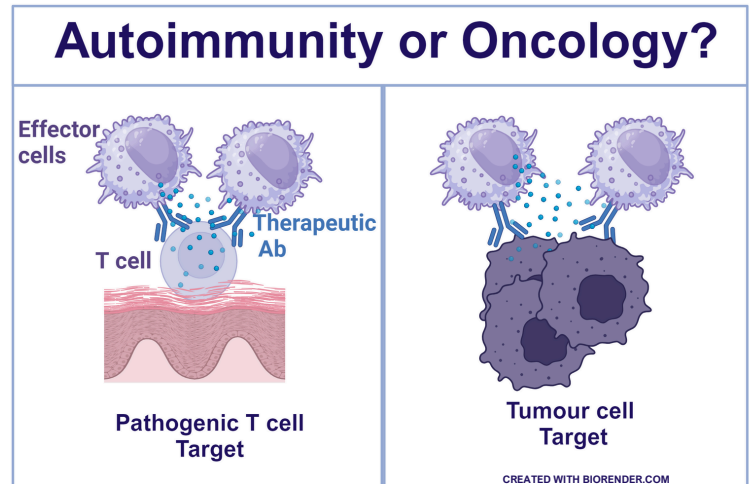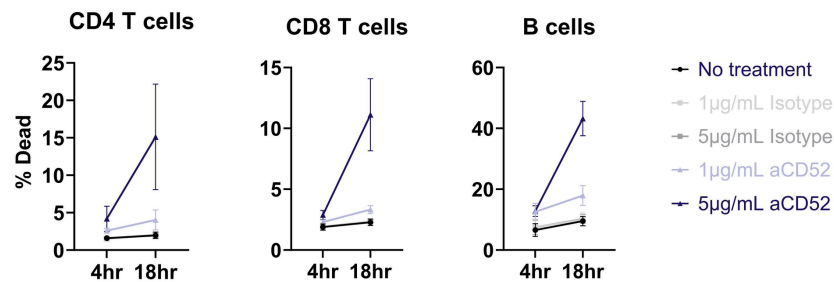# TARGETING IMMUNE CELLS OR TUMOUR CELLS BY ANTIBODY DEPENDENT CELL CYTOTOXICITY (ADCC)

Recently, oncology therapeutics such as CD19 CAR-T cells, used for treating B cell lymphoma, have been repurposed for depletion of pathogenic B cells in autoimmune disease such as SLE. This approach goes beyond cellular therapies, with an increasing number of biologics being investigated to target effector immune cells responsible for driving autoimmunity/inflammation. Here, we present example data of ADCC in two settings Autoimmune, using Alemtuzumab, as an example of an immune cell depleting antibody and Oncology, using Trastuzumab, as an example of a tumour targeting antibody. This illustrates how human primary immune cell in vitro assays can be used to investigate ADCC across multiple therapeutic areas.
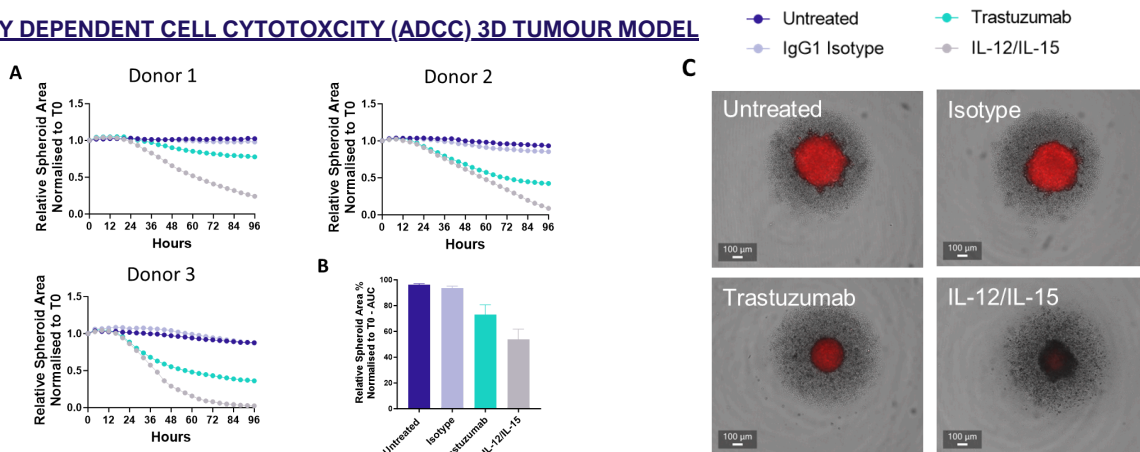

Autoimmunity or Oncology?

Effector cells

T cell

Therapeutic Ab

Pathogenic T cell Target

Tumour cell Target

CREATED WITH BIORENDER.COM

ANTIBODY DEPENDENT CELL CYTOTOXCITY (ADCC) OF PATHOGENIC IMMUNE CELLS

CD4 T cells   CD8 T cells   B cells

- No treatment
- 1µg/mL Isotype
- 5µg/mL Isotype
- 1µg/mL aCD52
- 5µg/mL aCD52

ADCC PBMC assay to determine which immune cell subsets are targeted by a therapeutic antibody. Example: Anti-CD52 antibody Alemtuzumab mediates killing via ADCC of CD52 expressing immune cells including T cells and B cells. The viability of CD4, CD8 and B cells was measured by flow cytometry after 4 or 18hr of culture in the presence of an anti-CD52 IgG1 (Alemtuzumab) antibody or isotype at two concentrations . Graphs show mean +/- SEM, n = 3 donors.

ANTIBODY DEPENDENT CELL CYTOTOXCITY (ADCC) 3D TUMOUR MODEL

- Untreated
- IgG1 Isotype
- Trastuzumab
- IL-12/IL-15

A   Donor 1   Donor 2   C

Donor 3

B

Untreated   Isotype

Trastuzumab   IL-12/IL-15

100 µm

ADCC in a PBMC/tumour spheroid co-culture system to determine if tumour populations expressing the appropriate antigen are targeted by a therapeutic antibody for ADCC. Example: anti-HER2 antibody Trastuzumab mediates killing via ADCC of HER2 expressing tumour cells by purified NK cells. Purified NK cells +/- Trastuzumab are added to SK-OV-3 tumour spheroids, tumour killing (spheroid reduction) is enhanced by targeted HER2 antibodies as compared to isotype control. (A). Therapeutic windows were driven in Trastuzumab and IL-12/IL-15 treated PBMC conditions as observed in AUC statistics calculated using GraphPad Prism v9.5.0 (B) and live cell imaging representative images (C). Bar graph shows mean of n=3 donor tumour killing +/- SEM.