

CALL FOR A RESEARCH FELLOWSHIP
Fellowship Reference IMM/BII/14-2024

Instituto de Medicina Molecular João Lobo Antunes (IMM) opens a call for one research fellowship under the project *“Dependence of IL-7R-mediated signaling on sphingosine kinase activity in acute lymphoblastic leukemia cells as an exploitable therapeutic vulnerability”* (FPJ001584), with the funding support from “Worldwide Cancer Research” Foundation.

Scientific Area(s): Oncobiology, Signaling in Cancer.

Fellowship recipients / Admission requirements: Any National, foreign and stateless candidate(s) that fulfill the necessary conditions to be enrolled in a non-academic degree course (in area related to the work plan) can apply. Are considered “Non-academic degree courses” the ones referred in [paragraph e\) of number 3 of article 4 of Decree-Law nr 74/2006, from 24th March](#), in its current version, as long as they are developed in association and cooperation between a higher education institution and at least one R&D Unit in accordance with the provisions of paragraph e) of Article 3 of FCT Fellowship Regulation.

Applicants must hold the following requirements:

- Master’s Degree in Bioinformatics or related areas, or in Biomedical Engineering or Biological Engineering, with clear evidence of expertise in bioinformatics (mandatory);
- Previous experience in cell culture (desirable);
- Previous experience in programming, e.g. Python, Matlab, Simulink, R+, Linux, GitHub, SQL (mandatory);
- Previous experience in bioinformatic techniques and tools (mandatory);
- High sense of responsibility, organization and method;
- Pro-active personality;
- Ability to work independently but also with team spirit;
- Excellent knowledge of English, spoken and written (mandatory).

Work Plan and Objectives:

Acute lymphoblastic leukemia (ALL), the most common childhood malignancy, is an aggressive cancer arising from B or T lymphoid progenitors. Although current therapies are highly effective, with 5-year survival rates reaching 80-90%, they associate with substantial short and long-term side effects, and a significant number of cases still relapse and have dismal prognosis. Importantly, therapeutic success in adults lags significantly behind, with only 30-40% of the cases surviving long-term. Thus, the current challenge is to develop novel, more efficient therapeutic strategies that specifically target the leukemic cells and minimize the detrimental side effects associated with conventional therapies. A majority of ALL cases express the IL-7 receptor (IL-7R) and ALL cells benefit from IL-7/IL-7R pro-survival and proliferative effects. Our preliminary data strongly indicate that there is a therapeutic window arising from the fact that IL-7R-mediated signaling depends on sphingosine kinase activity in leukemia cells but not in healthy lymphoid precursors. In this project we propose to validate this possibility, understand the molecular reasons for the differential dependence of IL-7R-mediated signaling on SK activity between leukemia and healthy lymphoid cells, and exploit them for therapeutic purposes. The selected candidate will be a highly organized, motivated and pro-active person that will participate in tasks that include:

- Single cell RNAseq analysis of B and T cell precursors collected from the BM and thymus, respectively, of 12-week old animals will be performed to evaluate transcriptomic alterations elicited by deletion of SKs in lymphoid cells in CD2-iCre.SK1fl/fl SK2-/- vs. SK1fl/fl SK2-/- control animals. This will be performed to evaluate transcriptomic alterations elicited by deletion of SKs in lymphoid cells;

- Single cell RNAseq analysis of CD2-iCre. IL7Rmutwt/fl.SK1fl/fl SK2-/- vs. CD2-iCre.IL7Rmutwt/fl.SK1wt/fl SK2wt/wt animals at 12 weeks, when most mice do not yet develop leukemia but are at a pre-leukemic stage with evidence of increased self-renewal ability and partial developmental block, and also upon leukemia-related death (at which time full transformation has evidently occurred);
- Bulk RNAseq analysis of a) an IL-7-responsive T-ALL cell line (HPB-ALL) that has been deleted for SK1, SK2 or SK1 and SK2 using CrispR-Cas9 vs respective negative control, b) human IL7R+ T-ALL cells vs human thymocytes, and c) mouse heterozygous IL7R mutant B-ALL cells (which retain a wild type allele and thus are still responsive to IL-7) vs healthy mouse B-cell precursors, in response to IL-7 in the presence or absence of SK1 (PF-543), SK2 (compound 55) or pan-SK (compound 49 and SKi) inhibitors (or respective SK KO for HPB-ALL cells);
- Bulk RNAseq and whole exome sequencing of leukemias developed in Vav-iCre.IL7Rmutwt/fl, CD2-iCre.IL7Rmutwt/fl, Mb1-Cre.IL7Rmutwt/fl, CD19-Cre.IL7Rmutwt/fl, pLck-Cre.IL7Rmutwt/fl and CD4-Cre.IL7Rmutwt/fl mice.

