

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

### PART A

**Title of the project:** Rational design of ligands targeting alpha-synuclein in Parkinson's Disease

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

**Project leaders:** Giulia Rossetti (Forschungszentrum Juelich), Paolo Carloni (Forschungszentrum Juelich), Luhua Lai (Chemistry Department, University of Peking, China)

**Co-Project Leaders:** Kamyar Hadian (Helmholtz Zentrum München, Germany), Tiago Outeiro (University Medical Center Goettingen, Germany), Claudio Fernandez (Max-Plank Institute, Rosario, Argentina).

**Web-address:** [http://www.fz-juelich.de/ias/ias-5/EN/Home/home\\_node.html](http://www.fz-juelich.de/ias/ias-5/EN/Home/home_node.html)

#### **Description of the project:**

Parkinson's disease (PD) is the second most common fatal neurodegenerative disease, affecting approximately four million people worldwide. Unfortunately, there is currently no cure for this devastating disorder.

The pathological hallmark of PD is the accumulation of proteinaceous deposits, known as Lewy bodies, in the brain. The protein alpha-synuclein (AS), is the major component of these deposits. AS is an intrinsically disordered protein (IDP) and it undergoes a structural transition from the innocuous, monomeric conformational ensemble to neurotoxic oligomers to the aggregates. Unfortunately, the potential of rational drug design has not been yet fully exploited because of the well-known difficulties of studying IDPs/ligand interactions. Here, we will capitalize on molecular-simulation-based approaches developed and used by our team for IDPs to identify ligands inhibiting (proto)fibril formation, with possible beneficial effects against PD. The anti-(proto)fibril formation activity of the ligands will be tested *in vitro* by biophysical assays and the structural basis behind their effects characterized NMR-based experiments. The most promising compounds will finally undergo *in cell* experiments.

This multidisciplinary project will involve a scientific consortium, where the expertise of Forschungszentrum Jülich and the University of Peking will be complemented by the ones in other three Research Institutions, namely the Helmholtz Zentrum München, Germany, the University Medical Center Goettingen, Germany and the Max-Plank Institute, Rosario, Argentina.

**Description of existing or sought Chinese collaboration partner institute:**

Collaboration has been planned for a long time between the INM-9 at Forschungszentrum and Professor Luhua Lai's group at the University of Peking, on the topic of this proposal. Professor Luhua Lai's group works on protein design, structural and systems-based drug design by using combined approaches of modeling and experimental studies. They develop computational methods and use them to study biomolecules and systems of interest. The recent research interests of the group include: (1) Intrinsically disordered proteins and function regulation; (2) Disease network modeling and drug design method development; (3) Metabolic network dynamics and chemical intervention; (4) Functional protein design; (5) Application of artificial intelligence in cheminformatics and drug discovery. Additionally, we welcome collaboration with any Chinese institution that deals with the same subjects and shares our 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.
- Availability to carry out some of the experiments planned in this research.

**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