

TITLE

Unravelling genetic modifiers of Incontinentia Pigmenti and their role in the NF-kB pathway

DESCRIPTION

The main interest of our group is to unravel the pathogenetic mechanism of the Incontinentia Pigmenti (IP, OMIM308300), a disease affecting the NF-kB pathway. IP is a monogenic disease, X-dominant, caused by mutation of NEMO/IKBKG, which encodes the IKKgammma regulatory protein of the NF-kB. The symptoms of IP (e.g., the appearance of severe defects of the Central Nervous System (CNS)), vary between individuals, whose NEMO/IKBKG mutations all abolish protein expression. Whereas the expression of Mendelian diseases can be influenced by factors independent from the pathogenic mutation, we aim to (1) identify modifier genes that influence the IP CNS severity (epilepsy and mental retardation), (2) define the main functional pathway(s) and the molecular mechanisms involved/affected and (3) establish the relationship, if any, between the candidate modifier and the NF-kB pathway activation.

To achieve this objective we will take advantage of the availability within our group of a large collection of IP patient samples completed with all clinical information, of a long-standing experience in the study of the effect of NEMO/IKBKG mutation on NF-kB activation and of an animal facility hosting mouse models of IP. Finally, data of exome targeted sequencing performed on IP trios with intra-familial CNS heterogeneous presentation is already available and a first step towards the identification and validation of the candidate modifier is in progress.

We offer a position for a PhD student. The PhD project will aim to identify, validate and characterize candidate modifier genes of CNS phenotype in IP. The functional characterization will include in-depth investigation on the NF-kB pathway impairment, generation of targeted engineered cellular model and the use of mouse model already available within our group to perform proof-of-concept validation.

We are looking for a young motivated and independent person with a strong background in molecular biology, and good experience in human genetic and bioinformatics.

SELECTION CRITERIA

Eligibility Criteria

- Academic degree: Applicants shall have a master degree 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 her/him 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 Valeria Ursini

<http://www.igb.cnr.it/staff/people/ursini>