

IGSN - SYMPOSIUM

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Human Brain Development and the Use of Cerebral Organoids to Decipher Cellular and Molecular Mechanisms

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Human brain organoids: from novel models to studies of development and disease

The brain is one of the organs that has undergone the deepest changes during evolution. For this reason, the latest years have seen a surge of human-relevant models, including organoids, that allow a more in-depth understanding of human brain development. In this talk, I will firstly discuss the latest advances in the brain organoid field that have led to state-of-the-art human-relevant models to study aspects of development and disease. I will then present recent work from our laboratory, in which we discovered that the human foetal brain possesses the intrinsic capacity to self-organize into organoids, i.e. foetal brain tissue-derived organoids (FeBOs). These organoids can be cultured and expanded long-term, due to the maintenance of tissue integrity and production of their own sustaining extracellular matrix (ECM) niche. Moreover, we found that perturbation of specific ECM-mediated signalling determines a dramatic reduction in the size and growth capacity of FeBOs. Amongst key differentially-expressed genes under newly described FeBO growth-impairing conditions, we identified a specific enzyme involved in key steps of ECM production, constituting a novel regulator of brain expansion. Generation of genetically engineered brain organoids showed a key role of this enzyme in the pace of brain development, with impaired neural stem cell expansion and accelerated differentiation. Interestingly, we provide indications that ECM perturbation also alters regional identity of the neural stem cells. Finally, I will discuss how combining different brain organoid models is a powerful approach to unravel novel aspects of human brain development..

Host:

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