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| **Research Theme: Cell Biology and Structural Biology** |
| **PhD Research Project Title: Investigating the nanoscale organization of epithelial cell junctions using correlative light and cryo electron microscopy** |
| **Principal Investigator/Supervisor: Alexander Ludwig** |
| **Co-supervisor/ Collaborator(s) (if any):** |
| **Project Description**  **a) Background:** Tight junctions and adherens junctions are large membrane protein complexes that play fundamental roles in all epithelial tissue. They mediate cell-cell adhesion, establish and maintain epithelial polarity, control the passage of molecules across epithelial barriers, and they regulate signaling and mechanotransduction. Detailed knowledge of their molecular and structural organization is critical to understand how these cell junctions function, and how their loss or deregulation leads to a loss of epithelial integrity and human disease.  **b) Proposed work:** This PhD project intends to study the native architecture of tight and adherens junctions under normal conditions and in perturbed or disease-related states using the latest technology for correlative light and cryo electron microscopy (cryoCLEM). CryoCLEM allows unprecedented insight into the nanoscale architecture of cells and cellular components under close-to-native conditions. The preparation of cells for cryoCLEM is technically challenging; it is a multi-step process involving imaging of frozen-hydrated cells by cryo-fluorescence microscopy, site-specific thinning of target cells using cryo focused-ion-beam milling, and cryo electron tomography of the desired subcellular target structure. This is followed by segmentation and computational approaches to generate high-resolution structural information on tight and adherens junctions and their components.  **c) Preferred skills:** The PhD candidate should have a degree in Biology, Chemistry or related discipline, and should have sufficient background incell biology, structural biology, and biochemistry. Experience in coding (R, Python) and bioinformatics are desirable. |
| **Supervisor contact:**  **If you have questions regarding this project, please email the Principal Investigator:**  **Alexander Ludwig**  [**aludwig@ntu.edu.sg**](mailto:aludwig@ntu.edu.sg)  **Check out the Ludwig homepage for more information: https://blogs.ntu.edu.sg/alabntusg/** |
| **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> |