

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

Title of Project : **ROLE OF NK CELLS AND NKG2D IN
CHEMOTHERAPY OF CANCER**

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Short Description

Anticancer agents that target DNA are among the most effective in clinical use and have produced significant increases in the survival of patients with cancer. Chemotherapeutic agents are usually administered at or near the maximum-tolerated dose resulting in severe toxicities that are life threatening in a significant number of patients. Even at these doses some tumor cells are resistant to chemotherapy because a cell intrinsic suicide programme, which is activated by chemotherapeutic agents, is often disrupted in such cells. Combining chemotherapies with treatments that eliminate tumor cells by additional means might therefore be a more effective strategy to treat cancer and decrease the frequency of relapses. We recently demonstrated that chemotherapeutic agents not only activate the suicide programme, but also render tumor cells more sensitive to natural killer (NK) cell-mediated lysis by inducing the expression of ligands for the activating NK cell receptor NKG2D. It is therefore plausible that part of the efficacy of cancer chemotherapy stems from enhanced NKG2D-mediated rejection of tumor cells. In this project, we propose to test the role of NKG2D and NK cells in the efficacy of chemotherapy using mouse tumor models and samples of human acute lymphoblastic leukemia patients that have undergone chemotherapy. Moreover, we will determine the potential of combining chemotherapy with simultaneous NK cell activation protocols or infusion of NK cells to further potentiate the immunomodulatory effects of some chemotherapeutics. The combination of immunotherapy and chemotherapy may offer a new strategy to improve the efficacy, specificity and safety of cancer treatments. 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).