TITLE
Exploring The Pathogenetic Basis of ICF Syndrome With Human Induced Pluripotent Stem Cells

DESCRIPTION

Immunodeficiency, Centromeric instability and Facial anomalies typeI (ICF1) syndrome is an autosomal recessive disorder mainly affecting the immune system. Most patients carry genetic mutations in the DNA methyltransferase DNMT3B gene, which severely interfere with the methyltransferase activity of the protein. Despite the disease has been described more than twenty years ago, ICF1 syndrome pathogenetic mechanisms are far from being completely clarified. Being a rare disease, samples from patients are scarce and often come as immortalized fibroblasts or transformed B-lymphocytes, which greatly restricts the possibility to analyze certain cellular phenotypes or even molecular defects. Thus, the development of models to study specific phenotypic aspects of the ICF1 syndrome are thus of great importance. Recent generation and characterization of ICF1 patients'-derived induced pluripotent stem cells (ICF1-iPSCs) and their CRSPR/Cas9-based corrected counterparts in which DNMT3B is restored (c-ICF1-iPSC) provided us with a valuable tool to in vitro modelling the molecular pathogenesis of ICF1 syndrome.
The research project aims at (i) comparing the hematopoietic differentiation of control and ICF-mutant iPSCs to determine the mechanisms by which DNMT3B deficiency gives rise to immune dysfunction and at (ii) identifying the earliest transcriptional and epigenetic defects caused by DNMT3B dysfunction and verify whether and at what extent they are restored through an integrated multi-omic approach.
The proposed research is expected to establish a more appropriate model to clarify the pathogenesis of ICF syndrome and the role of DNMT3B in human cell physiology. A background in molecular biology and knowledge of chromatin-related techniques and stem cell biology would be preferred.

SELECTION CRITERIA

Eligibility Criteria

- Academic degree: Applicants shall have a master degree or equivalent in **Life** or **Natural sciences** (e.g. Biology, Biochemistry, Biotechnology, Molecular Biology, or related fields), corresponding to the second level of studies.
- Mobility rule: There will be no nationality restrictions. Applicants can be from any Country. However, according to the mobility rule, at the time of the application deadline researchers should not have resided or carried out their main activity (work, studies, etc.) in Italy for more than 12 months in the 3 years immediately prior to the reference date. Compulsory national service and/or short stays such as holidays will not be taken into account.
- Research experience: Applicants shall, at the time of the application deadline, be in the first four years (full-time equivalent research experience) of their research careers and not yet awarded a doctoral degree.

Full-Time Equivalent (FTE) Research Experience will be determined from the date when a researcher obtained the degree which would formally entitle him or her to embark on a doctorate, either in the country in which the degree was obtained or in Italy, irrespective of whether or not a doctorate is or was ever envisaged.

Evaluation Criteria

Step 1 -Evaluation of documentation provided by the candidate: a) Academic record and training b) Research activities c) CV/motivation letter; d) Level of English; e) Reference letters.
Step 2 - Interview: a) Scientific knowledge in the field of interest; b) Research experience in the field of interest c), Motivation; d) English proficiency.

Supervisor

Dr. Maria Matarazzo
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