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Abstract

The T cell Repertoire as a biomarker for breast cancer detection

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Abstract:

To study the T-cell repertoire during tumor progression, we followed 10 female mice of a transgenic mouse strain that expresses the un-activated rat neu (Erbb2) oncogene, along with 5 control mice. These mice develop mammary tumors spontaneously over 5-8 months. To quantify the peripheral T cell repertoire, we extracted T cells from blood, every month, over the period of 9 months. Cells from these samples were sorted and later processed through a cDNA TCR and library preparation protocol using single-molecule barcoding and then NGS sequenced.

We were able to use the repertoire to classify tumor and non-tumor mice, using their immunological repertoire. Using feature selection algorithms, we were able to provide superior classification using a small subset (3 to 6 clones) of the T cell repertoire. Thus, machine learning

and feature selection allowed us to reduce the hundreds of thousands of TCR alpha and beta sequences obtained during repertoire sequencing, to a set of six clones, with which we can identify the source of a blood sample as tumor or control. We can further stratify older transgenic mice (older than 5 months) and those of older control mice, using the same small T cell clones' subset. This latter classification has been obtained with as little as three T cell clones.

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