TITLE

Identification of druggable disease paths in Aristaless-related Homeobox Epilepsy mouse model

DESCRIPTION

The Aristaless-related homeobox gene (ARX) is one of the most frequently mutated genes in a spectrum of X-chromosome phenotypes with ID and chronic Epilepsy, including infantile spasms. It is a morphogenetic gene codifying a homeo−Transcription Factor with a crucial role in GABAergic maturation and cortex development. Unfortunately, seizures associated to mutations in ARX are severe, occur very early in the post-natal life and are resistant to all standard epileptic drugs. The overall objective of our research is to dissect the ARX-dependent pathways to better understand the biological mechanisms through which defects in ARX and its effectors cause malignant seizure, with the final goal of identifying druggable target molecules. To achieve this objective, our research activity includes molecular and cellular methods and animal models.

Objectives

- Transcription factor targeting and application of non-coding RNA technology

- in vitro and in vivo analyses of epileptogenic pathways

- Development of new disease mouse models

Job description

Development of treatments to prevent or alleviate the early-onset of epilepsy in ARX patients is a field only at the beginning. Here, we have pointed out the opportunity to identify ARX-target genes with a crucial role during cortex development and at early-stage of postnatal life.

This understanding will be achieved through the application of molecular biology methods (expression constructs, epigenetic modifications), cellular biology methods in in vitro (neuron cultures), ex vivo (brain slices), and in vivo (mice) systems.

This PhD project will provide cutting-edge training for candidates who wish to pursue a career in human genetics and neurobiology diseases. Specifically, the student will have the opportunity to join a research programme within a multidisciplinary research network. We are seeking a highly talented student with a high quality Masters degree in biology, chemistry or material science. Students with a background in related disciplines are encouraged to apply.

Recent publication related to this project:

Poeta L, Fusco F, Drongitis D, Shoubridge C, Manganelli G, Filosa S, Paciolla M, Courtney M, Collombat P, Lioi MB, Gecz J, Ursini MV, Miano MG. 2013. A Regulatory Path Associated with X-Linked Intellectual Disability and Epilepsy Links KDM5C to the Polyalanine Expansions in ARX. Am J Hum Genet. 92:114-25.

SELECTION CRITERIA

<u>Eligibility Criteria</u>

- Academic degree: Applicants shall have a master degree or equivalent in **Life** or **Natural sciences** (e.g. Biology, Biochemistry, Biotechnology, Molecular Biology, Pharmacy or related fields), corresponding to the second level of studies.
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- 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.