



Life Sciences Seminar

Targeting aberrant Cl⁻ homeostasis and GABAergic transmission in Down syndrome to design innovative therapeutic approaches

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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 GABA_A receptors (GABA_ARs) 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 GABA_AR 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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