



BIOINFORMATICS 2016 FALL SEMINAR SERIES

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<http://bioinformatics.udel.edu/Seminars/Current>

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3:30pm
DBI Room 102

What makes T cells tick? Modeling the immune system across multiple spatio-temporal scales

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ABSTRACT: T cells play the critical role of orchestrating functional responses across multiple spatio-temporal scales in the adaptive immune system. Dissecting how T cells can bridge their rapid yet sloppy detection of non-self antigens into efficient pathogen eradication has fundamental consequence for understanding immune responses as emergent properties of collection of cells, and for the development of immunotherapies. Here we present results derived from our study of the dynamics of immune responses uncovering new modes of regulation of the immune responses.

First we show how studying T cells' response to small-drug inhibitors with single-cell resolution reveals two perpendicular modes of activation: digital (e.g. when the fraction of activated cells diminishes upon drug treatment, but cells remaining active appear unperturbed), versus analog (e.g. when the fraction of activated cells is unperturbed while their overall activation is diminished). We demonstrate that this digital/analog dichotomy of cellular response as revealed on the short timescales of cell signaling, translates into similar dichotomy on the long timescales of cell proliferation.

Second, we present experimental data documenting how integration of multiple signals (e.g. antigen- and cytokine-derived) enables T cells to fine-tune its self/non-self discrimination. In particular, we will discuss how antigen persistence plays a critical role in mediating the decision to proliferate or not.

To conclude, we will discuss how our systematic method of tracking how decisions are made in the immune system ushers new avenues in the development of immunotherapies. By combining immune monitoring at the single cell level, with computational modeling, we have uncovered novel modes of regulation of the immune response. We will present how these new modes create new opportunities to boost the immune responses in clinical settings (e.g. to eradicate tumors).