgoreanu MV, White WD, Morris RW, Mathew JP, Stafford-Smith M, Welsby IJ, Grocott HP, Milano CA, Newman MF, Schwinn DA. **(2006)** Perioperative Genetics and Safety Outcomes Study (PEGASUS) Investigative Team **Circulation** 114(1 Suppl), I275-81
	TCTTTCTGCATCCCCGTCTTTCTCCA[C/T]GTTTTTTTCTCTCCATCCCTCCCTA	Podgoreanu MV, White WD, Morris RW, Mathew JP, Stafford-Smith M, Welsby IJ, Grocott HP, Milano CA, Newman MF, Schwinn DA. **(2006)** Perioperative Genetics and Safety Outcomes Study (PEGASUS) Investigative Team **Circulation** 114(1 Suppl), I275-81
	GTTGAATGCCTGGAAGGTGAATACAC[A/G]GATGAATGGAGAGAGAAAACCAGAC	Israni AK, Li N, Cizman BB, Snyder J, Abrams J, Joffe M, Rebbeck T, Feldman HI. **(2008)** Association of donor inflammation- and apoptosis-related genotypes and delayed allograft after kidney transplantation **Am J Kidney Dis.** 52(2), 331-9
MANEA	CATTTTACAATAGATAAATGCTTGTG[C/T]TACCTAAAGCACTTAGCACACAGTT	Yu Y, Kranzler HR, Panhuysen C, Weiss RD, Poling J, Farrer LA, Gelernter J. **(2008)** Substance dependence low-density whole genome association study in two distinct American populations**. Hum Genet**. 123(5), 494-506
Leptin OB	gctctgggaatgtctatcctatgcaa[C/T]ggagataaggactgagatacgccct	Jiang Y, Wilk JB, Borecki I, Williamson S, DeStefano AL, Xu G, Liu J, Ellison RC, Province M, Myers RH. **(2004)** Common variants in the 5' region of the leptin gene are associated with body mass index in men from the National Heart, Lung, and Blood Institute Family Heart Study **Am J Hum Genet.** 75(2), 220-30

	atgcaatggagataaggactgagata[C/T]gccctggtctcctgcagtaccctca	Jiang Y, Wilk JB, Borecki I, Williamson S, DeStefano AL, Xu G, Liu J, Ellison RC, Province M, Myers RH. **(2004)** Common variants in the 5' region of the leptin gene are associated with body mass index in men from the National Heart, Lung, and Blood Institute Family Heart Study **Am J Hum Genet.** 75(2), 220-30
	GGAGCCCCGTAGGAATCGCAGCGCCA[A/G]CGGTTGCAAGGTAAGGCCCCGGCGC	Jiang Y, Wilk JB, Borecki I, Williamson S, DeStefano AL, Xu G, Liu J, Ellison RC, Province M, Myers RH. **(2004)** Common variants in the 5' region of the leptin gene are associated with body mass index in men from the National Heart, Lung, and Blood Institute Family Heart Study **Am J Hum Genet.** 75(2), 220-30
	AAGTTCCTGACCTCTGAATGAGAGGG[A/G]CTGTGTAAGGCCAATGCCTGGGAGG	Jiang Y, Wilk JB, Borecki I, Williamson S, DeStefano AL, Xu G, Liu J, Ellison RC, Province M, Myers RH. **(2004)** Common variants in the 5' region of the leptin gene are associated with body mass index in men from the National Heart, Lung, and Blood Institute Family Heart Study **Am J Hum Genet.** 75(2), 220-30
	aataaaaataaaTGTTCTTCCTTGCA[A/T]TGAAGTTAAATATGTAAATTCTCAA	Jiang Y, Wilk JB, Borecki I, Williamson S, DeStefano AL, Xu G, Liu J, Ellison RC, Province M, Myers RH. **(2004)** Common variants in the 5' region of the leptin gene are associated with body mass index in men from the National Heart, Lung, and Blood Institute Family Heart Study **Am J Hum Genet.** 75(2), 220-30
	ACTTAGGTATTAGAGGGTGGCCATTA[C/T]TTGAGAGTGACTATGACCACAGTTA	Jiang Y, Wilk JB, Borecki I, Williamson S, DeStefano AL, Xu G, Liu J, Ellison RC, Province M, Myers RH. **(2004)** Common variants in the 5' region of the leptin gene are associated with body mass index in men from the National Heart, Lung, and Blood Institute Family Heart Study **Am J Hum Genet.** 75(2), 220-30
	TGGGTGAATGTGTTATGCTCTCTCCC[A/G]CCACCATGTCTTTATACCCCCTGAT	Jiang Y, Wilk JB, Borecki I, Williamson S, DeStefano AL, Xu G, Liu J, Ellison RC, Province M, Myers RH. **(2004)** Common variants in the 5' region of the leptin gene are associated with body mass index in men from the National Heart, Lung, and Blood Institute Family Heart Study **Am J Hum Genet.** 75(2), 220-30
	CTCCCAGTGGGTGGGAGAGAAAGGAC[A/G]TAAGGAAGCAAGTGGTAAAGGCCCT	Jiang Y, Wilk JB, Borecki I, Williamson S, DeStefano AL, Xu G, Liu J, Ellison RC, Province M, Myers RH. **(2004)** Common variants in the 5' region of the leptin gene are associated with body mass index in men from the National Heart, Lung, and Blood Institute Family Heart Study **Am J Hum Genet.** 75(2), 220-30
PEMT	atcccttcaccAGAGTGATTTCCTCG[A/C]GGCAGGTGCCTGGGGTAGCCACTGG	Liu Y, Zhang H, Ju G, Zhang X, Xu Q, Liu S, Yu Y, Shi J, Boyle S, Wang Z, Shen Y, Wei J. **(2007)** A study of the PEMT gene in schizophrenia **Neurosci Lett** 424(3), 203-6
	GGACTGCCTGGTTGTGCTTCGGACCC[A/G]GAGGCAGACAGAGGAGGCCTTTGAA	Liu Y, Zhang H, Ju G, Zhang X, Xu Q, Liu S, Yu Y, Shi J, Boyle S, Wang Z, Shen Y, Wei J. **(2007)** A study of the PEMT gene in schizophrenia **Neurosci Lett** 424(3), 203-6
MAO-A	CCCACTAGGCAAGCCTCCTAAAAGCA[A/G]TATGGTTGTAGATCACTGGAAAATA	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak association with acute post-surgical pain in humans. **Mol Pain** 2,24
	GTAAACATGCAAACTGAAACATTAGC[A/G]CCCATTTATTCAGCATCTTAGAAGA	Lin YM, Davamani F, Yang WC, Lai TJ, Sun HS. **(2008)** Association analysis of monoamine oxidase A gene and bipolar affective disorder in Han Chinese **Behav Brain Funct.** 4,21
	GAGTGAAGGCCAGGTACAGAGGAAAT[A/G]AAGCATTCCAAATAATGCCAGGTAA	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak association with acute post-surgical pain in humans. **Mol Pain** 2,24
	CCAAAGTTAACTTGTGAACCCTTCTA[A/G]TAAACTGCTCCAAGATATGACAAAA	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak association with acute post-surgical pain in humans. **Mol Pain** 2,24
	GTTTGCCATGGATGAACCACCAGGAT[A/G]GTGG	Rommelse NN, Altink ME, Arias-Vasquez A, Buschgens CJ, Fliers E, Faraone SV, Buitelaar JK, Sergeant JA, Oosterlaan J, Franke B. **(2008)** Differential association

