Abstract ID: 93364

Student: Krivic Denis

Area of Research: Immunology, microbiome research and respiratory diseases

PhD Programme: PhD Metabolic and Cardiovascular Disease (DK-MCD)

Semester: 7

TRPC6 Photopharmacology Allows for Dissociation of Mast Cell Degranulation and Transcription Factor Activation

Denis Krivi?; Bernadett Bacsa; Kathrin S. Maitz; Annarita Graziani; Julia Kargl; Klaus Groschner

Besides a key role in allergic diseases, mast cells confer important modulatory functions in innate and adaptive immunity. The communication between mast cells and other immune cells is not only based on the acute or long-term release of pre-stored mediators involving distinct processes of degranulation but also on the expression of specific surface proteins. Activation of mast cells typically involves Ca2+ signalling, which evokes both transcriptional activation and degranulation. To dissect the complex functions of mast cells in human pathology and to explore new therapeutic strategies we aimed towards specific manipulation of mast cell phenotype. Characterization of an optochemogenetic protocol for activation RBL-2H3 mast cells revealed that repetitive photocycling of OptoBI-1 to generate oscillatory Ca2+ signals elicits rapid and efficient NFAT nuclear translocation without concomitant degranulation. By contrast, conventional pharmacological activation of overexpressed TRPC6 channel was strictly associated with CD63-associated secretion. Our results suggest that the specific modulation of mast cell phenotype as obtained by TRPC6-OptoBI-1-mediated activation, arises from introduction of a highly specific conformational and functional state of the TRPC6 channel, resulting in unique Ca2+signatures. Further understanding of these phenomena may lead to new approaches for (photo)pharmacological immunomodulation.