

## Report Research Visit: Boston, 2<sup>nd</sup> Cohort

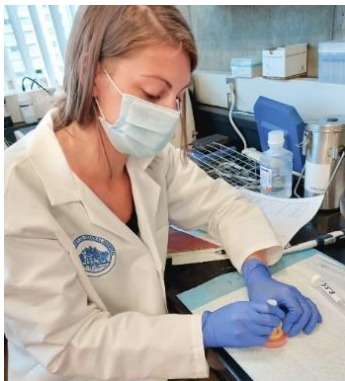
Between April and July 2022 four PhD students from the 2<sup>nd</sup> cohort of the GRK 2381 in Tübingen had the chance to join different laboratories in Boston for a three-month research visit, just like several students from the 1<sup>st</sup> cohort did in the months before.

**Jennifer Schulz** (P1 – cancer) joined the E. L. Steele laboratories for Tumor Biology at the Massachusetts General Hospital and Harvard Medical School. Here, she worked with the group of Associate Professor Dai Fukumura. The focus of the laboratory is to understand vascular, interstitial and cellular barriers to the drug delivery in solid tumors with the aim to discover and test new treatment strategies to overcome the physiological barriers.



*Assoc. Prof. Dai Fukumura (middle) with J. Schulz (right) and M. Barresi (left, PhD candidate of the 1<sup>st</sup> cohort).*

During her research stay she investigated, how different drug treatments (in combination with radiation) affect the tumor microenvironment in pancreatic adenocarcinoma (PDAC). She was able to learn and practice various techniques, such as radiation and immune-checkpoint blockade treatment of tumor-bearing mice, which all of them are standard-of-care treatments for patients, offering the potential to translate research results from bench to bedside.



*J. Schulz working in the E. L. Steele laboratory, isolating stroma cells.*

In addition, she expanded her skills in isolating tumor stroma cells through complex flow cytometry panels to reveal how the distribution of certain stroma cells within the tumor microenvironment is affected by various drug combinations.

Furthermore, she was able to improve her knowledge about melanoma mouse models due to the great expertise of the laboratory and the excellent training she received.



*J. Schulz on a ferry to Charlestown Navy Yard (CNY) Campus.*

Back in Tübingen she will implement the newly acquired techniques in her own PhD project and stay in touch with the great scientific community in Boston.



*Boston University Medical Campus*

**Aylin Balmes** (P3 – vascular biomechanics) joined the laboratory of Associate Professor Francesca Seta at the Boston University School of Medicine as a visiting scholar. The main focus of the laboratory is the investigation of basic mechanisms of vascular disease, with a focus on the role of vascular smooth muscle cells (VSMCs) in vascular remodeling.

During her stay she learned how to measure pulse wave velocity (PWV), the gold standard measure of arterial stiffness, in vivo in mice. These experiments are a great complement to her experiments in Tübingen where she studies stiffness on the cellular level using scanning ion conductance microscopy (SICM) and atomic force microscopy (AFM).

During her research visit she investigated if vascular smooth muscle cell stiffness is linked to actin cytoskeleton remodeling. This can be quantified using different techniques. One of those is filamentous (F)-actin immunostaining, which she previously used in Tübingen. Another one is Western Blot quantification of filamentous (F)- and globular (G)-actin, which she learned in Boston. Additionally, she learned a lot about the molecular biology of VSMCs particularly the role of the cyclic guanosine monophosphate (cGMP) pathway.



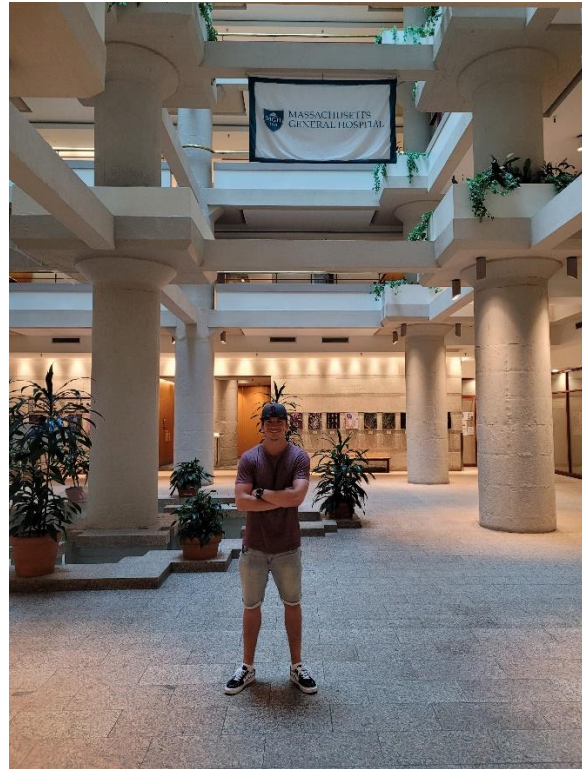
*A. Balmes at the Charles River in Cambridge*

**Timo Kopp** (P4 – atherosclerosis) joined the laboratory of Associate Professor Dr. Dmitriy Atochin at the Charlestown Navy Yard in Boston to conduct vascular research. The laboratory focuses on ischemic stroke models and possible treatment options for patients experiencing a stroke. Investigating the role of vascular smooth muscle cells (VSMCs) in reperfusion and limiting the damaged area in the brain is of particular interest in this regard.