	GGGAGACAGAAAAGGTTGATG	between MAOA, ADHD and neuropsychological functioning in boys and girls**. Am J Med Genet B Neuropsychiatr Genet**. 147B(8), 1524-30
	GGAAAATTCCCCTTCCCCTAAGACAT[C/T]CACCCTTCTGGTTTGGGTAATTCCT	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak association with acute post-surgical pain in humans. **Mol Pain** 2,24
	GCAGAGAGAAACCAGTTAATTCAGCG[G/T]CTTCCAATGGGAGCTGTCATTAAGT	Lin YM, Davamani F, Yang WC, Lai TJ, Sun HS. **(2008)** Association analysis of monoamine oxidase A gene and bipolar affective disorder in Han Chinese **Behav Brain Funct.** 4,21 Ni X, Sicard T, Bulgin N, Bismil R, Chan K, McMain S, Kennedy JL. **(2007)** Monoamine oxidase a gene is associated with borderline personality disorder. **Psychiatr Genet** 17(3), 153-7
	GTGCATGATGTATTACAAGGAGGCC[G/T]TCTGGAAGAAGAAGGGTAGGCTGCT	Lin YM, Davamani F, Yang WC, Lai TJ, Sun HS. **(2008)** Association analysis of monoamine oxidase A gene and bipolar affective disorder in Han Chinese **Behav Brain Funct.** 4,21 Li J, Kang C, Zhang H, Wang Y, Zhou R, Wang B, Guan L, Yang L, Faraone SV. **(2007)** Monoamine oxidase A gene polymorphism predicts adolescent outcome of attention-deficit/hyperactivity disorder **Am J Med Genet B Neuropsychiatr Genet.** 144B(4), 430-3
	AGAGAAGGAAGTGGTGTCCCCACAAA[G/T]GAATTGCTAAGGAGTTCCACAGCCT	Rommelse NN, Altink ME, Arias-Vasquez A, Buschgens CJ, Fliers E, Faraone SV, Buitelaar JK, Sergeant JA, Oosterlaan J, Franke B. **(2008)** Differential association between MAOA, ADHD and neuropsychological functioning in boys and girls**. Am J Med Genet B Neuropsychiatr Genet**. 147B(8), 1524-30
	AAGAGAAAACAAAGCTGAAATGCTGC[A/G]AGTCAATAATATCGTTGCTTTAACA	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak association with acute post-surgical pain in humans. **Mol Pain** 2,24
	TTTGACAACTATTTCTAGAATTTGCA[C/T]TGAACTCTGCTTTTCCTTTTAAATT	Kim H, Lee H, Rowan J, Brahim J, Dionne RA. **(2006)** Genetic polymorphisms in monoamine neurotransmitter systems show only weak association with acute post-surgical pain in humans. **Mol Pain** 2,24
	GGTCTCGGGAAGGTGACCGAGAAAGA[C/T]ATCTGGGTACAAGAACCTGAATCAA	Rommelse NN, Altink ME, Arias-Vasquez A, Buschgens CJ, Fliers E, Faraone SV, Buitelaar JK, Sergeant JA, Oosterlaan J, Franke B. **(2008)** Differential association between MAOA, ADHD and neuropsychological functioning in boys and girls**. Am J Med Genet B Neuropsychiatr Genet**. 147B(8), 1524-30 Li J, Kang C, Zhang H, Wang Y, Zhou R, Wang B, Guan L, Yang L, Faraone SV. **(2007)** Monoamine oxidase A gene polymorphism predicts adolescent outcome of attention-deficit/hyperactivity disorder **Am J Med Genet B Neuropsychiatr Genet.** 144B(4), 430-3 Huang S, Cook DG, Hinks LJ, Chen XH, Ye S, Gilg JA, Jarvis MJ, Whincup PH, Day IN. **(2005)** CYP2A6, MAOA, DBoH, DRD4, and 5HT2A genotypes, smoking behaviour and cotinine levels in 1518 UK adolescents **Pharmacogenet Genomics** 15(12), 839-50
CRH	CTGTCCCACAACATGGGGTCTTACAG[C/T]TCTTTGATGTATCCCCCCACAGGGG	Binder EB, Bradley RG, Liu W, Epstein MP, Deveau TC, Mercer KB, Tang Y, Gillespie CF, Heim CM, Nemeroff CB, Schwartz AC, Cubells JF, Ressler KJ. **(2008)** Association of FKBP5 polymorphisms and childhood abuse with risk of posttraumatic stress disorder symptoms in adults **JAMA** 299(11), 1291-305 Bradley RG, Binder EB, Epstein MP, Tang Y, Nair HP, Liu W, Gillespie CF, Berg T, Evces M, Newport DJ, Stowe ZN, Heim CM, Nemeroff CB, Schwartz A, Cubells JF, Ressler KJ. **(2008)** Influence of child abuse on adult depression: moderation by the corticotropin-releasing hormone receptor gene. **Arch Gen Psychiatry** 65(2), 190-200

	GCCTCTGGGGTCACCAG GTACATCTT[C/T]GATCT TGGCCACACTGGAGAGT CAA	Bradley RG, Binder EB, Epstein MP, Tang Y, Nair HP, Liu W, Gillespie CF, Berg T, Evces M, Newport DJ, Stowe ZN, Heim CM, Nemeroff CB, Schwartz A, Cubells JF, Ressler KJ. **(2008)** Influence of child abuse on adult depression: moderation by the corticotropin-releasing hormone receptor gene. **Arch Gen Psychiatry** 65(2), 190-200 Wasserman D, Sokolowski M, Rozanov V, Wasserman J. **(2008)** The CRHR1 gene: a marker for suicidality in depressed males exposed to low stress**. Genes Brain Behav** 7(1), 14-9
	TTTCTAAACACAGAGGA CTGGTGTTG[C/T]GTTAT GCAAAGAAAAATGCTTC TTA	Bradley RG, Binder EB, Epstein MP, Tang Y, Nair HP, Liu W, Gillespie CF, Berg T, Evces M, Newport DJ, Stowe ZN, Heim CM, Nemeroff CB, Schwartz A, Cubells JF, Ressler KJ. **(2008)** Influence of child abuse on adult depression: moderation by the corticotropin-releasing hormone receptor gene. **Arch Gen Psychiatry** 65(2), 190-200
	AAGACACTCAGGTGCA GGGACCCTCT[A/C]CATT TTTGCCCAGCAGCAGCC ATGC	Bradley RG, Binder EB, Epstein MP, Tang Y, Nair HP, Liu W, Gillespie CF, Berg T, Evces M, Newport DJ, Stowe ZN, Heim CM, Nemeroff CB, Schwartz A, Cubells JF, Ressler KJ. **(2008)** Influence of child abuse on adult depression: moderation by the corticotropin-releasing hormone receptor gene. **Arch Gen Psychiatry** 65(2), 190-200 Binder EB, Bradley RG, Liu W, Epstein MP, Deveau TC, Mercer KB, Tang Y, Gillespie CF, Heim CM, Nemeroff CB, Schwartz AC, Cubells JF, Ressler KJ. **(2008)** Association of FKBP5 polymorphisms and childhood abuse with risk of posttraumatic stress disorder symptoms in adults **JAMA** 299(11), 1291-305
	AGGGCCAGGAACCATG AACCAGCGCG[G/T]GTG GGGGCAGCCTCTTCAGG CCTGG	Liu Z, Zhu F, Wang G, Xiao Z, Wang H, Tang J, Wang X, Qiu D, Liu W, Cao Z, Li W. **(2006)** Association of corticotropin-releasing hormone receptor1 gene SNP and haplotype with major depression **Neurosci Lett** 404(3), 358-62 Licinio J, O'Kirwan F, Irizarry K, Merriman B, Thakur S, Jepson R, Lake S, Tantisira KG, Weiss ST, Wong ML. **(2004)** Association of a corticotropin-releasing hormone receptor 1 haplotype and antidepressant treatment response in Mexican-Americans **Mol Psychiatry** 9(12), 1075-82
	GGCACACCAGTCCTTTT GAGCCCCAG[C/T]GTCC CCAGGTTAATAACCTAG AATT	Bradley RG, Binder EB, Epstein MP, Tang Y, Nair HP, Liu W, Gillespie CF, Berg T, Evces M, Newport DJ, Stowe ZN, Heim CM, Nemeroff CB, Schwartz A, Cubells JF, Ressler KJ. **(2008)** Influence of child abuse on adult depression: moderation by the corticotropin-releasing hormone receptor gene. **Arch Gen Psychiatry** 65(2), 190-200
	TGAACACGGAGGCCAC ACAAGAGTGG[A/G]TTC CAAGTGAAGGAGTGAC CAACTC	Liu Z, Zhu F, Wang G, Xiao Z, Tang J, Liu W, Wang H, Liu H, Wang X, Wu Y, Cao Z, Li W. **(2007)** Association study of corticotropin-releasing hormone receptor1 gene polymorphisms and antidepressant response in major depressive disorders **Neurosci Lett** 414(2), 155-8 Liu Z, Zhu F, Wang G, Xiao Z, Wang H, Tang J, Wang X, Qiu D, Liu W, Cao Z, Li W. **(2006)** Association of corticotropin-releasing hormone receptor1 gene SNP and haplotype with major depression **Neurosci Lett** 404(3), 358-62 Licinio J, O'Kirwan F, Irizarry K, Merriman B, Thakur S, Jepson R, Lake S, Tantisira KG, Weiss ST, Wong ML. **(2004)** Association of a corticotropin-releasing hormone receptor 1 haplotype and antidepressant treatment response in Mexican-Americans **Mol Psychiatry** 9(12), 1075-82
	TCCTTTCCTGGGATCAC AGAGGGAAG[C/T]GCGG GGGAGCCTAGAGAGCA CCACA	Blomeyer D, Treutlein J, Esser G, Schmidt MH, Schumann G, Laucht M. **(2008)** Interaction between CRHR1 gene and stressful life events predicts adolescent heavy alcohol use **Biol Psychiatry** 63(2), 146-51
	TACAGGTGAAGGAAAG TGATTCTTTC[C/T]CCGT TAACTTTGTTTCACGCC AGAT	Bradley RG, Binder EB, Epstein MP, Tang Y, Nair HP, Liu W, Gillespie CF, Berg T, Evces M, Newport DJ, Stowe ZN, Heim CM, Nemeroff CB, Schwartz A, Cubells JF, Ressler KJ. **(2008)** Influence of child abuse on adult depression: moderation by the corticotropin-releasing hormone receptor gene. **Arch Gen Psychiatry** 65(2), 190-200
	CCCCCAACCAGAGATGA TGATGGGGG[A/G]CAGG GGAGGCACCAAACCCT	Blomeyer D, Treutlein J, Esser G, Schmidt MH, Schumann G, Laucht M. **(2008)** Interaction between CRHR1 gene and stressful life events predicts adolescent heavy alcohol use **Biol Psychiatry** 63(2), 146-51

