MAGNETIC RATCHETING CYTOMETRY TOWARDS MANUFACTURING SCALE SEPARATIONS OF “BEST IN CLASS” CART-T CELLS

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Adoptive cell therapies taking advantage of engineered Chimeric Antigen Receptors (CAR) or T-Cell Receptors (TCR) have shown incredible potential as “living drugs” that achieve personalized immunotherapies for cancer patients. However, variations in T cell transduction efficiency during genetic modification can lead to widely varied levels of expression\(^1\) (~2-orders of magnitude) which can possibly dilute therapeutic effectiveness and potentially contribute to off-tumor toxicity\(^2\). While research has shown that isolation of cell sub-populations with tightly controlled expression could lead to improved therapies\(^3\), limitations of current cell separation technologies prevent implementation at manufacturing scale workflows. Quantitative separation techniques (e.g. fluorescence assisted cell separation-FACS) do not scale for production of therapeutic doses, and magnetic assisted cell separation (MACS) techniques do not allow precise selection of cell sub-populations based on surface expression. Because of these limitations, enrichment of “best in class” CAR-T/TCR sub-populations at manufacturing scale throughputs remains impractical and non-economical.

To address this we are developing a quantitative magnetic cell separation platform for purifying “best in class” CAR-T/TCR cell sub-populations at manufacturing scale throughput utilizing a disruptive technology called magnetic ratcheting cytometry\(^4\). The technology operates by manipulating magnetically labeled cells in a massively parallelized manner with chips composed of Nickel-Iron pillar arrays. Using a micro-pillar arrays with increasing pitch cells can be rapidly separated based on the quantity of magnetic particles bound to their surface (Figure 1a). Because the quantity of bound magnetic particles is proportional to surface expression, cells can be separated quantitatively similar to FACS (Figure 1b). Moving towards a therapeutic cell manufacturing application, we performed preliminary experiments using anti-CD19/EGFR transduced Jurkat cells which demonstrated successful separations on a small prototype chip (Figure 1c).

Our goal is to validate and scale this technology to achieve quantitative purification of “best in class” CAR-T/TCR cells at manufacturing scale throughputs.

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