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| **Research Theme: Proteomics and Protein** |
| **PhD Research Project Title:**  High throughput screening of potential antimicrobial molecules via native mass spectrometry |
| **Scholarship category (Please indicate the type of scholarship for this project):**   1. **SBS Research Student Scholarship (for SBS faculty only)** 2. **NTU Central RSS** |
| **Principal Investigator/Supervisor: Xueming Dong** |
| **Co-supervisor/ Collaborator(s) (if any):** |
| **Project Description**  **a) Background:**  The increasing occurrence of resistant bacteria necessitates the discovery of new classes of antibiotic compounds. In recent years, researchers have successfully identified numerous potential compounds demonstrating antibacterial properties. However, detailed investigations into the underlying mechanisms are still needed before the potential antibacterial compounds can be further tested for clinical application. Unfortunately, several challenges in drug discovery remain unresolved. For example, membrane proteins, which constitute the target of approximately 60% of currently clinically approved drugs, face limitations in related studies due to their inherent hydrophobicity, flexibility, and instability.  Native mass spectrometry (MS) is a relatively recently emerged technology that has been employed in the pharmaceutical industry at multiple stages of drug discovery, including compound library screening, hit validation, and lead optimization. Native MS measures intact protein-small molecule interactions in the gas phase and is a powerful and versatile tool for determining protein-ligand interaction stoichiometry, specificity, dissociation constant, and the mechanism of action of inhibitors. Reports have shown the successful application of native MS in studying the interaction between G protein-coupled receptors, one of the most pharmaceutically targeted membrane protein families, and several orthosteric small molecules. Additionally, native MS offers several advantages compared to conventional means of studying protein-ligand interactions: (1) requiring a low sample amount, (2) high throughput with < 5 minutes analysis time, (3) direct detection of protein-ligand interactions, and (4) the ability to analyze heterogeneous samples. Therefore, native MS is well-suited for rapid kinetical screening of potential antimicrobial drugs.  **b) Proposed work:**  This project has two stages: (1) instrumentation and validation of a native MS system, and (2) automated high-throughput screening of potential antimicrobial molecules in collaboration with other groups.  **c) Preferred skills:**   1. Mass spectrometry is a plus but not required. 2. Experience in native MS, micropipette pulling, and related publication is highly desired. |
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| **SBS contact and how to apply:**  Associate Chair-Biological Sciences (Graduate Studies) : [AC-SBS-GS@ntu.edu.sg](mailto:AC-SBS-GS@ntu.edu.sg)  Please apply at the following:  **Application portal:** <https://venus.wis.ntu.edu.sg/GOAL/OnlineApplicationModule/frmOnlineApplication.ASPX> |