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Neural actions of luteinizing hormone and Alzheimer's disease

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Elevation of luteinizing hormone (LH) during aging has been implicated in association with the incidence of Alzheimer's disease (AD), but the underlying pathophysiology remains largely unexplained. We demonstrated that the brain expressed LH receptors (Lhr). Eliminating the actions of LH via knocking-out the receptor (LhrKO) resulted in a remarkable reduction of brain amyloid-β (Aβ) plaques in an AD animal model that expresses a mutant human amyloid precursor protein (APP). This reduction was not associated with a change in APP production. Several Aβ mediated neuropathologic and functionally relevant molecules were markedly improved, which included relief of astrogliosis, reductions of elevated phosphorylated tau and α7-nicotinic acetylcholine receptor, and restorations of altered neuropeptide Y receptors Y1 and Y2. To investigate the underlying mechanism for the reduction of Aβ accumulation, the expression of brain interleukin-6 (IL6) was examined because LhrKO animals exhibited dramatically elevation of serum IL6 and IL6 is known to enhance microglial removal of Aβ. Indeed, brain IL6 mRNA and protein were significantly increased. The elevated IL6 also led to a marked increase in the activity of IL6 signaling pathway evidenced by an increase in Stat3 phosphorylation. In accordance, upregulation of several microglial activity markers, such as H2AB1, Chi3l3, Sra and S100a9 were observed, supporting that Lhr ablation enhances microglial phagocytic activity. These findings indicate that chronic elevation of LH during aging may significantly impact the pathogenesis of AD by inhibiting clearance of Aβ and development of specific and effective LH antagonists may be promising for prevention and treatment of this disease.

Biography

After graduation from Fujian Medical University and completing master degree in Tianjin Medical University, Dr. Zhenmin Lei spent the period from 1987 to 1990 as a postdoctoral fellow in the Department of OB/GYN at the University of Louisville. He received his Ph.D. from the Department of Biochemistry, University of Louisville in 1995 and joined the faculty of the Department of OB/GYN, University of Louisville, where he became a full professor in 2009. His research has focused on understanding the molecular mechanisms and pathophysiological significances of gonadotropin actions in gonadal and nongonadal tissues. He has authored over 150 scientific papers.

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