IBMC - Instituto de Biologia Molecular e Celular

Research fellowship (f/m)

Internal Code: Norte2020NEURO34

Project: NORTE-01-0145-FEDER-000008 – Porto Neurosciences and Neurologic Disease Research Initiative at i3S
PortoNeuro Drive

Title: Setting a rational screening program for transthyretin-Abeta binding stabilizing compounds that may lead to potential Alzheimer´s disease modulating drugs

IBMC/i3S is opening **1 (one) Research Fellowship** to join its Research Program in **Modulation of Aβ toxicity in Alzheimer's Disease**

Applicants should hold a **MSc** degree in Biochemistry, Microbiology, Biology, or related fields with a final score ≥ 17. The candidate should have full autonomy in working in Molecular Biology. Preference will be given to candidates with previous experience in protein production and purification and with transgenic mice models for Alzheimers Disease (AD), behavioral animal studies and cell culture, and hold a certificate for the Animal Science course (cat B). Applicants should be fluent in English and good inter-personal relationships in the context of a multidisciplinary research team is essential. The candidate should be available to join the team immediately.

Group: Modulation in Neurodegenerative disorders (MiND)

PI: Isabel Cardoso

Work Plan:

TTR is a neuroprotective protein known to bind Aβ in CSF and plasma, avoiding Aβ accumulation and deposition in the brain, although the underlying mechanism is not yet unraveled. Supporting a protective role for TTR in AD are its decreased levels both in the CSF and in plasma. It has also been reported that plasma TTR from AD patients has a decreased ability to carry T_4, suggesting ttr is destabilized which can accelerate its clearance, thus explaining its lower levels, both in CSF and plasma. Further, such instability can also affect the Aβ sequestration properties of TTR.

It is also known that, *in vitro*, different TTR mutations bind differently to Aβ, correlating inversely with the amyloidogenic potential of TTR, further suggesting that TTR stability is a key factor in TTR/Aβ interaction. Interestingly, TTR genetic stabilization has been shown to be associated with decreased cerebrovascular disease and increased life expectancy. Although TTR mutations were not found in AD patients, protein destabilization can result from other factors, such as metal ions concentration, protein environment and protein quality control systems.

TTR tetrameric stabilization can also be achieved or improved by small chemical compounds that, in most cases, bind in the T_4 binding channel. Importantly, we have shown that some of the TTR stabilizers compounds result as we predicted, in enhanced TTR/Aβ affinity in vitro, resulting in amelioration of AD features in vivo.

This project aims at screening compounds able to promote TTR/Abeta interaction through TTR stabilization and at investigating the mechanism underlying TTR protection in AD.

This project is within the scope of a collaborative work with 4 different research groups in Spain and the selected candidate should be available to travel to one of these laboratories, if necessary.

The work will be developed at Instituto de Investigação e Inovação em Saúde - i3S, Porto, Portugal.

Selection of candidates:

Candidates will be selected according to theirs Cvs and if necessary, through an interview.

The BIM Fellowship will be for 6 months, eventually renewable for a maximum of 18 months and it is expected to start in February 1st 2017.

The fellowship amount is 980 euros, paid by bank transfer, preferentially.
(http://alfa.fct.mctes.pt/apoios/bolsas/valores)

Fellowships are regulated by current laws relating to the Statute of Science Research Fellows, namely Law 40/2004 of August 18, amended and republished by Decree-Law No. 202/2012 of 27 August and the Regulation of Scientific Research Studentships of IBMC approved by Fundação para a Ciência e Tecnologia (http://www.fct.pt/apoios/bolsas/docs/RegulamentoBolsasFCT2015.pdf)

Selection Committee:
Isabel Cardoso, PhD
Rosário Almeida, PhD
Maria João Saraiva, PhD

Applications are open from December 20th of 2016 to January 20th of 2017.

To apply for the Research Fellowship interested candidates must hold a MSc degree and submit the following documents a) Complete CV; and b) Letter of Motivation, *via* the online application system:
http://www.ibmc.up.pt/gestaocandidaturas/index.php?codigo=Norte2020NEURO34

The ranking list of candidates will be published at IBMC website, and the selected candidate will be notified by email.