



CONCEPT LIFE SCIENCES

Immuno-Oncology

Drug Discovery & Development
from Concept through to Clinic

October 2023



Our Custom IO Services

Immuno-oncology is an exciting and progressing area of research that uses manipulation of the immune system to successfully target cancer.

Concept Life Sciences can help you understand the immunomodulatory effects of your drug candidates within the tumour microenvironment and/or in combination with other immune modulators, efficiently progressing your route to clinic.

We have extensive *in vitro* immunology, pre-clinical immunology and specialist multiplex histology experience. Our suite of available immuno-oncology services and assays can be specifically tailored to your project.

- ▶ Exhausted T Cell Assay
- ▶ Tumour Cell Killing Assay
- ▶ Macrophage Suppression Assay
- ▶ T Cell Activation Assays
- ▶ Antigen-Specific T Cell Activation Assay
- ▶ Tailored Histology Services
- ▶ Molecular Biology Services

Oncology

- ▶ Bespoke assay & screening cascade development
- ▶ High content phenotypic profiling
- ▶ Biophysical expertise, novel MOAs
- ▶ Biomarker/patient selection strategies
- ▶ PROTACs, ADCs
- ▶ Medicinal chemistry and PK models

Immunology

- ▶ Specialist human *in vitro* and *ex vivo* models
- ▶ Collaborative and tailored experimental design
- ▶ Advice on cell types, mono- or co-culture assays
- ▶ Customisation and development of novel assays
- ▶ Medicinal chemistry design for multiple target classes including PPIs

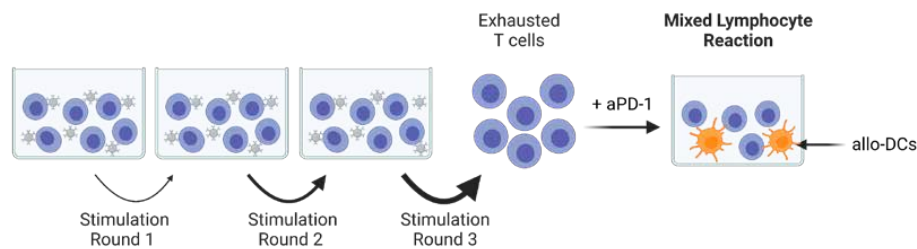


Exhausted T Cell Assay

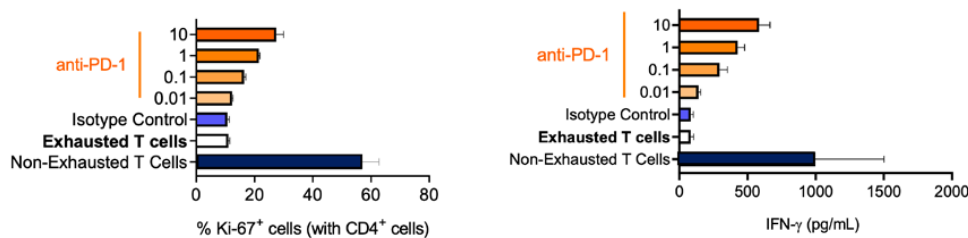
Concept Life Sciences have developed an *in vitro* human exhausted T cell model that phenotypically and functionally recapitulates the exhausted T cells found within the tumour microenvironment.

This assay can be used as a valuable tool to assess the ability of candidate immuno-oncology therapeutics to prevent establishment of exhaustion, rescue an exhausted T cell phenotype, restore T cell function and permit tumour cell clearance.

Compound effects can be determined by assessment of phenotypic status and cytokine production as well as using functional assays including mixed leukocyte reaction (MLR) and tumour cell killing assays.



