Seminar/Talk

Targeting aberrant Cl- homeostasis and GABAAergic transmission in Down syndrome to design innovative therapeutic approaches

Laura Cancedda
Italian Institute of Technology

Host: Simon Hippenmeyer

Down syndrome (DS) is the most frequent genetic cause of intellectual disability, and individuals with DS often present also sleep and anxiety disorders. A large body of literature demonstrated that altered GABAergic transmission through Cl?- permeable GABAA receptors (GABAARs) considerably contributes to learning and memory deficits in DS mouse models. However, the efficacy of GABAergic transmission had never been directly assessed in DS. Recently, we have shown that GABAAR signaling is excitatory rather than inhibitory, in the hippocampi of adult DS mice. Accordingly, hippocampal expression of the cation Cl? cotransporter NKCC1 is increased in both trisomic mice and individuals with DS. Notably, NKCC1 inhibition by the FDA-approved diuretic bumetanide restores inhibitory GABAergic signaling, synaptic plasticity and hippocampus-dependent memory in adult DS mice. Based on these findings, a pilot clinical trial will soon start on adult individuals with DS patients. Yet, there are open issues related to Cl- homeostasis that, if addressed in DS mice, will provide new knowledge into DS molecular mechanisms and will offer a larger scientific background for designing future clinical trials. In this talk, I will summarize all findings from our laboratory on DS, and show preliminary results we recently collected on some of these open issues.

Tuesday, May 23, 2017 11:30am - 12:30pm
Seminar Room, Lab Building East

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