Applications are invited for a Postdoc position available 1.1.2018 in the Computational Pharmaceutical Chemistry & Molecular Bioinformatics group (Prof. Dr. Holger Gohlke; http://cpclab.uni-duesseldorf.de) at the Heinrich-Heine-University, Düsseldorf, Germany.

TOPIC: Inhibition of the oncogenic function of RUNX1 / ETO in t(8;21) acute myeloid leukemia: Establishment of a lead structure

Background: Acute myeloid leukemia (AML) is particularly common among middle-aged adults. One of the most frequent causes of an AML is the formation of the chimeric fusion protein RUNX1 / ETO. RUNX1 / ETO-dependent AML have an unfavorable prognosis and show a high (45%) rate of regression after standard chemotherapy, which leads to a 5-year survival rate of only 10 to 20% for over 60 years. Targeted therapies have so far been almost completely lacking.
Essential for the leukemogenic function of RUNX1 / ETO is a tetramerization via the so-called NHR2 domain of ETO. In previous work (see http://cpclab.uni-duesseldorf.de/publications/publications/97.pdf and http://cpclab.uni-duesseldorf.de/publications/publications/143.pdf), we have identified the small molecule **7.44** that inhibits this tetramerization and can serve as the lead structure for the development of novel, specific, structurally related compounds that exhibit an anti-leukemic effect by inhibiting the oncogenic function of RUNX1 / ETO. **7.44** is first-in-class with regard to its operating principle.
In this project, a lead structure based on 7.44 is to be established, which will allow for further lead optimization and (pre-)clinical trials. To do so, I) compounds analogous to **7.44** will be identified by virtual screening or synthesized and (II) biophysically and cell biologically characterized; III) for **7.44** and further analogues, the binding site and the binding mode will be elucidated; IV) a quantitative structure-activity relationship will be derived; and V) *in vitro* and *ex vivo* studies of metabolism and pharmacokinetic (DMPK) properties of **7.44** and analogs will be performed.

Requirements: Ideal candidates will have a record of excellence (PhD plus publications in highly visible journals) and a strong background in chemistry, biochemistry, molecular biology, cell biology, and/or structural biological as well as a high interest in working in an interdisciplinary research field.

Applicants should submit applications (a one-page letter of motivation *why* they are interested in the respective project and *how* they can contribute to the project's success, a current CV, and contact data of three references) by email to gohlke@uni-duesseldorf.de . **Please provide all documents as one PDF file.**

Detailed information about living and studying in Düsseldorf is provided here: http://www.uni-duesseldorf.de/home/leben-in-duesseldorf.html