ROLE OF T-CELL SUBSETS IN REGULATION OF IMMUNE RESPONSE

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Cancer cure 'may be available in two years'

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Cancer sufferers could be cured with injections of immune cells from other people within two years, scientists say.

*Red tape hinders cancer research, says report*

US researchers have been given the go-ahead to give patients transfusions of “super strength” cancer-killing cells from donors.

Dr Zheng Cui, of the Wake Forest University School of Medicine, has shown in laboratory experiments that immune cells from some people can be almost 50 times more effective in fighting cancer than in others.

Dr Cui, whose work is highlighted in this week’s New Scientist magazine, has previously shown cells from mice found to be immune to cancer can be used to cure ordinary mice with tumours.
Adoptive lymphocyte transfer

1. Isolate lymphocytes from blood or tumor infiltrate
2. Expand lymphocytes by culture in IL-2
3. Transfer lymphocytes into patient, with or without systemic IL-2
4. Tumor regression
~ $5 \times 10^{11}$ lymphocytes in human body

- 2% in peripheral blood
- 98% in all organs
- $5 \times 10^{11}$ lymphocytes travel through the blood each day
- Most lymphoid and non-lymphoid organs are included in migration / circulation routes
Central dogma of cancer immunology
CD4+

Th1

Th2
Balance between Th1 and Th2

Precursor Helper T Cells Differentiate into Two Types

- Th1
  - T-Bet
  - Delayed-type hypersensitivity
  - Macrophage activation

- Th2
  - GATA3, cMaf
  - Antibodies
  - Allergic responses

The T-bet Knockout

- Th2
  - Asthma
  - Autoimmunity
  - Tumor immunity
  - Transplant rejection
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Elimination of Tregs

Enhancing antigen presentation: anti-CD40

Provision of antigen from lysed tumour cells

CD4\(^+\) T cell

CD8\(^+\) T cell

Co-stimulation to T cells: anti-4-1BB, anti-OX40

 CTL

 CTL

 CTL

 Tumour cell

Counteracting immunoregulation: anti-CD25, anti-CTLA-4
CD4+

Th17  Treg
CD8+

CD28+/CD57-  CD28-/CD57+
Reciprocal relationship between CD28 ir CD57

CD3+CD8+CD28- = CD8hi CD57+
CD8+CD28+
CD8+CD28-
Flow cytometry of CD8+ lymphocytes

CD8 PE

CD57 FITC

CD8hCD57+

CD8+CD28- (CD8h CD57+)

- Clonal expansion
- Short telomeres
- Anergy
- Increase with age
- Consequence of chronic antigenic stimulation
- Alcoholism
CD8+CD28- (CD8h CD57+)

- Biomarker of poor prognosis in RCC
- Biomarker of good prognosis in multiple myeloma, melanoma
CD8hCD57+ lymphocytes in RCC

RCC - IFNα

Survival

Non-treated
Treated

p = 0.02

CD8hCD57+ ≥ 30%

RCC - IFNα

CD8hCD57+ < 30%

Survival

- - - Non-treated

Treated

p = 0.11

Months

Changes of CD8highCD57+ lymphocytes in melanoma patients after IFNα

Prognostic significance of CD8hCD57+ lymphocytes in melanoma after IFNα

Prognostic significance of CD8highCD57+ lymphocytes in bladder carcinoma patients after intravesical IL-2

Perioperative immunomodulation in RCC

Jankevičius F, Characiejus D, Pašukonienė V, et al.
PALDIES PAR UZMANĪBU!