

Stefan SCHILD (ORCID: 0000-0001-7842-0177): Patho-physiological roles of bacterial membrane vesicles

Research interest and scientific background: The release of membrane vesicles (MVs) is a common feature of all bacteria, but information on their patho-physiological roles is still limited. Recent reports indicate that bacterial MVs are able to modulate host cells signaling and shape the immune system. Additionally, MVs can diffuse into regions bacteria may not reach, e.g. MVs can be internalized by host cells, penetrate into deeper tissues - especially during barrier dysfunction - and thereby spread systemically. Despite general awareness that MVs can induce pro- and anti-inflammatory immune responses in a range of tissues resulting in beneficial or adverse effects for the host, the mechanisms involved have not been well studied^[1].

Along on our expertise on bacterial MVs ^[2-5] we currently study the impact of MVs derived from gastrointestinal bacteria on gut homeostasis or inflammatory bowel disease (see also BioTechMed flagship project SECRETOME: <https://biotechmedgraz.at/en/programs/flagship-projects/call-2016/secretome/>). Within the doc.funds project the student will characterize MV-host cell interactions and analyze the impact of pathogenic and probiotic MVs on alterations of the intestinal microbiome.

Approach and methods: Besides standard techniques in molecular biology and microbiology, the student will learn cultivation and genetic engineering of bacterial species pathogens. A non-exhaustive list of methods includes MV isolation and composition analyses, bacterial cell fractionation and membrane isolation, Cell culture assays, ELISA, cytokine profiling, reporter-based MV internalization assays, protein-protein interaction assays, inflammation and colonization assays using the mouse model (willingness on animal handling is compulsory for this position). Naturally, the student will strongly interact with other research groups of the doc.fund Molecular Metabolism and the research and training network NAWI Graz and BioTechMed Graz.

Affiliation: The student will work at the Institute of Molecular Biosciences at the University of Graz. This project is directly connected to the doc.fund Molecular Metabolism.

References:

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- [2] Roier, S., Zingl, F.G., Cakar, F., Durakovic, S., Kohl, P., Eichmann, T.O., Klug, L., Gadermaier, B., Weinzerl, K., Prassl, R., Lass, A., Daum, G., Reidl, J., Feldman, M.F., Schild, S. A novel mechanism for the biogenesis of outer membrane vesicles in Gram-negative bacteria **Nature communications** 2016, 7, 10515. 10.1038/ncomms10515
- [3] Leitner, D.R., Lichtenegger, S., Temel, P., Zingl, F.G., Ratzberger, D., Roier, S., Schild-Prüfert, K., Feichter, S., Reidl, J., Schild, S. A combined vaccine approach against *Vibrio cholerae* and ETEC based on outer membrane vesicles **Frontiers in microbiology** 2015, 6. 10.3389/fmicb.2015.00823
- [4] Schild, S., Nelson, E.J., Camilli, A. Immunization with *Vibrio cholerae* outer membrane vesicles induces protective immunity in mice **Infect Immun** 2008, 76 (10), 4554-4563.
- [5] Roier, S., Leitner, D.R., Iwashkiw, J., Schild-Prüfert, K., Feldman, M.F., Krohne, G., Reidl, J., Schild, S. Intranasal Immunization with Nontypeable *Haemophilus influenzae* Outer Membrane Vesicles Induces Cross-Protective Immunity in Mice **PLoS One** 2012, 7 (8), e42664.