1. Introduction

Cancer is one of the most threatening diseases nowadays and immunotherapy is a successful field of research. Therefore, oncology immunotherapy has become a potential source of investigation, and its main results are related to cell therapy and monoclonal antibodies.

My work is based on cell therapy, main results are related to cell therapy and monoclonal antibodies. Immunotherapy has become a potential source of investigation, and its main results are related to cell therapy and monoclonal antibodies.

2. Natural Killer T cells

Characteristics
- Antigen-CD1d complexes recognition
- They express TCR and NK receptors
- They develop and mature in the thymus

Features

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<tr>
<th>TCR α chain</th>
<th>Type I (INKT)</th>
<th>Type II (vNKT)</th>
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<td>CD4+CD8+ (DN)</td>
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Main role in cancer
- Enhance immune response
- Suppress immune response

3. NKT cell-based immunotherapy of cancer

Therapy objectives
- Elimination of MHC +/- cells in order to avoid tumor relapse
- Use of adjuvants as tumor cells are low immunogenic
- To induce DC maturation to promote efficient responses

- Free α-GalCer injection

It activates antitumor immune responses directed by iNKT cells, but it shows conflicting effects as it induces Th-0-like cell responses (cytokine mix)

α-GalCer analogs
- Hydrophobic pro-inflammatory, Th-1 cytokines
- Solubility anti-inflammatory, Th-2 cytokines

Trial outcomes
- Tolerated, safety and transient increase of NKT cells have been observed but it also has shown inefficient immune responses with a long period of energy

- Autologous DCs loaded ex vivo with α-GalCer

It increases INKT cell expansion and its INF-γ production. Moreover, it is tolerated and less likely to generate anergy of INKT cells than a plain α-GalCer injection. Finally, various routes of administration have been successful.

Trial outcomes
- Tumor size and necrosis reduction have been observed
- It has shown disease stabilization in some cases

- Tumor cells loaded with α-GalCer

It has high specificity, yet it needs adjuvants so as to be effective.

Trial outcomes
- IFN-γ route enhancement: activation of iNKT, NK and CTL

Novel: Immune memory after its combination with anti-4-1BB Ab reported

- Other α-GalCer immunotherapies

Anti-PDL1 Ab: it promotes INKT Th-1 cytokine production and NK activation

Anti-ganglioside GD2 Ab: it shows INKT-NK interaction and enhancement

Antibody + CD1d/αGC complexes: they induce tumor-specific CTL activation

Live bacteria as αGC vector: it activates tumor-specific CTL

- Ex vivo expansion of autologous iNKT cells

Trial outcomes
- Tolerance and safety
- Disease stabilization
- No tumor regression

Ex vivo expanded autologous iNKTs and α-GalCer-pulsed DCs

- Combination immunotherapy

Trial outcomes
- Tolerance and no severe side effects reported
- It shows moderate responses in NKT and NK cell activities
- It induces partial response, stable disease and tumor regression

4. Conclusions

- Immunosuppressive TME eradicates antitumor responses
- Small NKT population, which is even lower in cancer patients, is associated with worse prognosis
- All studies are small scale trials without long monitoring
- Differences between mouse and human in CD1d and INKT frequencies
- Novel: research in humanized mouse models, αGC analogs, delivery vectors
- Trials with mature DCs or PBMCs have shown better results than DCs
- Combination immunotherapy is not as good as expected theoretically
- Irradiated tumor approaches are the best candidate for vaccination

- Novel
- PS: reinfusion of larger numbers of NKT promotes CTL activation
- CARs: NKT transduced with CAR.GD2 induces persistent activity

5. Bibliography