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

PART A (Info about the Position)

Helmholtz Centre and institute: Helmholtz Institute for Pharmaceutical Research Saarland (HIPS)

Title of the project: **Deciphering and remoulding the biosynthesis of active and promising compounds from actinobacteria and myxobacteria**

Project leader: Prof. Dr. Rolf Müller,

Web-address: https://www.helmholtz-hzi.de/en/research/research_topics/anti_infectives/microbial_natural_products/our_research/

Description of the project (max. half page)**:**

Natural products contribute greatly to human health via providing promising compounds as drugs/leads combating various diseases. We have isolated series of active compounds from actinobacteria and myxobacteria, which displayed potent anti-tumor and antibiotic activities. We are willing to spend efforts on the mechanisms of biosynthesis and structure modifications due to the potential novel chemistry in biosynthesis andpromising activities. This project includes several topics as follows:

1. Confirmation of the corresponding gene cluster. According to retro-biosynthesis analysis, all candidate clusters will be predicted from the genomeof the producer strain firstly, and then gene deletion will be employed to confirm the corresponding gene cluster. The boundaries and functionalities of the cluster will be confirmed by further gene knockouts.
2. Characterization of the biosynthesis. After the confirmation of gene cluster, a hypothetic biosynthetic pathway will be proposed via bioinformatic analysis. And then genetic manipulations on these genes will be performed to revise the pathway. The biosynthesis pathway of the novel building block is one of the top aims in this project, which needs gene knockout/complementation as well as in vitro enzymatic assays of key enzymes in its pathway.

3. Heterologous expression. Based on the characterized cluster, we will try to express the compounds in heterologous hosts, which will facilitate the engineering of the pathway as well as compounds isolation.
4. Structure diversification. Three distinct ways might be employed to diversify compound structures: (1) To improve the production of small portion of analogs (detected level) in the producer via heterologous expression and synthetic biology; (2) To obtain the intermediates in tailoring gene deleted mutants; (3) To produce new analogues via alter the substrate specificity of enzymes responsible for building block incorporation; (4) To introduce various modified unusual units via engineering its sub-pathway or via feeding chemical synthesized substrates into the sub-pathway broken mutant.

In summary, our final goal is to learn new chemistry from nature and to produce novel compounds with better activities based on the acquired knowledge.

Description of the existing or planned collaboration with a Chinese institution (max. half a page)

We have established Shandong University-Helmholtz Joint Institute of Biotechnology and recently achieved funding for one of three Helmholtz International Laboratories in this collaboration.

Required qualification of the post-doc:

- A PhD on natural product or a related field
- Extensive hands-on experience in genetics and biochemistry
- Experience in writing publications, conference papers and research proposals
- Fluency in spoken and written English and excellent oral and written communication skills
- Planning and organisational skills, prioritisation of multiple tasks, meeting strict deadlines
- Demonstrated project and laboratory management skills in multiple tasks
- Capability of creative and critical thinking, independent thought and experimentation, decision making, problem solving with discretion, self-motivation and curiosity