	GGGCC	
	AGCAGCATACCCCTAGG GACCTAGGA[A/G]CAGG GAGGGAGAGAGGCAGC CCTGG	Liu Z, Zhu F, Wang G, Xiao Z, Tang J, Liu W, Wang H, Liu H, Wang X, Wu Y, Cao Z, Li W. **(2007)** Association study of corticotropin-releasing hormone receptor1 gene polymorphisms and antidepressant response in major depressive disorders **Neurosci Lett** 414(2), 155-8 Liu Z, Zhu F, Wang G, Xiao Z, Wang H, Tang J, Wang X, Qiu D, Liu W, Cao Z, Li W. **(2006)** Association of corticotropin-releasing hormone receptor1 gene SNP and haplotype with major depression **Neurosci Lett** 404(3), 358-62 Licinio J, O'Kirwan F, Irizarry K, Merriman B, Thakur S, Jepson R, Lake S, Tantisira KG, Weiss ST, Wong ML. **(2004)** Association of a corticotropin-releasing hormone receptor 1 haplotype and antidepressant treatment response in Mexican-Americans **Mol Psychiatry** 9(12), 1075-82
	CAGCTGGCACTGACAGC CTGGGGGGG[-/C/G]CGCTCTCCCCCTGC AGCCGTGCAGG	Keck ME, Kern N, Erhardt A, Unschuld PG, Ising M, Salyakina D, Muller MB, Knorr CC, Lieb R, Hohoff C, Krakowitzky P, Maier W, Bandelow B, Fritze J, Deckert J, Holsboer F, Muller-Myhsok B, Binder EB. **(2008)** Combined effects of exonic polymorphims in CRHR1 and AVPR1B genes in a case/control study for panic disorder **Am J Med Genet B Neuropsychiatr Genet** 147B(7), 1196-204
	GAGCACAAGAAGGCCA GCCCACTGGG[C/G]CCT GGGGCTGCCCTCGGCAA CCGTG	Keck ME, Kern N, Erhardt A, Unschuld PG, Ising M, Salyakina D, Muller MB, Knorr CC, Lieb R, Hohoff C, Krakowitzky P, Maier W, Bandelow B, Fritze J, Deckert J, Holsboer F, Muller-Myhsok B, Binder EB. **(2008)** Combined effects of exonic polymorphims in CRHR1 and AVPR1B genes in a case/control study for panic disorder **Am J Med Genet B Neuropsychiatr Genet** 147B(7), 1196-204
	CTGCTTCCCACCAATCA GCACAGCTC[A/C]TGCCT GGGGCTGGGACACACTC CCG	Bradley RG, Binder EB, Epstein MP, Tang Y, Nair HP, Liu W, Gillespie CF, Berg T, Evces M, Newport DJ, Stowe ZN, Heim CM, Nemeroff CB, Schwartz A, Cubells JF, Ressler KJ. **(2008)** Influence of child abuse on adult depression: moderation by the corticotropin-releasing hormone receptor gene. **Arch Gen Psychiatry** 65(2), 190-200
ADIPOQ	ATCAGAATGTGTGGCTT GCAAGAACC[A/G]GCTC AGATCCTGCCCTTCAAA AACA	Goyenechea E, Collins LJ, Parra D, Abete I, Crujeiras AB, O'Dell SD, Martinez JA. **(2009)** The 11391 G/A polymorphism of the adiponectin gene promoter is associated with metabolic syndrome traits and the outcome of an energy-restricted diet in obese subjects **Horm Metab Res.** 41(1): 55-61 Cauchi S, Nead KT, Choquet H, Horber F, Potoczna N, Balkau B, Marre M, Charpentier G, Froguel P, Meyre D. **(2008)** The genetic susceptibility to type 2 diabetes may be modulated by obesity status: implications for association studies **BMC Med Genet.** 9,45
	GTTCTACTGCTATTAG	Ahituv N, Kavaslar N, Schackwitz W, Ustaszewska A, Martin J, Hebert S, Doelle H, Ersoy B, Kryukov G, Schmidt S, Yosef N, Ruppin E, Sharan R, Vaisse C, Sunyaev S, Dent R, Cohen J, McPherson R, Pennacchio LA. **(2007)** Medical sequencing at the extremes of human body mass **Am J Hum Genet**. 80(4), 779-91
STS	GATGACAAGCCAGGCA GGGAGGAATG[A/G]ACC TGGATTCCTGGTGAAGG ACGTG	Brookes KJ, Hawi Z, Kirley A, Barry E, Gill M, Kent L. **(2008)** Association of the steroid sulfatase (STS) gene with attention deficit hyperactivity disorder **Am J Med Genet B Neuropsychiatr Genet** 147B(8), 1531-5
VDR	GTCAGCGATTCTTAATA TAAGAAAAA[A/G]TGGT GAAATGTGTTTAGAGTG TGCT	Jiang H, Xiong DH, Guo YF, Shen H, Xiao P, Yang F, Chen Y, Zhang F, Recker RR, Deng HW. **(2007)** Association analysis of vitamin D-binding protein gene polymorphisms with variations of obesity-related traits in Caucasian nuclear families **Int J Obes (Lond).** 31(8), 1319-24
	CCTGGGGTGCAGGACGC CGCGCTGAT[C/T]GAGG CCATCCAGGACCGCCTG TCCA	Handoko HY, Nancarrow DJ, Mowry BJ, McGrath JJ. **(2006)** Polymorphisms in the vitamin D receptor and their associations with risk of schizophrenia and selected anthropometric measures **Am J Hum Biol**. 18(3), 415-7
	GTTCCTGGGGCCACAGA CAGGCCTGC[A/G]CATT CCCAATACTCAGGCTCT GCTC	Dvornyk V, Long JR, Xiong DH, Liu PY, Zhao LJ, Shen H, Zhang YY, Liu YJ, Rocha-Sanchez S, Xiao P, Recker RR, Deng HW. **(2004)** Current limitations of SNP data from the public domain for studies of complex disorders: a test for ten candidate genes for obesity and osteoporosis **BMC Genet.** 25,5:4
	CATAAGACCTACGACCC CACCTACTC[C/T]GACTT	Dvornyk V, Long JR, Xiong DH, Liu PY, Zhao LJ, Shen H, Zhang YY, Liu YJ, Rocha-Sanchez S, Xiao P, Recker RR, Deng HW. **(2004)** Current limitations of SNP data from

	CTGCCAGTTCCGGCCTC CAG	the public domain for studies of complex disorders: a test for ten candidate genes for obesity and osteoporosis **BMC Genet.** 25,5:4
	TGGCCTGCTTGCTGTTC TTACAGGGA[C/T]GGAG GCAATGGCGGCCAGCA CTTCC	Dvornyk V, Long JR, Xiong DH, Liu PY, Zhao LJ, Shen H, Zhang YY, Liu YJ, Rocha-Sanchez S, Xiao P, Recker RR, Deng HW. **(2004)** Current limitations of SNP data from the public domain for studies of complex disorders: a test for ten candidate genes for obesity and osteoporosis **BMC Genet.** 25,5:4 Handoko HY, Nancarrow DJ, Mowry BJ, McGrath JJ. **(2006)** Polymorphisms in the vitamin D receptor and their associations with risk of schizophrenia and selected anthropometric measures **Am J Hum Biol**. 18(3), 415-7
	TGTGGGGGTGGGCCAGC CCAGCTTAG[A/G]TTATC TTGGCTCATTGTCCACT AGT	Dvornyk V, Long JR, Xiong DH, Liu PY, Zhao LJ, Shen H, Zhang YY, Liu YJ, Rocha-Sanchez S, Xiao P, Recker RR, Deng HW. **(2004)** Current limitations of SNP data from the public domain for studies of complex disorders: a test for ten candidate genes for obesity and osteoporosis **BMC Genet.** 25,5:4
DBI	TCTGTCCTCAGGCCAGG GCTTCGCTG[A/C]AGCCC CGGCCACTCCCTAGTGC CTG TACGAACTCACTGTAAA ACTCACCTT[C/T]GCCAT AAGACCTTCTTCAACTA AGT ACAGAGTTTACGAACTC ACTGTAAAA[C/T]TCACC TTCGCCATAAGACCTTC TTC GGAGAGAAAACAAAGT CAATGGGGCA[C/T]GTG TGGGAAACCAGCCTGAC CTGTG TTACAGGGACTTCCAAG GAAGATGCC[A/G]TGAA AGCTTACATCAACAAAG TAGA	Thoeringer CK, Binder EB, Salyakina D, Erhardt A, Ising M, Unschuld PG, Kern N, Lucae S, Brueckl TM, Mueller MB, Fuchs B, Puetz B, Lieb R, Uhr M, Holsboer F, Mueller-Myhsok B, Keck ME. **(2007)** Association of a Met88Val diazepam binding inhibitor (DBI) gene polymorphism and anxiety disorders with panic attacks **J Psychiatr Res** 41(7), 579-84
GABRA6	TTGGGAAAGGAGAGTCT GAAGGGACA[A/G]TGCA TGGTCGGAGAGCAGTG ACAAT	Ma DQ, Whitehead PL, Menold MM, Martin ER, Ashley-Koch AE, Mei H, Ritchie MD, Delong GR, Abramson RK, Wright HH, Cuccaro ML, Hussman JP, Gilbert JR, Pericak-Vance MA. **(2005)** Identification of significant association and gene-gene interaction of GABA receptor subunit genes in autism **Am J Hum Genet.** 77(3), 377-88
	AAATTGGAAATCTGTAA CGCAGCTTC[C/T]GTAAG CATGTGTGGGCAAAAA AGCA	Uhart M, McCaul ME, Oswald LM, Choi L, Wand GS. **(2004**) GABRA6 gene polymorphism and an attenuated stress response **Mol Psychiatry** 9(11), 998-1006
	TTCTTTCCATCTGGCAC CTATTTATT[C/G]ACTAT TTATGCATTCGTTGAAT TAT	Ma DQ, Whitehead PL, Menold MM, Martin ER, Ashley-Koch AE, Mei H, Ritchie MD, Delong GR, Abramson RK, Wright HH, Cuccaro ML, Hussman JP, Gilbert JR, Pericak-Vance MA. **(2005)** Identification of significant association and gene-gene interaction of GABA receptor subunit genes in autism **Am J Hum Genet.** 77(3), 377-88
	CTCTTTCACCATTGACA AATATTTAT[G/T]GACGA CTTACTTTCTATGTAAG GTC	Ma DQ, Whitehead PL, Menold MM, Martin ER, Ashley-Koch AE, Mei H, Ritchie MD, Delong GR, Abramson RK, Wright HH, Cuccaro ML, Hussman JP, Gilbert JR, Pericak-Vance MA. **(2005)** Identification of significant association and gene-gene interaction of GABA receptor subunit genes in autism **Am J Hum Genet.** 77(3), 377-88

