Post-doc position on nicotinic acetylcholine receptors & organophosphorus nerve agents

Background

The use of organophosphorus nerve agents (OPNA) against civilian populations has renewed research interest in the development of new antidotes. In the battlefields or terrorist attacks, conventional emergency treatment of OPNA poisoning consists on rapid administration of pyridinium oxime for reactivation of acetylcholinesterase (AChE), diazepam for relaxation and atropine to block muscarinic acetylcholine receptors (mAChR). However, the current treatment does not target nicotinic acetylcholine receptors (nAChR). MULTIDOTE (Development of multi-targets antidotes against organophosphorus nerve agents) is an ANR granted project (ANR-17-ASTR-0012). MULTIDOTE aims at developing original multitarget antidotes against NOP poisoning by reactivating human AChE, and by simultaneously blocking nAChR so as to limit peripheral nicotinic effects (*i.e*. paralysis of respiratory muscles) and counteract the overload of acetylcholine in the Central Nervous System. The multidisciplinary integrated approach (organic chemistry, computational chemistry, molecular docking, enzymology, structural biology, neuropharmacology and animal experimentation) is the major asset of MULTIDOTE. Docking studies and molecular dynamics are being carried out on OPNA/ AChE, OPNA/ nAChRs and OPNA/ mAChRs to synthesize multi-target antidotes. Electrophysiological and binding tests on nAChRs and mAChRs receptors will validate *in-vitro* the specificity and the activity of these antidotes that will be also tested in animal models.

The post-doc scientist will work in the Laboratory of Toxins, Receptors and Ionic Channels that possesses long-standing experience and up-to-date electrophysiology setups, ***i.e.*** manual and automated two-electrodes voltage clamp (HiClamp), patch-clamp and *ex-vivo* and *in-vivo* electrophysiological systems. MULTIDOTE Consortium has recently characterized multitarget compounds harboring an inhibitor of AChE and a partial agonist of α7 nAChR. Potent AChE-oxime reactivators were as well synthesized and tested in animal models. The laboratory of Toxins, Receptors and Ionic Channels is located at CEA-Saclay, Ile de France and the work will be performed in collaboration with Ludovic JEAN and Pierre Yves RENARD (COBRA, Rouen), Florian NACHON (IRBA, Brétigny sur Orge) and Martin WEIK (IBS, CEA-Grenoble).

Candidates profile

A strong background in two-electrodes voltage clamp electrophysiology on *Xenopus laevis* oocytes and/or patch-clamp on transfected cell lines is essential for this position. An expertise in cell culture, molecular biology, animal experimentation and biochemistry will be highly appreciated. The recruited post-doc will work in close collaboration with the multidisciplinary Consortium Team MULTIDOTE.

Applications

Please, send a letter of interest, a CV (containing a detailed list of publications, a description of all relevant experience, and two recent letters of reference or contact information of two referees). Please, send your complete application by email to romulo.araoz@cea.fr. The candidate will have the opportunity to have an attractive 1-year post-doc grant with possibility for extension starting in November 2020 at CEA-Saclay.