



International Lecture Series

Disease Biology and Molecular Medicine

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Dr. Adrianos Skaros

Postdoctoral Research Fellow
Human Technopole, Neurogenomics Centre, Laboratory of High Definition
Disease Modelling, Lab: Stem Cell and Organoid Epigenetics

9 November 2022
16:00 h

Kleiner Hörsaal

Institut für Biochemie
und Biotechnologie
Kurt-Mothes-Straße 3

“Cerebral Cortical Genetic Circuits Selected in Anatomically Modern Human Evolution: A dissection via Orthogonal CRISPR Perturbations”

Adrianos received a BSc (Hons) in Biotechnology from Northumbria University Newcastle in 2016, which was followed by a MSc in Applied Biomolecular Technology from the University of Nottingham. In 2018, he began his PhD in the lab of Giuseppe Testa in IEO/University of Milan, under the Marie-Curie ITN “EpiSyStem”. Since 2021 he has been a Leverhulme Trust Fellow where he now conducts his work at the newly opened Human Technopole institute, in Milan, Italy.

His research interests address the crossroads between evolution and neurodevelopment. Anatomically modern humans (AMHs) have evolved neural features that differ significantly from those of archaic hominins and underlie their cognitive-behavioural specificities; their evolution, however, has thus far been predominantly inferred from the fossil record and from the comparison of modern and archaic genomes. In doing so, a vast number of genes have been found to harbour changes within protein-coding regions, rendering these different between the AMH genome and Neanderthal and Denisovan genomes. To investigate the functional importance of amino acid changes in the modern human cortex, he prioritised and curated evolutionary- and neurodevelopmentally-relevant genes (15) in order to create a dependency network via CRISPR technologies, by combining two orthogonal Cas9 proteins from *Streptococcus pyogenes* and *Staphylococcus aureus*, to carry out a dual screen in which one gene is activated whilst a second gene is deleted in the same cell; understanding the direction of information flow is vital for characterising how genetic networks affect phenotypes, but also to fully understand single gene functions. Specifically, he integrates hiPSC-based cortical organoid developmental modelling at single cell resolution, multiplex gene editing and gene network reconstruction to enable the first empirically tested, systems-level definition of the molecular logic underlying our recent cortical evolution. These technologies are versatile and can be used in different disciplines, whether that be in understanding protein function for drug discovery in cancer or understanding the role of certain genes in disease.

Selected publications

Zanella, M. et al., 2019. *Sci. Adv.* 5, eaaw7908.

Lopez-Tobon, A. et al., 2022. doi.org/10.1101/2022.10.10.511434.

Mihailovich, M. et al., 2022. doi.org/10.1101/2022.10.10.511483.

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