H12O-CNIO CANCER IMMUNOTHERAPY CLINICAL RESEARCH UNIT

Luis Álvarez-Vallina
(since November)
Clinical Research Unit Head

Research Scientists
Belén Blanco, Anáis Jiménez

Post-Doctoral Fellows
Rodrigo Lázaro, Ángel Ramírez, Antonio Tapia, Ivana Zagorac

OVERVIEW

Our Unit focuses on understanding the molecular and cellular mechanisms of cancer immune escape in order to design next-generation cancer immunotherapies. For example, we have developed a novel strategy based on the secretion of bispecific T cell-engaging antibodies by engineered human T (STAb-T) cells, which has been shown to be effective in solid and haematological malignancies and is currently being tested in clinical trials. The Cancer Immunotherapy Clinical Research Unit has several research areas of interest: 1) reactivation of tumour-specific endogenous T cells; 2) development of tumour-reactive "artificial" T cells; and 3) development of multi-targeting approaches recognising extra- and intracellular tumour antigens. Our group also has a strong interest in the generation of multi-specific antibodies and the use of engineered mRNA-based delivery systems. Finally, our Unit is firmly committed to introducing new immuno-oncology drugs and adoptive cell therapies in the clinic, to provide high-quality personalised treatments.

Gradutate Students
Francisco Javier Arroyo, Laura Díez, Carmen Domínguez, Marina Gómez, Laura Rubio, Alejandro Segura, Miriam Velasco

Technician
María de La Yedra Pacheco

RESEARCH HIGHLIGHTS

The year 2022 saw the consolidation of the "STAb-T" cancer immunotherapy strategy as a viable therapeutic option for many cancer patients. The "STAb-T strategy" is a novel adoptive cell therapy (ACT) designed by our Unit, based on the endogenous Secretion of T-cell engaging (TCE) Antibodies (STAb) by T cells (FIGURE 1). The secreted TCE antibodies recruit and activate T cells against cancer cells expressing a predefined tumour antigen. STAb-T cells offer several potential advantages over current T redirection strategies (FIGURE 1). First, *in vivo* secretion might result in effective concentrations of TCEs. Second, *in vivo* secretion can remove potential concerns regarding the formulation and long-term storage of TCEs in a manner that prevents aggregation and deterioration. Third, in STAb-T strategy, T cell recruitment is not restricted to engineered T cells, as in the case of CAR-T cell approaches. The polyclonal recruitment by TCEs of both engineered and unmodified bystander T cells, present at the tumour site, might lead to a significant boost in antitumour T cell responses (FIGURE 1). During 2022, we demonstrated the remarkable therapeutic impact in preclinical models of haematological cancers (B cell leukaemia, T cell leukaemia and multiple myeloma), with a cell product (STAb-T19) currently in a phase I, first-in-human clinical trial in patients with B cell malignancies. Throughout this period, the implementation of this strategy in solid tumours, as well as the design of dual targeting strategies, has been considerably improved. ■

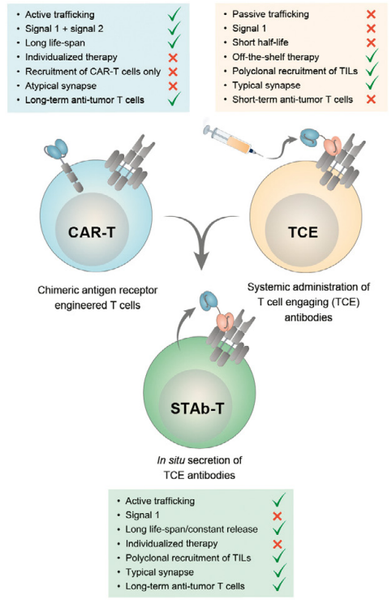

FIGURE 1 Schematic diagram summarising the advantages (green tick) and limitations (red cross) of T cell-redirecting strategies.

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