GM-CSF modulates the migratory phenotype of vaccine-induced T cells by enhancing CXCR3 expression

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Background

Selective chemokine receptor

Local microenvironment

Tissue specific dendritic cells

CXCR3

CCR4

CCR9

Inflammatory tissue
Tumor tissue

Skin

Small intestine
Aim of the study

Analysis of

• Expression of chemokine receptors CXCR3 and CCR4 on vaccine-induced T cells.

• Influence of GM-CSF as vaccine adjuvant on chemokine receptor expression.
Materials & Methods

- **Patient samples**: stage III/IV melanoma
  - 2 cohorts
    1) Tyrosinase peptide + KLH + GM-CSF
    2) Tyrosinase peptide + KLH

- T cell response assessment
  by IFNγ flow cytometry analysis
Phase I trial of tyrosinase peptide with adjuvants GM-CSF and KLH

IFNγ-secreting T cells / 10^6 PBMC

Patient identification

Tyr specific

KLH specific

Scheibenbogen et al. 2003
CXCR3 expression on KLH-specific T cells

- **no antigen**
  - CXCR3
  - IFNγ
  - Tyr + KLH cohort
  - Tyr + KLH + GM-CSF cohort

- **KLH**
  - CXCR3
  - IFNγ
  - Tyr + KLH cohort
  - Tyr + KLH + GM-CSF cohort
CXCR3, CCR4 and CCR9 expression on KLH-specific T cells

- % CXCR3+ T cells
- % CCR4+ T cells
- % CCR9+ T cells

With GM-CSF
- Total CD4+ T cells: n=8
- KLH-specific T cells: n=7

Without GM-CSF
- Total CD4+ T cells: n=7
- KLH-specific T cells: n=6

P-value: p=0.001

Total CD4+ T cells
- KLH-specific T cells

n=4, n=7
Follow up of CXCR3 profile of KLH-specific T cells

- Total CD4+ T cells
- KLH-specific T cells

**With GM-CSF**
- 1 month: 30% CXCR3+ T cells
- 6 months: 40% CXCR3+ T cells
- 17 months: 50% CXCR3+ T cells

**Without GM-CSF**
- 1 month: 20% CXCR3+ T cells
- 4 months: 30% CXCR3+ T cells
- 18 months: 30% CXCR3+ T cells
Summary

• These results show for the first time in humans that it is possible to modulate chemokine receptor expression on T cells generated by vaccination by modifying the local vaccine milieu.

• Immunization protocols that induce T cells expressing CXCR3 may be of considerable value for improvement of immune therapy strategies.