



PhD Program between the Freie Universität Berlin (FUB) and the China Scholarship Council (CSC) Open PhD position for CSC scholarship candidates 2015

Please note: the PhD position is only offered to Chinese PhD candidates for application in the framework of the FUB-CSC Program.

<u>Department/Institute:</u>	Department of Biology, Chemistry and Pharmacy Institute of Chemistry and Biochemistry
<u>Subject area:</u>	Cell biology, biophysics, ion imaging
<u>Name of Supervisor:</u>	Dr. Tobias Stauber
<u>Number of open positions:</u>	1
<u>Project title:</u>	Generation and application of subcellular chloride sensors

Project description:

The intracellular chloride concentration does not only play an essential role in regulating neuronal excitability, but it also seems to crucially contribute to basic cell biological processes such as cell migration (1). In addition, organellar chloride concentrations play pivotal roles in vesicular trafficking and function (2). However, precise quantitative measurements of spatial and temporal alterations of both cytosolic and vesicular chloride are lacking due to technical difficulties. Cytosolic chloride sensors may display insufficient K_{on}/K_{off} values and/or sensitivity in the required range for monitoring transient chloride alterations and gradients. Chloride dyes targeted into organelles face the problem of an acidic environment and potentially too high chloride concentrations (as seen with a lysosomal chloride sensor we developed recently (3)).

In this project, we aim at testing cytosolic chloride sensors for the fluorescence-microscopic detection of spatial and temporal alterations in chloride concentrations upon various cues and at different physiological states of the cells. Existing chloride dyes can be modified chemically to improve their physical-chemical parameters for our purposes (characterization also includes testing for disturbance-tolerance to other ions). The dyes will be used to test the role of a number of chloride channels, such as the volume-regulated anion channel which we have identified on a molecular level (4). Besides this, we aim at improving our previously described lysosomal chloride sensor (3) by chemical modification to be able to measure chloride concentrations under physiological conditions (not by systemic depletion of chloride as done in (3)) and monitor alterations during lysosomal acidification, fusion events and various manipulations, including the use of available cell lines deficient for certain lysosomal ion transporters.

References:

- (1) Schwab A, Fabian A, Hanley PJ and Stock (2012) Role of ion channels and transporters in cell migration. *Physiol Rev* 92, 1865-1913

- (2) Stauber T and Jentsch TJ (2013) Chloride in vesicular trafficking and function. *Annu Rev Physiol* 75, 453-477
- (3) Weinert S, Jabs S, Supanchart C, Schweizer M, Gimber N, Richter M, Rademann J, Stauber T, Kornak U, Jentsch TJ (2010) Lysosomal pathology and osteopetrosis upon loss of H⁺-driven lysosomal Cl⁻-accumulation. *Science* 328, 1401-1403
- (4) Voss FK, Ullrich F, Münch J, Lazarow K, Lutter D, Mah N, Andrade-Navarro MA, von Kries JP, Stauber T, Jentsch TJ (2014) Identification of LRRC8 heteromers as an essential component of the volume-regulated anion channel VRAC. *Science* 344, 634-638

Language requirements:

Working language in our lab is English, and the PhD thesis can be written in English or German. German is not required.

Academic requirements:

Master's degree in chemistry, biochemistry, biophysics or related. Ideally experience with ion imaging in cell biology and/or with the generation and use of fluorometric sensors.

Link to professor and further information:

Homepage: <http://www.bcp.fu-berlin.de/en/chemie/biochemie/ag/agstauber>

Please note: In a first step the complete application should be submitted to the Beijing Office for evaluation by January 4th. The professor will then get in contact with you after having received the complete application in January.