PROFILE

The Research Group, at **Centro Nacional de Biotecnología,** is focused in generating novel immunotherapies using the ability of bacteria to modify the immune responses. It has been discovered that conventional CD4+ T cells can be trained by bacteria engineered to express tumor antigens. Bacteria-trained CD4+ T cells (bacT) became potent antigen presenting cells activating naïve CD8+ T cells that became effective anti-tumor cytotoxic cells and generating central memory (resistant to tumor induced exhaustion). Antitumor activity of BacT cells was tested in proof-of-concept models.

SPEAKER

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PRODUCT

Bacteria-trained lymphocytes as novel anti-cancer immunotherapy

MECHANISM OF ACTION

Bacteria-trained CD4+ T (BacT) cells are conventional Cd4+ T cells (extracted from the patient) and later "trained" by bacteria engineered to express tumor antigens. BacT cells are able to activate naïve CD8+ T cells that recognize these tumor antigens. BacT-activated CD8+ T cells migrate to the tumor locations and are able to trigger a potent cytotoxic response against the tumor cells. In addition, BacT-activated CD8+ T cells differentiate into central memory CD8+ T cells, the population more resistant to tumor induced exhaustion, which in addition expressed very low levels of PD1, the major check point inhibitor molecule.

BacT became potent antigen presenting cells able to (1) activate naïve CD8+ T cells that became effective tumor cytotoxic cells and (2) generating central memory; activities involved in the removal of tumors. Note that actually there exist huge efforts to generate central memory CD8+ T cells from tumor infiltrating lymphocytes. These effects, together with (3) the localized secretion of inflammatory cytokines by bacT cells, which could block the immunosuppressive environment generated by solid tumors, prompted us to hypothesized that bacT cells could be useful in antitumor therapies. This hypothesis was tested, mice treated with bacT cells were protected against tumor development.

TARGET INDICATIONS

The present product is a novel cancer immunotherapy that could act against immunogenic tumors (the vast majority). It could be use against any tumor (solid or liquid) with identified tumor-associated antigens.

CURRENT STATUS

- Proof of concept experiments have been performed, demonstrating that BacT cells impeded the implantation of the tumor as well as tumor growth.
- Mice vaccination with bacT cells impeded the implantation of aggressive melanoma.
- BacT cells were useful not only at preventive but also at therapeutic level, we tested BacT against already established tumors using B16 melanoma and MC38 (colon cancer; non orthotopic). In both models a clear reduction of tumor growth was observed.
- In order to achieve this task, we engineered bacteria expressing tumor-associate antigens. In these preliminary experiments, we used 100x less cells than the equivalent (taking into account the weight differences between species) used in TILs therapies in humans, and we used only 3 doses when other experiments use up to seven inoculations of the treatment.

INNOVATIVE ASPECTS

- The closest technology is the use of dendritic cells as anti-cancer vaccines. DC-based cancer vaccines unfortunately show very low responses, underlining the need for novel therapies.
- Note that BacT cells is superior in generating effective antitumor CD8+ T cells which in addition are more resistant to exhaustion.
- Other cellular technologies are TILS (tumor infiltrating lymphocytes) or CAR-T. Here also, BacT technology generate improved anti-tumor responses against solid tumors, and more resistance to exhaustion.

IPR

The use of bacT cells in cancer immunotherapies has been protected by patent, and this has been extended to USA, Canada, EU and Australia.

PARTNERING OPPORTUNITIES

We would like to strengthen the possibility to transfer these discoveries to the society. Ideally be by founding a Spin-Off company or by licensing the patent.