POSITION

Project Title/ Job position title

Molecular characterization of endometrial carcinoma: Prognostic and predictive impact/ Pre-doctoral Fellowship

Area of Knowledge

Life Science Panel

Human Biology, Microbiology, Genetics, Cell Biology, Genomics and Proteomics, Biochemestry

Research Project/Research Group Description

Our group is focused in the identification of prognostic and predictive biomarkers related to different types of tumors.

Last years, endometrial carcinoma has been pointed in the research focus due to recent advances in its molecular biology knowledge, with a possible impact in the patients stratification regarding targeted therapies.

Endometrial carcinoma is the most common gynecological tumor in females. Classically subdivided in type I or endometrioid, accounting for more than 80% of cases, and type II, including the serous variant, with a worst prognosis. Both are supposed to be different entities also at the molecular level, with *KRAS*, *PTEN*, *PI3KCA* or *CTNBB1* alteration for the type I, and *mTOR* components pathway of T*P53* mutations in type II.

More recently, the TCGA study revealed the existence of 4 molecular subtypes with impact in the prognosis of the patients: *POLE* mutated group, microsatellite instable group, and the high and low copy number alterations groups.

The identification of surrogate markers to identify these molecular subgroups, mainly by easily to perform techniques in the pathology departments is a big challenge. Combination of *POLE* mutation, and p53 , PMS2 and MSH6 inmunohistochemistry has been proposed.

The study of the clinical evolution of these subgroups is very interesting. As exemplifying paradigm, the *POLE* mutated group, accounting for 10% of cases, present aggressive features by the pathological point of view, but usually behave with a better outcome than expected. Another opposite example are the low grade tumors that present a worse outcome, and that will need to further molecular characterization. To date, surgery is the cornerstone for the treatment of these tumors. To identify those patients with medium-high risk of relapse will be very helpful in order to consider adjuvant treatment.

Other points under research are the targeted therapies. To date, there is not a clinical benefit supporting the standardization of targeted therapies, but there are multiple clinical trials

exploring some hallmarks for tumor development, including tumor growth signaling, angiogenesis, DNA repair and immunotherapy. The characterization of the effect of these drugs in preclinical models, ideally form different molecular subtypes, could be a very interesting way to explore the rational use of these drugs.

Job position description

The Research Project has three major goals:

1. Validate published molecular classification of EC and relate to patient´s outcome.
2. Explore biomarkers for the identification of intermediate or high risk of relapse in low grade tumors
3. Preclinical studies in EC established cell lines.

To tackle these issues, the student will employ a broad array of highly specialized techniques, including molecular analysis on tissue sections by PCR and inmunohistochemistry, and cellular and functional analysis of culture cell. These skills will be acquired by the student under supervision of the laboratory scientific staff, and mentored by the PI of the project.

Previous experience in any of the tasks will be positively valuated, but not mandatory for consideration of the application.

GROUP LEADER

Title: MD, PhD

Full name: Andrés Redondo

Email: aredondo12@gmaill.com

Research project/Research group website:

http://www.idipaz.es/PaginaDinamica.aspx?IdPag=252&Lang=EN