GABRB3	CGTTCAGTTTAGTAAC	Hogart A, Nagarajan RP, Patzel KA, Yasui DH, Lasalle JM. **(2007)** 15q11-13 GABAA receptor genes are normally biallelically expressed in brain yet are subject to epigenetic dysregulation in autism-spectrum disorders **Hum Mol Genet** 16(6), 691-703
	AGCTTACCATTTAAGTA GAACTGTTT[A/G]AGAT GCTGGACATTCTAATAC AATC	Ma DQ, Whitehead PL, Menold MM, Martin ER, Ashley-Koch AE, Mei H, Ritchie MD, Delong GR, Abramson RK, Wright HH, Cuccaro ML, Hussman JP, Gilbert JR, Pericak-Vance MA. **(2005)** Identification of significant association and gene-gene interaction of GABA receptor subunit genes in autism **Am J Hum Genet.** 77(3), 377-88
	CCAAATCTGAAATTTAC TTGTCACTT[C/T]AGAGT TGTCTTTGAACGGAAAG ATT	Ma DQ, Whitehead PL, Menold MM, Martin ER, Ashley-Koch AE, Mei H, Ritchie MD, Delong GR, Abramson RK, Wright HH, Cuccaro ML, Hussman JP, Gilbert JR, Pericak-Vance MA. **(2005)** Identification of significant association and gene-gene interaction of GABA receptor subunit genes in autism **Am J Hum Genet.** 77(3), 377-88
	TCTGTTGAGTGATAATC TTTCTCGCA[A/G]ATAAC TCACAATATTTAAAAAT TGT	Ma DQ, Whitehead PL, Menold MM, Martin ER, Ashley-Koch AE, Mei H, Ritchie MD, Delong GR, Abramson RK, Wright HH, Cuccaro ML, Hussman JP, Gilbert JR, Pericak-Vance MA. **(2005)** Identification of significant association and gene-gene interaction of GABA receptor subunit genes in autism **Am J Hum Genet.** 77(3), 377-88
	AAGAACTCTTCCATGAT TGAAATGGT[A/C]GCAC ATGGAATAACATCGATA AGTT	Kim SA, Kim JH, Park M, Cho IH, Yoo HJ. **(2006)** Association of GABRB3 polymorphisms with autism spectrum disorders in Korean trios **Neuropsychobiology** 54(3), 160-5
	ACAGCAGGTTGGAGCA CAGGGCCTAA[A/G]TGG GAGGCCAGGGAGGTGG GCAGAG	Kim SA, Kim JH, Park M, Cho IH, Yoo HJ. **(2006)** Association of GABRB3 polymorphisms with autism spectrum disorders in Korean trios **Neuropsychobiology** 54(3), 160-5
	ATTGCTGATTTTCAGGC AAACTATGT[A/T]ACAT GGCTTTCAATGGGTGCT TGGC	Ma DQ, Whitehead PL, Menold MM, Martin ER, Ashley-Koch AE, Mei H, Ritchie MD, Delong GR, Abramson RK, Wright HH, Cuccaro ML, Hussman JP, Gilbert JR, Pericak-Vance MA. **(2005)** Identification of significant association and gene-gene interaction of GABA receptor subunit genes in autism **Am J Hum Genet.** 77(3), 377-88
MTHFR	GAAGCAGTTAGTTCTGA CACCAACAA[A/G]TGGT GATAAGAGGTTGATAGC CTAG	Liu X, Zhao LJ, Liu YJ, Xiong DH, Recker RR, Deng HW. **(2008)** The MTHFR gene polymorphism is associated with lean body mass but not fat body mass **Hum Genet**. 123(2), 189-96
	GTGGGGGGAGGAGCTG ACCAGTGAAG[A/C]AAG TGTCTTTGAAGTCTTTGT TCTT	Shi J, Gershon ES, Liu C. **(2008)** Genetic associations with schizophrenia: Meta-analyses of 12 candidate genes **Schizophr Res** 104(1-3), 96-107
	CTTGAAGGAGAAGGTGT CTGCGGGAG[C/T]CGAT TTCATCATCACGCAGCT TTTC	Shi J, Gershon ES, Liu C. **(2008)** Genetic associations with schizophrenia: Meta-analyses of 12 candidate genes **Schizophr Res** 104(1-3), 96-107
	AGATGTTCCACCCCGGG CCTGGACCC[C/T]GAGC GGCATGAGA	Liu X, Zhao LJ, Liu YJ, Xiong DH, Recker RR, Deng HW. **(2008)** The MTHFR gene polymorphism is associated with lean body mass but not fat body mass **Hum Genet.** 123(2), 189-96
MLXIPL (carbohydrate binding element)	GACAAAAAGCAATTGA GGTCCAGGAG[C/G]TGC CGCCCACCCGGCTCCTC CTCTG	Kooner JS, Chambers JC, Aguilar-Salinas CA, Hinds DA, Hyde CL, Warnes GR, Gomez Perez FJ, Frazer KA, Elliott P, Scott J, Milos PM, Cox DR, Thompson JF. **(2008)** Genome-wide scan identifies variation in MLXIPL associated with plasma triglycerides **Nat Genet**. 40(2), 149-51 Vrablik M, Ceska R, Adamkova V, Peasey A, Pikhart H, Kubinova R, Marmot M, Bobak M, Hubacek JA. **(2008)** MLXIPL variant in individuals with low and high trigylceridemia in white population in Central Europe **Hum Genet.** 124(5), 553-5
	CAGGTAACTGACCCTTC ACACATTTA[C/T]GGTGC CCATCTGACATTCATAG CAT	Wang J, Ban MR, Zou GY, Cao H, Lin T, Kennedy BA, Anand S, Yusuf S, Huff MW, Pollex RL, Hegele RA. **(2008)** Polygenic determinants of severe hypertriglyceridemia **Hum Mol Genet.** 17(18), 2894-9

VEGF	GCGCGCGGGCGTGCGA GCAGCGAAAG[C/G]GAC AGGGGCAAAGTGAGTG ACCTGC	Harris SE, Fox H, Wright AF, Hayward C, Starr JM, Whalley LJ, Deary IJ. **(2007)** A genetic association analysis of cognitive ability and cognitive ageing using 325 markers for 109 genes associated with oxidative stress or cognition **BMC Genet.** 8,43
	AGACATGTCCCATTTGT GGGAACTGT[A/G]ACCC TTCCTGTGTGAGCTGGA GGCA	Harris SE, Fox H, Wright AF, Hayward C, Starr JM, Whalley LJ, Deary IJ. **(2007)** A genetic association analysis of cognitive ability and cognitive ageing using 325 markers for 109 genes associated with oxidative stress or cognition **BMC Genet.** 8,43
	AGACATGTCCCATTTGT GGGAACTGT[A/G]ACCC TTCCTGTGTGAGCTGGA GGCA	Harris SE, Fox H, Wright AF, Hayward C, Starr JM, Whalley LJ, Deary IJ. **(2007)** A genetic association analysis of cognitive ability and cognitive ageing using 325 markers for 109 genes associated with oxidative stress or cognition **BMC Genet.** 8,43
	ACATCCTGAGGTGTGTT CTCTTGGGC[C/T]TGGCA GGCATGGAGAGCTCTGG TTC	Harris SE, Fox H, Wright AF, Hayward C, Starr JM, Whalley LJ, Deary IJ. **(2007)** A genetic association analysis of cognitive ability and cognitive ageing using 325 markers for 109 genes associated with oxidative stress or cognition **BMC Genet.** 8,43
	AGCATTCCCGGGCGGGT GACCCAGCA[C/T]GGTC CCTCTTGGAATTGGATT CGCC	Harris SE, Fox H, Wright AF, Hayward C, Starr JM, Whalley LJ, Deary IJ. **(2007)** A genetic association analysis of cognitive ability and cognitive ageing using 325 markers for 109 genes associated with oxidative stress or cognition **BMC Genet.** 8,43
	ATCCTCTTCCTGCTCCCC TTCCTGGG[A/G]TGCAG CCTAAAAGGACCTATGT CCT	Harris SE, Fox H, Wright AF, Hayward C, Starr JM, Whalley LJ, Deary IJ. **(2007)** A genetic association analysis of cognitive ability and cognitive ageing using 325 markers for 109 genes associated with oxidative stress or cognition **BMC Genet.** 8,43

