Scan the QR code to view more exemplar assay data here:

NEXUS BIOQUEST

3D tumour killing model

Tool for screening immunotherapeutics

Introduction

Tumour cell line spheroids co-cultured with immune cells allow the assessment of the therapeutic effect of novel checkpoint inhibitors, targeted monoclonal/ bi-specific antibodies, small molecule therapeutics or cell therapies in a system which more closely recapitulates solid in vivo tumours by including 3D structure. Here we present data demonstrating that this 3D spheroid model is fit for purpose for checkpoint inhibitor targeting antibodies and ADCC modalities. The 3D spheroid model provides a robust model for lead candidate selection for in vivo immuno-oncology studies and can be performed with a bank of tumour line cell types and immune subsets.

Methodology

Fluorescently labelled tumour cells are seeded in 96 well plates and tumour spheroids generated. Immune cell subsets are added to the spheroids and immune mediated killing of tumour cells is measured by reduction of tumour spheroid area via live cell imaging on the CellCyte X. The ability of large molecules, small molecules or cell therapies at enhancing immune mediated tumour killing is assessed, alone or as a combination.

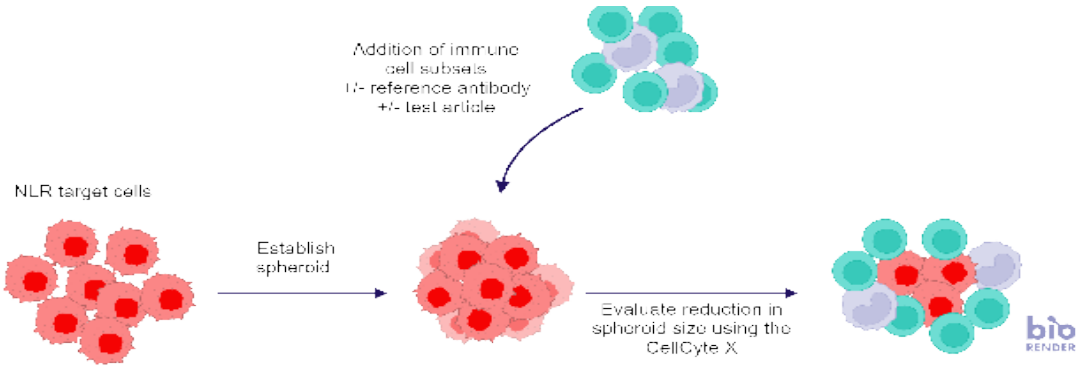


Figure 1: Checkpoint inhibitor sensitive 3D model

These data show the therapeutic window for checkpoint inhibitors (CPI) in a 3D immune mediated tumour killing assay (n=3 PBMC donors). When PBMC +/- Pembrolizumab or IgG4 control are added to SK-OV-3 spheroids, tumour killing (spheroid reduction) is enhanced by CPI as compared to isotype control. Relative spheroid area (%) was measured **(A)** This therapeutic window was shown in n=3 donors with AUC statistics calculated using GraphPad Prism v9.5.0 **(B)** tumour killing +/- SEM.

