Ph.D. Project Number	**9**
in Project cluster	Pathoblockers as Novel Anti-infectives
Supervisors + Affiliations	**PD Dr. Martin Empting** HIPS Saarbrücken, Department Antiviral and Antivirulence Drugs https://www.helmholtz-hips.de/en/research/teams/team/antiviral-and-antivirulence-drugs/ **Prof. Dr Gabriela Krasteva-Christ** UKS Homburg, Department Anatomy, cell biology and developmental biology https://www.uniklinikum-saarland.de/de/einrichtungen/fachrichtungen/anatomie_zellbiologie_und_entwicklungsbiologie/univ_prof_dr_med_vet_gabriela_krasteva_christ_anatomie/forschung_research
Description research focus/environment	The group “Antiviral & Antivirulence Drugs (AVID)” headed by PD Dr. Martin Empting focuses on the generation of novel antimicrobial compounds against viral and bacterial infections. To this end, state-of-the-art medicinal chemistry methodologies are applied to explore unprecedented modes-of-action and resistance-breaking approaches. Prof. Dr. Gabriela Krasteva-Christ heads the Department for Anatomy and Cell Biology and focuses on chemosensation phenomena in the course of infections.
Project title	Exploring inter-kingdom cross-talk as a new strategy for the modulation of Pseudomonas aeruginosa infections
Short description Ph.D. project	Doctoral candidate (DC) 9 will study the impact of Pseudomonas Quorum Sensing (QS) molecules and their inhibition on TRPM5-mediated host responses. Pseudomonas aeruginosa (PA) is a prime pathogen in the hospital setting with especially severe impact on patients with chronic lung diseases like cystic fibrosis, COPD and bronchiectasis. The bacterial signal molecules, which comprise an alkylquinolone structural scaffold, have been demonstrated to mediate host-pathogen interactions. DC9 will investigate the effect of natural and synthetic alkylquinolone (AQ) derivatives on the “Transient receptor potential cation channel subfamily M member 5” (TRPM5) as well as on other TRP channels present on immune cells and on sensory neurons. TRPM5 mediates important cellular functions of epithelial brush cells essential for mucociliary clearance of bacteria from the airways. Furthermore, structure-divergent QS inhibitors, which potently inhibit AQ biosynthesis and other important virulence factors, have been designed and optimized in our labs. DC9 will assess the impact of AQ biosynthesis inhibition by QS inhibitors and their potential impact on the TRPM5-AQ host-pathogen interaction axis. To this end, the DC will apply advanced assay systems and work e.g. with HPLC-MS-based quantification methods as well as ex vivo video microscopy for estimation of the mucociliary clearance, studying barrier function, and Ca-imaging for the investigation of signaling mechanisms.
Secondment	The secondment with Prof. Susanna Zierler at the Johannes Kepler University Linz, Austria will train the DC in Patch-Clamp techniques using primary human immune cells.
Required or advantageous skills/competences	MSc (or equivalent) in life sciences, pharmacy or medicine; open-minded person motivated to work in a multidisciplinary team
Career perspectives	Scientific career in biomedical or pharmaceutical area in academia or industry
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