

Click enrichment proteomics catalogues blood-brain-barrier permeable plasma proteins with age (Master's thesis project at Stanford University, CA, USA)

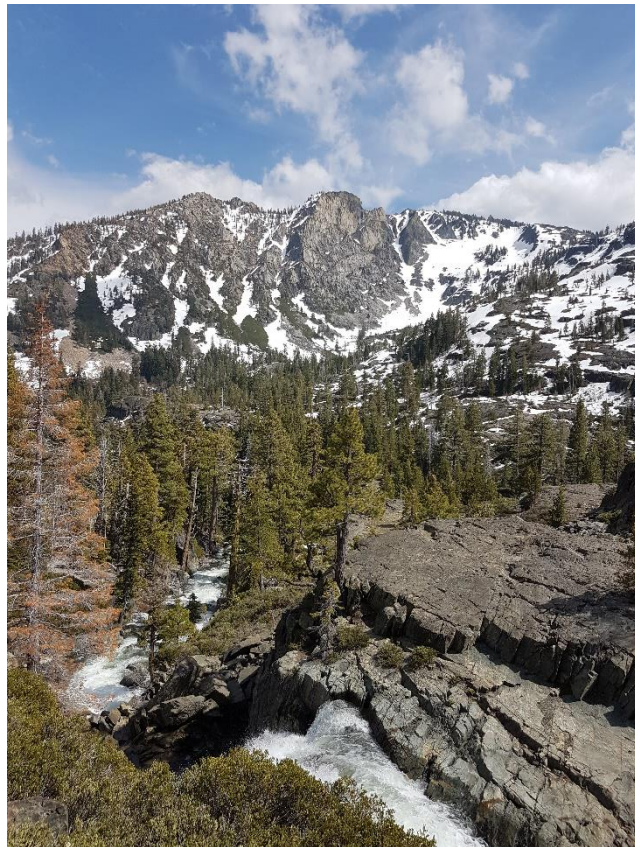
Daniel Stähli, December 2019

Stanford University is among the leading universities in the world located in one of the most innovative and creative areas in the world - the bay area. I had the great privilege to join the lab of professor Tony Wyss-Coray, one of the best labs in the field of aging. I worked together with Andrew Yang, a brilliant Ph.D. student, who invested a lot of time and effort in training me. I also learnt a lot from the other lab members (around 30 people) and our many collaborators. At Stanford University brainpower, hard work, collaboration and money all come together, creating this unique place. Among other things I learnt how to handle mice and do behavior experiments, prepare and analyze samples for fluorescence microscopy and transmission electron microscopy and how to perform mass spectrometry-based proteomics. In our project we investigated how the blood-brain-barrier (BBB) ages. Using NHS-chemistry, we labeled the whole plasma proteome as a means to test and visualize BBB permeability. We show that plasma enters brain endothelial cells (BECs) and the brain parenchyma to a larger extent than expected. Further we developed a tool with which we could identify BBB permeable proteins. By flow cytometry and single cell RNA sequencing we elucidated how plasma is taken up by BECs and how this transcriptional program changes with age. The results and methods are described in more detail in my master's thesis. At the end of my stay we submitted a manuscript to the journal Nature which is currently under review. Next to this main project I could also briefly work on the project "A Single Cell Transcriptomic Atlas Characterizes Aging Tissues in the Mouse" which has been pre-published on bioRxiv.com. During my time there I learned a lot about science, method wise and otherwise. I had an amazing time there and I can only recommend this lab and university.

California is a beautiful state but also extremely expensive, especially the bay area. Funding is a major concern when going there (my stay cost around \$30-35k). There is basically no housing for visiting students on campus and outside rents for a single room with shared bathroom are around \$1500. Things are widespread and there is almost no public transportation. Thus, it is almost inevitable to have a car. The admission process is long and time consuming. Both, reward and effort for going to Stanford University are huge.



Half Moon Bay west of Palo Alto



Lab retreat at Fallen Leaf, close to Lake Tahoe