Universität Zürich[UZH]

Institute of Medical Microbiology

University of Zurich
Institute of Medical Microbiology
Gloriastrasse 28/30
8006 Zurich
+41 44 634 27 00
imm@imm.uzh.ch
www.imm.uzh.ch

Tigecycline Resistance mechanisms in pathogenic non-tuberculous mycobacteria

Members of the *Mycobacterium abscessus* complex (MABC) are opportunistic environmental pathogens. MABC frequently infects the lungs of immunocompromised patients, often with underlying lung diseases such as cystic fibrosis (CF) or chronic obstructive pulmonary disease (COPD). The treatment of these infections is challenging due to the high intrinsic resistance mechanisms of MABC, which include enzymes that modify the antibiotic or its target, efficient drug efflux, and a specialized hydrophobic cell wall that limits antibiotic uptake. Furthermore, the rapid emergence of acquired resistance mechanisms further complicates the treatment. MABC is thus deserving of its reputation as an antibiotic nightmare. To overcome the reduced availability of effective antibiotic agents against MABC infections, second-line antibiotics like Tigecycline (TIG), a third-generation Tetracycline (TET), are more frequently used in clinical treatment. However, the resistance mechanisms against TIG in MABC are still elusive, even though other resistance mechanisms have recently been closely investigated.

What you will do:

- Selecting TIG resistant mutant in engineered and WT MABC strains
- Whole genome sequence analysis to pinpoint TIG resistant determinants
- Further characterization of the TIG resistance determinants

What you will learn:

- Basic Microbiology techniques
- Working with difficult to handle bacteria (BSL-2)
- General and advanced genetic techniques
- MIC determination

We are offering a 1-year Master thesis project in the field of medical microbiology for early 2025. If you interested pls send a short introduction letter and your CV to Prof. Peter Sander (psander@imm.uzh.ch)

References:

Luthra S, Rominski A, Sander P. The Role of Antibiotic-Target-Modifying and Antibiotic-Modifying Enzymes in *Mycobacterium abscessus* Drug Resistance. Front Microbiol. 2018 Sep 12;9:2179. doi: 10.3389/fmicb.2018.02179. PMID: 30258428; PMCID: PMC6143652.
Phelps GA, Cheramie MN, Fernando DM, Selchow P, Meyer CJ, Waidyarachchi SL, Dharuman S, Liu J, Meuli M, Molin MD, Killam BY, Murphy PA, Reeve SM, Wilt LA, Anderson SM, Yang L, Lee RB, Temrikar ZH, Lukka PB, Meibohm B, Polikanov YS, Hobbie SN, Böttger EC, Sander P, Lee RE. Development of 2nd generation aminomethyl spectinomycins that overcome native efflux in *Mycobacterium* abscessus. Proc Natl Acad Sci U S A. 2024 Jan 9;121(2):e2314101120. doi: 10.1073/pnas.2314101120. Epub 2024 Jan 2. PMID: 38165935; PMCID: PMC10786304.

https://www.imm.uzh.ch/de/research/sander/virulencemabscessus.html

https://www.imm.uzh.ch/de/Nationales-Zentrum-f%C3%BCr-Mykobakterien.html