



The epigenetics of metabolites

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Metabolites mediate essential cellular responses to the environment, ensuring our survival. Changes in metabolic pathways are also key to how tumors evolve and thrive. Metabolites are not just substrates for enzymes, but act as signaling molecules that can directly and indirectly dramatically influence gene activity. Our team has a world-leading record in pioneering the discovery of novel interactions between gene regulatory factors and cellular metabolites or their products and to translate these discoveries toward novel therapies. We discovered that metabolites act as allosteric regulators of chromatin structure in the context of DNA damage and have now identified human transcription factors that act as metabolite receptors. We characterize these novel types of health-relevant gene–metabolism crosstalk.

We seek postdocs for two exciting frontline projects. First, we identified human transcriptional receptors for endogenous metabolites and characterized how they recognize and alter their structure upon metabolite binding. This knowledge enables drug discovery. We will develop small molecule regulators of transcription factor activity (this project is covered by an m⁴ Award of the Bavarian Government). In a second project, we will take this paradigm further to target the activity of other important cancer-relevant transcription factors. Together, we will investigate at the biochemical, cell biological, structural and chemical level how the activity of these transcription factors is directly modulated by small molecules. Our new knowledge and expertise will allow us to address one of the biggest challenges in drug discovery, the targeting of transcription factors via small molecules, for the benefit of patients.

Recent publications:

- Guberovic et al. *Nature Struct Mol. Biol*, 2021. [10.1038/s41594-021-00692-5](https://doi.org/10.1038/s41594-021-00692-5)
- Valera-Alberni et al. *Cell Reports*, 2021. [10.1016/j.celrep.2021.109565](https://doi.org/10.1016/j.celrep.2021.109565)
- Blessing et al. *Molecular Cell*, 2020. [10.1016/j.molcel.2020.10.009](https://doi.org/10.1016/j.molcel.2020.10.009)
- Murawska et al. *Molecular Cell*, 2020. [10.1016/j.molcel.2019.11.016](https://doi.org/10.1016/j.molcel.2019.11.016)
- Singh et al. *Molecular Cell*, 2017. [10.1016/j.molcel.2017.11.019](https://doi.org/10.1016/j.molcel.2017.11.019)
- Kistemaker et al. *Angewandte Chemie*, 2016. [10.1002/anie.201604058](https://doi.org/10.1002/anie.201604058)
- Hondele et al. *Nature*, 2013. www.nature.com/articles/nature12242

Our group is located at the LMU Biomedical Center, a state-of-the-art research and teaching center that targets cellular plasticity in health and disease. Further info at: www.ladurnerlab.de. We are generously funded by grants from the EU, DFG, LMU and Bavarian Government. Excellent in-house core facilities ensure access to specialized equipment and leading expertise. We are integrated within a robust R&D environment for innovative research in gene expression, chromatin dynamics, epigenetics and chemical biology, including through the DFG-funded Collaborative Research Centers SFB1064 (www.sfb1064.med.uni-muenchen.de) and SFB1309 (www.sfb1309.de). Our outstanding campus includes local partnerships with the two Max Planck Institutes for Biochemistry and Neurobiology, the Helmholtz Center Munich, the LMU Faculty of Biology, LMU Faculty of Chemistry and one of Europe's largest biotech hubs, including the IZB and our startup Eisbach Bio (www.eisbach.bio).

Candidates should be motivated, curious, project-, task- and team-oriented, communicate well and enjoy working together on pioneering projects at the forefront of biomolecular recognition. Ideally, you have a background in oncology, gene expression, chromatin or metabolism, and this technical expertise:

- Biochemistry and biophysical analysis of proteins, X-ray crystallography, cryo-EM
- Chemical biology, synthesis, pharmacy, enzymology and drug discovery
- Physiology and genetic models of metabolic disease, model organisms (*Drosophila*)

The successful candidate will collaborate within our team and across our outstanding academic and biotech campus. The salary is based on the public scale TV-L E13. The employment is planned for 3 years and can be extended. Please send any questions and your motivation letter, CV and names of 3 referees (in one PDF) by email to: andreas.ladurner@med.lmu.de.