

**NUS Graduate School for Integrative Sciences and Engineering
Research Project Write-up**

Title of Project : **The role of the DNA damage response in the regulation of the tumor-associated antigen 1 (CD155) expression.**

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Short Description

Some of the most effective cancer chemotherapies cause DNA damage and trigger the p53-dependent DNA damage response to induce apoptosis in a cell-autonomous manner. However, disruption of p53 function is very common in human cancers. The combination of chemotherapies with treatments that do not rely on p53 function might therefore be an effective strategy to treat cancer. Recently, we have shown that chemotherapeutic agents via the DNA damage response alert the immune system by inducing the expression of NKG2D ligands and other yet unidentified ligands in a p53-independent manner. Preliminary experiments suggest that the expression of tumor-associated antigen 1 (CD155) is upregulated in response to DNA damage. CD155 is a ligand for the activating receptor DNAM-1 and CD96, which are constitutively expressed on most immune cells. **Our hypothesis is that the efficacy of cancer chemotherapies partially depends on the p53-independent induction of CD155 on tumor cells and the consequent increased sensitivity to NK cell and T cell lysis.** Strategies to enhance CD155-mediated activation of the immune system after chemotherapy may hold great promise for the treatment of cancer. The experiments herein are designed 1) to identify the molecular mechanisms of the DNA damage response-mediated CD155 regulation 2) to assess the functional consequences of CD155 upregulation in response to DNA damage and 3) to study regulation of CD155 expression *in vivo* using an AML mouse model and AML patient samples. Through the knowledge gained from these studies we hope to optimize NK cell immunotherapy protocols currently undertaken at the National University Hospital (Singapore) and St. Jude Hospital (USA).