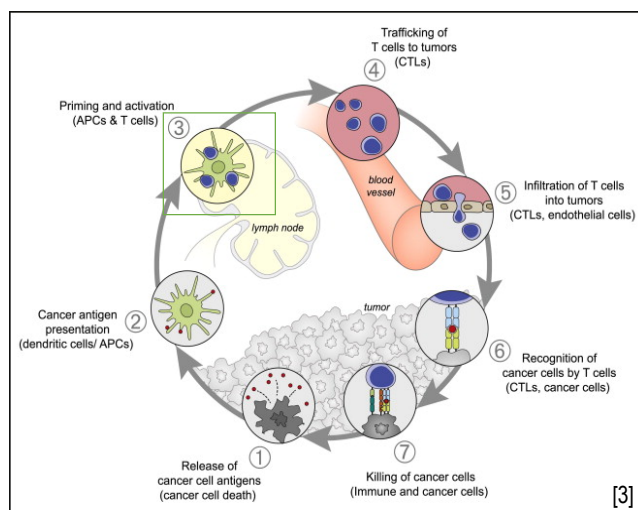


# Modeling and bioinformatics of combination immunotherapy in T cells

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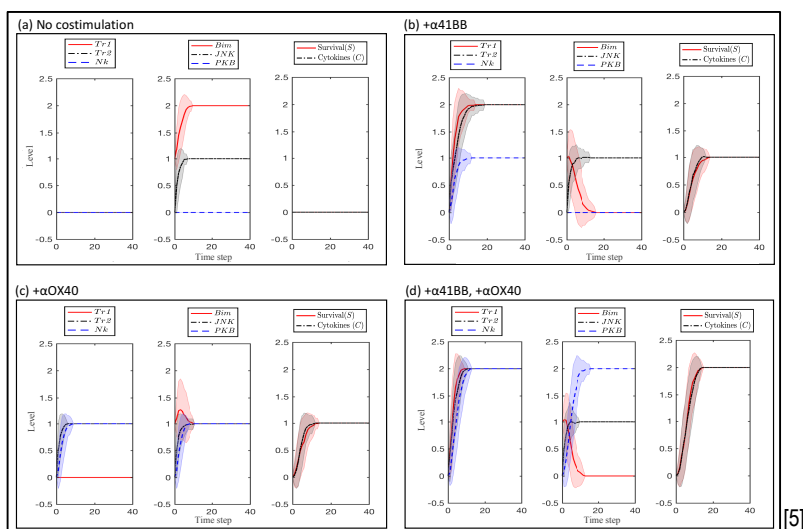
## Subproject 1: Model response to T cell dual costimulation

- OX40 (CD134) and 4-1BB (CD137) are T cell coreceptors that can boost anti-tumor T cell activity when stimulated by agonists [1].
- Dual costimulation (DCo) of both receptors results in a 'supereffector' T cell response [2].
- **Goal:** to develop and use a mathematical model of CD8+ T cell response to OX40 and/or 4-1BB agonists in order to better understand the mechanisms for supereffector T cell generation under DCo.



For a concise introduction to mathematical modeling for immunotherapy, please see our review in the Journal of Royal Society Interface [4].

**Results:** We developed a discrete, dynamic model that shows increased T cell response to dual costimulation vs. mono-costimulation, recapitulates known experimental outcomes, and provides insight into the underlying mechanisms for supereffector T cell generation [5].



