DEVELOPMENT OF A CELL-BASED IL-12 CANCER IMMUNOTHERAPY USING A GENETICALLY ENGINEERED MOUSE MODEL OF BREAST CANCER

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Interleukin-12 (IL-12) is a pro-inflammatory cytokine that plays a major role in the immune response. IL-12 causes increases in interferon-gamma (IFN-g) production, leads to a Th1 differentiation bias and cell-mediated immunity. Due to its many potent pro-inflammatory effects, the use of IL-12 for cancer immunotherapy continues to be the subject of clinical interest. Many of the IL-12 mediated therapies developed in the past failed clinical trials due to toxicity associated with high systemic IFN- g. To reduce systemic levels of IL-12 we are using autologous cancer cells to deliver high levels of IL-12 at the local site where the immune system meets the cancer cell. Upon injection, these IL-12 transduced host tumour cells cause sustai3ned immune mediated rejection, even to challenges with the original non-transduced parent tumour. The effectiveness of this model has thus far been demonstrated in murine leukaemias and various solid tumour models. Current work in our lab looks at the development of a transgenic model of breast cancer, which will be used to demonstrate that IL-12 cancer immunotherapy can be expanded to clinical relevant models. Our objective is to develop a clinically relevant model of cell-based IL-12 cytokine immunotherapy using the MMTV-PyMT breast cancer model

It has been demonstrated that primary MMTV-PyMT breast cancer cells can be maintained in culture and enriched for an epithelial tumour forming population. From this enriched population, clones of non-transduced and IL-12 transduced cell lines have been generated. Subcutaneous injection of non-transduced PyMT cells results in tumour development, while injection of IL-12-transduced PyMT cells results in tumour clearance.