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FABRY DISEASE: MOLECULAR MECHANISMS AND EMERGING THERAPEUTIC APPROACHES

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Abstract:

Fabry Disease is a rare X-linked inherited metabolic disorder caused by mutations in the *GLA* gene, which result in deficient activity of the lysosomal enzyme α-galactosidase A. The enzymatic deficiency leads to progressive accumulation of glycosphingolipids, particularly globotriaosylceramide (Gb3), within lysosomes of various cell types. This accumulation contributes to multisystem involvement affecting the kidneys, heart, nervous system, and skin. Clinical manifestations may include neuropathic pain, angiokeratomas, renal dysfunction, cardiomyopathy, and cerebrovascular complications. Due to the variability of symptoms and lack of awareness, the disease is frequently underdiagnosed, especially in developing countries. Advances in molecular biology have improved the understanding of the underlying pathogenic mechanisms and facilitated the development of targeted therapeutic strategies. Current treatment primarily involves enzyme replacement therapy aimed at restoring α-galactosidase A activity and reducing substrate accumulation. In addition, emerging therapeutic approaches such as pharmacological chaperone therapy, gene therapy, and substrate reduction therapy are being investigated to provide more effective and long-term management options. This chapter discusses the molecular mechanisms underlying Fabry disease, its clinical manifestations, diagnostic approaches, and recent advances in therapeutic strategies, highlighting future perspectives for improved patient outcomes.

Keywords: Fabry disease, α-galactosidase A deficiency, globotriaosylceramide (Gb3), enzyme replacement therapy, gene therapy.

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