

## Evaluation of Checkpoint Inhibitor Therapies using a Mixed Lymphocyte Reaction (MLR) Assay

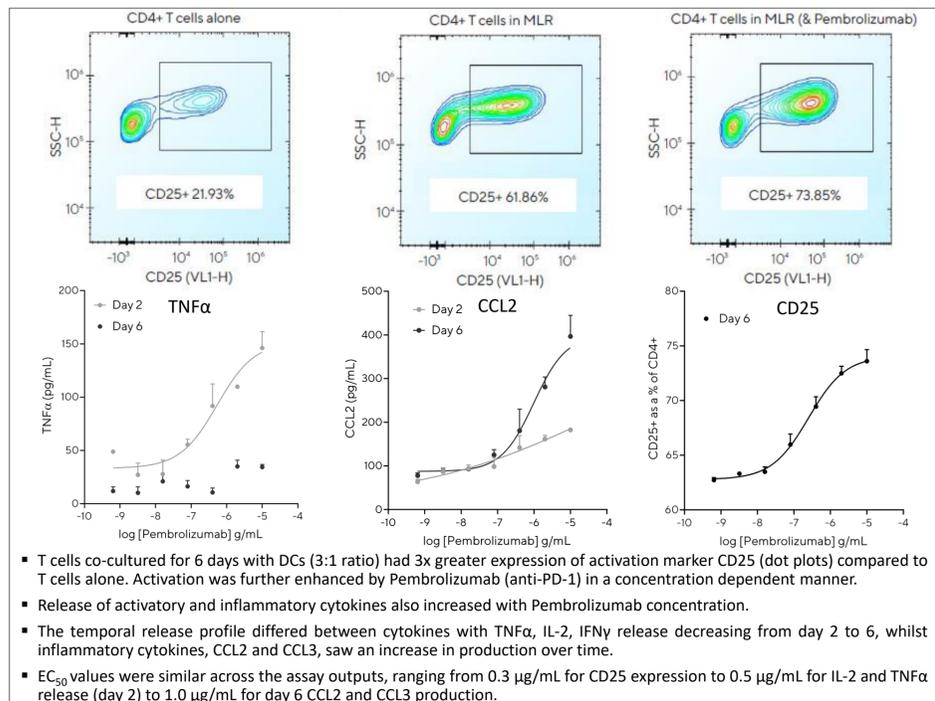
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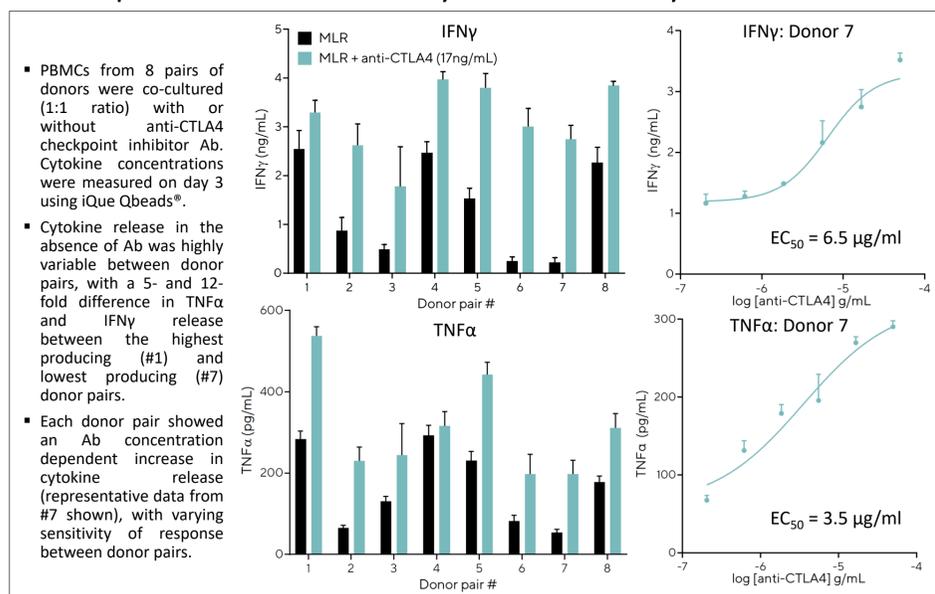
### Summary & Impact

- Checkpoint inhibitor antibodies target receptors in the synapse between T cells and antigen-presenting cells, such as dendritic cells (DCs), to increase T cell activation and enhance the T cell response against cancer.
- Common side effects of these immunotherapeutics are due to inflammation, in which an over-activation of the immune response can result in T cell attack of healthy body cells.
- A mixed lymphocyte reaction (MLR) assay, which mimics the T cell:DC synapse, can be used to evaluate these drugs *in vitro*.
- Here we present an assay for quantification of T cell response in MLR in 96- or 384-well plates using the iQue<sup>®</sup> advanced flow cytometry platform.
- Samples of cells and supernatants are analyzed using kits from the iQue<sup>®</sup> portfolio for measurement of T cell phenotypes, proliferation and cytokine release.
- These data exemplify the power of iQue<sup>®</sup> to generate pharmacological data for checkpoint inhibitor effects, with potential to enhance drug discovery or research applications.
- Sartorius outsourcing services can work with you to assess your molecules method of action using our platform MLR assay.