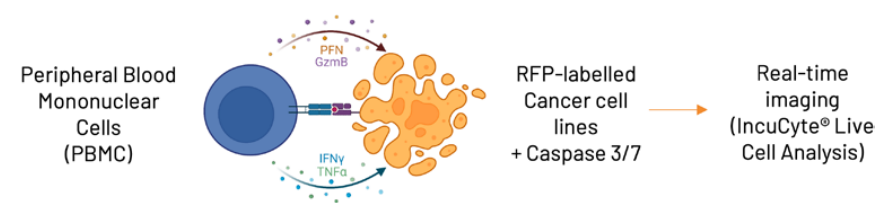
Reversal of T cell Exhaustion



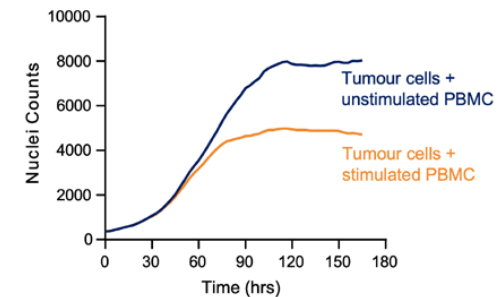
Tumour Cell Killing Assay

Understanding whether test biologics and/or small molecules can enhance tumour killing is a key component of an immuno-oncology drug discovery program. Cell-mediated cytotoxicity (CMC) or antibody dependent cytotoxicity (ADCC) can be measured using traditional label-release assays but data showing the kinetics of killing are increasing valuable.

Concept Life Sciences uses the IncuCyte® Live Cell Analysis System to assess immune cell-driven apoptosis of cultured tumour cells; designed to measure either a T cell-mediated (CMC) or NK cell-mediated (CMC or ADCC) killing. The system delivers real-time data for tumour cell proliferation and apoptosis.



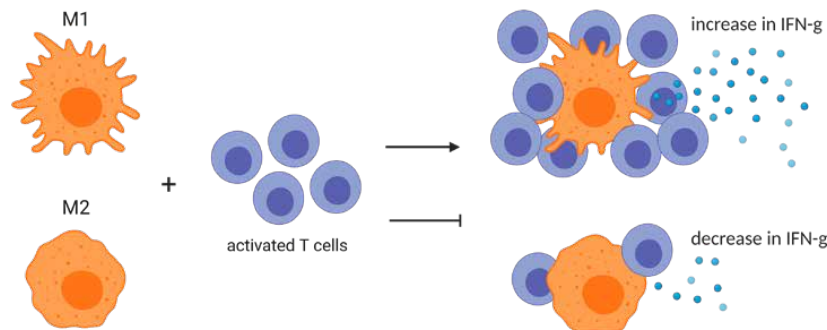
Activated PBMC Decrease Tumour Cell Number



Macrophage Suppression Assay

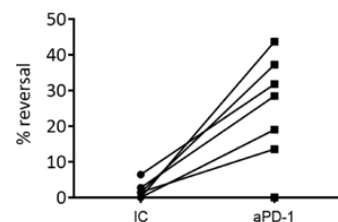
Understanding the role of macrophages in the tumour microenvironment (TME) is vital to an immuno-oncology research program.

Concept Life Sciences has developed a suite of *in vitro* assays to study macrophage suppression of autologous T cell responses, enabling screening of small molecules or biologics for their ability to reverse this suppression. M1 macrophages boost T cell activation, whereas M2 macrophages potentially suppress IFN- γ production. Macrophages are co-cultured with anti-CD3-stimulated PBMC. PD-1 blockade can partially reverse this suppression but can also show synergistic activity when combined with small molecule inhibitors.

