

ANNOUNCEMENT FOR THE OPENING OF AN INTERNATIONAL SELECTION TENDER PROCEDURE FOR DOCTORATE HIRING OF DECREE-LAW NO. 57/2016 OF 29 AUGUST, amended by 57/2017 Law of 19 july.

Internal Reference: PR401901

1. The meeting of the Board of Directors of IBMC deliberated the opening of an international selection tender for 1 vacancy of doctorate to perform duties of scientific research in the scientific area(s) of Life and Health Sciences- antimicrobial therapies, under a work contract with non-fixed term under the Portuguese labor Law in order to perform duties, as researcher within the project with the reference PTDC/BTM-SAL/29786/2017 and the title “Two4Three-A small couple against the big three” at IBMC, financed by FEDER - Fundo Europeu de Desenvolvimento Regional funds through the COMPETE 2020 - Operacional Programme for Competitiveness and Internationalisation (POCI), Portugal 2020, and by Portuguese funds through FCT - Fundação para a Ciência e a Tecnologia/Ministério da Ciência, Tecnologia e Ensino Superior.

2. Project summary: “A small couple against the big-three” (Two4Three) is an innovative and ambitious project where we propose to fight Malaria, Tuberculosis (TB), and HIV-1/AIDS (HIV) using Ionic Liquids (IL).

One of the major current societal challenges is the increasing resistance of pathogens against available drugs, a matter of great concern for the “Big Three Diseases” (BTD): malaria, AIDS, and TB. These diseases often emerge as co-infections, especially in Africa.

We intend to address this problem from a completely new perspective: to combine two known drugs to form an IL active against HIV/TB, TB/malaria or malaria/HIV co-infections. Such IL will act as new formulation, potentially exhibiting dual antimicrobial action, while possessing physico-chemical properties favoring oral bioavailability, more potent activity, and absence of resistance induction. In fact, pairing ionizable drugs with convenient counter-ions offers a means to modulate pharmacokinetics, especially at the absorption and membrane permeability levels, and also pharmacodynamics. This may help to circumvent some drug-related challenges, as poor oral bioavailability, toxicity, or even polymorphism issues. In this connection, our recent work highlights the promising properties of drug-based IL, as we developed ampicillin-derived IL active against resistant bacteria, and primaquine-based IL active against the three stages of malarial infection in the human host.

With this new project, we wish to demonstrate that development of drug-based IL must be pushed forward, both because it will favor the recycling of many drugs currently put on hold due to resistance and/or bioavailability issues, and because novel ionic structures can be envisaged where a cationic drug (e.g., an antimalarial) can be paired with an anionic one (e.g., an antiretroviral) to produce organic salts as low cost dual-function drugs. Our working hypothesis, if proven correct, will open brand new avenues towards

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cheap and effective dual-action medicines against the BTB. In other words, this is a low-cost innovative approach that may yield a major advance in the control of the most concerning infections of today.

Tasks in which the applicant will be involved: Determination of anti-mycobacterial activity

The objectives of this task will be to determine and compare the antimicrobial activity of different ILs against *Mycobacterium tuberculosis*. All the experiments will be performed inside an animal biological safety level 3 (ABSL3) lab, properly equipped to fulfil the requirements of this task. Firstly, the antimycobacterial activity will be evaluated against *M. tuberculosis* growing axenically and inside murine macrophages. For the measurement of the activity against axenic cultures, increasing concentrations of the compounds will be added to the mycobacteria growing in an appropriate broth. The viability of the mycobacteria will be evaluated by measuring the optical density of the cultures, and by the addition of resazurin and the fluorimetric determination of its conversion to resorufin. These results will be confirmed by the quantification of Colony Forming Units (CFU). For the determination of the effect of the ILs on the viability of mycobacteria growing inside macrophages, these cells will be differentiated from mouse bone marrow and infected in vitro. The different ILs will be added to the cultures, and 3 days later the bacterial viability for each condition will be determined by CFU.

These results will enable us to identify the most active and promising compounds. These will be further evaluated in an in vivo mouse model of *M. tuberculosis* infection. This will be made by the aerosol route. One month after infection, the compounds will be administered to the animals, and one to two months after the beginning of treatment, animals will be euthanized and the lung will be harvested for bacterial quantification by CFU.

3. Applicable Legislation

- Decree-Law no. 57/2016 of 29 August, amended by Law 57/2017 of 19 July, which approved the doctorate hiring regime destined to stimulate scientific and technological employment for all knowledge areas (RJEC),
- Portuguese labor law
- Regulatory Decree Nr 11-A / 2017, of 29th December.

4. Pursuant to article 13 of RJEC, the tender selection panel shall be formed by:

President: Salomé Gomes;

Other members: Margarida Saraiva; Ricardo Ferraz

5. Workplace shall be at IBMC, Rua Alfredo Allen, 208, Porto. Group: Iron and Innate Immunity

6. Monthly remuneration: Gross monthly Remuneration is 2.128,34€, in accordance with subsection a), section 1, article 15 from Law nr 57/2017, 19th July, and with the remuneration position at initial level predicted in article 2 of Regulatory Decree nr 11-A/2017, of 29th December, correspondent to level 33 at Tabela Remuneratória Única, approved by Order nr 1553-C/2008, 31st December, with the category Junior Researcher.

