INTERNATIONAL PHD PROGRAMME

Unveiling the Chromatin Biology of Rare Genetic Diseases to delineate innovative therapeutic solutions

The Chrom-Rare Consortium

Chrom_Rare is a EU-funded consortium relying on a collaborative effort of multi-disciplinary research teams all around Europe, that share the aim of working towards unveiling the molecular basis of chromatinopthies to delineate innovative therapeutic solutions.

The goal

Chromatinopathies (CPs) are a group of rare genetic diseases, which share clinical features as well as causal genetic alterations, leading to the inactivation of chromatin regulators involved in gene expression control and 3D chromatin organization.Within the framework of Chrom_Rare, our main goal is to set-up an intra-sectoral, cross-disciplinary training programme that would prepare the next generation of researchers equipped with advanced theoretical, technical and computational skills to study fundamental aspects of chromatin biology and their impact on chromatinopaties (CPs). In parallel, Chrom_Rare will devise new strategies to translate the molecular findings into new diagnostic and therapeutic approaches for patients affected by CPs. We are thus looking for Doctoral Candidates that will join this PhD programme and that will work towards understanding the molecular basis of chromatinopathies, specifically aiming at:
1) developing multiple disease models recapitulating the main clinical features of CPs (WP1).
2) investigating the genetic, epigenetic and topological determinants of CPs (WP2).
3) uncovering perturbed regulatory circuitries suitable for therapeutic intervention (WP3).

The project

DC8 (UNINA) will dissect the impact of pathogenic variants in KMT2D by combining Kabuki syndrome disease modelling with omics technologies and computational approaches. Specifically, DC8 will investigate the epigenetic and transcriptomic profiles and 3D genome organization using KS hiPSC-derived differentiated cells and organoids (e.g. brain and heart).

To reach these goals, DC8 will expand the existing biobank of CPs, mainly by increasing the KS patients' cohort as well as controls. After a training period, the DC8 will adopt quantitative array-based methylation measurement at the single-CpG-site level, offering high resolution for understanding DNA epigenetic changes of all the KS models generated.

Then, DC8 will adopt the most recent technologies at single cell level resolution to unveil the overall alterations affecting chromatin structure and function as consequences of KMT2D pathogenic variants. Specifically, single cell Multiome ATAC + scRNASeq will simultaneously provide profile gene expression and open chromatin state from the same cell, while single cell Hi-C technologies will define the 3D chromatin interaction landscape.

Overall, this project will provide insights into how changes in chromatin accessibility, 3D spatial organizations and associated epigenetics profiles will lead to the defects that are clinically relevant in Kabuki syndrome.

Apply by March 31st!
Follow the link associated to this QR code to get access to all information regarding the Chrom_Rare projects and instructions on how to apply.

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This project has received funding from the European Union's Horizon Europe research and innovation programme under the Marie Skłodowska-Curie grant agreement No 101073334

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The projects

The consortium provides 10 PhD projects (DCs), distributed among the different partner laboratories:

DC1: Role of chromatin factors in establishing nuclear mechanical properties - University of Trento, Italy
DC2: Characterizing cortical neurons in Kabuki syndrome to understand biology and identify therapeutic targets - University of Manchester, UK
DC3: Epigenome and transcriptome in depth analysis of patient-derived model for CPs, mapping of possible alterations and effects of epi-drugs on the profiles - University of Montpellier, France
DC4: Computational modelling of epigenome rewiring (walking pathways) during cell differentiation. Model validation by in depth analysis of epigenome and transcriptome data - Genexplain GMBH, Germany
DC5: Enhancer responsiveness in disease models of Cornelia de Lange and Wiedemann-Steiner syndromes - CSIC/IBBTEC, Spain
DC6: Genotype/phenotype and epi-genotype correlations, immune phenotype in CPs - University of Montpellier, France
DC7: Defining the molecular consequences of haploinsufficiency in CEBP and p300 histone acetyltransferases underpinning the RT syndrome - Nencki Institute of Experimental Biology of the Polish Academy of Sciences
DC8: Biobanking, DNA-methylation signature and 3D genome organization in the study of Kabuki syndrome - University of Naples “Federico II”, Italy
DC9: Defining the proximal proteome of mutant chromatin proteins associated with CPs - Radboud University, Netherlands
DC10: Dissecting alterations of nuclear compartmentalization in CPs: from LLPS to molecular dynamics - University of Trento, Italy

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