Table 2: Hapiness genes

GENE	ASSOCIATIONS
DRD2	Alcoholism, Substance abuse, craving behavior, cocaine dependence, smoking, ADHD, parenting, Obesity, video gaming, sexual activity, posttraumatic stress disorder schizophrenia, Parkinson's, brain metabolism, BMI, executive functioning, love styles (EROS) pathological gambling. Pathological aggression, schizoid/avoidant behavior, criminal activity, politics party attachment. Energy, hypertension. Hyperphagia, growth, sexual maturation, brain development, depression, anorexia, bulimia, fibromyalgia, pain sensitivity, hunger, novelty seeking, extraversion, early onset sexual intercourse, defense style (lying), oppositional defiant disorder, panic disorder, developmental personality, Tourette Syndrome, Parkinson's, executive dysfunctioning, pleasure "buzz"
ANNKI	Smoking dependence, parental rule-setting, Schizophrenia, cognition deficit, alcohol and opiate dependence, pleasurable "buzz",
5HT2A	Eating disorders, obesity, Insulin resistance, love styles (romantic), suicide, ADHD, Panic disorders, impulsive aggression, cognitive impulsivity, anger, sweet tooth, antidepressant treatment outcomes, fibromyalgia, obsessive-compulsive disorder, borderline personality, smoking behavior, cocaine dependence, BMI.
OPRK1 (kappa –opioid receptor)	Alcohol and heroin dependence. Pain mechanisms and tolerance.
OPRM1 (mu opioid receptorreceptor)	Pleasure "buzz", smoking addiction, heroin addiction, alcoholism, pain sensitivity, BMI, type 2 diabetes mellitus.
COMT	Psychiatric and affective disorders, alcoholism, substance use disorder, smoking, post-surgical pain, fibromyalgia, Parkinson's disease, ADHD.
SLC6A3	Post-surgical pain, cocaine abuse, alcohol dependence, smoking behavior, juvenile delinquency, pathological aggression, bipolar disorder, schizophrenia, ADHD, impulsive aggression, cognitive impulsivity.
HTR3B	Heroin addiction, migraine, impulsive behavioral aggression, cognitive –impulsivity, ADHD, alcoholism.
NOS3	Pain mechanism, healing mechanisms, circulation, hypertension, cardiovascular.
PPARG	Type 2 diabetes, Obesity, Insulin sensitivity, Body composition, eating disorders, BMI, physical exercise, common metabolic disorders, body mass, waist circumference, inflammatory response, immune system.

CHREBP	Plasma triglycerides, triglyceridemia, obesity ,,improves plasma glucose,
FTO	Severe obesity, food intake, adiposity, body mass, energy intake, BMI, fat mass, pleasurable "buzz".
TNFalpha	Inflammation, mortality, schizophrenia, bipolar disorder, BMI, Immune response.
PEMT	Proinflamamtory, immunoregulation, apotosis, substance use disorder.
MANEA	Substance dependence
LEPTIN-OB	BMI, Schizophrenia, stress, obesity risk, food intake, craving behavior, diabetes, insulin sensitivity, adiposity, body composition, linear growth, metabolic factors, hyperphagia, cocaine dependence, lipogenesis, modulation of sweet substances, anorexia, bulimia, cardiovascular effects, fertility, sexual maturation, brain development, depression, fatty acid metabolism, hunger,
MAO-A	Pain sensitivity, bipolar affective disorder, ADHD, alcoholism, Substance Use Disorder, violent behavior, juvenile delinquency, smoking, child abuse, suicide, criminal activity, posttraumatic stress disorder, anti-depressant treatment response, alcoholism, panic disorder, schizophrenia, pathological gambling.
ADIPOQ	Metabolic syndrome, adiposity, fat mass, energy intake, obesity, lipogenesis, type 2 diabetes, BMI.
STS	ADHD
VDR	Obesity, BMI, overeating, metabolic syndrome, anthropometric measures, schizophrenia, temporal lobe epilepsy, immune system, type 2 diabetes, physical activity, BONE DENSITY (OSTEOPOROSIS).
DBI	ANXIETY DISORDERS
GABRA6	Autism, alcoholism, stress response.
GABRB3	Autism, alcoholism, stress.
MTHFR	Cardiovascular disease, Homocysteine levels, obesity, fat mass, Schizophrenia.
MLXIPL (CARBOHYDRATE BINDING ELEMENT)	Plasma triglycerides, glucose craving behavior, obesity.
VEGF	Angiogenesis factor, cognition, tissue healing, pain sensitivity, oxidative stress.
DRD4	Financial risk taking, nicotine withdrawal, ADHD, novelty seeking, Alcoholism, aggression, impulsivity, delinquency, memory deficits, anger, temperament, schizophrenia, sexual intercourse, drug abuse, extraversion, obesity, stress, emotional reactivity, infant attachment, oppositional defiant disorder, fibromyalgia, hyperphagia, alcohol craving, pathological gambling, panic disorder, developmental personality, Tourette Syndrome, Parkinson's.
VMAT2	Antidepressant treatment outcome, Parkinson's, ADHD, cocaine and methamphetamine dependence, spirituality "GOD Gene".
CLOCK	Circadian system, mood, bipolar, endocrine and metabolic rhythms, stress, reproduction, morphine dependence
MELETONIN	Sleep anxiety, alcoholism
OREXIN	Hyperphagis and energy regulation

