

2020 Helmholtz – OCPC – Program for the involvement of postdocs in bilateral collaboration projects

PART A

Title of the project: Molecular Synaptosome of Autistic Spectrum Disorder

Helmholtz Centre and institute: Forschungszentrum Jülich, Institute for Advanced Simulations IAS-5 and Institute of Neuroscience and Medicine INM-9, Computational Biomedicine

Project leaders: *J Douglas Armstrong* [University of Edinburgh (U.K.) and Forschungszentrum Jülich], *Paolo Carloni* (Forschungszentrum Jülich), *Alejandro Giorgetti* [Forschungszentrum Jülich]

Co-project leaders: *Paolo Ruggerone* [University of Cagliari (Italy)], *Francesco Musiani* [University of Bologna (Italy)]

Web-address: http://www.fz-juelich.de/ias/ias-5/EN/Home/home_node.html

Description of the project:

Autistic spectrum disorder (ASD) is a neurodevelopmental disorder with dramatic impact on communication and social behaviour. More serious cases are often co-morbid with childhood epilepsy and intellectual disability. The World Health Organization estimates that at least one in 160 children has some form of ASD. Currently, there is no known cure for ASD, although psychosocial interventions can have a positive impact on the person's well-being and quality of life. ASD is predominantly genetic with some 10-20% of cases linked to specific mutations. However, the identification of the mutations alone is not sufficient to characterize a specific ASD, considering that patients with similar pathogenic variants may be diagnosed on very different levels of the spectrum. On the other hand, if mutations are located at protein interfaces or are able to impair protein-protein interactions (PPIs) through allosteric mechanisms, they may impact not only the function of a single protein but also the biological pathways at the synapses. Indeed, proteins do not function in isolation, rather they interact in complex biological networks. Understanding the impact of ASD-linked mutations on the synaptosome is crucial to develop drug leads which eventually may alleviate the devastating effects associated with the disease. **Here we will use computational biology approaches to uncover aspects related to PPIs involving partners of the synaptosome.**

In order to evaluate the role of these variants we plan to set up an automatic protocol that aims to: *i*) identify genetic variants that are likely to impact via protein-protein interaction and, *ii*) to predict the effect of that variant in the PPI. In this exciting and innovative project, the candidate will identify protein variants associated with neurological and neuropsychiatric

disorders and investigate their effects on the full protein interactome of the human synapses. A variety of computational tools, spanning from network modelling and machine learning to structural bioinformatics and to massively scaled protein-protein docking, will be used to quantify the effect of mutations on the protein-protein complex models recently developed by one of the PIs [Douglas Armstrong (University of Edinburgh, U.K.)].

This multidisciplinary project will involve a scientific consortium, where the expertise of FZJ and Fuzhou University will be complemented by the ones of other four academic institutions, namely University of Bologna, University of Cagliari in Italy, as well as the University of Edinburgh in Scotland.

Description of existing or sought Chinese collaboration partner institute:

Collaboration already exists between the College of Chemistry, Fuzhou University (FZU) and NM-9 at Forschungszentrum Jülich. College of Chemistry in Fuzhou University is specialized in computational chemistry, structural biology, chemical biology, medicinal chemistry, and anticancer drug development. The National & Local Joint Biomedical Engineering Research Center of FZU is engaged mainly in anticancer and antithrombotic drug design and development. Its major achievement is the development of a novel anticancer drug, named Photocynine, which is the first photodynamic drug developed in China and received approval by China Food & Drug Administration (CFDA) for clinical trial (currently in Phase II trial). In particular, Prof. Jinyu Li at the Fuzhou University is a former Ph.D. student of Paolo Carloni and a current collaborator of his group. The existing scientific interaction is confirmed by the several joint publications.

Additionally, we welcome collaboration with any Chinese institution that deals with the same subjects and shares out scientific interests.

Required qualification of the post-doc:

- PhD in chemistry, biology or physics.
- Experience with molecular simulations, structural bioinformatics and/or virtual screening.
- Additional skills in supercomputing and programming are desired.
- Basic knowledge of biochemistry and structural biology.

PART B

Documents to be provided by the post-doc, necessary for an application to OCPC via a postdoc-station in China, which is affiliated to a research institution like a university:

- Detailed description of the interest in joining the project (motivation letter)
- Curriculum vitae, copies of degrees
- List of publications
- 2 letters of recommendation
- Proof of command of English language

PART C

Additional requirements to be fulfilled by the post-doc:

- Max. age of 35 years
- PhD degree not older than 5 years
- Very good command of the English language
- Strong ability to work independently and in a team