TITLE

Study of *in vivo* models to investigate the role of the causative gene *ZNF687* in Paget's disease of bone

DESCRIPTION

The Laboratory of Molecular Genetics and Genomics (MGG) led by Dr. Gianfrancesco is focused on the identification of the molecular bases responsible for bone diseases, with particular attention to Paget's disease of bone (PDB) and its related neoplastic degenerations. A well-known expertise about next generation sequencing approaches defines the main focus of Gianfrancesco's Group: to identify novel genes underlying bone diseases. The correlation of genetic studies with functional approaches also allows to characterize the function of the identified genes. Recently, applying whole exome sequencing, we identified a missense germline mutation (c.2810 C>G, p.Pro937Arg) in *ZNF687* as responsible for PDB complicated by Giant Cell tumor of bone. ZNF687 is a transcription factor belonging to the endogenous co-regulator Z3 complex, involved in the interpretation of the histone code for remodelling of the chromatin and for the transcription. However, its exact biological role remains to be defined yet.

In this PhD project the student will investigate *ZNF687* biological and pathological role through the study and the phenotypic characterization of two different mouse models: Knock-out and Knock-in *Zfp687*. Specifically, the student will explore the involvement of Zfp687 in the skeletal system and in bone cells involved in PDB onset, applying *in vivo* and *in vitro* approaches.
Mice will be analysed at various stages of development and growth. Analysis methods will include histology and immunohistochemistry light and fluorescent microscopy, FACS, microCT, molecular biology techniques and *in vitro* culture assays using primary cells (bone marrow precursors to study *in vitro* osteoclast and osteoblast differentiation) and tissue explants. Bio-imaging analyses will be used to study tumor development in Knock-in mouse model.

We are looking for a bright and highly motivated student researcher that will belong to INCIPIT Programme, the novel international PhD programme, aimed to provide innovative multidisciplinary and intersectoral training in Life and Biomaterial Sciences, co-funded by the COFUND scheme (Marie Skłodowska - Curie Actions). In this context, the candidate will join the Gianfrancesco's group, team of postdoctoral, PhD students and master student. The eligible candidate for this position should have a Master degree in Biology and Biomedical Sciences. Good knowledge about the animal models phenotypic characterization, also referred to bone and skeletal system, is preferable. Experience in molecular biology, cell culture and histology will be seen as a distinctive advantage. Strong interest in basic research, excellent experimental skills, enthusiasm to learn and develop new techniques, and a critical mind are strongly required. The student will receive supervision on the project at multiple levels, and will be offered numerous possibilities to further grow scientifically including by writing papers and participating in international meetings.

SELECTION CRITERIA

Eligibility Criteria

- Academic degree: Applicants shall have a master degree or equivalent in **Biology or Biomedical Sciences**, 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.

Supervisor
Dr. Fernando Gianfrancesco