

## Evolutionary impact on dopaminergic genes and societal issues related to ethnicity, sex, drugs, music, politics, friendships, marriage, longevity and happiness: ancestral polymorphisms and society

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### Abstract

Novel molecular genetic approaches, at genome-scale in different species allowed characterizing genes that have undergone recent selection. The interest in this research field is not limited to the natural curiosity about our evolutionary past, but it is also to identify novel susceptibility genes for neuropsychiatric disorders by pointing to specific human traits, such as behavioral and cognitive abilities. A good example of this selection occurs with dopaminergic genes. Since our discovery in 1990 of associating one such dopamine gene polymorphisms (A1 and B1 alleles) with severe alcoholism the field of psychiatric genetics exploded and now accounts for at least 13,281 articles listed in PUBMED. From the work of Kidd's group at Yale it appears that the ancestral B2A1 haplotype was the starting point of the DRD2 haplotypes. Interestingly we found that both A1 & B1 forms of the DRD2 gene significantly associated with severe alcoholism. Thus, starting from the ancestral **B2A1** haplotype, separate mutations generated the B1 allele and the A2 allele. The frequency and disequilibrium data argue for the "parallel" scenario and not a sequential scenario such as B2A1-B2A2-->B1A2-->B1A1. This work suggests that carrying for example the A1 allele of the DRD2 gene occurred in the homozygote form (A1/A1) of Neanderthal genes and probably had important select survival advantages. Given that it has now been discovered that *homo sapiens* mated with Neanderthals whereby 2% of our DNA is derived from the Neanderthal genome the evolutionary picture becomes clearer. The hypothesis is extended (EOBD-R) to suggest Neanderthal as the ancestral source for bipolar vulnerability genes (susceptibility alleles) impacted by photoperiod (darkness induced dopaminergic changes leading to affective disorders and alcoholism). Over a number of decades now we have observed many important societal associations briefly described below: **Ethnicity:**DRD2-A1 allele was found to be dramatically different among the populations studied, from as low as 0.09 to as high as 0.75; **Sexual Activity:**DRD2-A1 allele associated with early onset of sexual activity and intercourse and erotic love not romantic; **Alcoholism and Drug Abuse:**DRD2-A1 allele associated with high vulnerability and relapse potential; **Food and weight gain:** DRD2-A1 allele associated blunted brain reward response to palatable food and weight gain ; **Music Aptitude:** Creative functions and other music related abilities have a strong dopaminergic genetic component ; **Politics:**DRD2-A1 allele associated with low voting, being non-partisan and accepting liberal ideation ; **Friendships:** Fowler and associates found that DRD2- A1allele exhibits significant homophilyamongst friendships and as humans are "metagenomic" by at least two degrees of separation; **Marriage:**DRD2-A1 allele carriers are less likely to be married ; **Longevity:** Carriers of the DRD4 7 repeat , least 5-10-fold "younger" than the more common 4repeat allele has been associated with a longer life; **Happiness:** Carriers of the DRD2- A1 allele are less likely to be happy and such seek our many reward deficiency behaviors. In summary, identification of novel candidate genes based on recent evolution selection, coupled to genome-wide strategies designed to detect rare structural variants, could lead to a better knowledge of the molecular mechanisms of neurodevelopmental disorders and might therefore help to develop new genomic therapeutic strategies.

### Biography

Kenneth Blum is currently Chairman of the Board and Chief Scientific Officer of LifeGen, Inc. San Diego, California and managing partner of Reward Deficiency Solutions, LLC, and San Diego, California. He has received numerous awards including NIDA Career Teacher Award; American Chemical Society Speakers Award; Gordon Conference Research Award; Presidential Excellence award (National Council of Alcoholism and Drug Abuse). Dr Blum has authored and edited eleven books, was an Editor "in chief of an Elsevier Journal, and has published over 400 peer reviewed papers. Coined Brain Reward Cascade and Reward Deficiency Syndrome RDS) and is credited as the lead author in the first association of the Dopamine D2 receptor gene with severe alcoholism (JAMA, 1990). He is considered by many as the father of Psychiatric Genetics and Neuroadaptagen Amino-Acid Therapy (NAAT). Dr. Blum holds both US & foreign patents on Nutrigenomics. He serves on 7 editorial boards and is the associate editor on two boards including section editor of Integrative Omics and Applied Biotechnology journal and is an ad hock reviewer for 40 journals world-wide.