Project 1.9 Defining the molecular consequences of haploinsufficiency in CEBP and p300 histone acetyltransferases underpinning the Rubinstein-Taybi syndrome (Chrome Rare)

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Background:

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.

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).

Aim:

In this project we aim to define the molecular consequences of the loss of one of the copies of CEBP and p300 histone acetyltransferases. Likewise, based on the mechanistic data we will obtain, we aim to suggest potential clinical intervention strategies to address RT syndrome.

Using CRISPR-Cas9, we will establish a panel of heterozygous human-induced pluripotent stem cell lines (iPS) which lack one of the copes of p300 or CBP. DC7 will next generate neural progenitors and neurons and astrocytes from these lines along with the heterozygous controls. At NENCKI, the project will aim to determine the impact of the loss of CBP and p300 on chromatin structure and gene activity using Hi-C, ATAC-seq, ChIP-seq, and RNA seq. By integrating this data, the project will determine a list of genes and possible pathways that could constitute relevant intervention points for the possible design of the future therapies.

Requirements:

- supported researchers must be Doctoral Candidates (DC), i.e., not already in possession of a doctoral degree at the date of the recruitment. Researchers who have successfully defended their doctoral thesis but who have not yet formally been awarded the doctoral degree will not be considered eligible
- recruited researchers can be of any nationality and must comply with the following mobility rule: Researchers are required to undertake trans-national mobility (i.e., move from one country to another) when taking up the appointment. At the time of selection by the host organization, researchers must not have resided or carried out their main activity (work, studies, etc.) in the country of their host organization for more than 12 months in the 3 years immediately prior to their recruitment. Short stays, such as holidays, are not taken into account.

- English language: Candidates must demonstrate that their ability to understand and express themselves in both written and spoken English is sufficiently high for them to derive the full benefit from the network training.