IMPACT OF INTERMEDIATE VOLUMES AND CELL DIAMETERS ON CELL RECOVERY: A PREDICTIVE MODEL FOR AUTOLOGOUS IMMUNOTHERAPY WORKFLOWS

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CAR-T immunotherapy workflows can vary from process to process and customer to customer. Variables that can alter overall processing efficiency include cell type, cell diameter, input cell numbers, input volumes, final volumes, and number of rinses, among others. These process-specific differences can make it difficult to estimate outputs, and equally challenging to select which processing parameters to use for which workflow. We hypothesized that intermediate processing volumes might vary as the size of the cell diameter increases, to accommodate the larger pellet created during centrifugation and other processing steps. From this, we developed a mathematical model and designed a study to test the validity of our hypothesis. Testing involved using Sepax™ C-Pro CultureWash v432 software to assess the calculated intermediate volume as a function of cell diameter by looking at percent recovery of the harvest. As shown in Equation 1 below, we predict the minimum intermediate volume required for the total number of cells to be function of cell size, total cell number, and an additional 20% buffer volume. Recoveries exceed 88% on a linear range up to 4 billion cells that are ~16 µm in size, where the formula holds true. While recoveries dropped to 68% for larger cell harvests, with a more optimized parameter set (e.g., altered flow rates), we rescued 86% on average for 6 billion cells. In summary, the model and associated data developed on the Sepax™ C-Pro around intermediate volumes provides a framework for future decision-making as scientists develop and adapt workflows to serve novel immunotherapy applications. Future work will address other variables of interest such as additional cell types, pump speed, and larger input cell numbers.

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$$IV = \frac{4\pi C(\frac{D}{2})^3}{3} * 1.2 * 1e6$$

Equation 1 – Formula to predict minimum intermediate volume in mL needed for the total cell number (C) at a given diameter (D) in meters.

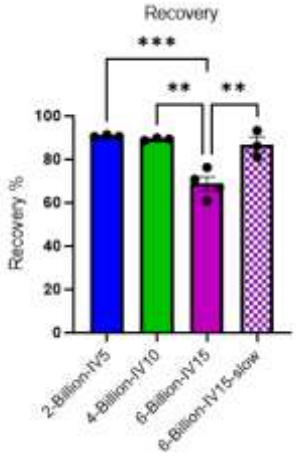

Figure 1 – Recovery in the final bag for each condition. Each bar represents the average of technical triplicate +/- SD, with each replicate shown in black. Differences are only significant when compared to 6-Billion-IV15, where great cell loss was experienced.