Journal for ImmunoTherapy of Cancer

POSTER PRESENTATION Open Access

Core skin DC signatures control immune tolerance to skin cancer and limit anti-tumor immunity

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From 30th Annual Meeting and Associated Programs of the Society for Immunotherapy of Cancer (SITC 2015) National Harbor, MD, USA. 4-8 November 2015

Background

Dendritic cells (DC) are gatekeepers of immunity, critical to both an initiate immune response upon infection and promote tolerance to self-antigens.

Methods

We have just established that DC subsets in the skin that constitutively migrate into LNs can individually and collectively temper an on-going immune response. Tissue DC originating in skin share a unique transcriptome signature geared towards immune dampening when compared to their lymphoid counterparts in both mouse and human.

Results

Here we demonstrate expression of unique core skin DC transcripts are closely associated with increased clinical aggressiveness of BCC in humans and the stratify stage 4 melanoma outcomes. In mice, loss of signature genes in DC, which include but are not limited to PD-L1/PD-L2, lead to enhanced antigen-specific immunity, decreased tumor growth, and improved anti-tumor vaccine priming to melanoma skin cancer by distinguishable molecular control of T cell effector function and clonal proliferation.

Conclusions

These data suggest core skin DC signatures regulate the immune-epithelial interface.

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Published: 4 November 2015

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doi:10.1186/2051-1426-3-S2-P205
Cite this article as: Nirschl *et al.*: Core skin DC signatures control immune tolerance to skin cancer and limit anti-tumor immunity. *Journal for ImmunoTherapy of Cancer* 2015 **3**(Suppl 2):P205.