

BOLSA DE INVESTIGAÇÃO (M/F)

Referência: PIC/IC/83221/2007

Título do Projecto: “Risk for cardiovascular events in chronic kidney disease patients under haemodialysis. Lipid profile, anemia, vascular access and inflammation.”

Código interno: PR 842207

Está aberto concurso para recrutamento de um(a) bolseiro(a) de Investigação para colaborar no projecto acima referido, co-financiado pela Fundação para Ciência e a Tecnologia. A bolsa, em regime de exclusividade, terá a duração de 12 meses, com início previsto a 1 de Novembro de 2009. O valor mensal da bolsa será de € 745,00, pago por transferência bancária (preferencialmente).

Local de trabalho: Serviço de Bioquímica da Faculdade de Farmácia da Universidade do Porto e Instituto de Biologia Molecular e Celular (IBMC), Porto

Programa de trabalho: ver anexo.

Perfil pretendido: Os/as candidatos/as devem possuir Licenciatura em Ciências Farmacêuticas ou áreas afins, com média final igual ou superior a 15 valores. É condição preferencial possuir experiência na área de Biologia Molecular, Bioquímica Clínica, Hematologia e Imunologia no âmbito das doenças inflamatórias, e estar fortemente motivado para prosseguir estudos de pós-graduação. Os candidatos devem ter conhecimentos de língua inglesa e de estatística. As candidaturas serão avaliadas pelos responsáveis do projecto, podendo haver recurso a uma entrevista.

O prazo para recepção de candidaturas decorre de 22 de Setembro a 6 de Outubro de 2009. As propostas deverão incluir uma carta de motivação, CV, e ser enviadas por correio ou e-mail para:

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A contratação será regida pelo estipulado na legislação em vigor relativamente ao Estatuto de Bolseiro de Investigação Científica, nomeadamente a Lei 40/2004, de 18 Agosto, e o Regulamento de Bolsas de Investigação Científica do IBMC (www.ibmc.up.pt/fellowships.php).

**“Risk for cardiovascular events in chronic kidney disease patients under haemodialysis.
Lipid profile, anemia, vascular access and inflammation.”**

Supervisor: Alice Santos Silva

Project Summary: Chronic renal failure is associated with the development of anaemia and cardiovascular disease risk. Despite the technologic development of haemodialysis procedures and of medical support in the last years, the mortality and morbidity of these patients remain high, about 10 to 20 times higher than that found in general population. Therapy with recombinant human erythropoietin (rhEPO) allows the correction of the anaemia in these patients, though more than 35% of them require high doses of rhEPO or do not respond to the therapy. The underlying mechanism to this resistance is still controversial and poorly clarified, though inflammatory features seem to be enhanced.

Cardiovascular events are referred as the major cause of death, more than 50%, in these patients. Advanced age, a risk profile for cardiovascular diseases (CVD) and diabetes mellitus, common in these patients, per se, do not explain the high number and severity of the observed cardiovascular events. The association and the value of oxidative stress, inflammation and dislipidemia in the evaluation for risk of cardiovascular events are well known. The development of oxidative stress has been described in chronic renal failure patients, however, the mechanism(s) inducing inflammation and its value is controversial, as it may result from inflammatory cell activation due to direct interaction with dialysis membranes, or it may also be induced by the type of vascular access chosen for hemodialysis procedure – arteriovenous fistula or central venous catheter – or, even, by the process underlying resistance to rhEPO therapy. Central venous catheter access has been used more and more in the last years, as a permanent hemodialysis access. Some studies proposed an association of this type of hemodialysis access to thrombotic risk; preliminary studies in our lab also suggested an association with an enhancement in inflammatory process and with disturbances in endothelial function and hemostatic process.

In Portugal few data exists about the causes of mortality and its association with risk factors for cardiovascular events and with the type of changes induced by the type of vascular access used in hemodialysis and with the development of resistente to rhEPO therapy. With this project we intend to evaluate the causes of mortality in Portuguese chronic renal failure patients, under hemodialysis and rhEPO therapies, and to search for a correlation with i) type of vascular access; ii) dislipidemia; iii) inflammatory response; iv) anemia and erythrocyte damage; v) oxidative stress; vi) endothelial dysfunction; vii) resistance to rhEPO therapy. In that perspective and in collaboration with several Hemodialysis Clinics from the north region of Portugal, we intend to perform a retrospective study to evaluate the causes of death and, whenever possible, to establish a relation with an analytical profile, response therapy and type of vascular access used; clinical and laboratorial study in 200 chronic renal failure patients in a follow-up regime (starting time, 12 months, 24 months) in order to evaluate survival curves and the odds ratios for the different studied parameters.

The work plan will include i) clinical study and hemodialysis history; ii) basic analytical study: urea, urea reduction ratio and Kt/v , haemogram, reticulocyte count, bilirubin concentration, serum iron, ferritin, transferrin, vitamin B12, and folic acid; iii) lipid profile: total cholesterol, triglycerides, high density lipoprotein cholesterol, low density lipoprotein cholesterol and lipoprotein(a); iv) inflammatory markers: serum levels of c-reactive protein, interleukin (IL)-6 and soluble receptor of IL-2; v) endothelial dysfunction markers: prothrombin fragment 1+2, tissue factor, von Willebrand factor, tissue plasminogen activator (tPA), plasminogen activator inhibitor type 1 (PAI-1), and D-dimer; vi) thrombotic risk factors: proteins C and S, antitrombin III and plasminogen activities and the genetic risk factors, factor V G1691A, prothrombin G20210A, methylenetetrahydrofolate reductase C677T, PAI-1 4G/5G and tPA -7351 C>T genotypes.

This study aims to know the causes of morbidity and mortality of Portuguese chronic renal failure patients under hemodialysis and rhEPO therapies and establish a relation with different physiopathological changes of renal failure, with cardiovascular risk factors, anemia and/or resistance to rhEPO therapy and with the type of vascular access used in hemodialysis. Finally, we hope that the out coming data could contribute to improve the quality of life and longevity of these patients.