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Senior Thesis Abstract

Investigating the Effect of B Cell Treatment on Native B Cell Populations in Amyotrophic Lateral Sclerosis Via Waddington Optimal Transport Analysis

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease that afflicts more than 200,000 patients worldwide. Considering the inefficacy of current treatments and the substantial impact of ALS on the immune system, it is crucial to introduce new immune-targeting therapies. B cell treatment, an experimental therapy, has shown promise in tissue repair and may prove beneficial. The purpose of this project is to elucidate whether the therapy has any observable effects on the immune system in ALS by calculating the developmental trajectories of patients' native B cells post-transfusion. This was done using Waddington Optimal Transport, a mathematical optimization method that identifies optimal couplings of cell ancestor and descendant probability distributions. Cytometry by time of flight profiles were acquired from a diseased patient at baseline and several time points after treatment. Cytokine data for Naive B cells, Memory B cells, and CD11c+ B cells were analyzed in Python using the NumPy and wot packages. Probability distribution couplings were calculated for all time point ranges in the form of transport matrices. Ultimately, B cell treatment induced several consistent changes in the cell populations. After the first transfusion, the proportion of the Naive to Memory category consistently increased. After the second transfusion, Naive to Memory consistently increased, Naive to CD11c+ consistently increased, and Memory to Memory consistently decreased. B cell treatment stimulated the development of Memory and CD11c+ B cells from Naive B cell ancestors. Since CD11c+ B cells are associated with inflammation, however, their increase in prevalence post-treatment is a concern. The effect of B cell treatment on inflammation levels in ALS should be determined in future studies.