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Modelling CD8 T cell dynamics in adoptive T cell therapy of melanoma

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CD8+ T cells play a critical role in anti-tumour immunity by directly targeting and eliminating cancer cells. However, during chronic antigen exposure, as occurs in cancer, these cells progressively lose their effector functions through a process known as exhaustion, ultimately compromising tumour control. The differentiation trajectory of CD8+ T cells—particularly into effector or stem-like progenitor exhausted, progenitor exhausted, and terminally exhausted phenotypes—critically shapes the outcome of the immune response in cancer [1, 2].

To investigate this process, we analyse high-dimensional flow cytometry data from a murine melanoma adoptive T cell therapy experiment. Using unsupervised clustering [3], we identify and quantify distinct CD8+ T cell subsets across multiple organs and time points, enabling us to track their kinetics during tumour progression. We propose a set of candidate mathematical models representing alternative CD8+ T cell differentiation pathways, defined by distinct lineage relationships between subsets. Each model is fitted to the experimental data, and model selection criteria are used to identify the differentiation motif that best explains the observed dynamics.

This integrated data-driven approach allows us to reconstruct CD8+ T cell differentiation trajectories in vivo and offers a framework for testing mechanistic hypotheses about T cell fate in the context of tumour immunity.

References

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