Automatically Finding Leukemic Cells that React Differently to Chemotherapeutics

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Abstract: We present a method for automating much of the experimental and computational workflow for phosphoflow cytometry. Specifically, we have built an analytical pipeline that accommodates transitional cell populations that are normally lost during manual analysis. This is important for analyzing cancer therapeutics. Since many cancer therapeutics directly affect the cell cycle, a transitional process, it is imperative that we analyze these transitions. We applied known cancer therapeutics over 4 different doses in 2 leukemic cell lines. By measuring cell cycle and signaling markers at the single cell level, we are able to measure the effect of cancer drugs on thousands of single cells. From this, we extracted a feature set from the cell signaling and cell cycle parameters measured. Then, we clustered these feature vectors to determine groups of drugs with similar mechanism. From these treatments, we have found features that distinguish between different drug clusters. We were able to replicate traditional drug classes with these clusters, with the exception of a subset of therapeutics. Further analysis showed that these drugs have a very different mechanism from others in the same class. Finally, we applied a multidimensional clustering algorithm and visualized drug-drug differences for these individual therapeutics.

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