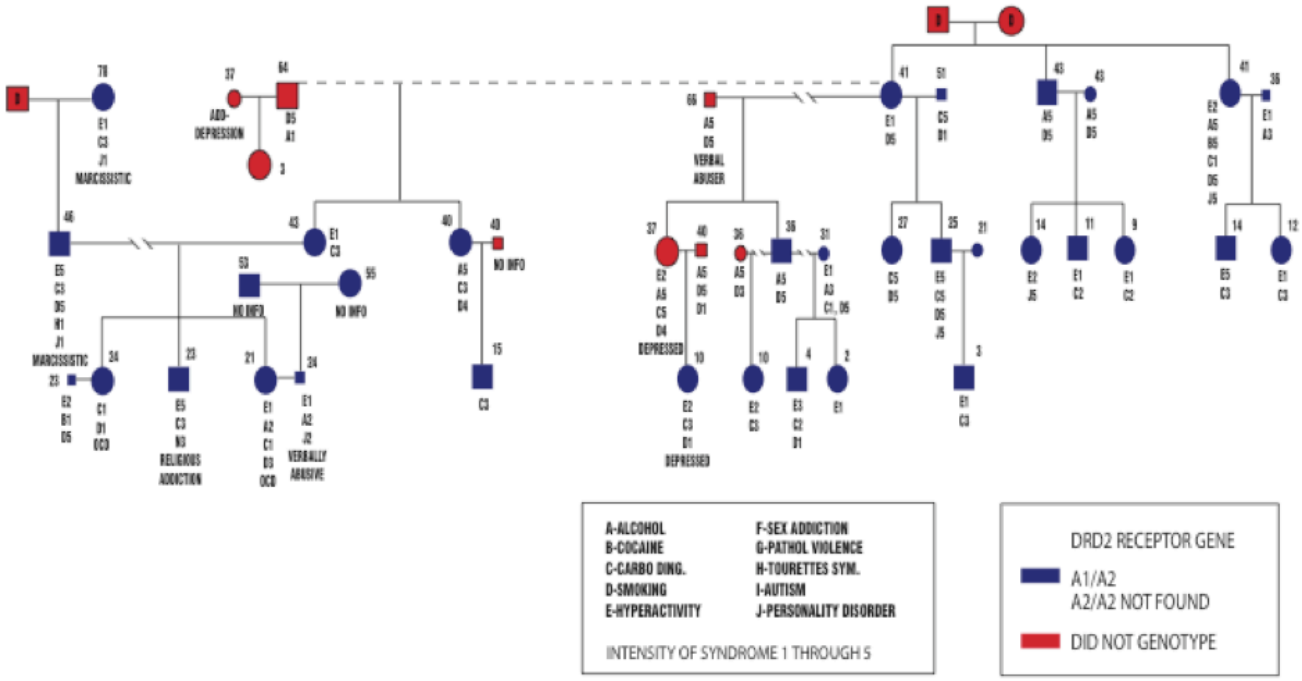

Figure 1: Five Generation of Dopaminergic Polymorphic genotyping in humans

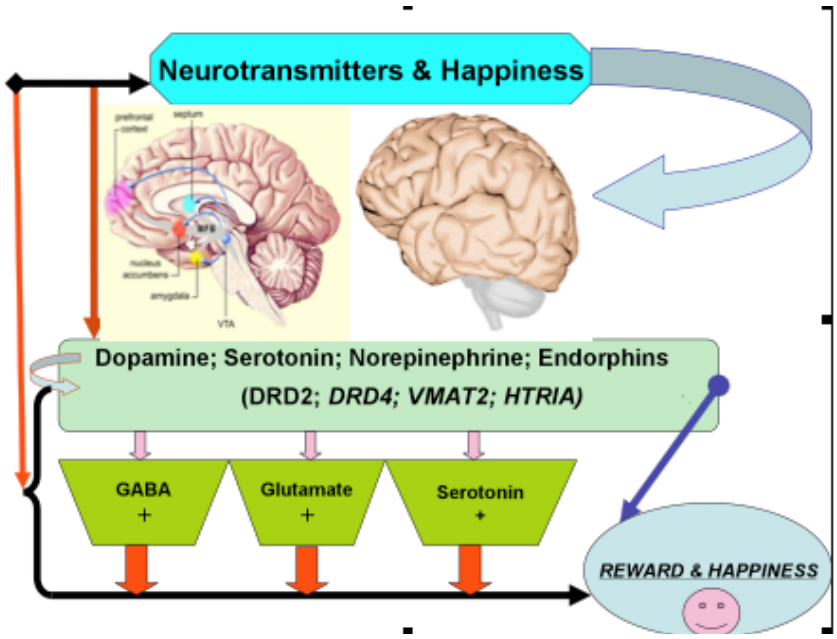

Figure 2: Neurotransmitters and Happiness

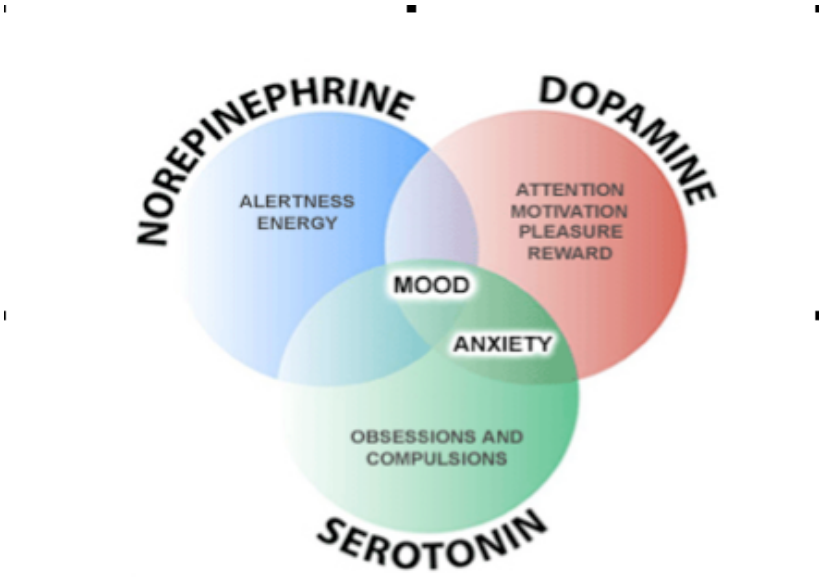

Figure 3: Neurotransmitters share emotional states leading to Happiness

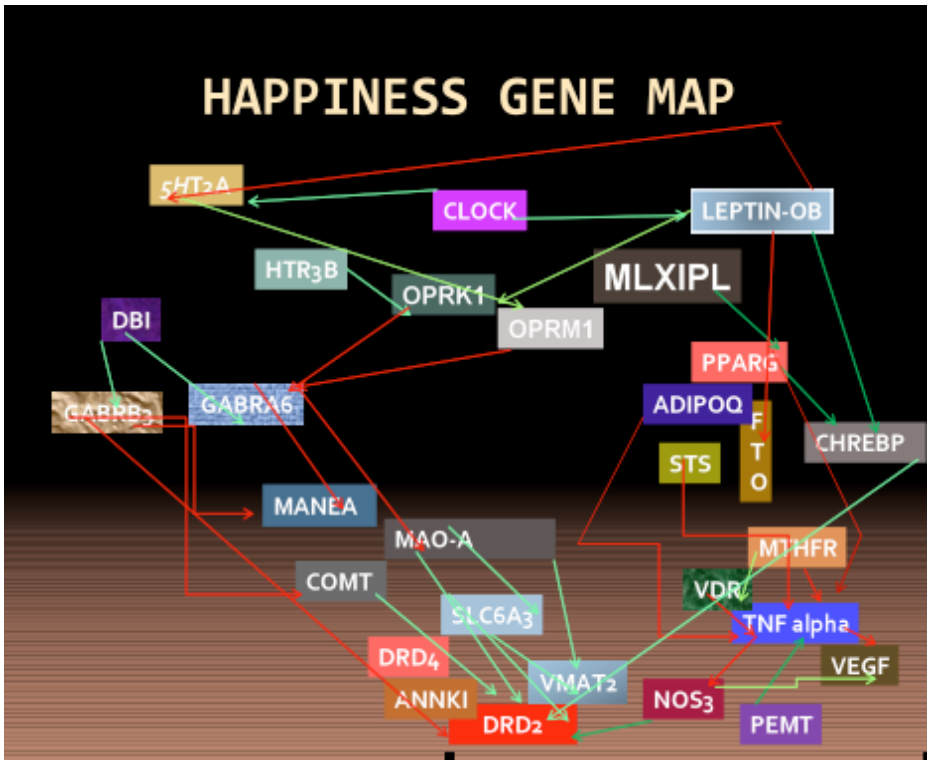

Figure 4: Proposed Happiness Gene Map

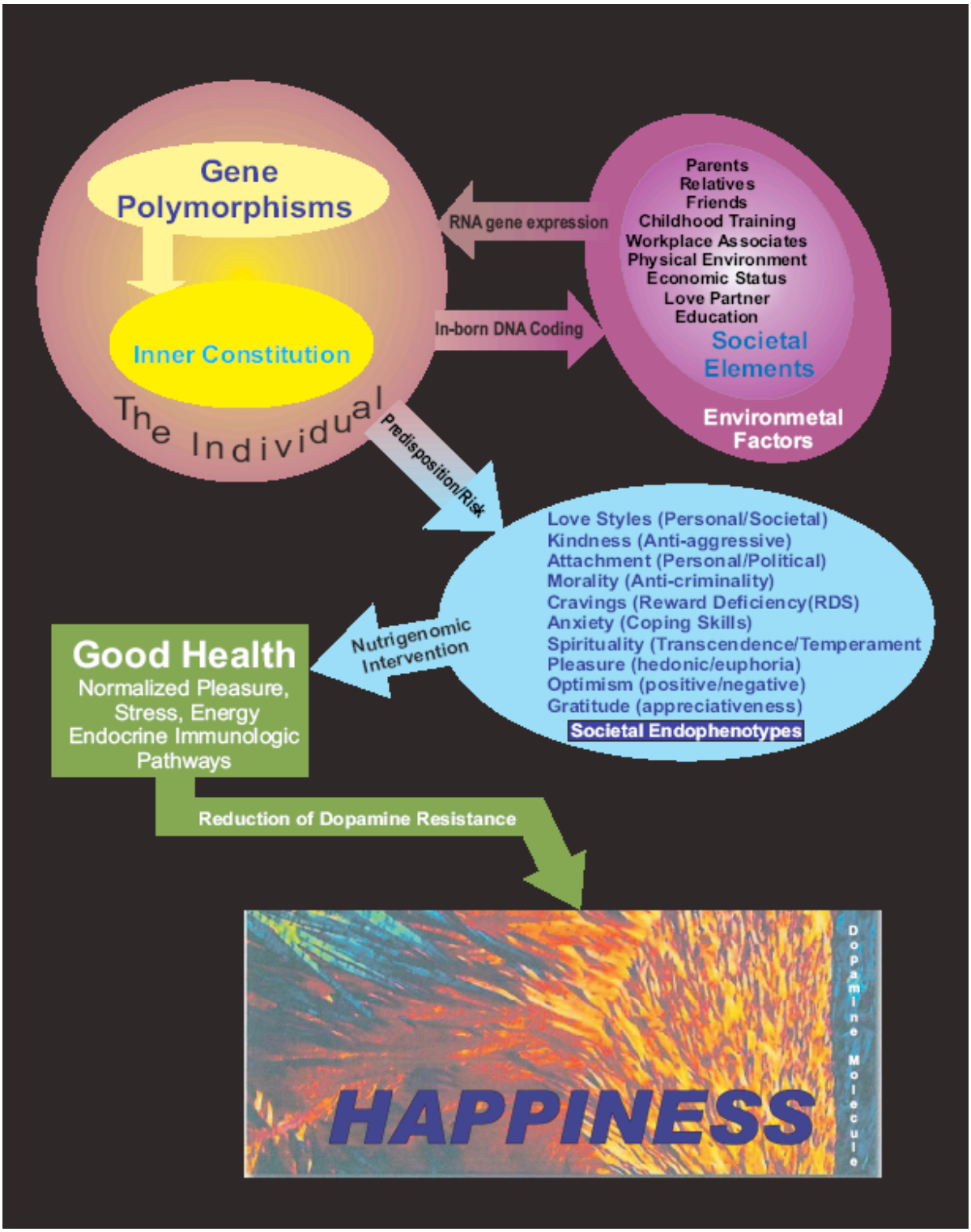

Figure 5: Schematic of genetic and environmental interactions leading to a reduction of "dopamine resistance" leading to a sdtate of Happiness

Figure 6: Schematic of Psychological Wealth (Published with Diener & Deiner (2008) permission)

IX. Conclusions

We merely have touched the surface of the complex relation between genes and happiness. We realize that over time many more gene polymorphisms will be tied to human emotions, including happiness. **Table 2** and **Figure 4** simply summarizes the current knowledge.

Based on a number of social science studies, it is well established that the behavioral characteristic known as attachment is tied to happiness (Fowler and Schreiber, 2008). In their book, "Loneliness: Human Nature and the Need for Social Connection" (2008), modern day philosophers John T. Carioppo and William Patrick suggested that isolation can be harmful to your health, just as is smoking or a sedentary lifestyle. A large part of this effect is driven by the subjective sense of social isolation we call loneliness. New research shows that human beings are far more intertwined, hardwired, and interdependent physiologically as well as psychologically than our cultural prejudices have allowed us to acknowledge. *"If you want to go fast," says an African proverb, "go alone. If you want to go far, go together."* Furthermore, it seems that spirituality also may be important for happiness (Charlton, 2008). In the latter scenario, it would be important to assess "genospitituality" polymorphisms as in the case of adrenergic and dopaminergic genes (Nilsson *et al*. 2007, Comings *et al*. 2008, Hamer, 2004, Benjamin 1996) (see **Table 1**). Keeping this in mind, if we add the associations between a number of genes, metabolic syndrome X, and/or obesity, including aberrant carbohydrate craving behavior (Stice *et al*. 2008) as a constraint against free will, then this will add another important barrier to happiness (Chopra 2007). Certainly there is no simple winning formula to assess happiness in an individual (Diener and Seligman 2002). Happiness is a transient state, but there are those who exude the positive while others dwell on the negative. It is not so simple as just being genetically programmed or hard wired at birth (Eisenberg *et al* .2007). In essence, it is always the interaction of genes and environment that provides a Bayesian view of predictability (Blum et al 1996). With that said, our laboratory focused its attention to the exploration of potential genetic antecedents and nutrigenomic solutions to achieve "gene guided precision nutrition" of obesity, for example. As we stated earlier, solve the obesity epidemic (over 30% of US population) and this will increase wellness in an individual. **Figure 5** provides a schematic that illustrates the various interactions involved in the ultimate release of Dopamine in the limbic system of the brain.

