

### Research Fellowship (m/f)

**Project title:** “The role of iron in the remodeling of the vascular niche in acute myeloid leukemia”

supported by a grant from the European Society of Haematology (EHA) in the following conditions:

**Internal Reference:** PR411902

#### **Candidate profile:**

We are looking for candidates with a Master's degree in Biology or related fields with a final score of 14 or higher. The candidate must have previous experience with animal work and flow cytometry and full autonomy in Molecular and Cellular Biology and performance of *in vitro* assays. Preference will be given to candidates with large experience in animal handling. Knowledge of English language, both spoken and written, and good interpersonal qualities in the context of a multidisciplinary research team are also essential attributes.

#### **Background and work plan:**

Acute myeloid leukemia (AML) is an aggressive blood cancer with poor prognosis and limiting treatment strategies. AML cell expansion and the survival of chemoresistant AML cells are thought to depend on interactions with the surrounding bone marrow microenvironment or niche. We have recently shown that the functionally unique endosteal vasculature is selectively lost in AML (Duarte D et al. Cell Stem Cell. 2018). Importantly, the use of the iron-chelator deferoxamine (DFO) in pre-clinical models of AML protects the endosteal endothelium as well as non-malignant hematopoietic stem cells (HSCs). It is likely that the three key compartments involved – vascular niche, HSCs and AML cells – respond differently to iron toxicity and are therefore differently affected by iron. To comprehensively study the toxic effect of iron and iron-containing heme on these compartments, we will use primary patient samples from IPO-Porto, leukemia mouse models and mouse mutants for key iron and oxidation-related genes. The candidate will perform transfection and transduction, *in vitro* assays, flow cytometry, immunofluorescence, confocal microscopy of the bone marrow and gene expression analysis. The project has a strong focus on *in vivo* experimental work. The project includes international collaborations and the opportunity to execute experimental tasks abroad. We aim to uncover new disease mechanisms in AML.

The work will be developed at the *Basic and Clinical Research in Iron Biology* group of i3S under the supervision of Delfim Duarte.

**Application procedure:**

Applications should include CV with 2 references (and respective contacts), the degree's certificate and a motivation letter and should be submitted between 16<sup>st</sup> August 2019 and 15<sup>th</sup> September 2019 on the IBMC webpage:

<http://www.ibmc.up.pt/gestaocandidaturas/index.php?codigo=PR411903>

**Legislation and applicable laws:** Employment at the IBMC is regulated by current laws relating to the Statute of Science Research Fellows of Fundação para a Ciência e Tecnologia, I.P. - 2015, namely Law 40/2004 of August 18, amended and republished by Decree-Law No. 202/2012 of 27 August and the Regulation of Scientific Research Studentships of the IBMC approved by Fundação para a Ciência e Tecnologia ([www.ibmc.up.pt/fellowships.php](http://www.ibmc.up.pt/fellowships.php)).

**Evaluation of applications:**

The candidates will be evaluated initially based on the written documentation: CV (60%) and motivation letter (40%). The top 3 most qualified candidates will be selected for a personal interview and the final score will be based on written documentation (CV + motivation letter, 50%) and interview (50%).

**Jury:**

President: Delfim Duarte (MD, PhD);

Ordinary members: Graça Porto (MD, PhD), Tiago Duarte (PhD)

**Grant conditions:**

The fellowship is due to start in October 1st 2019. The grant will be awarded for 6 months and is renewable for up to 17 months. The monthly amount of the fellowship is € 989.70 paid by bank transfer.