IBEC-VHIR INTERNATIONAL PhD PROGRAMME

Position

1. Project Title/ Job Position title:
   METAPHOR for Organoids: Metabolic Evaluation of Retinal Oganoids

2. Research project/ Research Group description

Hyperspectral imaging is an optical technique that provides full spectral information at every pixel of an image. The IBEC group has developed the METAPHOR pipeline, which combines hyperspectral imaging with artificial intelligence (AI) to extract metabolic fingerprints of living samples. The methodology, initially developed to assess embryo viability, is now poised to revolutionize the field of organoid research, such as retinal organoids (ROs).

At VHIR, human retinal organoids (RO) serve as valuable models for studying retinal degenerative diseases, particularly when suitable animal models are unavailable. We observed significant morphological and cellular changes, including lack of retinal structure, decreased expression of retinal markers, delayed cell maturation, particularly in photoreceptors, and altered neuronal activity in RO derived from retinitis pigmentosa patients (RP), further supporting the disease phenotype.

One of the most intriguing findings was the altered metabolic rate in RP-ROs, suggesting that metabolic dysregulation may be crucial in disease pathogenesis. By monitoring metabolic trajectories in real time, we can gain valuable insights into disease mechanisms and identify potential therapeutic targets. Moreover, aside from the biological insights, the hyperspectral and AI pipeline can provide 3D reconstruction and single-cell analysis of the RO to study its morphology and cell-cell interactions, as it allows for cell labelling and segmentation according to different metabolic profiles for each cell type. To validate our hyperspectral imaging findings, we will use qPCR, single-cell RNA sequencing, and immunohistochemistry, to help us understand the molecular and cellular mechanisms involved.

Preliminary data from the collaboration between both groups already showed the effectiveness of hyperspectral imaging in assessing the metabolic status of healthy and diseased RO, highlighting METAPHOR's potential applications in the organoid field.

3. Job position description

The PhD candidate will divide their time between the Bioengineering in Reproductive Health (BRH) group at IBEC and the Ophthalmology Research Group at VHIR. The aim of the project is to expand the horizons of hyperspectral technology on organoid research by developing new groundbreaking approaches to disease modeling.

At VHIR, the PhD candidate will learn how to cultivate retinal organoids from human pluripotent stem cells. They will also be involved in the *in vitro* modeling of rare degenerative retinal diseases. Additionally, the candidate will receive training in various molecular and cellular techniques, as well as in electron microscopy and calcium imaging. They will conduct their research in a highly multidisciplinary environment, which will be very advantageous to reinforce the translation between basic research and clinical applications.

At IBEC the PhD candidate will learn and perform the hyperspectral image acquisition and phasor analysis pipeline and apply it to the RO cultured at VHIR. They will also learn to code to develop the algorithm needed to build the AI classifier for metabolic profiling. Further training in image segmentation and object detection will be provided and the candidate will apply it to study the 3D structure of complex organoids. The group is a highly interdisciplinary team with extensive expertise covering developmental biology, biophysics, bioengineering, optics and data analysis.

The student will acquire a multidisciplinary profile with relevant expertise in a wide variety of techniques and scientific approaches, that include cellular and molecular biology, advanced imaging techniques and coding. Furthermore, the extensive experience of the BRH group in the field of knowledge transfer and innovation will offer the student valuable training in transferable skills.

Group Leader at IBEC

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