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CATALOGUE OF XLMR CONDITIONS (UPDATE 2009) AND TRANSCRIPTIONAL PROFILE OF XLMR GENES IN HUMAN TISSUES

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XLMR genes cloned to date are 86, including *PCDH19* (responsible for the unusual female-restricted epilepsy/MR condition) and the recently identified *CASK*, *SYP* and *ZNF711* genes. According to our listing, 9 more genes can be considered as potential cause of X-linked Mental Retardation. Data will be presented including the counts of all described XLMR conditions (syndromic, neuromuscular and nonspecific/MRX) either mapped or unmapped, updating our previous 2007 catalogue, also available online (<http://xlmr.interfree.it/home.htm>). In 2007 we proposed transcriptional profiling in human tissues as a useful strategy to identify candidate XLMR genes i.e. prioritizing candidate genes based on their relatively higher expression levels in brain. Since then we have analyzed several microarray datasets deposited in the Gene Expression Omnibus repository at NCBI (<http://www.ncbi.nlm.nih.gov/geo/>), including a large set (Human Body Index) deposited by Neurocrine (GSE7307) composed of 677 Affymetrix U133 Plus 2.0 arrays derived from 90 different human tissues. This allowed us to reconstruct the transcriptional profile of the 86 XLMR genes and to compare it with that of the 690 X-linked and 19432 autosomal genes. We calculated the brain-to-other organs ratio for all these genes and ranked them into classes. We found that 22.9% of XLMR genes are overexpressed more than 2-fold relative to the average of all other organs, while this is true for only 10.7% of all X-linked genes and for 8.2% of autosomal genes. However, we found a clear correlation between brain ratio and the clinical presentation i.e. genes involved in syndromic (10.5% with a brain ratio more than 2-fold) and those causing neuromuscular (31%) and nonspecific/MRX (37.5%) forms. This correlation logically explains that XLMR genes with the highest brain ratio have a brain/neurological phenotype, while XLMR genes expressed at comparable levels in other tissues will likely cause syndromes where MR is accompanied by manifestations in other organs.