



## PREDOCTORAL RESEARCHER POSITION GRANT

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The Hospital del Mar Research Institute is the research center of the Barcelona Mar Health Park Consortium and a member of the Barcelona Biomedical Research Park (PRBB). It provides an exceptional framework for translational research and offers state-of-the-art technological platforms (flow cytometry, animal facility, microscopy, etc.) as well as close collaboration with the Hospital del Mar.

### POSITION

Predocctoral researcher position as a part of the research group **Epithelial-to-Mesenchymal transition and tumor invasion** with a predocctoral contract supported by the grant reference **PID2022-136968OB-I00**, funded by MCIN/AEI/10.13039/501100011033 and the European Social Fund (FSE).

### OFFER

- Predocctoral researcher position.
- Predocctoral researcher employment contract governed by Article 21 of Law 14/2021, of June 1, on Science, Technology, and Innovation, and Royal Decree 103/2019, of March 1, on the Statute of Research Personnel in Training.
- Full-time contract.
- Salary according to the provisions of Royal Decree 103/2019, of March 1, on the Statute of Research Personnel in Training, paid in 12 instalments.
- Incorporation within 3 months from the definitive resolution.



## CANDIDATE REQUIREMENTS

- ✓ Degree in: **Chemistry, Biology, Biochemistry or similar; Master degree in a topic related to Molecular or Cellular Biology.**
- ✓ Training in: **Cell and Molecular Biology**
- ✓ Additional positive issues: **Work experience in a Cell Biology laboratory, preferably in topics related to Cancer Biology; also having the training course to work with experimental animals.**
- ✓ At the time of hiring, the candidate must provide proof of admission to a doctoral program.

Once the candidate has enrolled in the doctoral program, they will need to submit a copy of the formalized enrolment to the contracting institution.

## SELECTION CRITERIA

- 1) Academic and/or scientific-technical trajectory of the candidate. (Up to 50 points).
  - 1.a) Scientific-technical contributions: The academic record and other curricular merits of the candidate will be evaluated, as well as their suitability for the tasks to be carried out based on their training and professional experience. (Up to 45 points).
  - 1.b) Mobility and internationalization: The relevance and impact of the candidate's stays in national and international research centers and/or the industrial sector will be assessed, considering the prestige of the hosting entity and the activities carried out there. (Up to 5 points).
- 2) Suitability of the candidate for the research activities to be carried out. The candidate's suitability for the project or research activities will be evaluated based on their previous training and experience. This will include the added value that the completion of the project will bring to their research career, as well as the contribution to the institution and research group. (Up to 50 points).



## THE PROJECT

**TITLE: Oxidative and endoplasmic reticulum stresses during epithelial-to-mesenchymal transition: new vulnerabilities of metastatic cells**

**SUMMARY:** Epithelial tumors, such as those generated in colon or breast, often generate metastatic foci that eventually compromise the patients' life. Current chemotherapies mostly reduce tumor burden, but their efficacy is too limited since many tumor cells acquire resistance to the treatment. Cancer cells activate epithelial-to-mesenchymal transition (EMT) to dissociate from the primary tumor and invade the neighbour tissues; moreover, EMT also impinges in other tumoral traits since it provides stem cell characteristics, a higher resistance to chemotherapeutic drugs and even modifies the tumor cell metabolism. For instance, EMT promotes alterations in lipid metabolism decreasing the cholesterol levels and increasing membrane fluidity.

These modifications can uncover new vulnerabilities of tumor cells since mesenchymal cells show a higher sensitivity to ferroptosis inducers. Ferroptosis is an oxidative non-apoptotic form of cell death induced by endogenous lipid peroxides generated from polyunsaturated fatty acids. In this proposal we plan to analyze a hypothesis based on these results: active invasive tumor cells need elevated levels of unsaturated fatty acids to be fully functional and as consequence they undergo higher levels of lipid peroxidation. This makes these cells sensitive to drugs exacerbating the toxic effects of these lipids, such as ferroptosis inducers. Therefore, cells that have undergone an EMT are more sensitive to oxidative (OX) stress and need a functional system to counterbalance it. We plan to study how an EMT confers cell sensitivity to ferroptosis and how this is associated to other EMT-associated properties. We will also assess the impact of the changes observed in lipid metabolism such as fatty acid poly-unsaturation or cholesterol decrease on EMT and ferroptosis sensitivity.

We also plan to interconnect this OX stress with endoplasmic reticulum (ER) stress, since these two types of stress are associated: Sigma 1 receptor (S1R), a key modulator of ER stress also controls OX stress. Moreover, S1R activity is blocked by antipsychotics, drugs that prevent tumor



cell invasion in in vitro assays. We plan to investigate how these two types of stress are interrelated in EMT and if ER stress is also generated and is necessary for an extensive activation of mesenchymal genes and other EMT-related properties. We will also assess the effect of antipsychotics on EMT using primary tumor cells and animal models and elucidate their mechanism of action.

We believe that this research will shed light on the mechanisms controlling EMT and tumor metastasis, particularly those related to an integrated stress response, and allow us to determine why cells that have undergone EMT are more sensitive to OX stress-increasing compounds and maybe also to ER stress effectors and will allow antipsychotic drugs to be repurposed for antineoplastic use, either alone or in combination with other existing therapies.

Regarding the mentioned project, the person who joins will carry out the following tasks:

- o Formulation of working hypotheses and design of experiments to demonstrate them.
- o Carrying out experiments in the laboratory in the area of Cell Biology of Cancer.
- o Interpretation and communication of the results.

#### **APPLICATION OF CANDIDATES**

You can submit your application to: **Antonio Garcia de Herreros** ([agarcia@imim.es](mailto:agarcia@imim.es)) o **Josep Baulida** ([jbaulida@imim.es](mailto:jbaulida@imim.es)).

For more information: [https://www.imim.es/programesrecerca/cancer/en\\_ubcm.html](https://www.imim.es/programesrecerca/cancer/en_ubcm.html)