Unraveling killing kinetics: insights from real-time cell analysis in oncology

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Presenter's short bio:

Fetene Tekle is a principal statistician at Janssen Pharmaceuticals R&D, based in Beerse, Belgium. His current focus is on oncology discovery statistics, specializing in methods for dose response modeling, in-vitro assays, and high dimensional ML models. Over the past 9 years, Fetene has also been involved in drug safety statistics, collaborating with toxicologists and other scientists in nonclinical safety evaluation.

Abstract:

Real-time cell analysis (RTCA) technologies, like IncuCyte® and xCELLigence® have emerged as invaluable tools in oncology research, enabling the study of cell killing over time. RTCA deepens the understanding of the interactions between cancer cells and immune cells. This information helps establish compounds with tumor-killing potential.

To identify compounds that have cancer treatment potential, researchers need to determine both the maximum killing capacity and the kinetics of the compounds. In this work, we explore the analysis of 3-dimensional (i.e., cell counts, time, and compound concentrations) data obtained from RTCA. Our proposed analysis approach compares time profiles of cells in control wells with compound-exposed wells to establish metrics capturing the earliest statistically detectable time point between the compound and the control. By applying these metrics across varying compound concentrations, time-concentration kinetic profiles are created.

Often these experiments are performed using biological replicates or multiple donors of immune cells. By accounting for the experiment design through model specification, the marginal-level time-concentration kinetic profiles can provide insights on the interplay between time and

concentrations in cell killing dynamics. These profiles allow differentiation of anti-cancer treatments on their kinetics, potentially accompanied by other summaries like maximum killing capacity.

Keywords: cell killing, immunotherapy, treatment efficacy, time kinetics, compound profiling