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BOLSA DE PÓS-DOUTORAMENTO - BPD (m/f)

Encontra-se aberto concurso para a atribuição de uma Bolsa de Pós-Doutoramento no âmbito do projecto "Cell communication by *Leishmania* microvesicles" (**PTDC/BIA-MIC/118644/2010**), 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:

Refª Interna: PR300303

Área Científica: Imunoparasitologia

Requisitos de admissão: Doutoramento nas áreas em Bioquímica, Ciências Farmacêuticas, Biologia ou afins. Experiência em Imunologia, Parasitologia e Biologia molecular e Celular. Domínio da tecnologia da cultura de células e da área da proteómica.

Plano de trabalhos:
Since the discovery of exosomes in reticulocytes (Pan and Johnstone 1983), the release of membrane vesicles is accepted as a key factor of eukaryotic and prokaryotic (Ellis and Kuehn 2010) cell biology. The importance of extracellular vesicules in eukaryotic cell differentiation, homeostasis and in the regulation of the immune system with crucial roles in the processes of coagulation, inflammation and tumorigenesis has been extensively shown (van Niel, Porto-Carreiro et al. 2006; Al-Nedawi, Meehan et al. 2009; Cocucci, Racchetti et al. 2009). Although the concept of eukaryotic intercellular communication through the release of small vesicles was proposed a few decades ago (Bastida, Ordinas et al. 1984), it is now an accepted means of intercellular communication (Mathivanan, Ji et al. 2010). Several studies highlight the importance of this type of communication, especially in the context of the immune system (Al-Nedawi, Meehan et al. 2009; Cocucci, Racchetti et al. 2009; Mathivanan, Ji et al. 2010). The use of the secretion pathway to deliver effector molecules by microbial pathogens is almost a trademark in pathogenesis. At the beginning of the 21st century it was evident that to this paradigm a new one should be taken into consideration, the release of MVs by microbial pathogens (Silverman and Reiner 2011). It was then the dawn of a new era in the field of infectious diseases with many possibilities to explore in either pathogen-pathogen interactions or the relationship between the host and the pathogen. Although the capacity of many organisms to release MVs is still a matter of debate, some trypanosomatids were already shown to be able to secrete MVs (Silverman and Reiner 2011). It is then tempting to infer that the MVs released by these lower eukaryotes will have similar functions in inter-pathogen communication, playing a similar significant role in pathogen-host interaction.
Our research project will use the knowhow acquired over the last few years in the group to accomplish concise and specific goals concerning the importance of MVs in parasite-parasite communication and parasite-host interaction. In that sense, the current project will encompass the following objectives: 1) Characterization of *Leishmania infantum* MVs. This will be accomplished by parasite culture in a defined specific media developed by our group that enables the continuous growth of parasites in the absence of serum. The MVs will be recovered by ultracentrifugation, sorted by density gradient and characterized relative to size, protein content, and lipid content. This will allow the sub-characterization in exosomes, shedding MVs or apoptotic bodies. Further characterization will be performed recurring in several GFP (Green Fluorescent Protein) fusions with selected proteins already available in our laboratory. 2) Mechanisms of the fusion process with the

host cell. Murine macrophages and dendritic cells will be used to determine the fate of these vesicles using electron and confocal microscopy. These experiments will be carried out with the insect and mammalian parasite forms, promastigotes and amastigotes respectively 3) MVs as mediators of parasite-parasite communication. We will address two distinct possibilities of communication mediated through protein or RNA transfer. Our general strategy will consist in transferring MVs recovered from one defined parasite population to a second target one. Thus, MVs recovered from transgenic parasites expressing either GFP or Luciferase will be used to access the capacity of the recipient parasite population to transiently present GFP or Luciferase. To further clarify if the communication process is through protein or genetic material transfer we will recover exosomes from parasites grown with metabolic labeling (tritium or methionine-S^{35}), this will clarify if we have *de novo* synthesis of proteins in the recipient parasites. To confirm this theory we will try and induce the transfer of resistance to drugs using exosomes from resistant parasites and a recipient susceptible strain. 4) Importance of MVs in parasite-host cell interaction. An approach similar to the previous task will be used to confirm Parasite-Host interaction. Furthermore we it will be used a *in vitro* eukaryote transcription system to demonstrate that parasite RNA can be transcribed. Further, we will evaluate the *de novo* synthesis of parasite proteins in the cytosol of recipient cells. We will also sequence the parasite RNA inside the vesicles. If siRNA or miRNA are present, we will express them transiently in an eukaryote model to access for possible functions and effects.
The proposed project will be carried out in the Institute for Molecular and Cell Biology and it will provide ground breaking knowledge in the biological and pathogenic processes used by *Leishmania* parasites using a unique conjunction of multidisciplinary research groups taking advantage of the expertise and resources of each of the laboratories involved.

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 2010 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 no Grupo Parasite Disease do Instituto de Biologia Molecular e Celular, sob a orientação científica da Professora AnabelaCordeiro-da-Silva.

Duração da bolsa: A bolsa terá à duração de 6 meses, com início previsto a 1 de junho de 2012, renovável até ao máximo de três anos.

Valor do subsídio de manutenção mensal: O montante da bolsa corresponde a €1495 conforme tabela de valores das bolsas atribuídas directamente pela FCT, I.P. no País (http://alfa.fct.mctes.pt/apoios/bolsas/valores) e será paga mensalmente por transferência bancária (preferencialmente).

Métodos de selecção: Avaliação Curricular onde os candidatos serão seriados de forma quantitativa tendo em conta os seguintes critérios: possuírem Doutoramento nas áreas em Bioquímica, Ciências Farmacêuticas, Biologia ou afins; experiência em: Imunologia, Parasitologia e Biologia Molecular e Celular; domínio da tecnologia da cultura de células e da área da proteómica; Índice de impacto e citações de publicações científicas.
Quando necessário recorre-se numa segunda fase à entrevista dos candidatos em causa.

Composição do Júri de Selecção:
Presidente: Anabela Cordeiro-da-Silva, PhD, PI
Vogais efectivos: Ricardo Silvestre, PhD e Joana Tavares, 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 10 de maio a 23 de maio de 2012. As candidaturas devem ser formalizadas, obrigatoriamente, através de submissão electrónica de carta de motivação, CV detalhado e uma carta de referência em: http://www.ibmc.up.pt/gestaocandidaturas/index.php?codigo=PR300303