


## MEDICAL AND SCIENTIFIC COMMITTEE ANNUAL LAY REPORT 2008

<b>1</b>	<b>Lay Project Title:</b>	Identify the best anti-tumour T cell responses to optimize future vaccine
<b>2</b>	<b>Grant Holder:</b>	Dr Weisan Chen
<b>3</b>	<b>Unit/Institution:</b>	Ludwig Institute for Cancer Research
<b>4</b>	<b>Years Funded:</b>	2006-2008
<b>5</b>	<b>Funding 2008:</b>	\$70,000
<b>6</b>	<b>Lay Abstract</b>	<p>Killer T lymphocytes are one of the major immune surveillance mechanisms against tumour. They eliminate tumour cells upon recognising tumour-associated protein fragments (called epitopes) displayed by a molecule called HLA on the tumour cell surface. Each tumour cell could have different tumour-associated proteins and their fragments could be displayed by different HLA molecules from the HLA-A, HLA-B, and HLA-Cw families. Any given individual can express up to six distinct HLA. It is then very important to find out which fragment/HLA combination could stimulate the largest immune response, which might be more useful when incorporated in a real cancer vaccine.</p> <p>We hypothesize that such a combination is both tumour protein and individual HLA dependent. Therefore, we have systematically looked for evidence for that in both melanoma patients who had anti-NY-ESO-1, one of the most promising tumour proteins, response naturally and those after receiving NY-ESO-1 vaccination in our clinical trials.</p> <p>So far we have demonstrated that our hypotheses have been valid. Through screening specific T cell responses systematically, we have identified multiple novel epitopes derived from NY-ESO-1 to which the immune system mounts most vigorous responses. We have also shown that quite a few HLA molecules, such as HLA-Cw3, HLA-B7, HLA-B18, HLA-B35, are clearly more important in terms of displaying tumour epitopes than others.</p> <p>Due to our systematic screen approach and effort, rather than the common computer program-guided epitope mining, quite a few long and unexpected epitopes have been found. We now have studied the structure of these long epitopes when they are displayed by the corresponding HLA molecules and their intracellular routing properties. The knowledge acquired from our project will help us to speed up epitope discovery effort for this and other tumour proteins. Importantly, we hope through this kind of effort to identify the most useful tumour epitopes which might be used as future vaccine candidates. Our results emphasize the need for an individually tailored vaccine strategy.</p>
<b>7</b>	<b>Please list papers (NB: only papers arising from this research project), which have been published, or accepted for publication, in refereed journals by any of the principal investigators during 2008. Please include title, sequence of authors, first and last pages, name, volume and date of journal.</b>	<p>Javier Garcia Casado, Jozef Janda, Joe Wei, Laurence Chapatte, Sara Colombetti, Pedro Alves, Gerd Ritter, Maha Ayyoub, Danila Valmori, <b>Weisan Chen</b> and Frédéric Lévy. (2008) Lentivector immunization induces tumor antigen-specific B- and T-cell responses <i>in vivo</i>.</p>

	<p><u>European J Immunology. 38(7):1867-1876 IF=4.77</u></p> <p>Lisa M. Ebert, Yu Chi Liu, Craig S. Clements, Neil C. Robson, Heather Jackson, Jessica L. Markby, Nektaria Dimopoulos, Bee Shin Tan, Immanuel F Luescher, Ian D. Davis, Jamie Rossjohn, Jonathan Cebon, Anthony W. Purcell and <b>Weisan Chen</b> (2009). A long, naturally presented immunodominant epitope from NY-ESO-1 identified through vaccination reveals novel aspects of anti-tumor immunity. <i>Cancer Res in press</i> (accepted on Nov 13, 2008) <b>IF=7.672</b></p>
<p><b>8</b></p>	<p><b>Please list any symposia/plenary presentations relating to this research project, which were made at major national or international scientific meetings during 2008. Please indicate the level of your contribution, ie poster, speaker, invited speaker or session chair.</b></p> <p>I was an invited speaker for the <b>BIT Life Sciences' 1<sup>st</sup> Annual World Vaccine Congress 2008 held in San Shui, China.</b> The title of my talk was <b>“ISCOMATRIX™ adjuvant targets tumor antigen efficiently to cross-presentation pathway and induce broad CD4+ and CD8+ T cell responses in humans”.</b></p>
<p><b>9</b></p>	<p><b>Certification by Grant Holder</b></p>
	<p>I confirm that the above details are correct.</p> <p>Signature: _____  _____ Date: _____ <u>06-01-09</u> _____</p> <p>Name (please print): Weisan Chen</p> <p>_____</p>

**THANK YOU FOR YOUR ASSISTANCE**