#2550

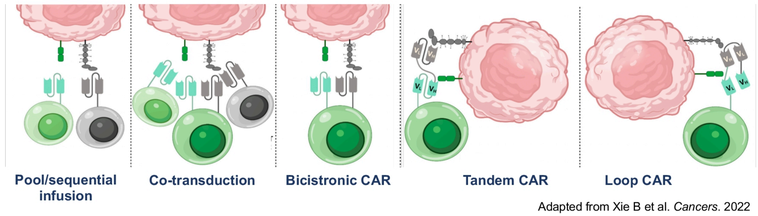
Effect of CD22-directed CAR-T cells secreting anti-CD19 T cell engagers on control of leukemia progression compared to tandem anti-CD19/CD22 CAR-T cells

Javier Arroyo-Ródenas[1,2], Laura Díez-Alonso[1,2], Aida Falgas[3], Alba Martinez-Moreno[3], FJ. Gil-Etayo[1], Óscar Aguilar-Sopeña[4], Miriam Velasco-Sidro[1,2], Clara Bravo-Martín[4], Ángel Ramírez-Fernández[1,2], Anaïs Jiménez-Reinoso[1,2], Belén Blanco[1,2], Pedro Roda-Navarro[4], Clara Bueno[3], Pablo Menéndez[3], Luis Álvarez-Vallina[1,2]

[1]Cancer Immunotherapy Unit (UNICA), Hospital Universitario 12 de Octubre, Madrid, Spain; [2] Spanish National Cancer Research Centre (CNIO), [3]Josep Carreras Leukaemia Research Institute, Barcelona, Spain; [4] Universidad Complutense, Madrid, Spain

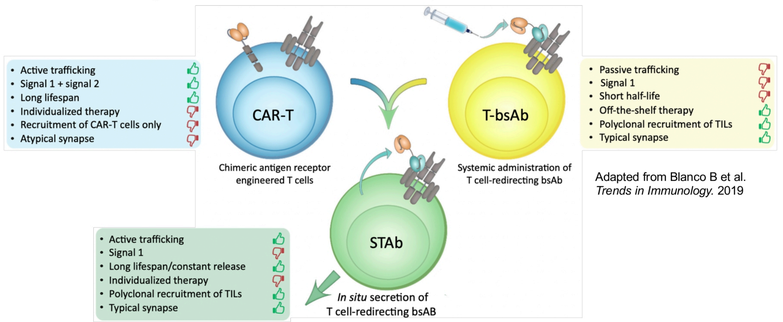
Introduction:

- Despite promising results, patients treated with CAR-T cells usually relapse due to tumor heterogeneity or antigen loss.
- Dual-targeting CAR-T cell strategies have been widely tested, although they have several shortcomings related to CAR design.



Adapted from Xie B et al. *Cancers*. 2022

- We have previously shown that T cells secreting T cell engagers (**STAb-T cells**) have advantages over i.v. administered bispecific antibodies and CAR-T cells.

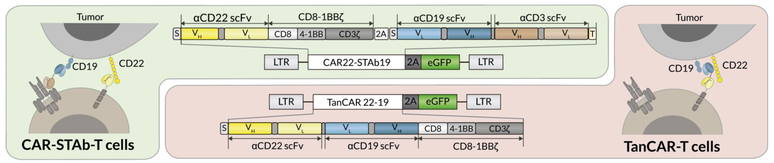


Adapted from Blanco B et al. *Trends in Immunology.* 2019

- STAb-T therapies against CD19, CD1a and BCMA have been developed and characterized, demonstrating superior tumor control compared to CAR-T cells.

Methods:

- We have developed a dual-targeting strategy for hematological malignancies based on T cells bearing an anti-CD22 CAR and secreting anti-CD19 T cell engagers (CAR-STAb-T cells).



- This work has primarily focused on the comparison between CAR-STAb-T cells and a previously validated tandem CAR construct (TanCAR-T) against the same two antigens.

