Decreased Cutaneous T Cell Immunity During Ageing
Basal Cell Carcinoma
VZV Re-activation (Shingles)
Human Cutaneous Antigen-Specific Memory T Cell Response

Reed J. et al, J. Exp. Med. 2004
Kinetics Of Antigen-Specific CD4⁺ T Cell Infiltration After Skin Challenge

Days post PPD injection

Perivascular T cells/unit area

%IFN-γ CD4⁺ T lymphocytes

T cell infiltrate
PBMC
Blister
Reduced Clinical Response To Antigen Challenge During Ageing

Young Day 3

Old Day 3
Reduced Clinical Response To Antigen Challenge
Reduced T Cell Infiltration After Antigen Challenge

Young

Old

Young Old

CD3

CD4
E-selectin Expression Reduced In Old Injected Skin

CD31	E-SELECTIN	MERGE

YOUNG

OLD
Cutaneous Defect To Antigen Challenge During Ageing

- Defective response to PPD, Candida, VZV challenge
- Decreased infiltration of antigen-specific CD4+ T cells (immunosurveillance)
- Not due to defects in chemokine receptor expression or physical capacity for migration
- Results from defective endothelial cell activation that prevents entry of T cells
- Why is there defective endothelial activation?

Agius et al J.Exp. Med 2009
Decreased TNF-α and IFN-γ in Old Skin After Antigen Challenge

- **TNF-α**: Young > Old, p = 0.01
- **IFN-γ**: Young > Old, p = 0.01
- **IL10**: NS

Concentration (pg/ml)
Defective TNF-α Production By CD163+ Macrophages During Ageing

A

YOUNG D3

OLD D3

CD163

CD163

B

OLD D3

CD163 and TNF-α merge

CD163 and TNF-α merge

C

TNF-α

TNF-α
Why Is TNF-a Secretion Defective In Old Macrophages?

**Modulation of monocyte/macrophage function by human CD4+CD25+ regulatory T cells.**
Taams LS, van Amelsfort JM, Tiemessen MM, Jacobs KM, de Jong EC, Akbar AN, Bijlsma JW, Lafeber FP.

*Tregs suppress TNF-α secretion by macrophages*

**CD4+CD25+Foxp3+ regulatory T cells induce alternative activation of human monocytes/macrophages.**
Tiemessen MM, Jagger AL, Evans HG, van Herwijnen MJ, John S, Taams LS.
Proc Natl Acad Sci. 2007;104:19446.

*By steering monocyte differentiation away from proinflammatory towards anti-inflammatory cytokine production*
Cutaneous Tregs are Increased In Old Subjects
Foxp3⁺ Cells In The Skin Have A Treg Phenotype

Blister

FOXP3

CD4

Foxp3⁺

Foxp3⁻

CD25

CD127

CD39

IFN-γ

IL-2
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