Bioelectric Characterization of T-cells With Electrochemical Impedance Spectroscopy

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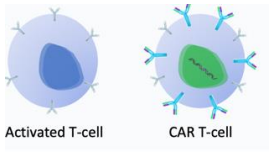
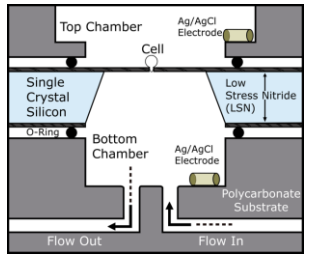
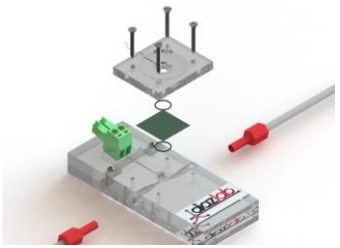


Novel immunotherapies use genetically engineered Chimeric Antigen Receptor T - cells (CAR T-cells) to target cancer cells.

Yet, during manufacture, not all T-cells express the CAR. The therapy has a higher efficiency if only potent CAR T-cells are supplied to a patient.

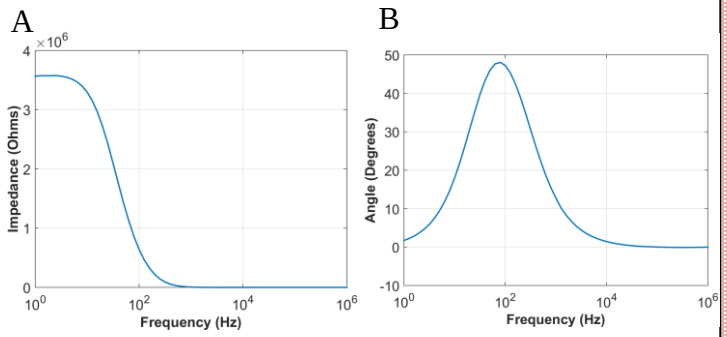




Electrochemical Impedance Spectroscopy (EIS) is a single-cell and label-free technique. EIS has proven to characterize cancer cells. Thus, it can be used to obtain a bioelectric fingerprint of the T-cells and the CAR T-cells. A fluidic device is used to trap a single cell in a silicon micropore chip.

The cell's impedance and phase angle are measured as a function of the frequency, for a given voltage (Figure 1). The data is transformed using Principal Component Analysis (PCA) (Figure 2).

Figure 1: EIS impedance (A) and phase angle (B) bode plots of a single cell



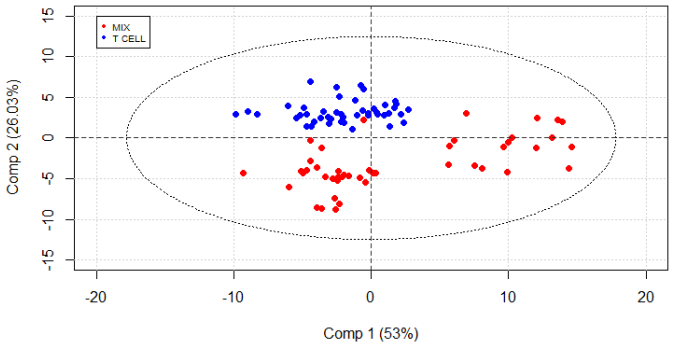


Figure 2: PCA plot which data points that corresponds to T-cells and a mix group (T-cells + CAR T-cells).

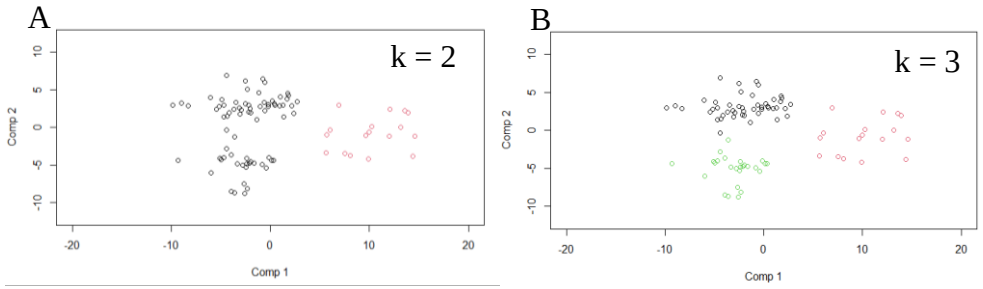
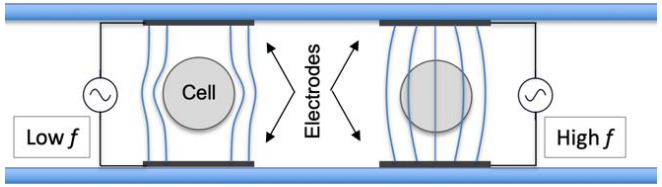


Figure 3: K-means clustering Figure 2 data in two (A) and three (B) groups

A clustering method was used to statistically segregate in groups PCA data (Figure 3).

K-means clustering algorithm groups data in, a user defined, k number of clusters by minimizing the Euclidian distance from each point to the centroid of the group. These statistical methods can not only be used to differentiate between T cells and CAR T-cell but can also identify sub-populations.

A drawback of this statistical method is its sensitivity towards outliers. Further analysis will use to identify and remove outliers in data



Future work also includes the design of another device that takes fast EIS data without the need of cell trapping.

It is known that EIS data for lower and higher frequencies provides information of the cell's surface and interior, respectively. Future work also aims to identify the frequency range where T-cells differ more from CAR T-cells.