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Cancer immunotherapy utilizing gene-modified T cells: From the bench to the clinic

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Adoptive immunotherapy involving genetic modification of T cells with chimeric antigen receptors (CAR's) is a promising approach for treatment of cancer although has resulted in on target toxicity in some trials. To explore this more fully, we utilized a self-antigen mouse model that expresses human Her-2 as a self-antigen in brain and mammary tissueto assess the ability of T cells expressing an anti-Her-2 chimeric receptor to eradicate Her-2+ tumor. In adoptive transfer studies, we demonstrated significant improvement in the survival of mice bearing Her-2+ tumor following administration of anti-Her-2 T cells compared to control T cells. Importantly, anti-tumor effects were not associated with any autoimmune pathology in normal tissue expressing Her-2 antigen.The reduction in tumor growth correlated with localization of transferred T cells at the tumor site andan antigen-specific recall response could be induced in long term surviving mice following rechallenge with Her-2+ tumor. In further studies we have also utilized gene-engineered T cells in combination with other immune-based therapies such as anti-PD1 which resulted in significantly enhancing therapeutic effects in mice. We have recently completed a Phase I clinical trial in patients with acute myeloid leukaemia targeting the Lewis Y carbohydrate antigen and demonstrated that the therapy was well tolerated.

Biography

Phillip K Darcy is currently a NHMRC Senior Research Fellow and Group Leader at the Peter MacCallum Cancer Centre. His work has focused on developing novel T cell based immunotherapy approaches for cancer in preclinical mouse models and translating this into patients. His most recent studies have involved the development of combination immune based therapies which is showing tremendous promise. He has received project support from numerous national and international funding bodies to support his work and has published his work in premier cancer journals.

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