ACT Cancer Council - Final Project Report

Application ID: **APP1028722**
First Named Investigator: **Joseph G. Altin.**

Project Title: ***A new plasmid DNA delivery system – for vaccine development and cancer immunotherapy.***

The body's natural defense mechanism against infections - the immune system - also plays an important role in defending us against cancer. The successful treatment of cancer by immunotherapy however, requires more effective means to enhance tumour immunity and to counteract cancer-induced immune-suppression. We recently developed a safe and effective lipid-based platform for targeting nucleic acids (genes encoded within plasmid DNA) directly to antigen-presenting cells, and to blood vessels within tumours, to enhance immune responses to cancer. The aim of the work supported by the CCACT was to show: firstly, that targeted pDNA-lipoplexes encoding immune-modulatory factors and tumour antigen (MUC1) directly to antigen-presenting cells can elicit potent anti-tumour responses; and secondly, that lipoplexes also can be targeted directly to established tumours to counteract tumour-induced immune-suppression. The potential of this approach to fight human cancer was tested in preclinical mouse models of human cancer. We produced 9Flg-lipoplexes containing DNA encoding antigen MUC1, a tumour–associated antigen that is highly expressed in many human cancers, and used these to vaccinate tumour-bearing mice. Our results show that vaccination of mice with pMUC1-lipoplexes elicit strong MUC1 anti-tumour responses; the mice showed an increase in the number of MUC1-specific cytotoxic T cells, and an increase in the level of MUC1-specific antibody in blood. Importantly, the mice vaccinated with pMUC1-lipoplexes exhibited strong inhibition in the growth of their established B16 melanoma tumours. These findings demonstrate that the approach can be used to vaccinate against human tumour antigens. Studies are currently underway to target lipoplexes to tumours to overcome tumour-induced immune suppression. Since the targeting strategies employed target both murine and human antigen presenting cells and tumours, successful completion of this work can immediately be followed by work to translate the findings to clinical trials to establish efficacy and improve treatment outcomes in patients.

Publication:

ALTIN JG (2012) Liposomes and other nanoparticles as cancer vaccines and immunotherapeutics. Book: Chapter 8 In: *Innovations in Vaccinology: from design, through to delivery and testing*. S. Baschieri Ed, Springer (In press, 31 July 2012).