

PhD fellowship

Adrenal gland - crossroads of stress response - epigenetic, transcriptional, and metabolic analyses

A PhD fellowship for three years is available starting August 1st 2021 at the Division of Endocrinology (Dept. of Internal Medicine I) of the University Hospital of Würzburg to join a collaborative project focusing on epigenetic, epitranscriptomic and metabolic modifications on cortisol production in adrenal tissues. Funding is provided by the German Research Foundation (DFG) within the Collaborative Research Program SFB/Transregio 205 „The Adrenal: Central Relay in Health and Disease“ (<https://adrenal-research.de>).

The hypothalamic-pituitary-adrenal (HPA) axis is the most important stress response orchestrating glucocorticoid actions with a wide range of cardiovascular, immune and metabolic effects. Even small disruptions of the HPA axis can have devastating consequences. Adrenal hypercortisolism leading to Cushing's syndrome may result from cortisol-producing adenomas, hyperplasias, and highly malignant adrenocortical carcinomas. The use of single-cell RNA sequencing in a murine chronic stress model (Lopez, ..., Sbiera et al., *Science Advances* 2021, PMID:33571131) allowed us to molecularly dissect cell types in the hypothalamus, pituitary, and adrenal that contribute to glucocorticoid dysregulation during chronic stress. Interestingly, the most prominent alterations were observed in the adrenal gland. This finding suggests a fine regulation of the stress response at the level of the adrenal gland beyond the canonical expression control, but the mechanisms are still largely unexplored. We hypothesise that secondary modifications at DNA, RNA and protein levels are paramount for in situ cellular control in different forms of adrenal Cushing's syndrome.

The successful candidate will utilize a combination of sophisticated bioinformatics tools, advanced optical methods like immunohistochemistry and MALDI mass spectrometry imaging as well as biochemical assays on tumor samples and cell lines to:

- investigate the impact of epigenetic DNA and epitranscriptomic RNA modifications in adrenal tissues leading to hypercortisolism
- verify consequences of epigenetic DNA and RNA modifications on steroid output in 3 D cell culture
- impact of the epigenetic modifications on the adrenal metabolic microenvironment using MALDI-MSI

The applicant will have access to a very stimulating research environment as both a member of an interdisciplinary TRR/SFB and of the prestigious Graduate School of Life Sciences of the University of Würzburg (http://www.graduateschools.uni-wuerzburg.de/life_sciences/). Furthermore, our group is one of the leading centres for the study of endocrine tumours with high ranking peer-reviewed publications (Beuschlein, Fassnacht, ..., Sbiera et al. *N Engl J Med* 2014, PMID:24571724; Assié, ..., Sbiera et al., *Nature Genetics* 2014, PMID:24747642; Reincke, Sbiera et al., *Nature Genetics* 2015, PMID:5485838; Weigand, ..., Sbiera *Science Reports* 2017, PMID:28250426; Sbiera, ..., Fassnacht *Neurooncology* 2019, PMID:31222332; Weigand, ..., Sbiera, *Science Advances* 2021, PMID:33608270).

Applicants should preferably have a background in genetics and biochemistry/cell biology. Applications are invited from all nationalities, with a Master's degree (or Diploma) in a relevant area.

Address applications (preferably by email) to:

PD Dr. Silviu Sbiera
Dept. of Internal Medicine I
University Hospital Würzburg
Oberdürrbacher Str. 6
97080 Würzburg
Germany
Email: sbiera_s@ukw.de