

This template should be used by Professor/Doctor interested in hosting post-doctoral fellows within the Marie Skłodowska-Curie fellowship programme.

1. Short Description of the Project idea

Cardiovascular safety liabilities of novel anticancer drugs and multidrug resistance reverting agents

Cardiovascular safety liabilities is the main cause of drug attrition during preclinical/clinical development, adverse drug reactions as well as post-approval withdrawal (Lavery et al, Br J Pharmacol 2011). These liabilities, which pertain to both cardiovascular- and non-cardiovascular-targeted drugs, can be discovered during early development (in the lead optimization or candidate selection phases) by addressing cardiovascular safety endpoints prior to the selection of a drug candidate.

Tasks

-acute and long-term cardiovascular toxicity assessment

Activities:

-evaluation of viability, mitochondrial function, apoptosis, autophagy, and redox state in endothelial cells, cardiac and vascular myocytes
-evaluation of the effects on Ca²⁺ channels (Cav1.2, Cav3.1, Cav3.2), Na⁺ channels (Nav1.5), K⁺ channels (KCa1.1, Kv11.1 - the target of virtually all QT interval-prolonging torsadogenic drugs) in cardiac and vascular myocytes, and hERG-HEK293 recombinant cell line
-evaluation of vascular responsiveness to various agents in rat aorta rings
-evaluation of cardiac function and ECG recording in Langendorff-perfused rat heart. Assessment of cardiac damage in homogenized hearts and concentrated coronary effluent (assessment of creatine kinase and troponin T, NT-proBNP)

1. DEPARTMENT/LABORATORY (Describe briefly the department/laboratory, where the researcher will be employed, including the research team expertise)

The Laboratory of cardiovascular pharmacology has a longstanding expertise in the field of cardiovascular pharmacology/toxicology (ion currents recording, vascular and heart contractility measurements, ECG recording) of natural and synthetic compounds.

Methodological expertise is provided in the following areas:

-isolation of cells from rat tissues, such as aorta, tail main artery, heart, etc.
-Cell and tissue cultures (A7r5; rat aorta cells; EA.hy926; human umbilical vein cells; hERG-HEK293 recombinant cells; rat aorta rings)
-isolated organs/tissue (rat aorta rings, rat atria, Langendorff perfused rat heart)

Associated techniques:

-isolated tissue/organ techniques, patch-clamp analysis of ionic currents (Ca²⁺ and K⁺ channels) in single cell; flow cytometry, western blot; cell survival and apoptosis, cell morphology and imaging, cell signaling

Available equipment:

2 patch-clamp set-ups, 1 Langendorff isolated perfused heart system, 10 multi-chamber tissue bath system, tissue and cell culture facility (sterile hoods, incubators, liquid N2 cell bank, centrifuges, UV/Vis-spectrophotometer, microplate-reader), Cytofluorimeter BD, Fluorescence microscope, Optical Microscopes (IX50 Olympus; DM2500 M Leica Microsystems)

1. Position, scientific requirements (es. n of publications), topic, discipline*:

Post-doc Position,

N of publications: >5

Topic: cardiovascular pharmacology/toxicology

*Please tick: (according to scientific subject areas, defined by MSCA)

Life Sciences X
Natural Sciences
Engineering Sciences
Chemistry

1. DESCRIPTION OF THE SUPERVISOR (max. 200 words)/Contact person: (name and e-mail address)/

Simona Saponara, PhD; Assistant Professor in Pharmacology

simona.saponara@unisi.it

BIBLIOMETRY:

39 full papers on indexed international journals subjected to peer-review (first author: 9, last author: 8);

2 book chapters,

10 proceedings of international meetings;

43 national and international meetings (1 talk as invited speaker at an international congress);

H index: 15; Total citations: 553

RESEARCH TOPICS

Polyphenols as modulators of ionic currents (Ca²⁺ and K⁺) in vascular smooth muscle cells

Cardiac as well as vascular effects of novel multidrug resistance reverting agents

TEACHING ACTIVITY:

Pharmacology, Over the counter drugs and Pharmacovigilance, Toxicology (Degree in Pharmacy; Chemistry and Pharmaceutical Technologies; Cardio-Circulatory Physiopathology and Cardiovascular Perfusion Methods)

1. Previous Related Projects / Research Experience

2012: FUTURO IN RICERCA 2012 (RBF12SQ1)

Agency: Italian Ministry of Education, University and Research

Principal investigator: Simona Saponara

Title: "Optimization of oncology therapy: novel drugs affecting multi drug resistance"

Funding: 989.437,00 €

Duration: 36 months

1. SPECIFIC REQUIREMENTS/PREFERENCES (Describe the specific requirements/preferences for the MSC fellow if necessary for the development/implementation of the project eg. required language, degree field, research experience, etc.)

Required language: English

Degree field: Pharmacy, medicine, biotechnology, medical biology, biophysics

Research experience: four years of full-time postgraduate research experience in cardiovascular pharmacology/toxicology

*Please consider that the preparation of a Marie Skłodowska-Curie proposal requires some time.

**Please consider that the preparation of a Marie Skłodowska-Curie proposal requires some time. Fellow and supervisor have to agree on a project and training opportunities for the fellow. If you want to extend your expression of interest to the third deadline in 2016, just leave this column open.