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Strong immunogenicity of membrane nanovesicles from dendritic cells

Interest in cancer immunotherapy has been bolstered by the recent success of T cell checkpoint blockade with specific antibodies. This approach might be especially effective if combined with methods for enhancing tumor immunogenicity, eg injection of dendritic cells (DC) expressing tumor antigens. Currently, DC therapy is successful in only a small proportion of patients, perhaps reflecting poor homing of injected DC. To overcome this problem, we have generated cell-surface membrane nanovesicles from in vitro-generated bone-marrow-derived mature DC. When loaded with specific peptide, the vesicles are stimulatory for naïve TCR transgenic CD8 T cells in vitro without APC, though only with aggregated vesicles and not with vesicles dispersed into nanovesicles by sonication. By contrast, after IV injection in vivo, the nanovesicles are much more immunogenic than aggregates and generate strong proliferation and effector function of CD8 cells in both spleen and LN, reflecting widespread distribution of the vesicles and uptake by host APC. Preliminary work has shown that injection of the vesicles can be used vaccinate against tumor growth and also reject established tumours in mice.

Biography

After PhD at the Walter Eliza Hall Institute in Melbourne and post-docs in Switzerland and UK, Jonathan Sprent worked for 30 years in the USA, first at the University of Pennsylvania in Philadelphia and then at The Scripps Research Institute in San Diego. During this time he worked on many aspects of T cell biology, including T-B collaboration during antibody production, role of T cells in graft-versus host disease after bone marrow transplantation, positive and negative selection during T cell differentiation in the thymus, T cell survival and homeostasis of mature T cells, construction of artificial antigen-presenting cells (APC) from insect cells, and the use of monoclonal antibodies (mAb) to enhance and target the activity of IL-2 and other cytokines. Jonathan moved from the USA in 2006 to form a research group at the Garvan Institute where he has continued to work on T cell differentiation and function. The lab is supported by several NHMRC grants and has collaborative interactions with many other investigators, both nationally and internationally.

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