186.11 - Neurotrophic-mimetic strategy to rescue synaptic plasticity and cognitive functions in a mouse model of Down syndrome

November 12, 2017, 3:30 - 3:45 PM

Session Type
Nanosymposium

Grant Support
Jérôme Lejeune Foundation Grant 254-CA2014A

Telethon Foundation Grant GGP15043

Authors
*A. Contestabile¹, M. Parrini¹, M. Alberti¹, D. Ghezzi¹, G. Deidda¹, L. Cancetta¹,²

¹Fondazione Inst. Italiano Di Tecnologia, Genova, Italy; ²Dulbecco Telethon Inst., Genova, Italy

Disclosures

Abstract
Down syndrome (DS) or trisomy 21 is the most frequent genetic cause of intellectual disability in children and adults. Although numerous studies have shown that cognitive impairment possibly arises from dysfunction of the hippocampal circuit, there has been little progress in defining effective treatments. Previous studies have shown that impaired synaptic plasticity of mature hippocampal neurons and decreased hippocampal adult neurogenesis are main determinants in reducing cognitive functions in DS animal models. Currently, most preclinical therapeutic approaches in DS mice have focused on rescuing either one or the other of these impairments. Here, we have found that the expression of Brain-Derived Neurotrophic Factor (BDNF) is decreased in the brains of individuals with DS. Interestingly, a large body of literature indicates that BDNF signaling modulates both synaptic plasticity, and adult neurogenesis. Therefore, we propose here to promote BDNF/TrkB signaling using a BDNF-mimetic drug with the twofold aim of rescuing synaptic plasticity and increase adult neurogenesis toward the rescue of cognitive functions in the Ts65Dn mouse model of DS. Our results indicate that indeed promoting BDNF/TrkB signaling rescued hippocampal synaptic plasticity, increased hippocampal adult neurogenesis and restored cognitive performances in different behavioral tasks in Ts65Dn mice. The molecular mechanisms of impaired BDNF/TrkB signaling in trisomic mice are currently under investigation. Overall, our experiments show in a reliable animal model of DS the efficacy of a novel and multifaceted therapeutic approach with good potential to be translated into clinical practice.