



Metabolite control of human transcription in obesity

Postdoctoral Fellow in sugar-to-lipid gene regulation and drug discovery

Munich, Germany

Metabolites mediate essential cellular responses to environmental change, which ensures our survival. Yet, we are maladapted to our modern diet, obesity rates have greatly increased and ~20% of Europeans will develop Type 2 Diabetes by 2030. Vital gene programs are responsive to the intake of dietary glucose, fructose and ethanol. They convert excess carbohydrates into fat, which promotes the metabolic syndrome. But how sugars actually promote specific changes in gene transcription is far from clear.

Our team has a world-leading record in the discovery of interactions between gene regulatory factors and cellular metabolites and to translate these discoveries toward novel therapies. We have now identified and validated a druggable metabolite-binding pocket in a vital factor. We will apply our know-how to develop small molecules that will therapeutically switch carbohydrate-driven gene programs.

We seek an enthusiastic and committed postdoc for an exciting frontline project at the interface of biomedical sciences, physiology and drug discovery. The fellow will investigate at the biochemical, cell biological, structural, chemical and small molecule level how the activity of our carbohydrate-regulated factor can be switched by the identified and validated small molecule probes and chemical leads. 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.

Selected publications:

- Blessing *et al.* *Nature Communications*, 2022. DOI: [10.1038/s41467-022-31820-4](https://doi.org/10.1038/s41467-022-31820-4)
- Guberovic *et al.* *Nature Struct Mol. Biol.*, 2021. DOI: [10.1038/s41594-021-00692-5](https://doi.org/10.1038/s41594-021-00692-5)
- Liu *et al.* *Chem Sci.* 2021. DOI: [10.1039/d1sc02340c](https://doi.org/10.1039/d1sc02340c)
- Valera-Alberni *et al.* *Cell Reports*, 2021. DOI: [10.1016/j.celrep.2021.109565](https://doi.org/10.1016/j.celrep.2021.109565)
- Hurtado-Bagès *et al.*, *Mol. Metab.* 2020. DOI: [10.1016/j.molmet.2020.01.014](https://doi.org/10.1016/j.molmet.2020.01.014)
- Kistemaker *et al.* *Angewandte Chemie*, 2016. DOI: [10.1002/anie.201604058](https://doi.org/10.1002/anie.201604058)

We are located at the LMU Biomedical Center, a state-of-the-art research center that targets cellular plasticity in health and disease (www.ladurnerlab.de). We are well-funded with 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 Collaborative Research Centers SFB1064 (www.sfb1064.med.uni-muenchen.de) and SFB1309 (www.sfb1309.de). Our outstanding campus includes partnerships with the 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 biotech cluster (www.izb-online.de/en) 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, metabolism, drug discovery or small-molecule chemistry. Technical and strategic expertise in one or more of these areas are advantageous:

- Biochemistry and biophysical analysis of proteins, X-ray crystallography, cryo-EM
- Chemical biology, pharmacy, enzymology, drug discovery and development
- Physiology and genetic models of metabolic disease, model organisms (*Drosophila*)
- Keen interest in drug discovery and developing a start-up company

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 a period of up to 3 years and can be extended. Opportunities exist to spin-off the project into an entrepreneur-led start-up company pending the achievement of project milestones.

Please send your CV, motivation letter and the names of three referees in a single PDF file by email to: applications.physiolchemistry@bmc.med.lmu.de. We look forward to your expression of interest.