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Importance of apolipoproteins in multiple sclerosis

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Multiple sclerosis (MS) is a multifaceted disease of the central nervous system. We discovered that progressive MS patients have lower levels of apolipoprotein A-I (ApoA-I) in serum and plasma compared to healthy age-matched controls or relapsing remitting patients. Apolipoproteins play important roles in cholesterol transfer and lipid metabolism in the central nervous system. Our data indicate that ApoA-I levels decline with disease progression. Therefore increasing ApoA-I levels might be beneficial for MS patients. We examined the role of ApoA-I in a mouse model of MS-Experimental Autoimmune Encephalomyelitis (EAE). ApoA-I deficient female mice (C57Bl/6-Tg (ApoA1)^{1Rub/J}) demonstrated a higher incidence and severity of the EAE in comparison to the wild type control mice (C57Bl/6J). EAE was accompanied by an increase in cytokines (INF- γ , TNF- α , TGF- β , IL-2, IL-23) and T cell differentiation into CD25⁺/Foxp3⁺ T cells in these animals. To further investigate the role of ApoA-I in MS, we have treated mice with GW3965, an orally active liver X receptor (LXR) agonist. The LXR form heterodimers with retinoid X receptor (RXR) and are important regulators of lipid metabolism. We found that mice treated with GW3965 had a lower disease incidence, EAE scores and cytokine expression compared to mice with regular EAE. Variation of ApoA-I levels correlated with disease incidence and severity. Our studies indicate that LXR activation resulted in increased ApoA-I production in the liver and in the spinal cord of experimental animals. Further investigation into the mechanisms of ApoA-I formation and disease-associated loss might lead to novel therapies in MS.

Biography

Lidia Gardner is an Associate Professor in the Department of Neurology at the University of Tennessee Health Science Center. She leads a Research program in Multiple Sclerosis at Memphis Veterans Administration Medical Center. She has extensive experience in biochemistry and molecular biology, basic and clinical research. She has published in leading biomedical journals. She is currently serving on the Institutional Animal Care and Use Committee. She received her MBA degree from the University of Memphis and a PhD from the Russian Academy of Sciences in Cell Biology and completed her Postdoctoral studies at the University of Tennessee Health Science Center.

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