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Regulator of G-protein signaling 10 modulates neuroinflammation and metabolic homeostasis: A potential role in alzheimer's diseases

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Insulin resistance and aging-related metabolic disorders constitute serious threats to human health as risk factors for Alzheimer's Disease (AD); especially impaired brain glucose homeostasis was related to the severity of the AD pathology. Regulator of G-protein Signaling proteins (RGSs) are a family of proteins that negatively regulate G-Protein Coupled Receptors (GPCR) through their GTPase Accelerating Protein (GAP) activity. RGS10 is one of the smallest RGS family proteins which we have shown to negatively regulate microglia activation and the level of RGS10 in microglia significantly decreased within the microglia by age. RGS10-deficient microglia displayed impaired phagocytic activity to amyloid-beta fibrils (fAβ). Interestingly, RGS10-deficient mice spontaneously gained weight with age (>15 months) and the level of RGS10 protein was decreased in postmortem brains of the AD and Frontal Temporal Dementia (FTD). Our data demonstrate that RGS10-deficient mice display impaired glucose tolerance, the high level of triglycerides (TG) in plasma. RGS10-deficient mice spontaneously gained weight with age (>15 months). We also tested whether RGS10 plays a role in high-fat-induced chronic inflammation and glucose metabolism as a risk factor for metabolic disorder in the periphery and the CNS. Indeed, HFD-fed RGS10-deficient mice gained significantly more weight compared to HFD-fed wild-type (WT) mice. Importantly, HFD-fed RGS10-deficient mice displayed an insulin resistance phenotype and impaired Long-Term Potentiation (LTP). These data implicate RGS10 may play a critical role of in insulin sensitivity during metabolic disorders in the periphery and the CNS. Importantly, peripheral metabolic disorders, including obesity and insulin resistance along with chronic inflammation have been shown to contribute to development and progression of cognitive impairment and alzheimer's disease through multiple mechanisms. Our data strongly implicate the role of RGS10 in modulating metabolic homeostatsis related to its role in neuroinflammation. Elucidating RGS10 function in maintaining metabolic homeostasis in the CNS and periphery may provide the mechanism to link aging associated chronic inflammation and metabolic disorders, which could be a potential therapeutic target for alzheimer's diseases with dual effects on both inflammation and metabolic disruption. Overall, our study produced highly novel data delineating potential mechanisms of RGS10 function in metabolic homeostasis in the brain.

Biography

Jae-Kyung Lee has completed her PhD in UNT Health Science Center and Postdoctoral studies from UT Southwestern Medical Center at Dallas. She had worked as an Assiatant Professor at Emory University until 2015. Currently, she is an Assistant Professor in University of Georgia, USA. She has published more than 24 papers in reputed journals. Her research focused on understanding how inflammation influences neurodegenerative diseases.

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