X-linked mental retardation

X-linked mental retardation refers to medical disorders associated with X-linked recessive inheritance that result in intellectual disability.

As with most X-linked disorders, males are more heavily affected than females.

Females with one affected X chromosome and one normal X chromosome tend to have milder symptoms.

Unlike many other types of intellectual disability, the genetics of these conditions are relatively well understood.

It has been estimated there are ~200 genes involved in this syndrome; of these, ~100 have been identified.[4] Many of these genes are found on the short 'p' arm of the chromosome, and duplications at Xp11.2 are associated with the syndromic form of the condition.

X-linked mental retardation accounts for ~16% of all cases of intellectual disability in males.

Huang et al. showed that temporal conditional deletion of Med12 in astrocytes in the adult central nervous system results in region-specific alterations in astrocyte morphology. Surprisingly, behavioral studies revealed rapid hearing loss after adult deletion of Med12 that was confirmed by a complete abrogation of auditory brainstem responses. Cellular analysis of the cochlea revealed degeneration of the stria vascularis, in conjunction with disorganization of basal cells adjacent to the spiral ligament and downregulation of key cell adhesion proteins. Physiological analysis revealed early changes in endocochlear potential, consistent with strial-specific defects. Together, studies reveal that Med12 regulates auditory function in the adult by preserving the structural integrity of the stria vascularis.

Mutations in Mediator protein complex subunit 12 (Med12) are associated with X-linked intellectual disability syndromes and hearing loss. Using temporal-conditional genetic approaches in CNS glia, we found that loss of Med12 results in severe hearing loss in adult animals through rapid degeneration of the stria vascularis. The study describes the first animal model that recapitulates hearing loss identified in Med12-related disorders and provides a new system in which to examine the underlying cellular and molecular mechanisms of Med12 function in the adult nervous system [1].

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Huang TW, Iyer AA, Manalo JM, Woo J, Bosquez Huerta NA, McGovern MM, Schrewe H, Pereira FA, Groves AK, Ohlemiller KK, Deneen B. Glial-Specific Deletion of Med12 Results in Rapid Hearing Loss via Degradation of the Stria Vascularis. J Neurosci. 2021 Jul 12:JN-RM-0070-21. doi: 10.1523/JNEUROSCI.0070-21.2021. Epub ahead of print. PMID: 34253626.