Novel regulators of CD8+ T-cell functions in the skin

Bridge, Jennifer A.; Overgaard, Nana Haahr; Cruz, Jazmina L. G.; Veitch, Margaret; Frazer, Ian H.; Steptoe, Raymond; Wells, James W.

Publication date:
2016

Document Version
Peer reviewed version

Link back to DTU Orbit

Citation (APA):

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.
Novel regulators of CD8$^+$ T-cell functions in the skin

Jennifer A. BRIDGE$^1$, Nana H. OVERGAARD$^1$, Jazmina L.G. CRUZ$^1$, Margaret VEITCH$^1$, Ian H. FRAZER$^1$, Raymond J. STEPTOE$^1$ and James W. WELLS$^1$.

$^1$ The University of Queensland Diamantina Institute, Translational Research Institute, Brisbane, QLD 4102, Australia, Email: j.bridge@uq.edu.au

Cancer Council statistics show that Australia has the highest rate of skin cancer in the world (twice that of the USA and UK), and predicts 2 in 3 Australians will be diagnosed with skin cancer before the age of 70. Tumour-specific CD8$^+$ T-cells are well-recognised for their importance in eliciting tumour-rejection, however, in many cases tumour-specific CD8$^+$ T-cells within the tumour microenvironment are dysfunctional. The regulation of CD8$^+$ T-cell activity in the tumour microenvironment is poorly understood. This study aimed to explore the mechanisms involved in the regulation of CD8$^+$ T-cells in the skin as a prelude to tumour studies. We have generated a new experimental mouse model in which activated CD8β$^+$ T-cells from donor mice were introduced into RAG1KO mice in order to assess CD8$^+$ T-cell deregulation in the absence of conventional-regulatory T-cells (Treg). When RAG1KO mice subsequently received CD4-depleting antibody, CD8$^+$ T-cell-mediated destruction of the ear skin occurred. However, this did not occur in mice administered control-antibody. Analysis of lymph nodes 30 days post CD8β$^+$ T-cell transfer showed no evidence of classical CD4$^+$FoxP3$^+$ Treg indicating regulation is mediated by a separate, distinct cell type. Using the model, we have identified CD4$^+$ cells, which are distinct from classical-Treg, and we are subsequently defining the mechanism by which these cells exert control of CD8$^+$ T-cell function in the skin. Uncovering novel pathways of CD8$^+$ T-cell regulation will shed new light onto regulatory influences of CD8$^+$ T-cell function within tumours and yield opportunities to develop better treatment options for cancer patients.