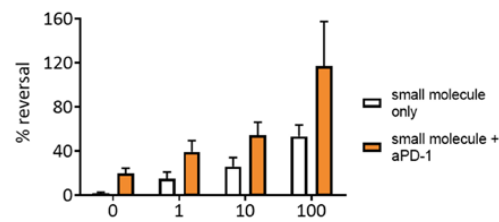


Reversal of Macrophage Suppression

Biologic



Combination treatment

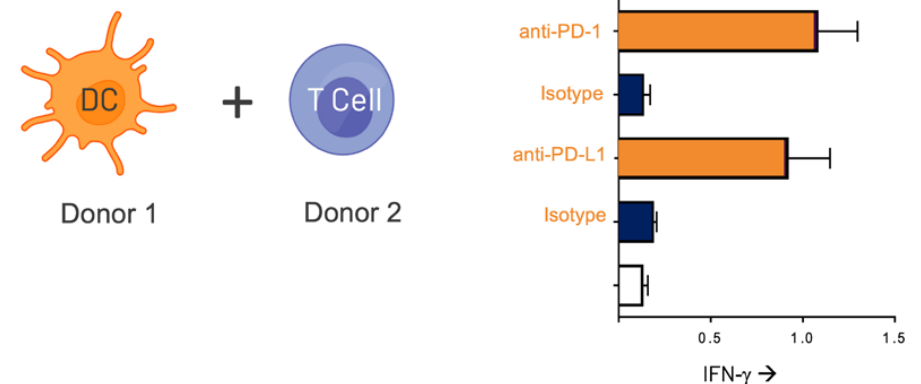


T Cell Activation Assays

MLRs are commonly used to understand the effects of biologics or small molecules on T cell activation, an important response in the tumour microenvironment. The assay relies on a proportion of the "responder" T cells bearing TCRs that will be triggered by allogeneic HLA molecules displayed by "stimulator" APCs. These APCs also have the capacity to provide costimulatory and coinhibitory signals in the assay.

Concept Life Sciences can advise on the most suitable MLR assay to understand your drug candidate mechanism of action and tailor the assay accordingly. The simplest mixes PBMCs from two donors as either "two-way" cultures, in which each PBMC population can act as stimulator and responder, or "one-way" MLRs where one PBMC population is first irradiated so that it can function as a stimulator but not a responder. A more refined MLR system uses monocyte-derived dendritic cells (Mo-DC), which can be immature or matured under varying conditions, depending on the target of interest. Responder T cells are isolated from HLA-mismatched donors providing a source of alloreactive T cells.

Mixed Leukocyte Reactions (MLRs)

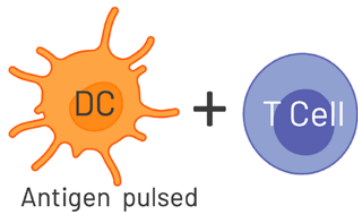


Antigen-Specific T Cell Activation Assay

Concept Life Sciences offers a comprehensive panel of T cell assays that can provide valuable efficacy data whether developing anti-cancer or anti-inflammatory therapies.

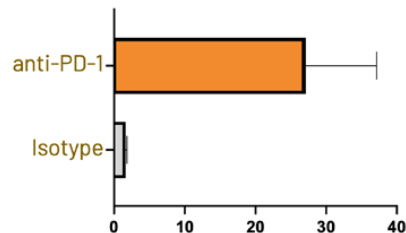
T cell assays can be performed using total PBMC, or isolated T cells, depending on the throughput required and the target of interest. T cells can also be activated in a variety of ways including via non-specific T cell receptor stimulation (anti-CD3) or via antigen-specific stimulation. Our various read-outs can be tailored to your requirements.

In the antigen-specific T cell activation assay, mixed peptide pools from CMV, EBV, and Influenza A can be utilised to differentially activate either CD4+ and CD8+ T cells. This allows for modulation of T cells upon antigenic stimulation to be assessed.



Assay Readouts Available

- ▶ Cytokine production
- ▶ Proliferation
- ▶ Cell cycle status
- ▶ Activation status
- ▶ Transcription factor expression
- ▶ Signaling pathways
- ▶ Gene expression



Other Available T Cell Assays

- ▶ PBMC Assays
- ▶ T cell Differentiation Assays (Th1, Th2, Th17, iTreg)
- ▶ Treg Suppression Assays