We are cognizant that there may be other pathways involved in this very complex human trait. Moreover, an understanding of the dynamic relationships between the various pathways offers a potential new therapeutic paradigm on how to more effectively achieve optimal wellness; and this will better enable the improvement of cellular health, fat reduction, and overall improved body composition.

In terms of wellness little is known about the genes that may regulate personality traits involved in the overall phenotype "well-being". Weiss *et al*. (2008) used a representative sample of 973 twin pairs to test the hypothesis that heritable differences in subjective well being are entirely accounted for by the genetic architecture of the Five-Factor Model's personality domains. Results supported this model. Subjective well being was accounted for by unique genetic influences from Neuroticism, Extraversion, and Conscientiousness, and by a common genetic factor that

influenced all five personality domains in the directions of low Neuroticism and high Extraversion, Openness, Agreeableness, and Conscientiousness. These findings indicate that subjective well being is linked to personality by common genes and that personality may form an "affective reserve" relevant to set-point maintenance and changes in set point over time. Other results also support a differentiated view of subjected well-being -health relations, and imply that both genes and environment play important roles in the associations between well being and health (Røysamb et. al. 2003).

The Psychology of Wealth has been proposed by others (Diener and Diener 2008) and can be summarized best by **Figure 6**. While we are not suggesting that the percentage of the various portions of the pie represent a true and accurate value the depiction of the enterties that impact our life have real meaning.

Finally it is very interesting that older cultures such as Bhutan, believe that enlightenment through multiple paths, including Mediatation, Yoga and Budhist spiritual teachings, lead the way to satistisfaction and ulfillment. In 1972 the then King of the country proclaimed that instead of measuring success by wealth or the "Gross National Product" it should be measured by "Gross National Happiness." Through many incarnations one may become enlightened and reach the ultimate state of Nirvana. Buddha described nirvana as the perfect peace of the state of mind that is free from craving, anger and other afflictive states (*kilesa*). The subject is at peace with the world, has compassion for all and gives up obsessions and fixations. This peace is achieved when the existing volitional formations are pacified, and the conditions for the production of new ones are eradicated. In Nibbana the root causes of craving and aversion have been extinguished such that one is no longer subject to human suffering (*dukkha*) or further states of rebirths in samsara.

With this in mind and being grateful for having this uplifting cultural mandate one could make a suggestion that NIRVANA is indeed an important acronym whereby it could be defined as "***Neurotransmitter Interaction at Reward Ventral tegmental Accumbens leading to Neuronal Adaptation*** (NIRVANA)" Or Happiness.

Acknowledgements

The authors would like to thank the editorial input of Margaret Madigan.

References

Althaus M, Groen Y, Wijers AA, Mulder LJ, Minderaa RB, Kema IP, Dijck JD, Hartman CA, Hoekstra PJ. **(2009).** Differential effects of 5-HTTLPR and DRD2/ANKK1 polymorphisms on electrocortical measures of error and feedback processing in children. **Clin Neurophysiol**. 120:93-107.

Aristole**, (1996)** in **"Cambridge Texts in the History of Political Thought"** S. Everson Ed. Cambridge Univ. Press, Cambridge.

Asghari, V., Sanyal, S., Buchwaldt, S., Paterson, A., Jovanovic, V., & Van Tol, H. H. **(1995).** Modulation of intracellular cyclic AMP levels by different human dopamine D4 receptor variants. **Journal of Neurochemistry**, *65*, 1157-1165

Avena NM, Rada P, Hoebel BG. (**2009**). Sugar and fat bingeing have notable differences in addictive-like behavior. **J Nutr**, 139(3): 623-628.

Benjamin J, Li L, Patterson C, Greenberg BD, Murphy DL, Hamer DH. (1996) Population and familial association between the D4 dopamine receptor gene and measures of Novelty Seeking.**Nat Genet**.12, 81-84

Blass EM. **2003** Biological and Environmental determinants of childhood obesity. **Nutr Clin Care**. 6, 13-19.

Blum K, Calhoun W. Merritt W, Wallace JE. **(1973)** L-Dopa: effect on ethanol narcosis and brain amines in mice. **Nature** 242 : 407-409.

Blum K, Chen TJ, Meshkin B, Downs BW, Gordon CA, Blum S, Mangucci JF, Braverman ER, Arcuri V, Deutsch R, Pons MM. **(2008a)** Genotrim, a DNA-customized nutrigenomic product, targets genetic factors of obesity: hypothesizing a dopamine-glucose correlation demonstrating reward deficiency syndrome (RDS). **Med Hypotheses** 68, 844-852.

Blum K, Chen AL, Chen TJ, Rhoades P, Prihoda TJ, Downs BW, Waite RL, Williams L, Braverman ER, Braverman D, Arcuri V, Kerner M, Blum SH, Palomo T.**(2008b)** LG839: anti-obesity effects and polymorphic gene correlates of reward deficiency syndrome. **Adv Ther.** 25, 894-913.

Blum K , Chen TJH, Williams L, Chen ALC, Downs BW, Waite RL, Huntington T, Sims S, Prihoda t, Rhoads P, Reinking J, Braverman D, Kerner M, Blum SH, Quirk B, Braverman ER. (**2008c**) A short term pilot open label study to evaluate efficacy and safety of LG839, a customized DNA directed nutraceutical in obesity: Exploring Nutrigenomics. **Geen Therapy & Mol Biol.** 12, 371-382.

Blum K, Chen ALC, Chen TJH, Rhoades P, Prihoda T, Downs BW, Baghi D, Bagch M,, Blum SH, Williams L, Braverman ER, Kerner M, Waite RL, Quirk B, White L. **(2008d)** Dopamine D2 Receptor ***Taq A1*** allele predicts treatment compliance of LG839 in a subset analysis of a pilot study in the Netherlands. **Gene Therapy & Mol Biol** 12, 129-140.

Blum K, Cull J G., Braverman ER, Comings DE**.(1996)** Reward Deficiency Syndrome. **American Scientist** 84, 132-145.

Blum K and Braverman ER.**(2000)** Reward Deficiency Syndrome (RDS): A biogeneic model for the diagnosis and treatment of impulsive, addictive, compulsive behaviors. **J. Psychoactive Drugs** 32, supplement 1-112.

Borg J., Andree B., Soderstrom H and Farde I.**(2003)** The serotonin system and spiritual experiences. **Am J Psychiatry 160, 1965-1969.**

Braverman ER**. (1987)** The religious medical model: holy medicine and the Spiritual Behavior Inventory. **South Med J** 80,415- 425.

Bruijnzeel AW, Repetto M, Gold MS. **(2004)**. Neurobiological mechanisms in addictive and psychiatric disorders. **Psychiatr Clin North Am** 27(4): 661-674.

Chang GO, Gaysinskaya V, Karatayev O , Leibowitz SF.**2008** Maternal high –fat diet and fetal programming: increased proliferation of Hypothalmic pepetide-producing neurons that increase risk for overeating and obesity. **J. Neurosci.** 28, 12107-12119.

Charlton BG. **(2008)** Genospirituality: genetic engineering for spiritual and religious enhancement. **Med Hypotheses** 71:825-828.

Chen TJ, Blum K, Waite RL, Meshkin B, Schoolfield J, Downs BW, Braverman EE, Arcuri V, Varshavskiy M, Blum SH, Mengucci J, Reuben C, Palomo T**. (2007a)** Gene \Narcotic

Attenuation Program attenuates substance use disorder, a clinical subtype of reward deficiency syndrome. **Adv Ther.** 24, 402-414.

Chen TJH, Blum K, Kaats G, Braverman ER, Eisenberg A, Sherman M, Davis K, Comings DE, Wood R, Pullin D, Arcuri V, Varshavskiy M, Mengucci JF, Blum SH, Downs BW, Meshkin B, Waite RL, Williams L, Schoolfield J, White L **(2007b)** Chromium Picolinate (CrP) a putative anti-obesity nutrient induces changes in body composition as a function of *Taq1* dopamine D2 receptor polymorphisms in a randomized double-blind placebo controlled study. **Gene Ther Mol Biol** 11, 161-170.

Chopra D. **(2006) Life After Death.** Crown Publishing Group (a division of Randomhouse) New York.

Cloninger CR, Svrakic DM, Przybeck TR (**1993**). A psychobiological model of temperament and character. **Arch Gen Psychiatry** 50, 975-990.

Cohen MX, Schoene-Bake JC, Elger CE, Weber B**.(2009)** Connectivity-based segregation of the human striatum predicts personality characteristics.**Nat Neurosci.** 12, 32-34.

Comings DE**.(2003)** In : **Nature Encyclopedia of the Genome.** MacMillan,.

Comings DE**.(2008) Did man create God?** Hope Press, Duarte, California,

Comings DE and Blum K. **(2000)** Reward Deficiency Syndrome: genetic aspects of behavioral disorders. In: Uylings,H.B.M. Van Eden , C.G. DeBruin, J.C.P. Feenstra, M.G. P. and Pennatz, C.M.A. **Progress in Brain Res.** Elsevier Science BV, Amsterdam.

