Neural Precursor Cells as a potential therapeutic approach for Rett Syndrome: identification of the involved molecular mechanisms

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Rett syndrome (RTT) is a rare neurodevelopmental disorder, mostly caused by MECP2 mutations, representing the leading cause of severe intellectual disability in females. Unfortunately, no cure is available.
Considering the effectiveness of NPCs in the treatment of other neurological and neurodevelopmental diseases, we decided to investigate their therapeutic potential in RTT.
Our research demonstrated their efficacy in both RTT in vitro and in vivo mouse models.
Through a transwell-based co-culture system, we observed that NPCs promote morphological and synaptic rescues in Mecp2 null neurons. In vivo, we demonstrated a significant amelioration of the cognitive and motor defects of RTT mice, together with an increased lifespan, after NPCs transplantation.
The results highlighted that NPCs-mediated beneficial effects arise through “bystander” and paracrine mechanisms: by sensing the pathological environment, they secrete beneficial factors that promote immunomodulation, neuroprotection and brain plasticity.
To identify the molecular mechanisms set in motion by NPCs, we performed bulk RNA sequencing analyses on both models. Even if one candidate molecule has been identified and its efficacy validated, more studies are ongoing to further clarify other pathways modulated in KO neurons in presence of NPCs.
All data will be presented in the poster session to illustrate the value of this cellular approach in treating RTT and/or in identifying new defective pathways with putative therapeutic value.