Title

What tool or method do you wish existed?

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Title: Real-time reporting of cell-based immunotherapies in action

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Cell-based immunotherapies have transformed the treatment landscape for some hematological malignancies, but their efficacy against solid tumors remains limited. CRISPR screens have generated a long and growing list of target genes whose manipulation may promote the proliferation and/or function of immune cells. Similarly, library screens of receptor designs have identified components such as signaling domains that could significantly enhance activity. However, such screens are typically performed either *in vitro*, or with *in vivo* assays that rely on a single readout—i.e., the number of cells bearing a certain design—to identify hits. While cell persistence and proliferation can contribute to efficacy, they are not a direct assessment of anti-tumor activity. For example, it is quite plausible that the CAR-T cell clones that survive and expand the most in a screen are not the same clones that did the hard work of eliminating tumor cells.

Ideally, one would like the ability to quantitatively assess cellular composition and function in the tumor microenvironment (TME) in real time. Parameters of interest include where a cell is located relative to the tumor and to other immune cells, what the cell is doing (degranulating, secreting cytokines, etc.), and how many copies of a particular clone are present in the TME and how its population size changes over time. A technology platform that combines intravital imaging with multiplex and repeatable assessment of protein and/or mRNA transcripts could dramatically enhance our ability to develop next-generation cell-based therapies.