Legislation and Applicable Regulation: Estatuto do Bolseiro de Investigação (Lei n.º 40/2004, de 18 de Agosto, republished in attachment to Decreto-Lei n.º 202/2012, de 27 de Agosto, changed by **Decreto-Lei n.º 123/2019, 28 de Agosto**), current Regulation of Fellowships of IMM and IMM Career By-Law and Assessment regulations.

Predicted start date, duration and renewal conditions: The fellowship contract is predicted to start in April 2024, for a period of 12 months on an exclusive basis, eventually renewable until the maximum stipulated in applicable regulations, not exceeding the eligibility period of the project.

Work place and Scientific orientation: The research activities will be developed at Signaling in Cancer Lab, at IMM, under the supervision of the professor João Barata.

Non-discrimination and equal access policy: IMM undertakes to ensure compliance with the principles of non-discrimination and equality and to that extent, provides that no candidate can be privileged, benefited, harmed or deprived of any right or exempted from any duty due in particular ancestry, age, gender, sexual orientation, marital status, family status, economic status, education, social origin or condition, genetic heritage, reduced working capacity, disability, chronic disease, nationality, ethnic origin or race, place of origin, language, religion, political or ideological convictions and trade union membership.

International environment and experience: Diversity is a fundamental aspect of the essence of IMM, where researchers and non-researchers of different nationalities, backgrounds and areas of study work together, promoting the exchange of experiences and interactions, contributing to the personal and professional development of each person and to the existence of an international, inclusive and stimulating environment.

Research Fellows Support Centre: The Research Fellows Support Centre works on Tuesdays and Thursdays from 08:30AM to 6:00PM at Human Resources Office.

Fellowship financial conditions: The fellow will benefit from a monthly stipend in the amount of 1259.64€. The amount will be paid by wire transfer at the end of each month. The fellow will also benefit from a personal accident insurance to execute the proposed research activities as well as the right to Social Security through Voluntary Social Insurance regimen, if wanted, under the terms of Código dos Regimes Contributivos do Sistema Previdencial de Segurança Social, and the contributions costs will be supported by the research project.

Application documents: - Motivation Letter; - Detailed CV; - MSc certificate; - Recommendation letter(s); - Candidate's declaration of honor indicating previous fellowships, if any, its typology and duration. ***The non-compliance with these requirements determines the immediate rejection of the application.***

In case the applicant does not have yet the required degree certificate, a declaration of honor stating the conclusion of the necessary qualifications for the purposes of this process will be accepted and must be sent by the end date of the call.

Jury evaluation and selection: Applications will be evaluated by João Taborda Barata (FMUL/ IMM), Rita Cascão (IMM) and Rita Fragoso (IMM).

Selection methods: Curriculum Analysis (50%), Motivation Letter (40%) and Reference letter(s) (10%). The Curriculum will be analyzed qualitatively, and in what concerns to its content and relevance for the tasks to be performed, with special emphasis on research experience and relevant knowledge in the area of the proposed work plan as described in the candidate profile (50%). The letter of motivation will be evaluated in what concerns the motivation and adequacy for the activities to be performed (25%), and command of the English language (15%). The recommendation letter(s) will be evaluated with regard to the work previously carried out by the candidate, reflecting autonomy, proactivity, responsibility, organization and method as well as the ability to work in a team (10%).

Deadlines and application process: The call will be open **from March 6th until March 19th 2024.**

Applications should be submitted through IMM website, by clicking in the "Apply" button below the position job ad. ***The non-compliance with these requirements determines the immediate rejection of the application.***

Notification of results: The evaluation results will be announced within 90 days after the termination of the applications submission deadline, by writing and publishing a jury meeting minute at IMM website at <https://imm.medicina.ulisboa.pt/jobs/#results> with all process of recruitment, evaluation and selection including a list of all excluded and admitted candidates and for these last ones, their classification. All admitted candidates will be notified by email.

Preliminary Hearing and Final Decision Deadline: After notification, all candidates have 10 working days to respond. Panel's final decisions are pronounced within a period of 90 days, from application deadline.

Fellowship contracting: The Fellowship is granted through the signature of a [contract](#) between IMM and the selected fellow and after the fellow send the following mandatory documents: copy of identification document (in case of non-European citizens is mandatory the work visa / valid resident permit), document proving the required academic degree and the document proving the enrollment in a non-academic degree course.

For each Fellowship period an [Activity Report](#) must be prepared by the fellow as well as the [Report](#) by the supervisor.

Lisbon, March 5th 2024