Primary Human Immune Cell Assays for the Evaluation of New Immuno-Oncology Therapies

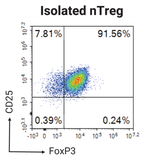
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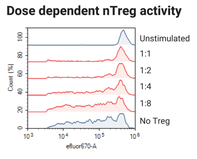
Introduction

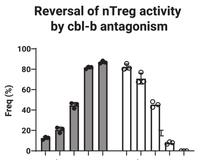
The field of immuno-oncology has gained significant attention in recent years due to the ability of the immune system to recognise and eliminate cancer cells. Different subtypes of primary human immune cells, such as regulatory T cells, NK cells, macrophages, T cells and exhausted T cells, play important roles in the tumour microenvironment. In vitro assays using these cells can support the evaluation of new immuno-oncology therapies.

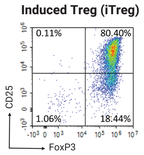
REGULATORY T CELLS

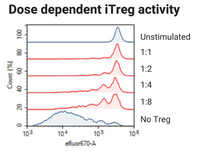
Regulatory T cells (Treg) can be isolated directly from PBMCs (nTreg) or naïve CD4 T cells can be induced to differentiate into Treg (iTreg). These can be used to suppress effector T cell responses such as proliferation and pro-inflammatory cytokine secretion. Isolated nTreg can used at defined ratios of Treg to target effector cells and used to suppress anti-CD3-induced proliferation of effector CD4 and CD8 T cells. Candidate therapeutics can be assessed for their ability to reverse regulatory T cell activity. Such assays can be performed at greater scale using iTreg, differentiated from naïve CD4 T cells in the presence of a proprietary cytokine cocktail.









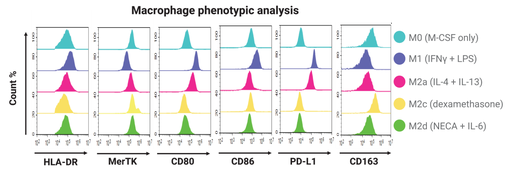


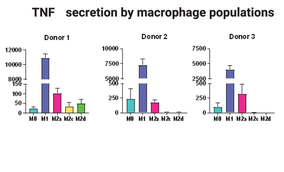
MACROPHAGES

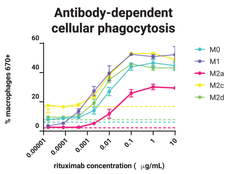
Isolated monocytes can be differentiated into macrophages for polarisation from M0 macrophages to M1 or M2 populations depending on what best reflects the in vivo conditions being modelled.

Macrophages can be used in the following assays:

- Phagocytosis assays
- Suppression assays
- Phenotyping & cytokine release
- Mixed lymphocyte reactions (MLR)

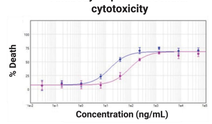






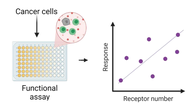
NK CELLS

Natural killer (NK) cells isolated from freshly collected whole blood or cryopreserved PBMCs can be phenotypically characterised by flow cytometry and used in cytotoxicity assays with readouts such as xCELLigence, luciferase activity or flow cytometry.



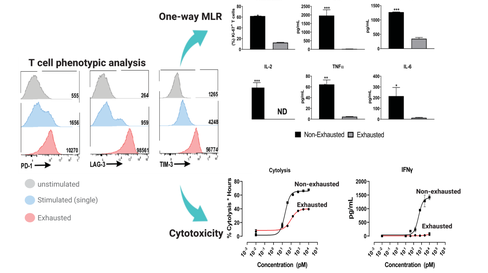
TUMOUR CELLS

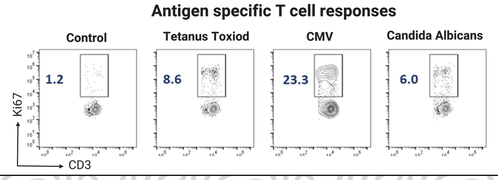
We have developed a novel model cell line platform that enables precise control of target antigen expression. This can be used in primary cell assays to determine activation thresholds and identify the potential 'on-target, off-tumour' side effects.



EXHAUSTED AND EFFECTOR T CELLS

Exhausted T cells are generated from human T cells isolated from PBMCs. These can be employed in a variety of functional assays to assess reinvigoration by test molecules. We are also able to study primary T cell responses employing model antigens (e.g. CMV), alloresponses (MLRs) or polyclonal stimulation utilising a variety of readouts e.g. flow cytometric phenotyping, proliferation, cytokine responses and target cell killing.





SUMMARY

In vitro assays with primary human immune cells are powerful tools for evaluating the impact of new immuno-oncology therapies on immune cell types that are relevant to cancer. These assays can help elucidate the mechanisms of action of the new therapies and assess their potential for clinical benefit, facilitating the discovery and development of new immuno-oncology therapies that can improve cancer treatment for patients.

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