Comings DE, Gade-Andavolu R, Gonzalez N, Wu S, Muhleman D, Blake H, Mann MB, Dietz G, Saucier G, MacMurray JP.(**2000**) A multivariate analysis of 59 candidate genes in personality traits: the temperament and character inventory. **Clin Genet.** 58:375-385.

Dackis CA, Gold MS. (**1985**). New concepts in cocaine addiction: the dopamine depletion hypothesis. **Neurosci Biobehav Rev**, 9(3): 469-477.

Davis VE, Walsh MJ.(1970) Alcohol addiction and tetrahydropapaveroline. **Science.** 169:1105-1106.

Davis CA, Levitan RD, Reid C, Carter JC, Kaplan AS, Patte AS, King N, Curtis C, Kennedy JL. (**2009)** Dopamine for Wanting" and Opioids for "Liking': A comparison of Obese adults with and without Binge Eating". **Obesity** (Silver Springs) (in press).

Dawes CT and Fowler JH. **(2008)** Two Genes Predict Voter Turnout. **Journal of Politics** 70, 579–594

(July 2008)Diener E, Lucas RE, Scollon CN.(**2006**)Beyond the hedonic treadmill: revising the adaptation theory of well-being. **Am Psychol.** 61, 305-314.

Diener E, Seligman ME. (**2002**)Very happy people. **Psychol Sci.** 13, 81-84.

Eisenberg DT, Campbell B, Mackillop J, Lum JK, Wilson DS. **(2007)** Season of birth and dopamine receptor gene associations with impulsivity, sensation seeking and reproductive behaviors. **PLoS ONE**. 2 : e1216.

Emanuele E, Brondino N, Pesenti S, Re S, Geroldi D**.(2007)** Genetic loading on human loving styles. **Neuro Endocrinol Lett.**28:815-21.

Fowler JH, Schreiber D. **(2008)** Biology, politics, and the emerging science of human nature. **Science**. 322: 912-914.

Gearhardt AN, Corbin WR, Brownell KD.**2009** Preliminary validation of the Yale Food Addiction Scale. **Appetite** 52:,439-436.

Gold MS, Dackis CA. (**1984**). New insights and treatments: opiate withdrawal and cocaine addiction. **Clin Ther**., 7(1): 6-21.

Gold MS, Kobeissy FH, Wang KK, Merlo LJ, Bruijnzeel AW, Krasnove IN, Cadet JL. (**2009**, Apr 2). Methamphetamine- and trauma-induced brain injuries: Comparative cellular and Molecular Neurobiological substrates. **Bio Psych** [Epub ahead of print].Grimm JW, Osincup D, Wells B, Manaois M, Fyall A, Buse C, Harkness JH.**2008** Environmental enrichment attenuates cue-induced reinforcement of sucrose seeking in rats. **Behav Pharmacol**., 19, 777-785.

Guo G, Roettger ME, Shih JC. **(2007)** Contributions of the DAT1 and DRD2 genes to serious and violent delinquency among adolescents and young adults. **Hum Genet.** 121(1):125-136.

Haeffel GJ, Getchell M, Koposov RA, Yrigollen CM, Deyoung CG, Klinteberg BA, Oreland L, Ruchkin VV, Grigorenko EL**.(2008**) Association between polymorphisms in the dopamine transporter gene and depression: evidence for a gene-environment interaction in a sample of juvenile detainees. **Psychol Sci.**19, 62-69.

Hamer D. **(2004) The God Gene: How faith is hardwired in our genes.** Doubleday, New York.

Hodgkins CC, CaHill KS, Seraphine AE, Frost-Pineda K, Gold MS.**2004** Adolescent drug addiction treatment and weight gain. **JAddict Dis** 23, 55-65.

Hoebel BG, Avena NM, Borcarsly ME, Rada P. **(2009)**. Natural Addiction: A behavioral and circuit model based on sugar addiction in rats. **J Addict Med**, 3(1): 33-41.

Joranby L, Frost-Pineda K, Gold MS. (**2005**). Addiction to Food and Brain Reward Systems. **Sex Addict Compuls**, 12(2): 201-217.

Kirk KM, Eaves LJ, Martia NG. (**1999)** Self –transcendence as a measure of spirituality in a sample of older Australian twins. **Twin Res.** 2, 81-87.

Kirk KM *et al*. **(1999)** Frequency of church attendance in Austrailia and the United Sates models of family resemblance. **Twin Res. 2**, 99-107.

Kobeissy FH, Baker HV, Husty T, Krasnova I, Cadet JL, Gold MS. (2008). Genomic analysis of chronic methamphetamine abuse in rat striatum. The Society for Neuroscience 38th Annual Meeting, Washington DC,

Krueger AB, Schkade D, Schwarz N, Stone AA. **(2006)**Would you be happier if you were richer? A focusing illusion. **Science** 312, 1908-910.

Langer E.J. **(1997) Mindfulness.** Addison-Wesley, Reading, MA.

Lykken DT**.(2007)** A more accurate estimate of heritability. **Twin Res Hum Genet.** 10:168-173.

Musick M.A., Herzog A.R. and House J.S. **(1999)** Volunteering and mortality among older adults: findings from a national sampling. **Journal Gerontol B Psychol Sci Soc Sci** 54, S173-180.

Newberg A., D'Aquill E and Rause V. (**2001) Why God Won't go Away .** Baltimore Books,New York.

Nilsson KW, Damberg M, Ohrvik J, Leppert J, Lindström L, Anckarsäter H, Oreland L**.(2007)** Genes encoding for AP-2beta and the Serotonin Transporter are associated with the Personality Character Spiritual Acceptance. **Neurosci Lett.** 2007 411:233-237.

North RJ, Holahan CJ, Moos RH, Cronkite RC.(**2008**) Family support, family income, and happiness: a 10-year perspective.**J Fam Psychol**. 22 , 475-483.

Ozkaragoz T, Noble EP**.(2000)** Extraversion. Interaction between D2 dopamine receptor polymorphisms and parental alcoholism. **Alcohol.** 22, 139-146.

Parducci A**. (1995) Happiness , Pleasure ,and Judgment: The Contexual Theory and its Application.** Lawrence Erlbaum Associates. Mahwah, New Jersey Hove, UK.

Post S.G. (**2005)** Altrusim, happiness and health: it's good to be good. **Int J Behav Med.**59, 66-77.

Post SG, Puchalski CM, Larson DB**.(2000)** Physicians and patient spirituality: professional boundaries, competency, and ethics**. Ann Intern Med.** 132, 578-583.

Rada P, Avena NM, Hoebel BG. **2005** Daily bingeing on sugar repeatedly releases dopamine in the accumbens. **Neuroscience** 134, 737-744.

Rothman RB, Blough BE, Baumann MH. **(2008)** Dual dopamine/serotonin releasers: potential treatment agents for stimulant addiction. **Exp Clin Psychopharmacol**. 16, 458-474.

Røysamb E, Tambs K, Reichborn-Kjennerud T, Neale MC, Harris JR**.(2003)** Happiness and health: environmental and genetic contributions to the relationship between subjective well-being, perceived health, and somatic illness**.J Pers Soc Psychol.** 85, 1136-46.

Shultes R.E. Hoffman A. and Ratsch C. **(1998) Plants of the Gods. Their Sacred Healing and Hallucinogenic Powers.** Healing Arts Press, Rochester , NY.

Scuteri A, Sanna S, Chen WM, Uda M, Albai G, Strait J, Najjar S, Nagaraja R, Orrú M, Usala G, Dei M, Lai S, Maschio A, Busonero F, Mulas A, Ehret GB, Fink AA, Weder AB, Cooper RS, Galan P, Chakravarti A, Schlessinger D, Cao A, Lakatta E, Abecasis GR. **(2007)** Genome-wide association scan shows genetic variants in the FTO gene are associated with obesity-related traits. PLoS Genet. 3, e115.

Serre l. Cantin F L . Ahmed SH.**2007** Intense sweetness surpasses cocaine reward. **Plos One** 2 , e698.

Seligman ME**. (2002)** How to see the glass half full. **Newsweek**. 140(12):48-49.

Stark R**.(2007) Discovering God: the origins of the great religions and the evolution of belief.** London: Harper One.

Stern C. (**1973) Principles of Human Genetics.** W.H. Freedman, San Fransico.

Stice E, Spoor S, Bohon C, Small DM. **(2008)** Relation between obesity and blunted striatal response to food is moderated by TaqIA A1 allele. **Science** 322, 449-452.

Sulmasy DP.(2006) Spiritual issues in the care of dying patients: ". . . it's okay between me and god"**.JAMA.** 296,1385-1392.

Thanos PK.et al**.(2001)** Overexpression of dopamine D2 receptor reduces alcohol –self-administration. **J Neurochem** 78, 1094-1103.

Volkow ND, Wise RA. (**2005**). How can drug addiction help us understand obesity? **Nat Neurosci**, 8(5): 555-560.

Wang G-J, Volkow ND, Thanos PK, Fowler JS. **(2009)** Imaging of Brain Dopamine Pathways: implications for understanding Obesity. **J. Addict Medicine** 3, 8-18.

Weiss A, Bates TC, Luciano M. **(2008)** Happiness is a personality thing: the genetics of personality and well-being in a representative sample. **Psychol Sci** 19:205-210.

Wenz FV. **(1977)** Neighborhood type, social disequilibrium, and happiness**. Psychiatr Q.** 49, 187-96.