Towards automated tracking and analysis of individual killer cell cytotoxicity

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Individualized immune therapy of cancer is at the cutting edge of medical advances. To assess the efficacy of new therapeutic treatments, the killing efficiency of human natural killer (NK) cells, specifically targeted at cancer cells needs to be assessed. Although population-based assessment of NK cell killing efficiency is an established analysis method, it inherits several shortcomings. For example, cell counts can vary on a frame-to-frame basis, due to temporary miss-detections or cells migrating out of the field of view. The fate of these cells needs to be heuristically determined, which can lead to biased analysis results. In addition, analyses on a population level cannot reflect alterations in induced cell death by individual killer cells, which is a critical factor for the success of a therapy. There is indeed emerging evidence for heterogeneity among single NK cells, ranging from inefficient killers to “super killers”.

Building on a novel time-resolved single-cell cytotoxicity assay, which allows the assessment of quality, quantity, and kinetics of target cell death induced by single primary human NK cells (Backes et al 2018, PMID: 30190323), we are developing measurements and analysis methods to allow automated quantification of single NK cytotoxicity on a large scale. To overcome the above-mentioned shortcomings, we propose an individual tracking and analysis on a per-cell level. This will not only generate more accurate analyses on population level but will most importantly allow the fate determination of each NK and cancer cell, their respective contacts, and the time point of cell death induction. The killing history of individual NK cells will give many insights into single NK cell cytotoxic efficacies.