E Sacide Caglayan, Human Genet Embryol 2016, 6:3(Suppl)
http://dx.doi.org/10.4172/2161-0436.C1.002

Generation of improved human cerebral organoids from single copy *DYRK1A* knockout induced pluripotent stem cells in trisomy 21: Hypothetical solutions for neurodevelopmental models and therapeutic alternatives in Down syndrome

E Sacide Caglayan
Ankara Yildirim Beyazit University, Turkey

Dual-specificity tyrosine phosphorylation-regulated kinase 1A (*DYRK1A*) is a strong therapeutic target to ameliorate cognitive functions of Down Syndrome (DS). Genetic normalization of *DYRK1A* is sufficient to normalize early cortical developmental phenotypes in DS mouse models. Gyrencephalic human neocortical development is more complex than that in lissencephalic mice, hence cerebral organoids (COs) can be used to model early neurodevelopmental defects of DS. Single copy *DYRK1A* knockout COs (sc*DYRK1A*KO-COs) can be generated from manipulated DS derived (DS-) induced pluripotent stem cells (iPSCs) and genetic normalization of *DYRK1A* is expected to result in corrected neurodevelopmental phenotypes that can be reminiscent of normal COs. *DYRK1A* knock-in (*DYRK1A*KI) COs can be derived after genetic manipulations of normal iPSCs and would be valuable to evaluate impaired neocortical development as can be seen in DS-COs. *DYRK1A* mutations cause severe human primary microcephaly, hence dose optimization studies of *DYRK1A* inhibitors will be critical for prenatal therapeutic applications in DS. Several doses of *DYRK1A* inhibitors can be tested in the neurodevelopment process of DS-COs and DS-sc*DYRK1A*KO-COs would be used as optimum models for evaluating phenotypic ameliorations. Overdose drug exposure in DS-COs can be explained by similar defects present in DS-ba*DYRK1A*KO-COs and *DYRK1A*KO-COs. There are several limitations in the current CO technology, which can be reduced by the generation of vascularized brain-like organoids giving opportunities to mimic late-stage corticogenesis and complete hippocampal development. In the future, improved DS-*DYRK1A*KO-COs can be efficient in studies that aim to generate efficiently transplantable and implantable neurons for tissue regeneration alternatives in DS individuals.

Biography

E Sacide Caglayan has completed her PhD in Medical Genetics from Afyon Kocatepe University in 2010 and worked as a Visiting Scholar in Ruohola-Baker Lab, Institute of Stem Cell & Regenerative Medicine, University of Washington. Presently, she is working as an Assistant Professor in Ankara Yildirim Beyazit University, Faculty of Health Science, Department of Nutrition in Ankara, Turkey.

escaglayan@gmail.com

Notes: