

**CANDIDATE GENE APPROACH IN TWO ARAB ISRAELI COHORTS
CONFIRMS AND REFINES SCHIZOPHRENIA SUSCEPTIBILITY LOCUS ON
CHROMOSOME 6Q23**

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A genome scan of Arab Israeli families, the TKT cohort (Lerer et al., 2003), yielded significant evidence for a schizophrenia susceptibility locus at chromosome 6q23 within a 23Mb genomic region. We initiated a study of candidate genes in the interval containing 93 defined genes and 21 putative genes. A total of 10 candidate genes were selected based on functionality and expression data. Within each candidate gene 4-6 SNP markers were chosen, the allele frequency determined, and the TKT cohort genotyped. Significant association was found with three SNPs within three consecutive genes, namely PDB7E, NMBR and EPM2A. Additional genotyping around these genes suggest a significant haplotype consisting of 3-4 SNPs between the PDB7E and NMBR genes being transmitted. A second cohort of similar ethnic background, the BT cohort, was genotyped for the 8 SNPs which yielded the strongest results within these three candidate genes for validation. The second cohort confirmed the presence of a schizophrenia susceptibility locus within the interval and excluded the EPM2A gene as a possible candidate gene. The results of these two rounds of genotyping on the two cohorts reduced the interval to about 3Mb, a region containing 28 known genes and 2 putative genes.