HIGH THROUGHPUT IMMUNO-ONCOLOGY POTENCY ASSAYS BASED ON MICROPATTERNING AND MACHINE LEARNING

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Adoptive cellular cancer therapies, especially the usage of autologous T cells expressing engineered antigen receptors (CAR-T cells) represent a promising new cancer therapy tool. The evaluation of quality, specificity and killing efficiency (potency) of CAR-T cell populations is crucial for the development of potent and safe patient specific CAR-T cell products.

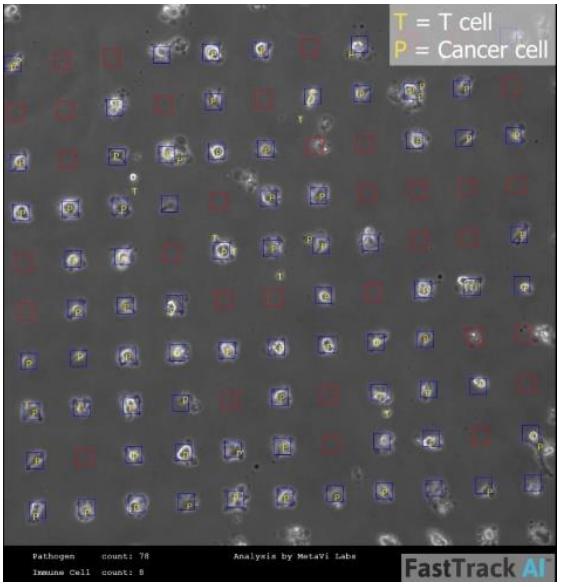

Figure 1: FastTrackAI analysis example; RCC 26 cancer cells immobilized on micropatterned adhesion pads interacting with JB4 T-cells.

Potency usually is evaluated on the population level by measurement of Interferon-gamma secretion or Cytotoxic T cell assays, such as Chromium-51 release assays. The evaluation on population scale, however, lacks sensitivity and fails in evaluating kinetic processes on a single cell level.

Live cell imaging allows for a quantitative, detailed and kinetic observation of CAR-T cell – cancer cell interaction and therefore yields a much more comprehensive potency analysis. To identify and track cells and intra and/or extracellular events, time-lapse series capturing multiple fluorescent probes at multiple positions are required. However, due to exposure and objective travelling times as well as data size, the throughput of such a comprehensive imaging approach is limited, implying a compromise between high content imaging and high throughput screening.

In order to overcome this limitation we developed a method which allows for high throughput, fluorescent probe independent CAR-T cell potency evaluation on a single cell level. Therefore, we combined an intelligent assay design which facilitates identification and tracking of CAR-T and target cells with machine learning based image analysis. Using our approach, we were able to analyze and track interaction and killing events, viability status and apoptotic body formation with high throughput and using just phase contrast imaging, qualifying our analysis as the only machine learning system currently being utilized in therapy development.