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Metachromatic Leukodystrophy: Diagnosis, Modeling, and Treatment Approaches

Shaimardanova A.A., Chulpanova D.S., Solovyeva V.V., Mullagulova A.I., Kitaeva K.V., Allegrucci C., Rizvanov A.A.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© Copyright © 2020 Shaimardanova, Chulpanova, Solovyeva, Mullagulova, Kitaeva, Allegrucci and Rizvanov. Metachromatic leukodystrophy is a lysosomal storage disease, which is characterized by damage of the myelin sheath that covers most of nerve fibers of the central and peripheral nervous systems. The disease occurs due to a deficiency of the lysosomal enzyme arylsulfatase A (ARSA) or its sphingolipid activator protein B (SapB) and it clinically manifests as progressive motor and cognitive deficiency. ARSA and SapB protein deficiency are caused by mutations in the ARSA and PSAP genes, respectively. The severity of clinical course in metachromatic leukodystrophy is determined by the residual ARSA activity, depending on the type of mutation. Currently, there is no effective treatment for this disease. Clinical cases of bone marrow or cord blood transplantation have been reported, however the therapeutic effectiveness of these methods remains insufficient to prevent aggravation of neurological disorders. Encouraging results have been obtained using gene therapy for delivering the wild-type ARSA gene using vectors based on various serotypes of adeno-associated viruses, as well as using mesenchymal stem cells and combined gene-cell therapy. This review discusses therapeutic strategies for the treatment of metachromatic leukodystrophy, as well as diagnostic methods and modeling of this pathology in animals to evaluate the effectiveness of new therapies.

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Keywords

arylsulfatase A, bone marrow transplantation, gene therapy, lysosomal storage diseases, mesenchymal stem cells, metachromatic leukodystrophy, replacement therapy, sulfatide

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