2018 Helmholtz – OCPC – Program
for the involvement of postdocs in bilateral collaboration projects

KIT-06

PART A

Title of the project: Development of a miniaturized solid-phase synthesis platform combined with on-chip high throughput cell screening

Helmholtz Centre and institute: Karlsruhe Institute of Technology (KIT), Institute of Toxicology and Genetics (ITG), Group of Biofunctional Materials

Project leader: Dr. Pavel Levkin

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Description of the project: The traditional pipeline of drug discovery includes individual synthesis and characterisation of drug candidates or acquisition of a drug library, followed by a biological screening, which is separated from synthesis in space and time. This approach suffers from low throughput and associated high costs, which in turn lead to the inefficiency in the field of drug discovery. The ultimate goal to advance drug discovery would therefore be a miniaturized platform that 1) facilitates high-throughput synthesis and 2) after completing synthesis can be directly used in cell screening with high spatial and temporal control.

Recently, we established a miniaturized screening platform (droplet microarray platform, DMA), which proved itself to serve as a convenient and versatile platform for high-throughput screening of cells. DMA comprises a glass slide, on which nanoporous poly(2-hydroxyethyl methacrylate-*co*-ethylene dimethacrylate) layer is covalently grafted. Polymer surface of the DMA is patterned with hydrophilic regions/spots, which are separated from each other by hydrophobic liquid-impermeable barriers. Due to extreme differences in wettability, different liquids (containing either chemicals or live cells) can be compartmentalized within DMA, forming an array of nanoliter-sized droplets, which can be subjected to cell screening.

The goal of this project is to further develop DMA to transform it into a platform for combinatorial solid-phase synthesis. The porous polymer inside the hydrophilic spots will be used as a solid support. In each spot, a unique compound will be synthesized. Each microspot will serve first as a confined microreactor, and then will provide the confined environment to perform cell screening in solution. By utilization of UV-cleavable linker, products of solid-phase synthesis can be released from the porous polymer and diffuse into separate droplets. The light-induced release of the products will be developed to control the release spatially, temporally and quantitatively. The aim of the project is to establish a repertoire of chemical reactions, that can be performed on the synthesis DMA, to form the framework for high-throughput solid-phase synthesis and screening.

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

Required qualification of the post-doc:

- PhD in organic chemistry
- Experience with organic synthesis, NMR, HPLC-MS, UV-Vis, IR,
- Additional skills in solid-phase synthesis are desired

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