UNIVERSITAT DE BARCELONA

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POSTDOCTORAL CANDIDATE INTERESTED IN APPLYING FOR A MSCA-IF IN NEUROSCIENCES

Neurodegeneration and Neuroprotection

Are you a postdoctoral researcher thinking about your next career move? The Marie Sklodowska-Curie Individual Fellowships (MSCA-IF) are a great option if you are an experienced researcher looking to give your career a boost by working abroad.

Institut of Neurosciences of the University of Barcelona allows you to work in a first class research environment while benefitting from an attractive salary to cover living, travel and family costs.

Group and project information

Applicants will be integrated into the research group "Neurodegeneration and Neuroprotection"; (P.I.Carme Auladell).

The research of our group is focused in the identification of new therapeutic targets to prevent neuronal degeneration through the study of cellular processes that occurs in epilepsy.
The most common form of chronic focal epilepsy is temporal lobe epilepsy (TLE) that is the most frequent type of refractory epilepsy.
Seizures that occur in epilepsy induce the activation of c-Jun N-terminal kinase (JNKs), also known as stress-activated protein kinase (SAPK). Aberrant activation of JNK has been implicated in the pathogenesis of different neurodegenerative diseases as Alzheimer and Parkinson and also Epilepsy. Accordingly JNKs could be a novel therapeutic target in human refractory epilepsy.
There are three JNK isoforms (JNK1, JNK2 and JNK3) which differentially mediate a plethora of physiological and pathological functions. However, only few data are available about the individual actions of JNKs in brain functions. To analyse the particular implication of the JNK isoforms in the molecular features that occurs in epilepsy we use genetically modified mice, *jnk1*$^{-/-}$*, jnk2*$^{-/-}$ *and jnk3*$^{-/-}$ treated with kainic acid (KA), an analogue of glutamate, that triggers temporal lobe epilepsy in humans.
We have evidenced that the lack of JNK1 or JNK3 has a neuroprotective effect against KA that is not observed in jnk2 null mice; moreover both isoforms preserve the increase of neurogenesis observed after KA. Therefore, JNK1 or JNK3 are a promising target for blocking the brain damage induced by excitability. One promising pharmacological inhibitor of the JNK1 belongs to the group of chalcones, which are found in many natural products (fruits, vegetables, spices, tea …). Our results showed that JNK1 inhibition by Lic-A, previous

to KA administration, has neuroprotective effects and that; it could be a new potential approach for the treatment of epilepsy and neurodegeneration.
Further understanding of the physiological function of JNKs requires the identification the proteins and /or genes which are activated or silenced in different knockouts for JNK, in physiological conditions, after KA treatment and in animals treated with Lic A and KA.

Functions and tasks

One of the pathological features observed following seizures in KA experimental mice model is an increase of neuroprogenitors in the subgranular zone of the hippocampus (SGZ), together with an alteration in migration of new born cells. Accordingly, we are studying the role that different JNKs isoforms (specifically JNK1 and JNK3) may play in the regulation of neural stem cells (NSC) and neural progenitor cells (NPC) in the SGZ.

Describe functions and task of the candidate (optional)

Work Plan
In order to carry out the effect of each JNK isoform in the neurogenesis that occurs in the hippocampus, it will be analysed

1.- The arborisation pattern of new formed cells in WT and Knockout mice (KO) mice in physiological conditions and after KA treatment.

Method: Production of high-titer retrovirus (RV) and intrahippocampal injection (will be done as ***Teixeira CM. et al 2018).*** It will be used RV stock of the genes encoded: CAG-GFP encoding for GFP.
For intrahippocampal injections, 8-week-old mice (Wild type, WT and knockout for JNK, KO) will be anesthetized with a ketamine/xylazine mixture and placed on a water-circulating heating blanket. After positioning in a Kopf stereotaxic frame, a midline scalp incision will be made, the scalp will be reflected by hemostats to expose the skull, and bilateral burr holes will be drilled. RV will be injected (1.5 uL of viral stock solution/site) into the left and right dentate gyrus over 20 min using a 5 uL Hamilton syringe, and the micropipette will be left in place for an additional 2 min. Coordinates for injections (in mm from bregma and mm depth below the skull) will be: caudal 0.2, lateral 0.16, depth 0.22.

2.- The neurogenesis activity in each genotype, both in wild type and in mice treated with KA.

Method: To address this purpose, 8-week-old mice Wild type (WT) and knockout (KO) mice for JNK will be treated with bromodeoxiuridine in order to label the new born cells. Thereafter, subpopulations cells in different timeframes of neurogenesis will be identified by immunostaining techniques in colocalization with BrDU. Thus, specific biomarkers will be

used, such as nestin, a protein that label neural stem cells (NSC) or early precursors that give rise to subsequent neuronal precursor (type I cells); doublecortin (DCX) protein and polysialic acid-neural cell adhesion molecule (PSA-NCAM) to detect neuroblasts, including transit-amplifying progenitor cells (PNC) and proliferative cells produced by symmetrically and asymmetrically dividing (type 2a and 2b cells); calretinin (CR), a calcium binding protein (CBP), as a marker that identify neuroblasts at late stage of precursor cell development (type 3 cells).

Requirements for candidates:

Skills/Qualifications:

- PhD or equivalent (Recognised Researcher R2)
- List other required skills:
- Stereotaxic Techniques
- Establishment of retroviral and lentiviral producer cells
- Immunohistochemical techniques
  Primary cell cultures

Languages:
English: Excellent

Specific Requirements:

- Candidates must fulfilled eligibility MSCA criteria described in the Guide for Applicants

Working conditions:

- Full time temporary contract
- Gross salary of about € 50,000
- Duration: ranging from 12 to 36 months depending on the typology of the fellow
- Starting date: flexible from beginning of May 2020

Support for candidates

The Institute of Neurosciences and the International Research Projects Office at the University of Barcelona could offer you:

- A travel grant to work on your proposal with your future supervisor
- One day course on “How to work a successful MSCA IF”
- Personalized support on the application
- Support on other national calls such as Beatriu de Pinós and Junior Leader
- Mentoring

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How to apply

Please submit your CV to: Carme Auladell Costa (cauladell@ub.edu); Reference: MSCA IF Candidate

Deadline: 24/06/2019