



**Universität
Zürich**^{UZH}

**Institute of
Medical Microbiology**
Gloriastrasse 30
8006 Zürich, Switzerland

Prof. Dr. Hubert Hilbi
Tel.: +41 44 634 2650
E-mail: hilbi@imm.uzh.ch

Postdoctoral/PhD/master positions – *Legionella*-host cell interactions

The environmental bacterium *Legionella pneumophila* causes a severe pneumonia termed Legionnaires' disease in humans. The opportunistic pathogen employs a conserved mechanism to grow in free-living amoeba and macrophages by forming a unique, ER-associated "Legionella-containing vacuole" (LCV) (**Fig. 1**). Pathogen-host cell interactions are governed by a bacterial type IV secretion system, which translocates more than 330 different "effector proteins". The effector proteins subvert pivotal host processes, such as signal transduction, vesicle trafficking, cytoskeleton dynamics and mitochondrial bioenergetics (1) (**Fig. 1**). However, the function of most of these effectors is not known.

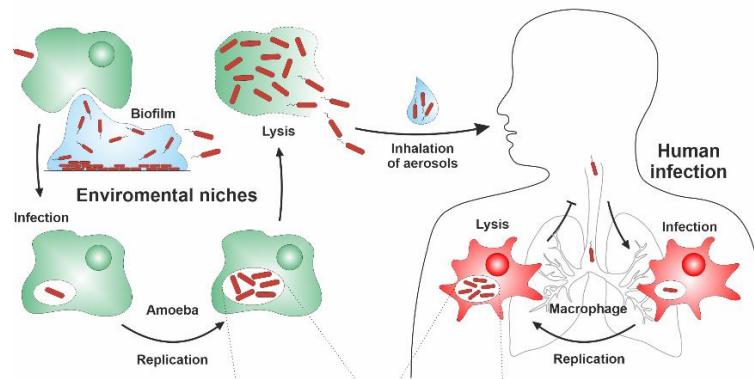
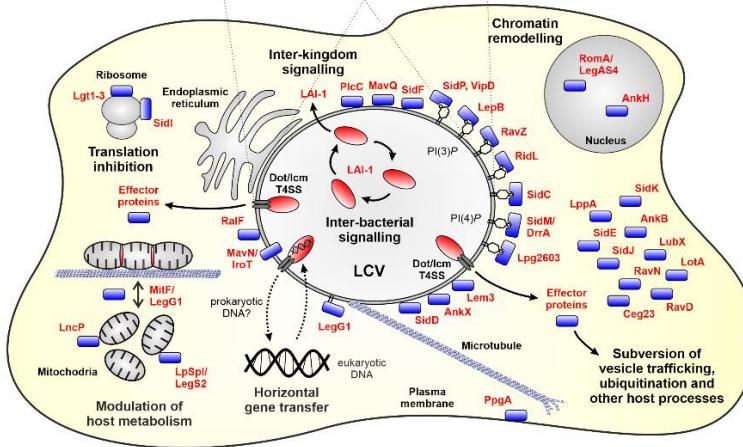


Fig. 1. Environmental niches, human infection, and intracellular replication of *L. pneumophila*. *L. pneumophila* replicates in phagocytes within a unique “*Legionella*-containing vacuole” (LCV). More than 330 secreted effector proteins target virtually all cellular processes. The small signaling molecule LAI-1 promotes inter-bacterial as well as inter-kingdom signaling (1).



Current research in our laboratory focuses on the molecular mechanisms of *Legionella* virulence (pathogen-host cell interactions), communication (cell-cell signaling) and persistence (dormancy). Recent studies in our group identified large dynamin-like GTPases, lipid droplets, LCV-ER membrane contact sites and mitochondria as crucial determinants of *L. pneumophila*-host cell interactions (2-8). Within this framework, the specific project will mechanistically elucidate the subversion of host targets by *L. pneumophila* effector proteins. The project allows to get familiar with a broad range of techniques in the disciplines Microbiology (handling of BSL-2 pathogens, infection analysis), Cell Biology (confocal fluorescence microscopy, (imaging) flow cytometry, RNA interference), Biochemistry (protein-protein and protein-lipid interactions, LCV isolation and characterization) and Molecular Biology (cloning, mutagenesis, reporter construction).

Highly motivated individuals with an interest and background in Microbiology, Biochemistry, Cell Biology, or a related area are invited to apply. For further information please contact Prof. Hubert Hilbi (hilbi@imm.uzh.ch) and visit our website (<https://www.imm.uzh.ch/de/research/experimental/Hilbi.html>).

References:

1. Hilbi H, Buchrieser C. 2022. Microbe Profile: *Legionella pneumophila* - a copycat eukaryote. *Microbiology* 168: doi: 10.1099/mic.0.001142.
2. Steiner B, Swart AL, Welin A, Weber S, Personnic N, Kaech A, Freyre C, Ziegler U, Klemm RW, Hilbi H. 2017. ER remodeling by the large GTPase atlastin promotes vacuolar growth of *Legionella pneumophila*. *EMBO Rep* 18: 1817-1836.
3. Katic A, Hüslér D, Letourneur F, Hilbi H. 2021. *Dictyostelium* dynamin superfamily GTPases implicated in vesicle trafficking and host-pathogen interactions. *Front Cell Dev Biol* 9: 731964.
4. Hüslér D, Steiner B, Welin A, Striednig B, Swart AL, Molle V, Hilbi H, Letourneur F. 2021. *Dictyostelium* lacking the single atlastin homolog Sey1 shows aberrant ER architecture, proteolytic processes and expansion of the *Legionella*-containing vacuole. *Cell Microbiol* 23: e13318.
5. Hüslér D, Stauffer P, Keller B, Bock D, Steiner T, Ostrzinski A, Vormittag S, Striednig B, Swart AL, Letourneur F, Maass S, Becher D, Eisenreich W, Pilhofer M, Hilbi H. 2023. The large GTPase Sey1/atlastin mediates lipid droplet- and FadL-dependent intracellular fatty acid metabolism of *Legionella pneumophila*. *Elife* 12: e85142.
6. Hüslér D, Stauffer P, Hilbi H. 2023. Tapping lipid droplets: A rich fat diet of intracellular bacterial pathogens. *Mol Microbiol* 120: 194-209.
7. Vormittag S, Hüslér D, Haneburger I, Kroniger T, Anand A, Prantl M, Barisch C, Maass S, Becher D, Letourneur F, Hilbi H. 2023. *Legionella*- and host-driven lipid flux at LCV-ER membrane contact sites promotes vacuole remodeling. *EMBO Rep* 24: e56007.
8. Vormittag S, Ende RJ, Derré I, Hilbi H. 2023. Pathogen vacuole membrane contact sites - close encounters of the fifth kind. *Microlife* 4: uquad018.