The Ottawa Hospital | L'Hôpital d'Ottawa

Research project summary

Understanding molecular control of lipid metabolism in brain aging

- Principal Investigator: Jing Wang
- Awarded $726,751 from the Canadian Institutes of Health Research (CIHR) in January 2018 (pending)

While perturbed lipid metabolism has been implicated as a risk factor for aging-related neurological degeneration, it remains unknown how the perturbed lipid metabolism arises during the aging process. Importantly, bioactive lipids have been shown as controllers to regulate neural stem cell function that plays an essential role in learning and memory by producing adult-born neurons. To this end, we are interested in understanding molecular mechanisms that control lipid metabolism to regulate neural stem cell function in the context of aging brain with the long term goal of identifying the molecular target for drug discovery to treat aging-associated cognitive decline. Recently, we discovered a signaling-induced molecular pathway that is required to maintain homeostatic neurogenesis and new memory formation during normal aging. This molecular pathway involves the direct phosphorylation of CBP, a histone acetyltransferase, by atypical protein kinase C (aPKC). We recently identified that monoacylglycerol lipase (Mgll), an enzyme that converts endocannabinoid (2-AG) into arachidonic acid, is a downstream target of the aPKC-CBP pathway. Importantly, we observe that the attenuation of the aPKC-CBP pathway causes upregulation of Mgll expression occurring in both normal and Alzheimer's Disease aging brain of animal models. Thus, we hypothesize that deregulation of the aPKC-CBP pathway in brain aging impairs lipid composition and adult neurogenesis that culminate in the cognitive decline, a phenotype associated with brain aging. Together, our experiments will provide important new information regarding regulation of lipid metabolism and provide fundamental knowledge towards the development of therapeutic strategies fighting against the aging process.

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