

<b>Research Theme:</b> DNA Damage and Repair (Future Healthcare)
<b>Research Project Title:</b> Perusing the role of a novel germline mutation in DNA repair factor: XPF/ERCC4 and its contribution to sarcoma tumorigenesis
<b>Principal Investigator/Supervisor:</b> A/P Andrew Tan
<b>Co-supervisor/ Collaborator(s) (if any):</b> Dr. Joanne Ngeow
<p style="text-align: center;"><b>Project Description</b></p> <p><b>a) Background:</b></p> <p>XPF endonuclease is one of the most important DNA repair proteins. Encoded by XPF/ERCC4 gene, XPF provides the enzymatic activity of XPF-ERCC1 heterodimer, an endonuclease that incises at the 5' side of various DNA lesions. XPF is essential for nucleotide excision repair (NER) and interstrand crosslink repair (ICLR). We have identified several novel germline mutations in patients suffering from soft tissue sarcomas affecting the catalytic domain. In the absence of its catalytic domain, we anticipate that ERCC4 interaction with ERCC1 will be affected, resulting in an impaired nuclear translocation upon DNA damage that culminates in cell death.</p> <p><b>b) Proposed work:</b></p> <p>There are at present no established treatment for GCTOB and the majority of sarcomas. Most of the commercially available chemotherapeutic drugs (platinum based) are DNA alkylating agents. The candidate will screen various drugs using cell viability assays, especially inhibitors (PARP/ATR) for checking synthetic lethality with ERCC4 deficiency using patient-derived cell lines. The project will also focus on the role of ERCC4 in telomeric regions. Recent reports suggest a putative role of ERCC4 in telomere length homeostasis. Most cancer cells adopt a mechanism of maintaining telomere stability through the Alternate Telomere Lengthening (ALT) pathway. The candidate will explore the role of ERCC4 in telomere stability.</p>
<p style="text-align: center;"><b>Supervisor contact:</b></p> <p style="text-align: center;"><b>If you have questions regarding this project, please email the Principal Investigator:</b></p>
<p style="text-align: center;"><b>SBS contact and how to apply:</b></p> <p style="text-align: center;">Associate Chair-Biological Sciences (Graduate Studies) : <a href="mailto:AC-SBS-GS@ntu.edu.sg">AC-SBS-GS@ntu.edu.sg</a></p> <p style="text-align: center;">Please apply at the following:</p> <p style="text-align: center;"><a href="http://admissions.ntu.edu.sg/graduate/R-Programs/R-WhenYouApply/Pages/R-ApplyOnline.aspx">http://admissions.ntu.edu.sg/graduate/R-Programs/R-WhenYouApply/Pages/R-ApplyOnline.aspx</a></p>