BOLSA DE INVESTIGAÇÃO (m/f)

Encontra-se aberto concurso para a atribuição de uma Bolsa de Investigação (BIL) no âmbito do projecto **"**The crosstalk between lipid antigen presentation and the pathogenic mechanisms of Lysosomal Storage Diseases**"** (PTDC/SAU-ORG/110112/2009), financiado por fundos nacionais através da FCT/MCTES (PIDDAC) e co-financiado pelo Fundo Europeu de Desenvolvimento Regional (FEDER) através do COMPETE – Programa Operacional Factores de Competitividade (POFC), nas seguintes condições

Área Científica: Ciências da Saúde - Órgãos e Sistemas: Mecanismos das Doenças

Referência Interna: PR984003

Requisitos de admissão: Os/as candidatos/as devem possuir Licenciatura em Biologia, Bioquímica ou Ciências Biomédicas, tendo obtido classificação final mínima de 14 valores.
É condição preferencial a experiência de investigação em Imunologia e Doenças Lisossomais de Sobrecarga bem como o domínio das técnicas de cultura de células e citometria de fluxo.

Plano de trabalhos:
Lysosomal storage diseases (LSDs) are a group of more than 50 inherited metabolic diseases in which the lysosome function is affected leading to the accumulation of undigested macromolecules. LSDs are classified, according to the biochemical nature of the stored material, into: lipidoses (mainly sphingolipidosis), mucopolysaccharidosis, glicogenoses, glycoproteinoses, neuronal ceroidlipofuscinoses and mucolipidoses. In Portugal, the prevalence of LSDs as a group is 1 in 4000 living births. Clinically LSDs are complex with different tissues and systems being involved. Common features of the LSDs include recurrent infections, organomegaly, and bone, ocular, cardiac and neurological alterations. These diseases are characterized by their progressive course, often resulting in severe disease and early death. In all LSDs, the central pathophysiological question is how the storage material affects the metabolism of a cell and subsequently leads to organ pathology and clinical symptoms. The aim of this proposal is to contribute for the understanding of the LSDs pathologic mechanisms. The strategy used in order to achieve this aim is based in the following background data: i) several LSDs mouse models present reduced number of the lipid specific invariant NKT (iNKT) cells due to deficient lipid antigen presentation by LSDs antigen presenting cells; ii) iNKT cells are immunoregulatory lymphocytes with a role in several pathologic conditions like atherosclerosis, allergy and hepatic, renal and intestinal disorders; iii) the mice model is not adequate to investigate the repertoire of lipid-specific T cells that is present in humans [lipid-specific T cells are subdivided into different sub-populations according to the CD1 isoform restriction, in humans, five CD1 isoforms are expressed while mice only express CD1d]. In this project we propose to study the lipid antigen presentation to CD1 restricted human T cells in six LSDs: four sphingolipidoses [Fabry, Tay-Sachs, Gaucher and Niemann-Pick Type C1 (NPC1) diseases] and two mucopolysaccharidoses (MPS II and MPS VI). These LSDs, with the exception of NPC1 disease, are caused by deficiency in specific lysosomal hydrolases leading to the accumulation of the respective undegraded subtract within the lysosomal and late endosomal compartments. NPC1 is a late endosomal/ lysosomal transmembrane protein involved in the cellular transport of glycosphingolipids and cholesterol. In addition to the specific storage, some LSDs have secondary storages. In the LSDs that will be studied in this project all, except Fabry disease, have some degree of GM2 and GM3 ganglioside accumulation. Patient characterization will included genetic, biochemical and clinical parameters. This project will contribute both for the understanding of Fabry, Tay-Sachs, Gaucher, NPC1, MPS II and MPS VI disease pathologic mechanisms and to the knowledge of lipid antigen presentation to CD1 restricted human T cells. More specifically with this project we will: i) clarify if the lipid antigen presentation by the

different CD1 molecules are equally affected or whether only the CD1 that traffic throw the endosomal compartments that are loaded in these diseases are affected; ii) elucidate whether the lipid antigen presentation to human T cells is equally affected by the different composition of the stored material; iii) identify links between the results obtained in in vitro immunological assays and the clinical presentation of the patients, that may explain the pathophysiology of the diseases. In addition it is our expectation that the results of this project will also be helpful in the understanding of the pathopysiology of related LSDs. One final note to point out that, in cancer and infectious diseases, several clinical trials are being done using iNKT cells as targets for immunotherapy. Therefore if the results coming out of this proposal identify this lipid specific T cells as major players in the LSDs pathologic development these results can be useful for disease treatment.
The successful candidate is expected to collaborate in the different laboratorial tasks mentioned above.

Legislação e regulamentação aplicável: Lei Nº. 40/2004, de 18 de Agosto (Estatuto do Bolseiro de Investigação Científica); Regulamento da Formação Avançada e Qualificação de Recursos Humanos 2011 e Regulamento de Bolsas de Investigação Científica do IBMC aprovado pela Fundação para a Ciência e a Tecnologia.

Local de trabalho: O trabalho será desenvolvido na Unidade de Biologia do Lisossoma e do Peroxissoma do Instituto de Biologia Molecular e Celular, sob a orientação científica da Doutora Fátima Macedo.

Duração da(s) bolsa(s): A bolsa terá duração de 3 meses, com início a 15 de Maio 2012.

Valor do subsídio de manutenção mensal: The monthly amount of the fellowship is €745- (http://alfa.fct.mctes.pt/apoios/bolsas/valores).

Métodos de selecção: Os candidatos serão avaliados segundo o seu CV.

Composição do Júri de Selecção:

Presidente: Fátima Macedo (PhD)

Vogais efetivos: Clara Sá Miranda (PhD), Andrea Balreira (PhD)

Vogais suplentes: Lorena Rodrigues (PhD)

Forma de publicitação/notificação dos resultados: Os resultados finais da avaliação serão publicitados, através de lista ordenada por nota final obtida, publicada no site do IBMC, sendo o candidato(a) aprovado(a) notificado através de e-mail.

Prazo de candidatura e forma de apresentação das candidaturas: O concurso encontra-se aberto no período de 09 de abril de 2012 a 20 de abril de 2012.

As candidaturas devem ser formalizadas, obrigatoriamente, através de submissão electrónica da candidatura acompanhada dos seguintes documentos: *Curriculum Vita,* carta de motivação e carta de referencia (opcional) em
http://www.ibmc.up.pt/gestaocandidaturas/index.php?codigo=PR984003