Position Profile for Chinese Applicants running for 2019 Helmholtz – OCPC – Program

PART A (Info about the Position)
Helmholtz Centre and institute: HZI – HIPS

Title of the project:

Project leader: Anna K. H. Hirsch

Web-address: www.helmholtz-hzi.de/hirsch

Description of the project (max. half page)**:**
To fight antimicrobial resistance we relied on several established and unprecedented hit-identification strategies such as structure-based design, virtual screening and dynamic combinatorial chemistry[1] on an unexplored anti-infective target to identify novel chemical classes with an unprecedented mode of action.[2] Energy-coupling factor (ECF) transporters are a class of ATP-binding cassette (ABC) transporters that mediate the uptake of essential vitamins in prokaryotes, making them an attractive unexplored target.[3] A structure-based virtual screening campaign[4] aimed at the unique mechanism of transport afforded the first allosteric inhibitors of the ECF transporters for all vitamins. The series of compounds displays *in vitro* activity, excellent ADMET properties antibacterial activity (MIC = 4 μM) against a range of pathogenic Gram positive bacteria (*Staphylococcus aureus*, *Enterococcus faecium*, Streptococcus *pneumoniae* and *Clostridium difficile*)[5] and good oral bioavailability (PK study). Thus, the inhibitors constitute an excellent starting point for the development of novel antibiotics and are currently being investigated in an *in vivo* infection model.[5] The aim of this project is the optimization of the available lead compounds. In parallel, the search for novel hit classes using kinetic target-guided synthesis, dynamic combinatorial chemistry or fragment-based design will be intitiated.

Bibliographic references:
1. M. Mondal, A. K. H. Hirsch, *Chem. Soc. Rev.* **2015**, *44*, 2455–2488.
2. S. Bousis, I. Setyawati, E. Diamanti, D. J. Slotboom, A. K. H. Hirsch, *Adv. Ther.* **2018**, *accepted.*
3. D.J. Slotboom. *Nature Rev. Microbiol*. **2014**, *12*, 79-87.
4. L. J. Y. M. Swier, A. Guskov, D. J. Slotboom, *Nat. Commun.* **2016**, *7*, 11072.
5. E. Diamanti, I. Setyawati, L. Monjas, L. J.Y.M. Swier, S. Bousis, W. K. Stanek, M. Jäger, J.

Haupenthal, J. Herrmann, R. Müller, D. J. Slotboom, A. K. H. Hirsch, *J. Am. Chem. Soc. under review.*

Required qualification of the post-doc:

- PhD in chemistry or pharmacy
- Experience with synthetic organic chemistry
- Additional skills in medicinal chemistry, docking/molecular modelling, biochemistry

PART B (Materials and Procedures)

The applicants shall submit the following documents to a Chinese postdoc station affiliated to a research institution or a university, after passing through the internal selection, the qualified application shall be forwarded to OCPC, and then to Helmholtz for evaluation:

- 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 (General Conditions)

Additional requirements on the postdoctoral fellows:

- Chinese citizenship from Mainland China (allows application while staying abroad)
- Max. age of 35 years, PhD degree not more than 5 years by submission of application
- Very good command of English language
- Strong ability to work independently and in a team