Open position for the LSM call of applications

Department/Institute: LMU Faculty of Biology, Microbiology

Subject areas/Research fields: Biophysics, Biochemistry

Keywords: membrane transporter, drug-Design, molecular biophyscs, fluorescence spectroscopy

Name of supervisor: Prof. Dr. Thorben Cordes, in collaboration with Prof. Kirsten Jung

Project title: ABC importers as targets for antibiotics of pathogenic bacteria

Project description:

Multidrug resistant bacteria and lagging development of novel antibiotics were the cause of >17 million deaths in 2006.1 As pointed out by the world health organization (WHO) new strategies against drug resistant bacterial infections are urgently required (www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed). Bacterial ATP Binding Cassette (ABC) import systems have a huge potential as targets for antibiotic development due to their involvement in a numerous biological processes, their extracellular localization and the absence of homologous proteins in the mammalian hosts.2 These transmembrane systems transport wide variety of substrates ranging from sugars and peptides to metal ions, osmolytes and vitamins by utilizing the energy from ATP-hydrolysis. Different studies have shown that certain ABC importers are involved in bacterial virulence or survival in the host organism.2 Here, we propose to disable the periplasmic or extracellular components of ABC import systems, substrate binding domains or proteins (SBPs). They initiate substrate transport via its delivery to the membrane-embedded ABC import system allowing selective and ATP-coupled transport. In the framework of this project, you will conduct a structural analysis of the selected SBPs, establish and optimize the methods for protein expression, purification and fluorophore labelling of the target SBP and test the established fluorescence assays using single-molecule3, bulk- and high-throughput fluorescence detection methods. Furthermore, you will identify SBP inhibitors in silico, test and optimize their ability to

bind the relevant SBPs in biochemical experiments. Finally, in collaboration with the lab of Kirsten Jung, you will test the impact of promising inhibitor molecules on the growth and infectivity of bacteria.

References:

Martens, E.; Demain, A. L., The antibiotic resistance crisis, with a focus on the United States. The Journal of antibiotics 2017, 70 (5), 520-526.

Garmory, H. S.; Titball, R. W., ATP-binding cassette transporters are targets for the development of antibacterial vaccines and therapies. Infection and immunity 2004, 72 (12), 6757-6763.

de Boer, M.; Gouridis, G.; Vietrov, R.; Begg, S. L.; Schuurman-Wolters, G. K.; Husada, F.; Eleftheriadis, N.; Poolman, B.; McDevitt, C. A.; Cordes, T., Conformational and dynamic plasticity in substrate-binding proteins underlies selective transport in ABC importers. eLife 2019, 8, e44652.

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Reseach group website:

https://www.mikrobiologie.biologie.uni-muenchen.de/forschung/ag_cordes/research/index.html

Apply: Please send your application through the online portal of the Graduate School Life Science Munich (LSM).