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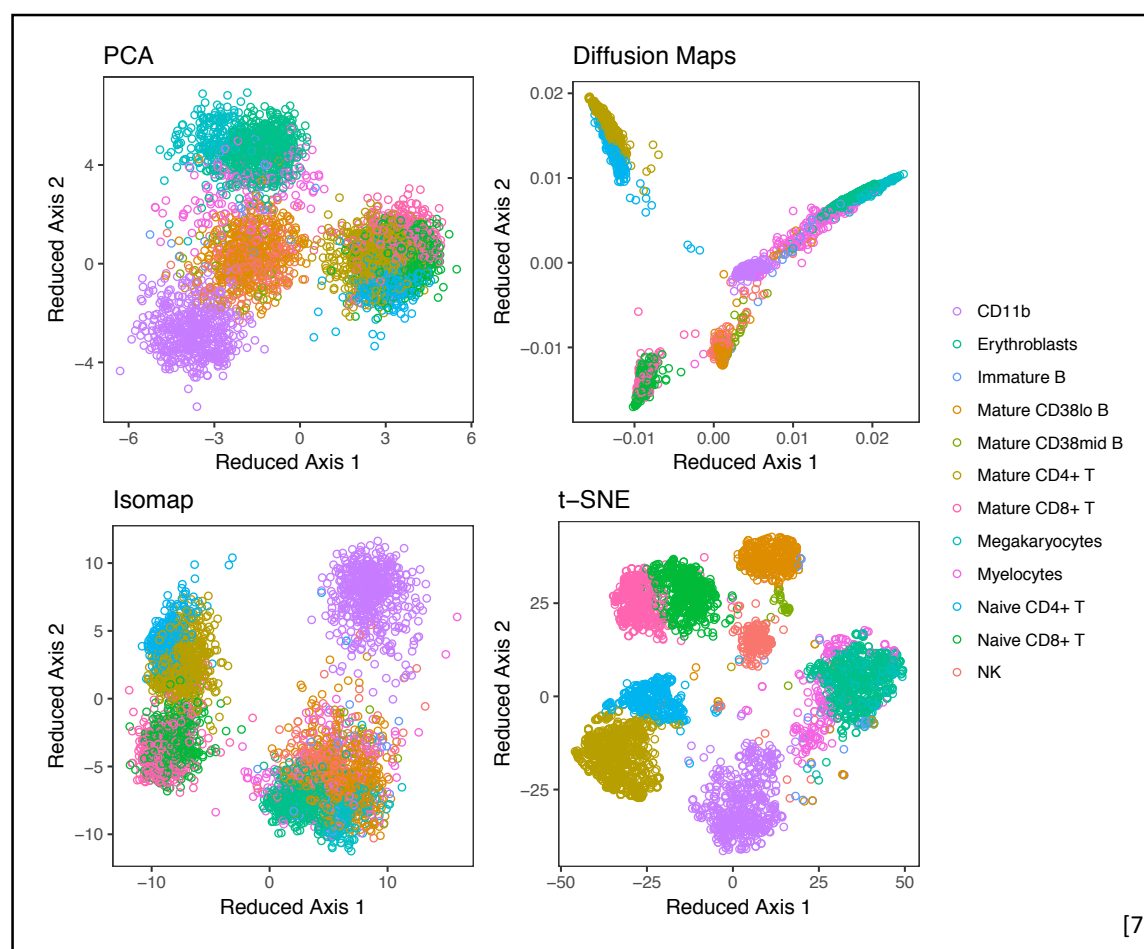
<sup>3</sup>Jackson Laboratory for Genomic Medicine, UConn Health

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## Subproject 2: Dimension reduction methods for CyTOF data

- In order to develop data-driven models of T cell activation and other immune-mediated processes, we need to use and develop algorithms to extract information from high-throughput data generated on experiments involving immune cells.
- Mass cytometry, also known as CyTOF, is a newly developed technology for quantification and classification of immune cells that can allow for analysis of >30 markers per cell [6].
- We conducted a comparative analysis of four dimension reduction techniques – principal component analysis (PCA), isometric feature mapping (Isomap), t-distributed stochastic neighbor embedding (t-SNE), and Diffusion Maps by implementing them on a benchmark mass cytometry data set [7].



Two-dimensional embeddings of a random sample of 10,000 cells from the benchmark dataset for the four dimension reduction techniques. Manually gated cell subtypes are labeled.

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Our preprint of this work is currently available here (link to <https://www.biorxiv.org/content/early/2018/12/03/273862>).

We are using the results to inform our analysis of data of both publicly-available and collaborator-generated T cell data.

### **Funding**

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