



Tübingen, 19.07.2018

Elisabeth and Franz Knoop-Stiftung
Report for the “Biochemie-Förderpreis für Forschungsaufenthalte 2017“

2017 IFIB Research Visit Award Report (14.05.2018 – 12.07.2018)

I received the 2017 Biochemie-Förderpreis für Forschungsaufenthalte and used the award money to fund a research collaboration from May 14, 2018 to July 12, 2018 between the lab of Prof. Dr. Robert Feil at Interfaculty Institute of Biochemistry at Tübingen University and the lab of Prof. Dr. Anna Devor in the department of Neurosciences at the University of California San Diego (UCSD), USA. The biochemical signaling molecule cGMP is implicated in various diseases and medications that modulate cGMP pathway are on the market for human use, such as the PDE5 inhibitor Sildenafil for erectile dysfunction, the guanylyl cyclase C agonist Linaclotide for chronic idiopathic constipation and irritable bowel syndrome, and the NO-GC stimulator Riociguat for some forms of pulmonary hypertension. Given the druggability of the cGMP pathway, it is important to further elucidate the cGMP signaling pathway in the nervous system. In the brain, it has been hypothesized that neuronal activity influences the cerebral vasculature through signaling cascades known as ‘neurovascular coupling’. Nitric oxide and cGMP are potential components of this physiological process. Our research collaboration aimed to investigate the biochemical cGMP signaling cascade in vivo in mouse models with 2-photon microscopy. The collaboration was with Dr. Martin Thunemann, an IFIB doctoral graduate student, previous postdoc and 2015 winner of the Knoop Preis für Biochemie, who investigates the nervous system under in vivo conditions in awake mice. The aim of the collaboration was to investigate cGMP signaling in the primary sensory cortex. Transgenic mice from Tübingen were sent to the imaging laboratory at UCSD and Michael Paolillo spent two months at UCSD working on this project.

We demonstrated a physiological effect (vasodilation) of a nitric oxide releasing compound in the primary sensory cortex. The combination of pharmacological tools, transgenic mice, surgical implantation of cranial windows and multiphoton imaging allowed us to collect data on a new methodology to elevate cGMP levels via a cell specific process. The data collected during this collaboration are crucial to improve our understanding of cGMP’s role in the nervous system. This collaboration produced results with implications for biochemistry researchers as it demonstrates a novel biochemical method to investigate the role of nitric oxide and thus cGMP in a cell specific manner in vivo.

This exchange has allowed me to increase my scientific outlook as well as my network. The data we collected in living mice increases the impact of our research and my doctoral thesis. I have also gained technical insights into multiphoton imaging of live mice, surgical implantation of cranial windows and analysis of the 2-photon data. I thank the Elisabeth and Franz Knoop-Stiftung for their support and it is my sincere hope that graduate students will have the opportunity to apply for this award in the future and that the Elisabeth and Franz Knoop-Stiftung continues to support the excellent research conducted at the Interfaculty Institute of Biochemistry at Tübingen University.

Sincerely,

Michael Paolillo