

Decreased TNF- α synthesis by macrophages restricts cutaneous memory T cell immunosurveillance ageing.

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Immunity declines during ageing, however the mechanisms involved are not known. In this study we show that cutaneous delayed type hypersensitivity responses (DTH) to recall antigens is significantly decreased in old individuals and that this was unrelated to CCR4, CLA or CD11a expression or physical capacity for migration of CD4⁺ T cells. Instead, there was defective activation of dermal blood vessels of these subjects that resulted from decreased TNF- α secretion by macrophages after antigen-challenge *in vivo*. However, isolated skin macrophages from these subjects could be induced to secrete TNF- α after stimulation with TLR 1/2 or TLR 4 ligands *in vitro*, indicating that the defect is reversible. The decreased conditioning of tissue microenvironments by macrophage-derived cytokines may therefore lead to defective immunosurveillance by memory T cells. This may be a predisposing factor for the development of malignancy and infection in the skin during ageing.