Laboratory title : CNRS UMR 5297 - Daniel Choquet

Supervisor

Name : Christel BAUDET

Thesis title : Studying the mechanisms of pain sensitization after a thermoinducible deletion of the Cav1.2 gene

Keywords : Chronic pain, Mouse transgenesis, Spinal network, HIFU (High-Intensity Focused Ultrasound), Calcium channel

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Abstract

Chronic pain states are characterized by long-term sensitization of spinal cord neurons that relay nociceptive information to the brain. Among the mechanisms involved in chronic neuropathic pain, we have recently shown a crucial role of the L-type calcium channel Cav1.2 (Cav1.2-LTC) in spinal dorsal horn has a crucial role. However Cav1.2-LTC null-mutation is embryonically lethal and dorsal horn specific genes are not known. So, to characterize further role of Cav1.2-LTC in neuropathic animal models, we need a conditional, inducible, adult knock-out mouse, in which we can specifically target the lumbar region of the spinal cord. For that purpose we are currently breeding existing Cav1.2-LTC conditional knockout mice with an activator strain expressing the Cre recombinase under the control of a thermally induced promoter. The newly created strain will then provide an original tool to delete the Cav1.2-LTC gene specifically in the lumbar spinal cord using High-Intensity Focused Ultrasound (HIFU) for a non-invasive, targeted thermal induction of the Cre-lox recombination. This very innovative approach of conditional gene deletion in mice, will allow us to further investigate the physiopathological role of Cav1.2-LTC in vivo using behavioral, molecular and electrophysiological techniques.

Méthodologies :
HIFU (High-Intensity Focused Ultrasound)
Histology (staining/immunofluorescence)
Imaging
in situ Hybridization
Behavior Tests: Dynamic Weight Bearing (DWB), Von Frey

Qualification required

Basic knowledge of neurobiology and cellular biology would be a plus.
Motivated individual.
Good knowledge of English (written/spoken).