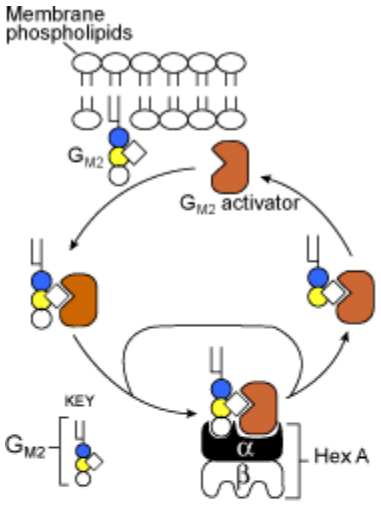
U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: National Center for Biotechnology Information (US). Genes and Disease [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 1998-. Tay-Sachs disease.
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Tay-Sachs disease



Model for G_{M2} ganglioside metabolism. Under normal conditions, β-hexosaminidase works in the lysosome of nerve cells to breakdown unwanted ganglioside G_{M2}, a component of the nerve cell membrane. This requires three components: an α-subunit, a β-subunit and an activator subunit. In Tay Sachs disease, the alpha subunit of hexosaminidase malfunctions, leading to a toxic build-up of the G_{M2} ganglioside in the lysosyme. [Adapted from: Chavany, C. and Jendoubi, M. (1998) *Mol. Med. Today*, 4: 158-165, with permission.]

Tay-Sachs disease, a heritable metabolic disorder commonly associated with Ashkenazi Jews, has also been found in the French Canadians of Southeastern Quebec, the Cajuns of Southwest Louisiana, and other populations throughout the world. The severity of expression and the age at onset of Tay-Sachs varies from infantile and juvenile forms that exhibit paralysis, dementia, blindness and early death to a chronic adult form that exhibits neuron dysfunction and psychosis.

Tay-Sachs is an autosomal recessive disease caused by mutations in both alleles of a gene (*HEXA*) on chromosome 15. *HEXA* codes for the alpha subunit of the enzyme β-hexosaminidase A. This enzyme is found in lysosomes, organelles that break down large molecules for recycling by the cell. Normally, β-hexosaminidase A helps to degrade a lipid called GM2 ganglioside, but in Tay-Sachs individuals, the enzyme is absent or present only in very reduced amounts, allowing excessive accumulation of the GM2 ganglioside in neurons. The progressive neurodegeneration seen in the varied forms of Tay-Sachs depends upon the speed and degree of GM2 ganglioside accumulation, which in turn is dependent upon the level of functional β-hexosaminidase A present in the body.

A mouse model has been developed for Tay-Sachs, although its usefulness is limited since Tay-Sachs mice possess a minor alternative pathway for breaking down GM2 ganglioside. Treatment of the late onset form of Tay-Sachs with a ganglioside synthesis inhibitor shows promise. The effectiveness this and other treatments on individuals with the infantile (the most common) form of the disease is extremely limited since the extent of neurological damage prior to birth is unknown. The difficulty in reversing such damage will make it hard to develop an effective treatment for the infantile form of the disease. It is hoped, however, that the latter onset forms of Tay-Sachs may prove responsive to treatment, and such treatment combined with the DNA and enzymatic screening programs currently in use will lead to the eventual control of this disease.

Related diseases

See other Diseases of the Nervous System

See other Nutritional and Metabolic Diseases