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| **Research Theme: Cancer Biology** |
| **PhD Research Project Title: Investigating R-Loop Biology for Therapeutic Applications in PARP inhibitor resistant and chemo-resistant Cancer** |
| **Scholarship category (Please indicate the source of funding for this project):**   1. **SBS Research Student Scholarship (for SBS faculty only)** 2. **Grant Scholarship (NMRC, MOE Tier 2, NRF, NTU Central RSS etc)** 3. **Others** |
| **Principal Investigator/Supervisor: Li Hoi Yeung** |
| **Co-supervisor/ Collaborator(s) (if any):** |
| **Project Description**  **a) Background: Resistance to PARP inhibitors and platinum-based chemotherapies presents a significant hurdle in treating homologous recombination-deficient (HRD) cancers. These resistances often arise from mechanisms like secondary mutations restoring DNA repair functions or increased drug efflux, rendering standard treatments ineffective. Our novel small molecule, derived from a Singapore medicinal plant, induces R-loop accumulation and transcription-replication conflicts (TRCs), selectively targeting cancer cells with compromised DNA repair pathways. This project aims to investigate whether this compound can overcome resistance in PARP inhibitor-resistant and chemoresistant cancer models, potentially offering a new therapeutic avenue for patients with limited treatment options.**  **b) Proposed work: We propose a comprehensive study to evaluate the efficacy of our small molecule in overcoming drug resistance. In vitro, we will treat PARP inhibitor-resistant and chemoresistant cancer cell lines with the compound, assessing cell viability, apoptosis induction, and R-loop accumulation using assays like MTT, flow cytometry, and DNA-RNA immunoprecipitation (DRIP). In vivo, we will employ mouse xenograft models implanted with resistant cancer cells to examine tumor growth inhibition and survival rates post-treatment. Additionally, mechanistic studies will explore how the compound affects DNA damage response and replication stress markers. The outcomes will determine the potential of the small molecule as an effective treatment against resistant cancers.**  **c) Preferred skills: The project requires a multidisciplinary skill set. Proficiency in cell culture techniques is essential for maintaining and treating cancer cell lines. Expertise in molecular biology methods, such as PCR, Western blotting, and immunofluorescence microscopy, will be crucial for mechanistic studies and detecting R-loop formation. Familiarity with apoptosis assays and DNA damage markers will aid in evaluating cellular responses to treatment. Experience in animal handling and conducting xenograft studies is necessary for the in vivo component. Additionally, strong data analysis skills and the ability to interpret experimental results are vital for drawing meaningful conclusions and advancing the research effectively.** |
| **Supervisor contact:**  **If you have questions regarding this project, please email the Principal Investigator:** |
| **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> |