Please add the affiliation (number) in each

A-03

Activation of antigen-specific T lymphocytes by CD137 ligand generated dendritic cells

Zulkarnain Harfuddin (?), Shaqireen Kwajah (?), Adrian Sim (?), Paul MacAry (?), and Herbert Schwarz(?)

(1) Department of Physiology and Immunology Programme, National University of Singapore, Singapore. (2) NUS Graduate School for Integrative Sciences and Engineering, National University of Singapore, Singapore.

Abstract

Dendritic cells (DC) are professional antigen presenting cells that play an essential role in regulating and orchestrating T cell-based immunity. Their unique property has prompted an intense research in the field of DC-based immunotherapy. Nonetheless, DC vaccination is still in its infancy and further improvements in terms of DC preparation, antigen-loading and increasing their immunostimulatory capacity are still being optimized. Here, we describe a novel form of potent dendritic-like cells generated by CD137-ligand (CD137L) reverse signalling into peripheral monocytes. The ligand for CD137 (CD137L) is expressed on peripheral human monocytes and delivers a potent activating signal via reverse signaling. Treatment of monocytes with a recombinant CD137 protein that induces reverse signaling through CD137L reduces typical macrophage characteristics such as phagocytosis and CD14 expression. However, typical characteristics of DC including endocytosis, costimulatory molecule expression and the ability to stimulate proliferation of allogenic naive T-lymphocytes are induced. CD137L-generated DC (CD137L-DC) can be further matured by a basic maturation cocktail which leads to an increase in DC markers such as CD83, CD86 and HLA-DR. This in turn enables a stronger activation of allogeneic T cells. We also tested the ability of CD137L-DC to initiate antigen-specific T cell activation in an autologous setting. Using cytomegalovirus (CMV) pp65 peptides, we show that matured CD137L-DC are able to activate pp65-specific T cells more potently than classical DC. These in vitro data show that CD137L-DC are potent antigen presenting cells and should be evaluated for human immunotherapy.