MEDICAL AND SCIENTIFIC COMMITTEE
ANNUAL LAY REPORT 2015

Lay Project Title:	Cancer specific nanoparticles for improved chemotherapy
Chief Investigator(s):	Dr Suzanne Cutts, A/Prof Paul Pigram, Prof Geoff Pietersz, Dr Carleen Cullinane
Unit/Institution:	Department of Biochemistry, La Trobe University
Years Funded:	2013-2015

1 Lay Abstract

The anthracyclines are amongst the most widely used and effective drugs for treatment of a broad range of cancer types. Of all the anthracyclines available doxorubicin is the major clinically used drug. We have discovered that the ability of doxorubicin to kill cancer cells is significantly increased by the simple molecule formaldehyde. To enable formaldehyde to be delivered to doxorubicin-treated cancer cells the aim of this research is to encapsulate the formaldehyde in delivery vehicles called nanoparticles. These nanoparticles can then be modified on their surface with tumour-homing peptides. The purpose of the nanoparticles is to prevent release of the formaldehyde in the bloodstream and specifically deliver their contents to tumour cells. We have found the best types of nanoparticle for our research are micelles. These micelles are very efficient at encapsulating doxorubicin for delivery to cancer cells. We have established reproducible methods to make the micelles, and test their size and appearance. We have successfully encapsulated several chemotherapy drugs inside the micelles for drug delivery purposes and found that the drug-micelle preparations are stable for at least two weeks when refrigerated. We have also prepared formulations with tumour-homing peptides on their surface. Furthermore we encapsulated four different formaldehyde-releasing drugs inside the micelles. However, these preparations are not stable as the formaldehyde-releasing drugs leak out of the micelles within 10 hours. After investigating this problem we found that the drugs that are able to stay inside the micelles have several predictable characteristics; they are positively charged molecules, and they also need to have a bulky uncharged portion incorporated into their structure. We now have developed three different nanoparticle formulations to deliver chemotherapy drugs and now these will be tested in the final year of the project. We are utilising a mouse model of metastatic breast cancer to determine whether our new formulations are superior to conventional chemotherapy.

2 **Please list <u>all papers arising from this research project</u>, which have been published, or accepted for publication, in refereed journals since the commencement of this grant. Please list in chronological order, include title, sequence of authors, first, and last pages, name, volume and date of journal.**

Briefly annotate major findings within these publications

N/A

3 **Please list any presentations relating to this research project that were made at scientific meetings during 2015.**

Please identify the meeting, provide the tile of your presentation and indicate the type of presentation

	(plenary, invited, selected, poster etc, or session chair) EACR-AACR-SIC Special Conference on Anticancer Drug Action and Drug Resistance: From Cancer Biology to the Clinic, June 20 - 23, 2015, Palazzo dei Congressi, Florence, Italy S. Cutts, S. Pepe, T. Robinson, A. Rephaeli, A. Nudelman, C. Cullinane, D. Phillips, D. Rayner. A new strategy to prevent anthracycline-induced cardiotoxicity while improving anti-cancer activity, Poster presentation
4	**Certification by Chief Investigator**
	I confirm that the above details are correct. Signature:  Date: 9/01/2015 Suzanne Cutts