2017 Helmholtz – OCPC – Programme
for the involvement of postdocs in bilateral collaboration projects

PART A

Title of the project: Design and synthesis of novel activity-based probes

Helmholtz Centre and institute: Helmholtz Zentrum München, German Research Center for Environmental Health (GmbH) (HMGU), Institute of Medicinal Chemistry (IMC)

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Description of the project (max. 1 page)**:**
Animal models resembling chronic diseases are frequently compromised by high inter-animal variability and heterogeneous disease development, resulting in the necessity to employ large groups of animals to reach statistical significance. A major challenge in the development of novel therapeutics for these diseases is therefore to properly assess the efficacy of the applied drug in vivo. To achieve this, methods to characterize the disease state of individual animals at a given point in time in ongoing longitudinal pharmacological studies would be highly useful.
Visualization of the individual activity of particular enzymes can provide invaluable insights into specific disease states and efficacy of treatment. We will set out to design novel activity-based probes with high specificity for the pursued target that will generate spectroscopic signals proportional to the activity of the measured enzyme.
Besides employing near-infrared probes suitable for in vivo monitoring in rodent models, we will also address alternative imaging modalities like optoacoustic imaging. In particular we will aim at developing conceptually new activity based MRI based probes that will allow utilization in larger animal species and possibly even in human, but also will be able to provide optimal spatial resolution. This research effort will be dedicated to target specific proteolytic enzymes, critically involved in disease development in diabetes, inflammation and cancer. Upon successful demonstration of proof-of concept we will design tissue targeting strategies and incorporate the obtained targeting moieties in the probe in order to retain it at the organ of interest. Eventually, we will extend this approach to other targets of interest.
The intended project will be located at the interface of chemistry and biology. The scientists' task will comprise the conception of probe design, chemical synthesis of prototypic probes and characterization of their properties, particularly with respect to selectivity and signal emission. The obtained probes will subsequently be thoroughly optimized for optimal signal intensity, selectivity and other parameters predictive for in-vivo behaviour. The utility of the obtained probes will then be examined in relevant cellular and animal disease models.

Examination of the probe will be performed at IMC, but also in close collaboration with other institutes at HMGU.

Description of existing or sought Chinese collaboration partner institute (max. half page)**:**

We are looking for a highly motivated postdoctoral candidate with profound experience in synthesis of complex organic molecules and a deep interest in chemical biology / imaging related questions, who will join our young team to contribute to the project sketched above. This exciting project will offer the chance to work in a highly interdisciplinary team located in a modern medicinal chemistry environment.

We already have a long standing and very successful collaboration with scientists at the Institute of Materia Medica (IMM) at CAMS and PUMC in Beijing on development of imaging agents. Its mission is to discover innovative drugs for treating or preventing important human diseases. The collaboration partner we are looking for should have a strong history in developing imaging agents for observing effects in diseases like inflammatory or infectious diseases, diabetes or cancer, using state-of-the-art synthetic and medicinal chemistry methods to develop drug candidates from screening hits and have experience in the development of novel activity-based or tissue- targeted probes.

We are looking forward to receiving applications of highly motivated scientists from IMM or other Chinese institutions meeting the above described criteria, who are interested in working on the described research project to establish an intense and long lasting collaboration between the IMC and the selected Chinese institute.

Required qualification of the post-doc:

- PhD in organic chemistry
- Profound experience in modern synthetic methods
- Additional skills in chemical biology, imaging, characterization of dyes
- Basic knowledge in biochemistry techniques (cell culture, biochemical assays, histology) is a plus