Cord blood: a source of antiktumour specific T cell clones?

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Most approaches targeting rapidly dividing cells, also affect normal cells and result in side effects that limit treatment.

Harnessing the immune system to precisely target cancer cells without harming normal cells represents the challenge of Cancer Immunotherapy.

The reasoning for cancer immunotherapy

The ultimate goal of cancer immunotherapy

Cancer vaccine modalities

Anti-cancer vaccination

Cancer vaccine principles

Thorough analysis of pre-existing anti-tumor T cell responses

Adoptive T cell cancer therapy

Cancer vaccine principles
Significance of cancer immunotherapy

20 years of cancer immunotherapy

Clinical response

T cell response

Group A
Group B
Group C
Group D

All trials
(antigen, immunostimulant, age, sex, type of Ca etc.)
< 3-5% of vaccinated patients present with short lived regressions

Immunosenescence

Senescence of CD8 T cells

Patients with cancer have x10 more pCTL than healthy subjects of same age
Senescence of CD8 T cells

CD8 T cell clones of healthy individuals multiply better and bind to MHC peptide stronger.

Senescence of CD8 T cells

Early (PD=5) vs. late (PD=125) T cell replicative senescence


What does the future hold for cancer immunotherapy?
The **FUTURE** of cancer immunotherapy

"**YOUNG**" (allogeneic) lymphocytes promise to be more efficient in combating homologous tumors than the senescent host lymphocytes.

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The **FUTURE** of cancer immunotherapy

<table>
<thead>
<tr>
<th>Trials</th>
<th># of pts</th>
<th>Response rate % (CR/PR/NS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crispi, 2005</td>
<td>39</td>
<td>50% (2/7)</td>
</tr>
<tr>
<td>Braghi, 2002</td>
<td>8</td>
<td>57% (5/9)</td>
</tr>
<tr>
<td>Pedrazzoli, 2002</td>
<td>6</td>
<td>0% (0/6)</td>
</tr>
<tr>
<td>Kiris, 2004</td>
<td>12</td>
<td>33% (4/12)</td>
</tr>
<tr>
<td>Hentrich, 2003</td>
<td>8</td>
<td>30% (2/6)</td>
</tr>
<tr>
<td>Lina, 2000</td>
<td>15</td>
<td>47% (7/15)</td>
</tr>
</tbody>
</table>

**RCC**

Braghi, 2002 | 6 | 33% (2/6) |
| Lina, 2000 | 8 | 38% (3/8) |
| Cancela, 2002 | 17 | 20% (3/17) |
| Bishop, 2004 | 16 | 38% (6/16) |

Clinical trials on RIST HSCT for RCC

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The **FUTURE** of cancer immunotherapy

**A.** Can allogeneic lymphocytes combat homologous tumors?

**B.** Can antigen-specific T cells be primed/expanded from naïve UCB lymphocytes?

- Successful attempts have been made in expanding functionally active virus-specific T cells of neonatal origin that target CMV, adenovirus and EBV from naïve UCB T cell populations
- UCB lymphocytes can be expanded in vitro by approximately 1000-fold with a phenotype and function equivalent to those of expanded peripheral blood lymphocytes

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The **FUTURE** of cancer immunotherapy

**C.** Can tumor-specific T cells be primed and expanded from naïve UCB lymphocytes?

- Her2/new-specific CTAs have been generated from UCB effective against human breast cancer cells

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The **FUTURE** of cancer immunotherapy

Cancer results from the development of a tumor cell escape phenotype sculpted by the immune system (during immunosurveillance).
The **FUTURE** of cancer immunotherapy

The issue........

tumor immunogenicity against adoptively transferred homologous **UCB lymphocytes**,
might be **sufficiently different** to when the tumors are seen by the host immune system

Cord blood can be a source of anti-tumour specific **T cell clones**

*Thank you for your attention*