CAR-T cells secreting T cell engagers are more effective than conventional CAR-T cells by **recruiting bystander T cells**

More info

Full presentation

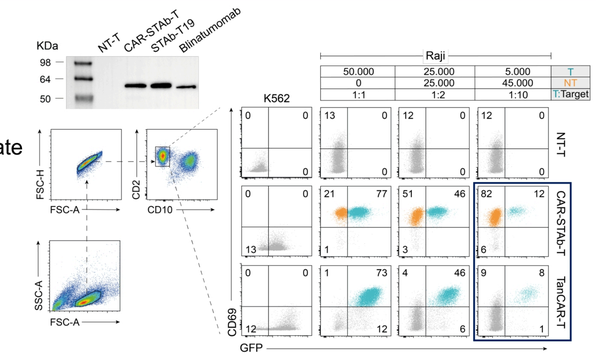
UNICA Cancer Immunotherapy Unit

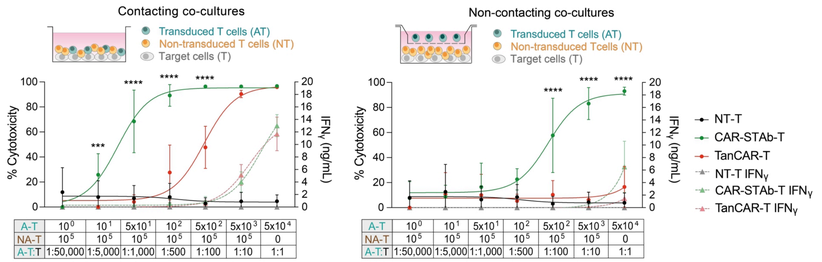
Contact : Javier Arroyo-Ródenas (farroyor@salud.madrid.org)
Luis Álvarez-Vallina (lav.imas12@h12o.es)

Copies of this poster/slide deck obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from ASCO® or the author of this poster/slides

Results:

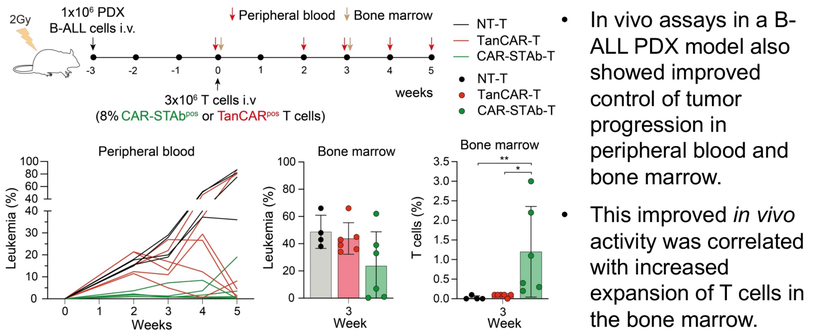
- CAR-STAb-T cells secrete functional anti-CD19 T cell engagers that activate all non-transduced bystander T lymphocytes in the presence of tumor cells, amplifying the response.





A-T	10^0	10^1	$5x10^1$	10^2	$5x10^2$	$5x10^3$	$5x10^4$
NA-T	10^5	10^5	10^5	10^5	10^5	10^5	0
A-T:T	1:50,000	1:5,000	1:1,000	1:500	1:100	1:10	1:1

- The effective recruitment of bystander T lymphocytes by CAR-STAb-T cells is translated into a superior cytotoxic activity at low E:T ratios.



- In vivo assays in a B-ALL PDX model also showed improved control of tumor progression in peripheral blood and bone marrow.
- This improved *in vivo* activity was correlated with increased expansion of T cells in the bone marrow.

Future research directions:

- CAR-STAb-T cells may be especially relevant in lymphodepleted patients with low T cell counts due to their high efficacy and recruitment properties.
- Safety concerns may be critical when targeting solid tumors. Therefore, our ongoing efforts are focused on the development of inducible STAb and CAR-STAb-T cells for specific and safe activation against tumor cells.