

## Genetic Addiction Risk Score (GARS) Predicts Severity, Relapse & Personalized Medicine

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**Background:** The P450 system genes involved in buprenorphine metabolism, and, 11 polymorphisms in 10 genes that based on extensive literature contribute most to the hypodopaminergic trait, called Reward Deficiency Syndrome (RDS), were selected for the genetic addiction risk scores (GARS) study.

**Methods:** Poly-drug users, n=393 from seven treatment centers were tested. The average age was 35.3 years; 57.8% were male 88.1%, and self-reported race as “white.” Statistical analysis compared GARS with clinical severity assessed in 273 subjects who completed the Addiction Severity Index (ASI-MV). A discrete analysis of the CYP3A4 included 144 African –Americans attending a drug treatment program.

**Results:** The GARS mean of 7.97 alleles ranged between 3 and 17 alleles, were within Hardy-Weinberg Equilibrium (HWE). Examination with the Fishers Exact Test revealed a significant predictive relationship ( $X^2 = 8.84$ ,  $df = 1$ ,  $p = 0.004$ , 2-tailed) after controlling for age ( $p < 0.01$ ) between GARS the Alcohol Severity. A chi-square linear regression ( $b = -0.122$ ,  $t = -1.91$ ,  $p = 0.10$ , 2-tailed), corrected along a priori lines revealed a p-value = 0.05 (1-tailed) for the association between the GARS and ASI Drug Severity score. Risk severity of ( $\geq$  seven alleles) alcohol and ( $\geq$  4 alleles) drugs was predicted. Allele exchange or weighting resulted in lost significance. African-Americans had the extended metabolic Buprenorphine allele \*1B (43%), and \*I/\*1B and \*1B/1B\* (42%) differed significantly from ~9000 Caucasians (26%).

**Conclusions:** GARS predicted ASI –MV alcohol and drug severity. This candidate, GARS panel approach, can be used for risk screening pain patients, relapse-prevention and nutrigenetic testing for personalized pro-dopamine regulation. The 1CYP3A4 Genotype can facilitate personalized buprenorphine dosing. Future funded research(1R41MD012318-01 grant) will involve \*1B and GARS testing to address diversity, provide appropriate substance addiction treatment and relapse prevention in an African-American population using personalized co-therapy with the goal of dopamine homeostasis.