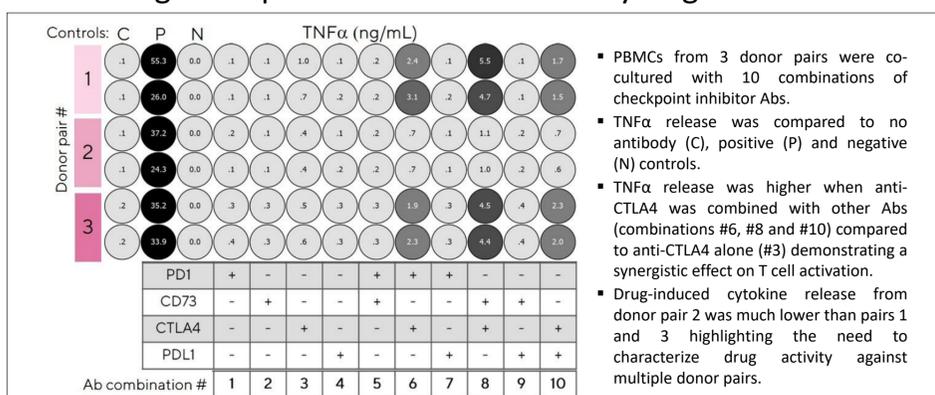
### Pembrolizumab (anti-PD-1) induces activation and inflammation



### Donor pairs differ in sensitivity to activation by anti-CTLA4



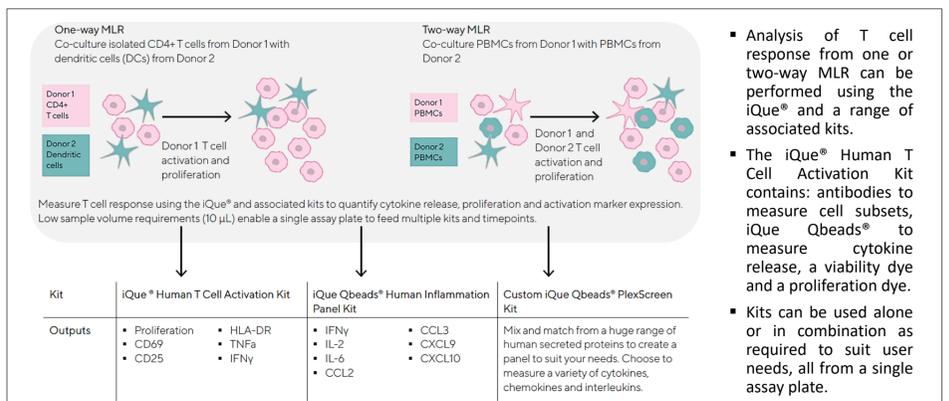
### Combining checkpoint inhibitors induces synergistic effects



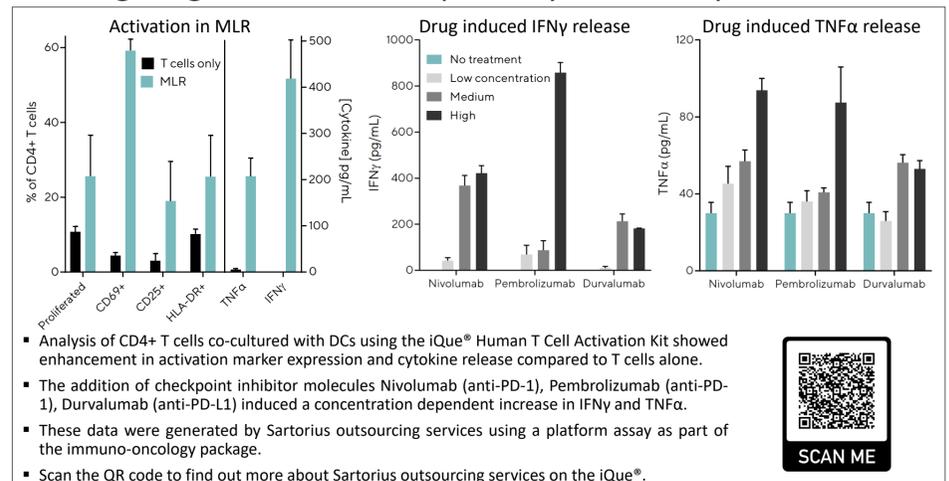
### iQue 3<sup>®</sup> System



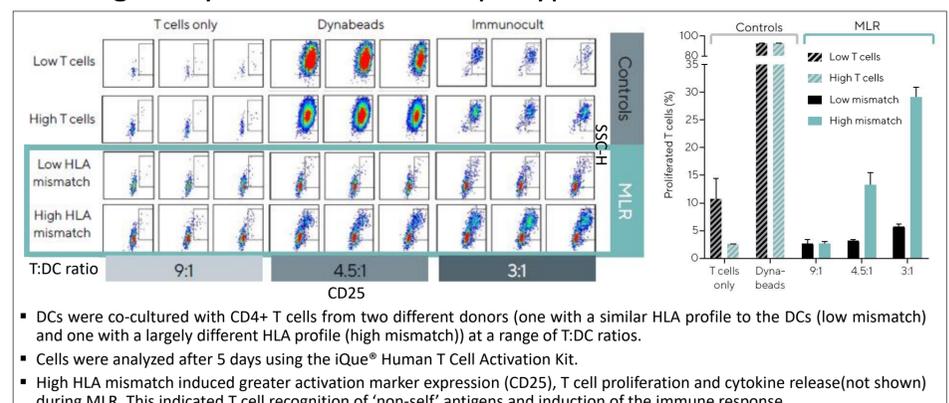
### Assay Concept



### Abs targeting the PD-1/PD-L1 pathway increase cytokine release



### Heterogeneity in donor's HLA haplotype induces T cell activation



### Dexamethasone (a corticosteroid) impacts cytokine release

