TREM2 in Health and Disease: A Comprehensive Review of Its Roles in Neurodegeneration and Metabolic Disorders

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Abstract

The transmembrane glycoprotein triggering receptor expressed on myeloid cells-2 (TREM2) is prominently found in peripheral tissue macrophages and brain microglia. It plays several critical roles, particularly in lipid metabolism, microglial function, immune response, and Alzheimer's disease. Polymorphisms of TREM2 are associated with a higher prevalence of neurodegenerative presentations such as Alzheimer's disease (AD), Parkinson's disease, and frontotemporal dementia. TREM2 is important for the energy metabolism of microglia; a lack of it impairs lipid and glycolysis metabolism, which compromises microglial function in AD. Furthermore, soluble TREM2 concentrations in cerebrospinal fluid are utilized as biomarkers for the early detection and monitoring of neurodegenerative conditions. TREM2 influences systemic lipid metabolism. It regulates the uptake, efflux, and intracellular processing of lipids in macrophages, affecting conditions such as atherosclerosis, non-alcoholic fatty liver disease, and obesity. TREM2 is vital for microglial function and central nervous system homeostasis, and its modulation offers therapeutic potential for neurodegenerative diseases. Continued research on TREM2's mechanisms is essential for progressing targeted interventions. This paper investigates the diverse roles of TREM2 in various physiological and pathological contexts, specifically focusing on metabolic syndromes, neurodegeneration (AD), and atherosclerosis. Despite significant advancements in our understanding of TREM2, the review addresses several critical gaps concerning its functions and potential for therapeutic applications.

Key words: Alzheimer's disease, lipid metabolism, microglia, neurodegeneration, phagocytosis, Triggering receptor expressed on myeloid cells-2