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The lipolysis stimulated lipoprotein receptor, LSR, as molecular link explaining the link between dyslipidemia, obesity and neurodegenerative diseases

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Dyslipidemia is often associated with obesity, and together represent significant risk factors for age-related diseases including cardiovascular, metabolic and neurodegenerative disorders. Lipoproteins provide the means by which lipid status is maintained through a number of complex regulatory pathways that involve lipoprotein receptors, enzymes, transporters, and transfer proteins. We have demonstrated the role of the lipolysis stimulated lipoprotein receptor, LSR in the removal of triglyceride (TG)-rich lipoproteins from the circulation during the post-prandial phase. Partial reduction of expression of LSR in LSR \pm mice leads to increased postprandial TG levels, as well as decreased capacity for the removal of lipid particles from the plasma. Furthermore, these moderately hyperlipidemic mice demonstrate higher weight gain as compared to their control littermates either with age, or when placed on a high-fat diet. When aged mice were subjected to amyloid stress by intracerebroventricular injection of the oligomeric form of β -amyloid peptide ($A\beta$), behavioral and biochemical analyses revealed increased deleterious effects in LSR \pm mice as compared to their control littermates. Furthermore, $A\beta$ -induced changes in cortical cholesterol content were negatively correlated with the behavioral changes measured. Immunohistochemical and GC MS analyses revealed potential changes in brain membrane cholesterol trafficking and metabolism which may be the underlying reason for the increased susceptibility of LSR \pm mice to $A\beta$ peptides. We therefore conclude that LSR and its dependent pathways may provide the missing link to explain the increased risk of neurodegenerative diseases associated with dyslipidemia and obesity, and may prove to be useful therapeutical targets for preventive and curative treatments.

Biography

Frances T Yen completed her PhD in Nutritional Biochemistry at the University of Illinois at Urbana-Champaign, and her Postdoctoral studies at Columbia University College of Physicians and Surgeons in New York and Louisiana State University Medical Center in New Orleans. She is a Director of research at INSERM, and is currently team leader of BFLA (Bioavailability and fonctionnalités of dietary lipids) of the URAFPA laboratory at the University of Lorraine. She has published over 30 papers in reputable journals, is co-inventor of 10 patents, and has served as reviewer for journals including Diabetes and PLoS One.

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