During his time there, his work focused on assessing the effects that a near-infrared laser has on the vascular reactivity in mice and how that effect might be beneficial for the outcome of stroke experiments. This series of experiments included breeding and genotyping mice of a specific genetic background (wild type, eNOS A-K.I.; eNOS D-K.I. and cGKI K.O. mice), checking for phosphorylation of eNOS and Akt after laser exposure by Western Blotting and most importantly, investigating changes to cerebral blood flow in mice that underwent stroke surgery, after their skull was exposed to the laser.



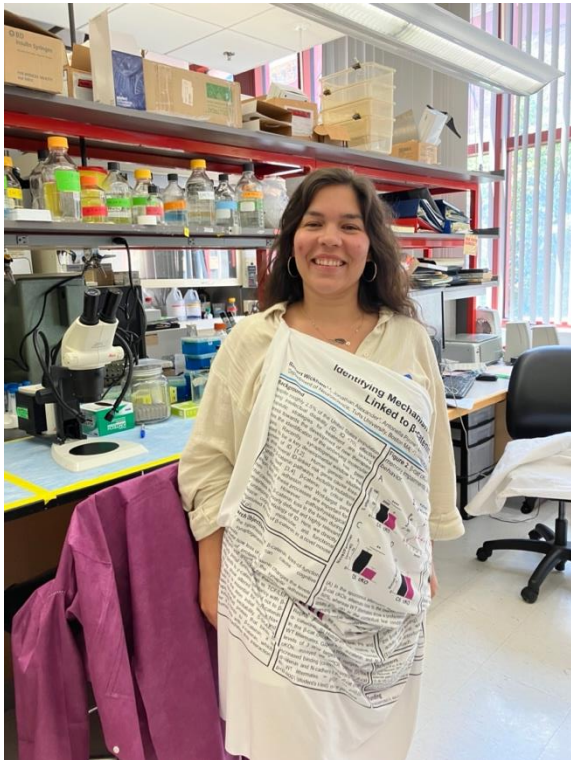
Lab meeting in the MGH library (left to right: T.Kopp, S. Yokomizo, D. Atochin, S. Kashiwagi)



T. Kopp in the main lobby of the Charlestown Navy Yard facilities

In addition to this, he was involved in a study about the effects of the same laser setup on a cancer cell line. Observed effects might give an indication that this technique can be used to treat the same cancer in humans as well.

As of August 2022, both projects resulted in co-authorships of two publications in the FASEB journal, underlining the mutual benefits of this research co-operation.



Dila Calis in Michele Jacob's Lab, wearing a poster (photo taken by Michele Jacob)

**Dila Calis** (P9 – brain) joined the laboratory of Professor Michele Jacob at the Tufts University Graduate School of Biomedical Sciences. The research team mainly focus on the Wnt-signaling pathway as an underlying mechanism for intellectual disability and autism spectrum disorder by determining the pathophysiological changes on behavioral, molecular, synaptic, and circuit levels.

During her visit, she was trained on different microscopy methods for imaging pyramidal neurons from hippocampus. For her research question she investigates synaptic spine density and structural morphology changes in hippocampal neuron. Synapses are unit structures that function in rapid information processing. It has been reported that spine density and morphology undergo alteration with hearing loss (either age-dependent or after acoustic trauma).

For this purpose, she used Golgi-Stained mouse brain sections that she prepared from different treatment groups, and acquired high-resolution images. In the next step, she was trained on the image analysis by using RECONSTRUCT software which helps to objectively measure density and classify spines.

Her preliminary findings suggest that, preventing the degradation of the cyclic guanosine monophosphate (cGMP) could be protective against the de-arborization of the neurons in the brain upon hearing loss and could be a potential therapeutic target.

She will establish the protocol that she learnt at Prof. Michele Jacob's lab in Tübingen where she will use this method in different mouse line (conditional KO) as a part of her PhD thesis.



Michele Jacob and Jonathan Alexander in the lab, discussing the imaging results.

We are convinced that the skills and knowledge we acquired during our research visit in Boston will be of great value for our continuing research in Tübingen.

Our gratitude goes to the GRK 2381 and the Reinhard Frank-Stiftung, for providing us with this great opportunity to broaden our scientific horizon and allowing us to connect with scientists from abroad. We would also like to thank Dai Fukumura, Francesca Seta, Dmitriy Atochin and Michele Jacob for allowing us to work at their laboratories and for the great mentorship.



*Get together after the Reinhard-Frank-Mini-Symposium.*



*Aylin Balmes (right), Jennifer Schulz (left) and Timo Kopp (middle) checking out the American "ALDI".*



*Dila Calis (left) and Jennifer Schulz (right) at the Harvard Football Stadium.*