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| **Research Theme: Protein degradation/Cancer Biology** |
| **PhD Research Project Title: Understanding the mechanistic basis of the Antizyme-mediated protein degradation system** |
| **Scholarship category (Please indicate the source of funding for this project):**  **SBS Research Student Scholarship (for SBS faculty only)** |
| **Principal Investigator/Supervisor: Prof Kanaga Sabapathy** |
| **Co-supervisor/ Collaborator(s) (if any): NA** |
| **Project Description**  **a) Background:**  The ubiquitin-proteasome system represents the well-studied, major mode of regulated proteolysis. However, other less explored proteolytic pathways exists, which are involved in diseases such as cancer. One such under-appreciated pathway involves Antizyme-1 (Az1), a 26kDa protein that was initially shown to bind to and lead to the degradation of ornithine-decarboxylase (ODC), through the proteasome in a ubiquitin-independent manner. Till now, there are six other substrates reported to be regulated by Az1, all of which are oncoproteins that are overexpressed or deregulated in cancers. The mechanistic basis of Az1-mediated substrate degradation and whether a common mode of action exists is unclear.  Furthermore, corroborating with its ability to degrade oncoproteins, Az1 overexpression retards the growth of cancer cells. Consistently, Az1 expression is decreased in cancers, concomitant with the overexpression of its inhibitor, Az inhibitor (AZIN). AZIN, which is highly homologous to ODC, binds to and inhibits Az1 from interacting with its substrates. The molecular details of Az1/AZIN interaction, and if it is amenable to disruption, thereby allowing for therapeutic benefit, is also unclear.  **b) Proposed work:**  The project will focus:  - uncovering novel Az1 substrates;  - exploring the mechanistic basis of Az1-mediated protein degradation, to determine if there is a common mode of action (on all the substrates);  - analyzing mice lacking Az1 to study its roles tumorigenesis.  This project involves molecular and cellular biology techniques, biochemistry, genome editing, mouse biology, etc. Candidates keen on exploring novel frontiers in protein quality controls and its impact on diseases such as cancers are welcomed to apply. indispensable    **c) Preferred skills:**  Preferred: Cell culture, biochemistry techniques, molecular cloning, mouse handling (though not all are indispensable). |
| **Supervisor contact:**  **If you have questions regarding this project, please email the Principal Investigator:**  **Prof Kanaga Sabapathy**  **Kanaga.sabapathy@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> |