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Evidence based clinical analytics supporting the Genetic Addiction Risk Severity (gars) assessment to early identify probands in Addiction psychiatry

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The first ever confirmed candidate psychiatric genetic association study was performed by Kennth Blum and Ernest Noble and their team, whereby that discovered a significant association of the minor DRD2 allele Taq A1 (rs 1800497 C>T) and severe alcoholism published in JAMA (1990)[1]. While this seminal finding has been the subject of significant controversy, it has been now confirmed in a number of high end and elaborate recent GWAS studies related to depression and suicide in 1.2 million veterans.[2, 3] In the latter case, the DRD2 rs1800497 was significantly associated with suicide behaviors at $P=1.77 \times 10.^{-7}$ In a recent meta-analysis Goldmans group reported on 62 studies showing a significant association with the DRD2 rs 1800497 and Alcohol Use Disorder (AUD).[4] Moreover, Gelernter's group at Yale, clearly showed an association of a haplotype block of the DRD2 gene A1 allele to associate with AUD and heroin dependence[5]. In 1996, our group using Bayesian theorem revealed a Predictive Value (PV) of 74.4% whereby carriers of the rs 1800497 will express one or more of "Reward Deficiency Syndrome" (RDS) behaviors (e.g. SUD, gambling, overeating, etc.[6] In 2004, Nevile et al., reported that the DRD2 rs 1800497is a single nucleotide polymorphism (SNP) that causes an amino acid substitution within the 11th ankyrin repeat of ANKK1 (p.Glu713Lys), which, while unlikely to affect structural integrity, may affect substrate-binding specificity[7]. In 2014, our group developed the GARS test consisting of ten genes and eleven SNPs across the finite neurotransmitter pathways representative of the Brain Reward Circuitry DNA hypodopaminergia antecedents to addiction psychiatry[8]. In 2022, involving 74,566 case-controls (AUD) we statistically validated the selection of these risk alleles measured by GARS, and showed significance for DRD2, DRD3, DRD4, DAT1, COMT, OPRM1, and 5HTT at 5% and these alleles captured post-risk for 8% estimation of the population's alcoholism prevalence post-risk for 8% estimation of the population's alcoholism prevalence.[9]Over 32 years as of 12-21-22, a PUBMED search using "dopamine Genes " revealed 11,495 articles mostly related to addiction psychiatry. Since 1990 and 2022, our laboratory published a number of studies showing the positive clinically relevant analyses of utilizing GARS to help identify not only AUD (N=393); SUD (N=110,241 cases and 122,525 controls; high Opioid risk in pain clinics (121 chronic opioid users); identified eating expectancy and other RDS behaviors in a bariatric post -surgical cohort (N=34); also utilized in drug Court to help convert DWI offenders facing prison time to rehabilitation based on genetic determinism rather than free will (N=31) saving over 225 prison time to mandated probation[10]. We genotyped over 3,000 people presenting with polysubstance abuse from at least one-dozen chemical dependency and Behavioral addiction clinics including general population mixed gender and race that resulted in a GARS score for drug and alcohol risk at over 90% and 72% respectively[11,12]. These results over 3 decades indicate that not only the DRD2 gene, but other polymorphic reward genes measured in GARS (5HTTLPR, MUOR, GABABR3, DRD1-4, DAT1, COMT, AND MAOA) have an important role in the unwanted induction of RDS behaviors. While we encourage the scientific community to perform additional required larger studies (GWAS and Candidate approaches), we believe we have found a very useful tool to help identify addiction risk even at birth not to label but inform parents of potential danger ahead.

Biography

Kenneth Blum (born August 8, 1939) is an American scientist who has studied neuropsychopharmacology and genetics. Until 1995 he was a professor of Pharmacology at the University of Texas Health Science Center at San Antonio. Blum received his B.S. in pharmacy from Columbia University in 1961, his M.S. in medical science in 1965 from the New Jersey College of Medicine, and his Ph.D. in pharmacology in 1968 from the New York Medical College. Blum completed post-doctorate research in psychopharmacology at the Southwest Foundation for Research and Education. He also completed a fellowship in pharmacogenetics under Gerald Mc Clearn at the University of Colorado College of Pharmacy (Boulder) in 1977. He retired in 1995 from his position as professor at the Department of Pharmacology, Texas Health Science Center, San Antonio, and University of Texas.