7. Any national, foreign and stateless candidate(s) who hold a doctorate degree in Biology and a scientific and professional curriculum whose profile is suited for the activity to be performed can submit their applications. In the event the doctorate degree was awarded by a foreign higher education institution, said degree must comply with the provisions of Decree-Law no. 66/2018 of 16 August, and all formalities established therein must be complied with at the application deadline.

8. The tender admission requirements are:

First author in at least 3 scientific publications in Q1/Q2 journals in relevant fields

Experience in supervision of undergraduate or Master students.

Participation in research projects.

At least 5 years of experience in experimental work in microbiology, including mycobacteria and other pathogens.

Laboratory experience in testing antimicrobial agents.

At least one year of experience in biosafety level 3 experimental work.

At least 5 years of experience in mouse models of infection and accreditation by DGAV to work with experimental animals.

Fluent in spoken and written English.

9. Pursuant to article 5 of RJEC, selection is to be made based on candidate scientific and curricular career evaluation.

10. Scientific and curricular career evaluation focuses on relevance, quality and up-to-dateness:

a) of scientific, technological, cultural or artistic production in the last five years, deemed most relevant by the candidate;

b) of research activities, applied or based on practical work, developed in the last five years, deemed most impactful by the candidate;

c) of knowledge extension and dissemination activities developed in the last five years, namely under the scope of the promotion of culture and scientific practices, deemed most relevant by the candidate.

11. The five-year period mentioned above can be extended by the panel, if requested by the candidate, whenever the suspension of scientific activities is reasoned by socially protected grounds like paternity leave, long-term serious illness, and other legal situations of unavailability to work.

12. Evaluation criteria are the following:

a) Detailed CV:

- List of scientific publications: relevance for the project, first authorship and journal impact factor and ranking will be valued (30%)
- Experience in supervision (15%)
- Relevant research experience in the project area. The previous participation in interdisciplinary projects, particularly those bridging the areas of chemistry, microbiology and immunology, will be valued (35%)

b) Letter of motivation:

- Interest and motivation for the research area of the project (15%)
- Proficiency in English and written communication (5%)

13. Candidate final classification system shall be given based on a scale 0-100.

14. The panel shall deliberate by means of roll-call vote justified under adopted and disclosed selection criteria, with no abstentions allowed.

15. Minutes of panel meetings shall be executed and shall include a summary of all occurrences of said meeting, as well as of all votes casted by the members and respective reasoning, and shall be provided to candidates whenever required.

16. After selection criteria application, the panel shall prepare a sorted list of approved candidates and respective classification.

17. Panel's final decision shall be validated by the leader of the institution, who is also in charge of deciding about the hiring.

18. Application formalization:

18.1 Applications shall include all supported documents encompassed by section 7 and 8 for tender admission, namely:

- a) Certificate or diploma copy;
- b) Curriculum vitae, detailed and structured pursuant to sections 10 and 12;
- c) Other documentation relevant for the evaluation of qualifications in a related scientific area;
- d) motivation letter (in English – mandatory)

18.2 Candidates shall submit their application filling in the required information and supporting documentation, in a digital form, in PDF format, from the 28th October 2019 to 11th November 2019 link:

<http://www.ibmc.up.pt/gestaocandidaturas/index.php?codigo=PR401901>

19. All candidates who formalize their applications in an improper way or fail to prove the requirements imposed by this tender are excluded from admission. In case of doubt, the panel is entitled to request any candidate to present further documentation supporting their statements.

20. False statements provided by the candidates shall be punished by law.

21. Both admitted and excluded candidate list and final classification list shall be published in the website of the Institute and the candidates are notified by email.

After publication, all candidates have 10 working days to respond. Panel's final decisions are pronounced within a period of 90 days, from the application deadline, published at IBMC website.

The expected starting date is January 1st, 2020.

22. This tender is exclusively destined to fill this specify vacancy and can be terminated at any time until approval of final candidate list, expiring with the respective occupation of said vacancy.

23. Non-discrimination and equal access policy: IBMC actively promotes a non-discrimination and equal access policy, wherefore no candidate can be privileged, benefited, impaired or deprived of any rights whatsoever, or be exempt of any duties based on their ancestry, age, sex, sexual preference, marital status, family and economic conditions, instruction, origin or social conditions, genetic heritage, reduced work capacity, disability, chronic illness, nationality, ethnic origin or race, origin territory, language, religion, political or ideological convictions and union membership.

24. The panel has approved this announcement in meeting held on 17/10/2019.

25. Pursuant to Decree-Law no. 29/2001 of 3 February, disabled candidates shall be preferred in a situation of equal classification, and said preference supersedes any legal preferences. Candidates must declare, on their honour, their respective disability degree, type of disability and communication/expression means to be used during selection period on their application form, under the regulations above.