Cutaneous immune system in health and disease

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Skin Worshop - NSC
19 Oct 2013
Skin immune resident cells

Epidermis
- stratum corneum
- stratum granulosum
- stratum spinosum
- stratum basale

Dermis
- dermal DC
- CD8+ T cell
- macrophage
- basal membrane
- basal keratinocyte
- fibroblasts
- pDC
- mast cell
- CD4+ TH2 cell
- CD4+ TH1 cell
Macrophages

Dendritic cells

Sentinels of the immune system
Antigen presenting cells

Scavengers of the immune system

Tissue immunity

Tissue homeostasis
Dendritic cells (DC)

Tolerance
Self antigens
Auto-immunity

Immunity
Pathogens
Vaccination
Why are DC important?

- **Basic science**: understanding immune responses

- **Clinical translation**: role in disease processes, therapeutic targets, vaccination

Define DC profile and function in infection/inflammation
CD11c (DCs)
FXIIIa (macrophages)
CD3 (T cells)

Wang et al. *J Invest Dermatol.* In press
CD11c (DCs)
FXIIIa (macrophages)
CD3 (T cells)
Cutaneous DC network

INSIST ON DC SUBSET FUNCTION

Epidermis

CD1c+ DC


(Nestle CD141+ DC)
CD14+ DC


FXIIIa+ dermal dendrocyte
a.k.a melanophages
a.k.a macrophages
‘FIXED’

Langerhans cell

Skin

Dermis
Cutaneous DC network

Role in anti-viral immune response
Major implications for vaccine design

Haniffa, Immunity, 2012
Schlitzer, Immunity, 2013
Human skin program: Dendritic cells in health and disease

I
Microscopy
Collagenase
Flow cytometry and cell sorting
Epidermis
Dermis
APC
Non-leucocytes
T cells

Gene expression
Antigen presentation
Cross presentation
Cytokine profile
Functional Composition
CD14+ DC
CD1a+ DC
CD141+ DC
macrophage

II
Identify molecular targets
Validation in preclinical model

Healthy vs Disease

I & II
Human skin program: 
Dendritic cells in health and disease

Skin platform: cutaneous inflammation and immune profiling

Identification of DC subsets in chronic inflammatory skin diseases using flow cytometric analysis (Dr Mark Tang)

Evolution of cutaneous DCs populations with age and in UV exposed zones (photo-aging)

Immune responses to Propionibacterium acnes: Role of dendritic cells subsets in the pathophysiology of Acne Vulgaris
Identification of DC subsets in chronic inflammatory skin diseases using flow cytometric analysis (Dr Mark Tang and Dr Amelie Seghers)

Atopic dermatitis  
Psoriasis  
Lichen Planus
Identification of DC subsets in chronic inflammatory skin diseases using flow cytometric analysis
(Dr Mark Tang and Dr Amelie Seghers)

Immune phenotyping

Blood

Skin
Identification of DC subsets in chronic inflammatory skin diseases using flow cytometric analysis
(Dr Mark Tang and Dr Amelie Seghers)

Immune phenotyping
Sorting of pure DC populations
Low-density array by nanostring

n=3 for condition 1
n=0 for condition 2
n=1 for condition 3

Immune profiling
Immune Pathways
Correlation with clinical score
- Adjunct Associate Prof, Program in Emerging Infectious Disease, DUKE-NUS
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Donovan Low
Laurent Renia lab
Lai Guan Ng lab
Microarray core facility (F. Zolezzi)
Bioinformatics core (M. Poidinger)
Flow cytometry core (A. Larbi)
Antibody platform (CI Cheng)