Research Fellowship BIM (M/F)

Title of the project: FOLSMART - Folate-Target Nanodevies To Activated Macrophages For Rheumatoid Arthritis"

Internal Reference: PR611801

We are recruiting a highly motivated pre-doctoral student to join the Gene Regulation research group at the IBMC/i3S. The work will involve, among other tasks, the *in vitro* differentiation and activation of macrophages to investigate the gene regulatory mechanisms modelling the effect of a drug in order to predict treatment outcome in rheumatoid arthritis patients, and to assess *in vitro* the genotoxicity and toxicology of novel folate-based nanodevices.

Requirements: The candidate must possess an M.Sc. degree in Biomedical Sciences, Biological Engineering, or related areas. We are looking for a highly motivated candidate, with a good track record and excellent practical knowledge on Molecular and Cellular Biology methodologies, and preferentially with experience in RNA biology and cell culture. The applicant must be willing to work as part of an interdisciplinary team.

Work plan: The successful applicant will be working within the H2020-funded FOLSMART project that brings together a multidisciplinary team of researchers from different EU Member States. The overall aim of FOLSMART is to bring to phase I clinical trials novel folate-based nanodevices for the treatment of rheumatoid arthritis (please see Abstract).

Legislation and Salary: The fellowship is regulated by current laws relating to the Statute of Science Research Fellows, namely Law 40/2004 of August 18, and the Regulation of Scientific Research Studentships of the IBMC (www.ibmc.up.pt/fellowships.php) approved by FCT. The monthly allowance is 980 € (net and tax free, http://alfa.fct.mctes.pt/apoios/bolsas/valores).

Location: The work will be developed at the Gene Regulation laboratory of the IBMC, i3S, under the supervision of Alexandra Moreira.

Duration: 1 year, non-renewable, to start on January 1st, 2019.

Selection method: The candidates will be listed according to their CV, experience in RNA methodologies, motivation letter and the requirements of the call. If necessary, the pre-selected top candidates will be interviewed (interview 75% and CV 25%).

Jury:
President: Alexandra Moreira (DPhil);
Members: Alexandre do Carmo (DPhil) and José Bessa (PhD).
Substitute: Isabel Pereira-Castro (PhD).

Application deadline and submission forms: The call will be open from 1-15 October 2018. Proposals must include CV, motivation letter and indication of two referees. Applications must be done by online submission:

http://www.ibmc.up.pt/gestaocandidaturas/index.php?codigo=PR611801

Form of notification of results: The final results of the evaluation will be publicized in the IBMC Web site, through a list sorted by final score, and the selected applicant will be notified by email.

Abstract
FOLSMART will bring to phase I clinical trials novel folate-based nanodevices (FBN) for the treatment of rheumatoid arthritis (RA). These nanodevices for folic acid (FA)-mediated targeting of activated macrophages showed improved clinical scores in a mouse model of RA when compared to methotrexate (MTX), a first-line drug therapy for the treatment of RA. In this way, FBN will be benchmarked against this drug. MTX has significant associated toxicity and second line biological therapies poses a great economic burden to hospital/public health systems. In parallel, nanodevices encapsulating Sulfasalazine (SSZ), will be tested. SSZ is a second line indication for the treatment of RA, unresponsive to MTX or MTX–intolerant patients. Furthermore, FOLSMART propose the optimization of mechanisms for the release of the drugs, through pH and temperature sensitive nanodevices. An exploitation and business plans will be elaborated. In parallel, initial economic evaluation of all proposed treatments will be performed to validate these claims.
Specific technological objectives of FOLSMART will be:
Good Manufacturing Practice (GMP) production of the FBN based therapies which have been positively bench-marked in the previous FP7 European project NANOFOL in comparison with the use of MTX in a RA mouse model:
-Liposomal MTX and SSZ with FA-“neck domain” peptide as targeting agent
-Nanoparticles from HSA-FA/MTX conjugates and SSZ
-Optimization of mechanisms of drug release and application to other fields
Pre-clinical development on RA models
-Toxicology and pharmacokinetics, to determine tolerability and efficacy benefit in two animal models rat and dog, under Good Laboratory Practice (GLP) standards
-Genotoxicity and Carcinogenicity
Phase I clinical trials of the best therapies bench marketed against MTX
-Nanodevices with MTX and SSZ will offer improved tolerance and greater efficacy meaning that patients who do not do well on MTX will have cost-effective alternatives