Immune evasion is a critical step in cancer progression in which tumour cells modulate the host immune system to evade destruction. Our Unit focuses on understanding the molecular and cellular mechanisms of cancer immune evasion to develop more effective and safer cancer immunotherapies. The Cancer Immunotherapy Clinical Research Unit has several areas of interest:

- Reactivation of tumour-specific endogenous T cell repertoires through the design of multi-specific antibodies against a combination of immunomodulatory targets. Preclinical and early clinical data show that this is a promising approach to enhance the clinical benefit of conventional checkpoint blockers.

- Generation of tumour reactive “artificial” T cell effectors by redirecting T cell activity towards cancer cells, targeting tumour-associated antigens (TAA) with bispecific T cell-engaging (TCE) antibodies and/or membrane-anchored chimeric receptors (chimeric antigen receptors and/or chimeric costimulatory receptors).

- Development of multi-target approaches that simultaneously recognise extracellular and intracellular tumour antigens.

- Rational design of mRNA-based therapeutics.

- Provision of personalised cancer treatments by bringing new immuno-oncology drugs and adoptive cell therapies to the clinic.

“At the Cancer Immunotherapy Clinical Research Unit, we aim to develop immunotherapies that synergistically stimulate T cell immunity against cancer.”
STAB T cancer immunotherapy

The "STAB-T strategy" is a novel adoptive cell therapy (ACT) developed by our Unit, based on the in vivo secretion of TCE Antibodies (STAB) by T cells (FIGURE 1). The secreted TCE antibodies redirect T cells against cancer cells expressing a predefined TAA. STAB-T cells offer several potential advantages over current T redirection strategies (FIGURE 1): in vivo endogenous secretion could result in effective concentrations of TCEs, and T cell recruitment is not restricted to engineered T cells, as in the case of CAR-T cell approaches. Polyclonal recruitment by TCe of both engineered and unmodified bystander T cells, present in the tumour microenvironment, could lead to a significant boost in antitumour T cell responses (FIGURE 1). In 2023, we confirmed the remarkable therapeutic impact of single-targeted STAB-T cells in haematological cancers, B cell leukaemia, T cell leukaemia and multiple myeloma (Diez-Alonso L., Álvarez-Vallina L., Sci Trans Med, in press), and shown that dual-targeted STAB-T therapies (FIGURE 1) have superior control of leukaemia progression than dual-targeted CAR-T cells. We also showed that TCE-secretion tumour-infiltrating lymphocytes (STAB-TILs), but not conventional TIL, induce responses in solid tumours (non-small cell lung cancer) when administered intratumorally and systemically.

Dendritic cell-mediated cross-priming by bispecific antibodies

Dendritic cells (DCs) are professional antigen-presenting cells that play a central role in the induction of antigen-specific adaptive immune responses. DC natural killer group receptor-1 (DNGr-1) is a C-type lectin receptor (CLR) selectively expressed at high levels by mouse CD8α+ adaptive immune responses. DCs and their natural killer lectin group cells that play a central role in the induction of antigen-specific Dendritic cell-mediated cross-priming by bispecific and systemically.

Early clinical trials

Our Unit, in collaboration with the Haematology and Medical Oncology Departments of the Hospital Universitario 12 de Octubre, has launched 2 independent clinical trials funded by the Carlos III Health Institute: a phase I, first-in-human clinical trial to evaluate the safety of STAB-T99 cells (genetically modified autologous T lymphocytes (STAB-TILs), but not conventional TIL, induce responses in solid tumours (non-small cell lung cancer) when administered intratumorally and systemically.

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