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### Adult neurogenesis stimulation as an anti-alzheimer's disease therapeutic approach

Sox2 is a transcription factor that controls the balance between stem cells self-renewal and differentiation, thereby contributing to the control of neurogenesis. Importantly, Sox2 deficiency triggers neurodegeneration in the adult brain. Moreover, Sox2 co localizes with the Amyloid Precursor Protein (APP) in stem cells and Sox2 levels are decreased in the brain of Alzheimer's Disease (AD) patients. We have recently reported the existence of functional network engaging Sox2, the APP Intracellular Domain AICD and the secretase ADAM10 *in vitro* in human cells. Indeed, Sox2 is a potent activator of the non-amyloidogenic processing of APP by increasing the expression of ADAM10. Secondly, transient overexpression of the pro-apoptotic C-terminal APP-derived AICD50 metabolite reduces Sox2 transcription whereas inhibiting AICD production with a -secretase inhibitor augments Sox2 expression, and consequently ADAM10 protein levels, in HEK293 and SH-SY5Y cell lines. Experiments carried out *in vivo* indicate that Sox2 levels are diminished in the hippocampus of mouse models of AD when compared to control animals. Whether ADAM10 and Sox2 co-localize in neurogenic areas of the adult mouse brain and determining if this co-localization is impaired in transgenic AD models is currently under investigation. Finally, the impact of the pharmacological or the genetic modulation of this network on the reprogramming of human induced pluripotent stem cells into neurons is currently monitored in an *in vitro* model of neurogenesis. Altogether, our data suggest that enhancing the Sox2/ADAM10 axis may favor neuroprotection and neurogenesis during the development of AD.

### Biography

Bruno Vincent has completed his PhD from the University of Nice, France in 1996. He has then joined the Rockefeller University in New York as a Postdoctoral Fellow. He returned back to France in 1999 at the Institute of Molecular and Cellular Pharmacology in Sophia-Antipolis and took the position of permanent Researcher at the National Center for Scientific Research (CNRS) in 2001 and was promoted to Research Director. In 2010, he moved to Mahidol University in Bangkok where his research team is working on the identification of new AD-regulating factors. He has published 60 articles in reputed international journals.

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