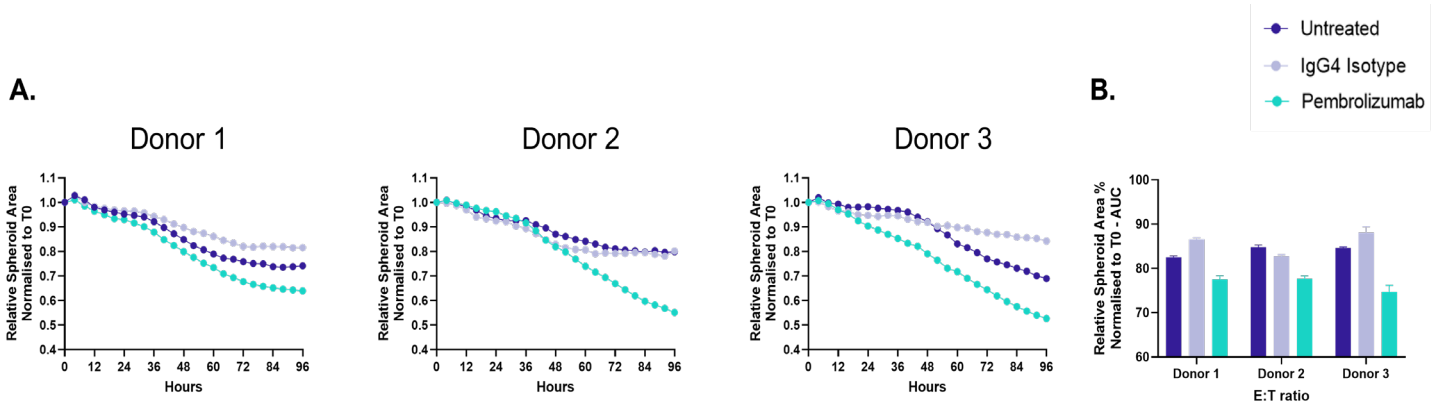
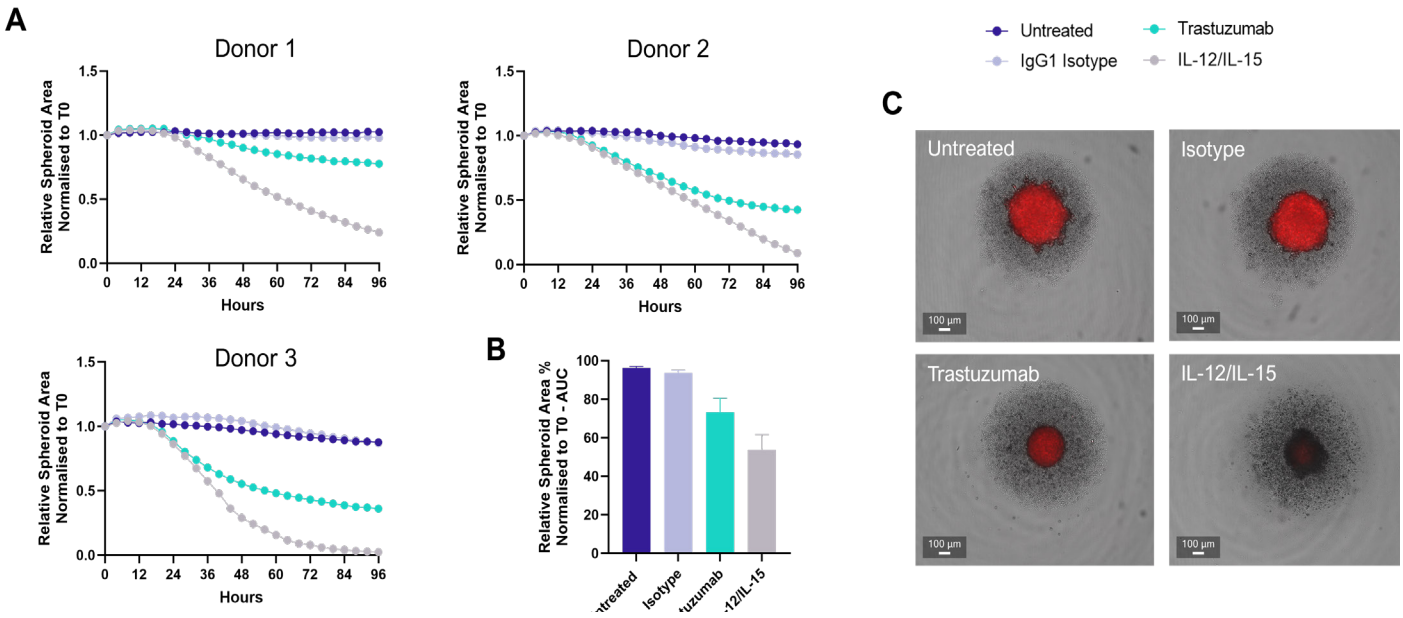


Figure 2: Antibody dependent cell cytotoxicity (ADCC) 3D model

These data demonstrate the therapeutic window for targeted monoclonal antibodies (ADCC) in a 3D immune mediated tumour killing assay (n=3 donors). When 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. Relative spheroid area (%) was measured (A)and the 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



Conclusion

- At Nexus Biouest, we offer a selection of clinically relevant tumor cells labelled with NUCLight Red, ideal for use in 3D spheroid assays. These spheroids enable the testing of antibodies, antibody-drug conjugates, small molecules, and cellular therapeutics.
- Our 3D spheroids can also be customised by incorporating additional stromal components or modifying immune cells to recreate the tumor microenvironment.

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