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| **Research Theme:** Structural Biology and Drug Discovery in Infectious Disease |
| **PhD Research Project Title:** Insights into the *Mycobacterium abscessus* energy converter F-ATP synthase to discover novel compound targets |
| **Scholarship category (Please indicate the source of funding for this project):**  **Grant Scholarship (NRF)** |
| **Principal Investigator/Supervisor:** Professor Dr Gerhard Grüber |
| **Co-supervisor/ Collaborator(s) (if any):** |
| **Project Description**  **a) Background:** Infections caused by non-tuberculous mycobacteria (NTM) are increasing globally, including *Mycobacterium abscessus* (Mab), which comprises three subspecies. This rapidly growing mycobacterium is one of the most commonly identified NTM species responsible for severe respiratory, skin and mucosal infections in humans. It is often regarded as one of the most antibiotic-resistant mycobacteria, leaving us with few therapeutic options. In Singapore, *Mab subsp. abscessus* is the most common subspecies, causing mostly pulmonary disease in patients with structural lung disorders like cystic fibrosis and bronchiectasis, cutaneous infections leading to abscesses or inflamed cysts, and increasing numbers of peritonitis- and catheter-related infections. The Mab disease area is underserved, and drug discovery efforts are limited. The rational development of new agents, leading to potential anti Mab-drugs, requires the identification and understanding of essential biochemical pathways within the Mab bacterium so that they can be specifically targeted with new molecular entities. The oxidative phosphorylation pathway (OXPHOS) includes the key enzyme for the final formation of ATP, essential for the pathogen. This class of enzyme is an interesting and novel target for therapeutic intervention as disrupting its function would compromise the ability of Mab to respond to stress adaptation.  **b) Proposed work:**  In order to perform structure-based design of drugs to the Mab F-ATP synthase, structural and mechanistic insights into the parts responsible for OXPHOS catalysis and regulation are required. Such information will open the door for a) a novel understanding of communication between the catalyzing- and regulating parts of the enzymes, b) identification of possible targets for new anti-Mab compounds, c) the design and synthesis of novel molecules to inhibit the enzyme and to eradicate the pathogen.  **c) Preferred skills: computation work on data analysis would be a big plus, but not indispensable**  Have fun with science, be open for new approaches and enjoy working together in a lovely team.  Find more about us under: [http://labs.sbs.ntu.edu.sg/ggrueber/](https://urldefense.proofpoint.com/v2/url?u=http-3A__labs.sbs.ntu.edu.sg_ggrueber_&d=DwMGaQ&c=-35OiAkTchMrZOngvJPOeA&r=HV1fZYhfXUUwy6dDeaQAAp6RV8MkzdW4gglgDMYJPM8&m=AJ-xqFx8earTT6JIB522XZQpVBHAnkExhJUeN2XQQlE&s=V69JteuFJYWiGP_1O2vTv32cPU9HVHFU6UERkYrnwOY&e=) |
| **Supervisor contact:**  **If you have questions regarding this project, please email the Principal Investigator:**  Email: [GGrueber@ntu.edu.sg](mailto:GGrueber@ntu.edu.sg) |
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