

## Open PhD Position in GRG2158: Hiring in October 2022

**Name of PI:** Prof. Dr. Thomas Kurz

Email: [thomas.kurz@hhu.de](mailto:thomas.kurz@hhu.de)

**Title of Ph. D. Project:** Development of selective histone deacetylase inhibitors (HDACi) and HDAC-based targeted protein degraders (TPD)

### Abstract:

The targeted treatment of epigenetic dysregulation is a valuable therapeutic option in cancer treatment. Zn-dependent histone deacetylases are clinically validated cancer drug targets. Five Histone deacetylase inhibitors (HDACi) vorinostat, belinostat, panobinostat, romidepsin, and tucodinosat are currently approved for the treatment of hematological malignancies. HDACis induce for example growth arrest, cell differentiation, and apoptosis in cancer cells. Especially the use of HDACi as chemosensitizers that improve the efficiency of currently used cancer drugs has shown great potential in drug development. Most of the approved HDACi are pan-inhibitors that cause in part significant side effects and off-target toxicity. Therefore, the development of less toxic but effective and selective HDACi is one goal of the described research project. Other goals include the development of dual-target HDACi to delay the development of resistance in cancer cells and the development of HDAC targeting protein degraders. Targeted protein degraders (TPD) are chemical tools that use endogenous pathways to degrade intracellular proteins e.g. HDACs. Established examples of TPD are proteolysis targeting chimeras (PROTAC), autophagy targeting chimeras (AUTAC) and molecular glues. First PROTACs are already in clinical development for cancer treatment.

### Requirements:

*The ideal candidate will have a record of excellence and a strong background in pharmaceutical & medicinal chemistry, and/or in biochemistry & organic chemistry (organic synthesis) and as well as a high interest in working in an interdisciplinary research environment.*

### Recommended literature:

1. Terence C. S. Ho, Alex H. Y. Chan, A. Ganesan. Thirty Years of HDAC Inhibitors: 2020 Insight and Hindsight *J. Med. Chem.* **2020**, 63, 12460.
2. Alves Avelar LA, Schrenk C, Sönnichsen M, Hamacher A, Hansen FK, Schliehe-Diecks J, Borkhardt A, Bhatia S, Kassack MU\*, Kurz T\*. Synergistic induction of apoptosis in resistant head and neck carcinoma and leukemia by alkoxyamide-based histone deacetylase inhibitors. *Eur. J. Med. Chem.* **2021**, 211, 113095.
3. Fischer F, Alves Avelar LA, Murray L, Kurz T. Designing HDAC-PROTACs: lessons learned so far. *Future Med. Chem.* **2021**, doi.org/10.4155/fmc-2021-0206.