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IDENTIFICATION OF NOVEL GENES FOR AUTOSOMAL RECESSIVE MENTAL RETARDATION IN PAKISTANI POPULATION

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Mental retardation (MR) is defined by an intelligence quotient (IQ) less than 70. It is a common and distressing group of disorders that imposes one of the most important unsolved problems in health care. While in recent years considerable progress has been made to elucidate X-chromosomal genes involved in MR, the identification of the larger group of autosomal MR genes is lagging far behind. So far, few genes have been identified in a small number of families. The slow rate of elucidation of the genetic defects is due to the extreme heterogeneity in autosomal recessive MR (ARMR) and the paucity of families that are suitable for genetic research. Our project aims to identify new genes for ARMR, by exploiting the high degree of consanguineous marriages (70%) in the Pakistani population. Twenty-four ARMR families were ascertained with multiple affected individuals resulting from consanguineous parents. Clinical assessment, blood collection and processing are being conducted in Pakistan and additional families are being ascertained. We used one proband per family on 6.0 Gene Chip array from Affymetrix to check possible copy number variations. For homozygosity mapping all other affected and non-affected individuals are analyzed on the Illumina 6K array. As a first batch the homozygosity mapping data from 12 families revealed several families in which a single locus was found whereas other families also have limited (2-3) loci. Some families also shared common loci that could be regions of prime interest and priority to consider for candidate selection. The identification of genes responsible for ARMR will improve possibilities for DNA diagnostics tremendously both in developed and in developing countries.

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