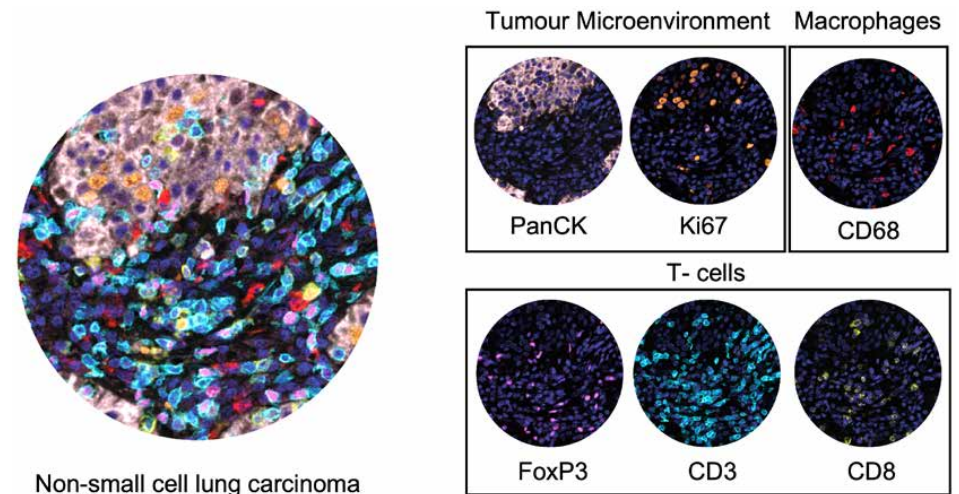
Research-Specific Histology Services

Providing target validation and in-depth insight into mechanisms of action and biological processes

Visualise and quantify cellular responses to your drug treatment through detection of multiple biomarkers on the same tissue section.

Our highly experienced scientists can:

- ▶ Utilise their extensive knowledge of immunology, immuno-oncology, neuroscience, and fibrosis.
- ▶ Recommend suitable pre-optimised antibodies for biomarkers.
- ▶ Help design and develop up to 8-plex (9-colour) mIF panels.
- ▶ Assist with data interpretation throughout the study and provide guidance on next steps.



Non-small cell lung carcinoma

Interrogate your biomarkers using our **image analysis capabilities** to obtain quantifiable data on cell parameters incl. cell number within select regions of interest (e.g., tumour versus stroma), cell distances, and protein expression levels.

Tailored Molecular Biology Services

Providing target validation and in-depth insight into mechanisms of action and biological processes

Isolation & Purification

- ▶ Fresh frozen & FFPE tissues
- ▶ Purification of total RNA
- ▶ Nanodrop™, Qubit™ & Agilent® instruments



NGS Library Preparation

- ▶ Bulk RNA-Seq
- ▶ ATAC-Seq
- ✔ Recommended for drug response, target identification, and mechanism of action



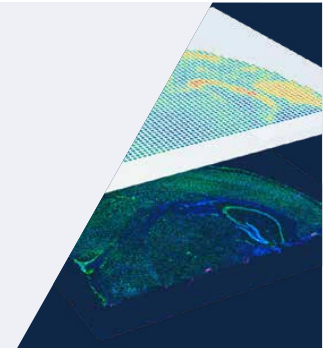
Single-Cell Assays

- ▶ 10X Genomics Chromium Controller™
- ▶ Gene Expression, V(D)J & CITE-Seq
- ✔ Recommended for tissue characterisation, mechanism of action, and target identification



Spatial Transcriptomics

- ▶ 10X Genomics Visium™ Platform
- ▶ Fresh Frozen or FFPE Tissue
- ✔ Recommended for tissue characterisation, biomarker analysis and target identification



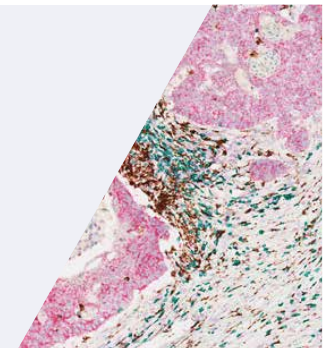
Quantitative PCR (qPCR)

- ▶ Primer design & efficiency testing
- ▶ Tissue-specific validated housekeeper genes
- ✔ Recommended for drug response, biomarker analysis, and target validation



RNAscope & BASEscope

- ▶ Chromogenic or fluorescent
- ▶ Up to 4-plex
- ▶ Up to 2 proteins + mRNA multiplex
- ✔ Recommended for target validation, screening & distribution





Let's talk about your
unique Drug Discovery &
Development journey

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Drug discovery & development from concept through to clinic



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