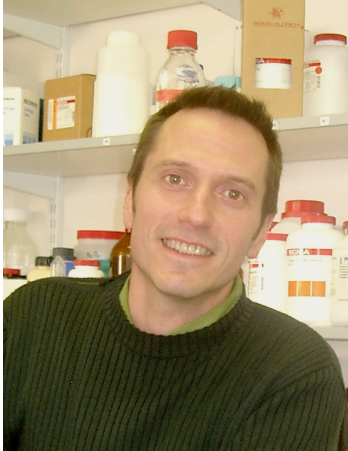


LES CONFÉRENCES DE L'ICM



Frédéric SAUDOU

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Hosted by Alexis BRICE

If you would like to meet the speaker, please use
the following contact: *alexis.brice@upmc.fr*

Frédéric SAUDOU - September 19, 2011 at 11:00

Huntington's disease: huntingtin from axonal transport to ciliogenesis

Huntington's disease (HD) is a fatal neurodegenerative disorder characterized by neuronal dysfunction and the selective death of striatal neurons in the brain. The mutation that causes disease is an abnormal expansion of a polyglutamine (polyQ) stretch in the N-terminus of the 350 kD protein huntingtin. The mechanisms by which huntingtin induces dysfunction and death of neurons in the brain are not clearly understood but they involve in part the loss of the protective properties of wild-type huntingtin.

We previously reported that huntingtin is subjected to phosphorylations such as S421 by the IGF-1/Akt pathway that modify its toxicity, suggesting that protein context, and thereby huntingtin function is a crucial regulator of the toxicity elicited by the polyQ expansion. In support, we demonstrated that huntingtin controls the microtubule-based transport of neurotrophic factors such as BDNF. This function is altered in disease, leading to a decrease in neurotrophic support and death of striatal neurons.

We recently demonstrated that huntingtin phosphorylation at S421 by the IGF-1/Akt pathway restores huntingtin ability to transport vesicles along microtubules in HD. We also analyzed the function of this phosphorylation on wild type huntingtin and found an unexpected role in transport directionality. This further demonstrates the important role of htt as a key regulator of axonal transport in health and disease. Here, we will extend the function of huntingtin as a critical protein that control dynamic processes and how these processes are altered in normal and pathological conditions.

Lundi 19 Septembre 2011 à 11H00
Auditorium de l'ICM
Hôpital Pitié-Salpêtrière
47, boulevard de l'hôpital - 75013 Paris