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| **Research Theme: Cell Biology** |
| **PhD Research Project Title: Regulation of the tight junction paracellular permeability barrier by the junctional actin cytoskeleton** |
| **Scholarship category (Please indicate the source of funding for this project):**  **NTU Research Scholarship** |
| **Principal Investigator/Supervisor: Alexander Ludwig** |
| **Co-supervisor/ Collaborator(s) (if any):** |
| **Project Description**  **a) Background:**  The Ludwig lab at the School of Biological Sciences (<https://blogs.ntu.edu.sg/alabntusg/>) is interested in the molecular organisation, regulation and function of epithelial tight junctions (TJs). The TJ is a complex membrane structure found at the apical most tip of the epithelial lateral membrane. TJs physically separate body compartments and control the paracellular flux of ions and macromolecules across epithelial tissue barriers. Breakdown of TJs or deregulation of paracellular transport have been implicated in human diseases, including kidney diseases and Inflammatory Bowel Disease. TJs are also linked to several signaling pathways to control cell growth and tissue morphogenesis and are tightly associated with the cortical actin cytoskeleton. We recently found that TJs can regulate paracellular flux by fine-tuning junctional actin assembly and tension. We now wish to uncover the underlying cellular and molecular mechanisms.  **b) Proposed work:**  The goal of this PhD project is to understand how the junctional actin cytoskeleton controls the mechanics of TJs to regulate the flux of macromolecules across the TJ permeability barrier.  The PhD candidate will use CRISPR/Cas9 genome editing to generate genetically modified cell lines, several biochemical and biophysical approaches to study protein-protein interactions, 2D and 3D epithelial tissue culture models and assays to study protein function, as well as high resolution light and electron microscopy to visualize the junctional actin cytoskeleton. The candidate will also be given the opportunity to use zebrafish genetics and imaging to analyse gene function and paracellular transport.  **c) Preferred skills:**  The PhD candidate should have a comprehensive theoretical background in cell biology, molecular biology, and biochemistry, and should have experience in working in a cell biology laboratory. The candidate should also be proficient in English, in both verbal and written form, and be a team player. |
| **Supervisor contact:**  **If you have questions regarding this project, please email the Principal Investigator:**  **aludwig@ntu.edu.sg** |
| **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> |