Spectroscopic imaging system for high-throughput viability assessment of ovarian microtumors in a microfluidic system

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ABSTRACT

There is a growing effort in the biomicrosystems community to develop a personalized treatment response assay for cancer patients using primary cells, patient-derived spheroids, or live tissues on- chip. Recently, our group has developed a technique to cut tumors in 350 µm-diameter microtissues and keep them alive on-chip, enabling multiplexed in vitro drug assays on primary tumor tissue. Two-photon microscopy, confocal microscopy and flow cytometry are the current standard to assay tissue chemosensitivity on-chip. While these techniques provide microscopic and molecular information, they are not adapted for high-throughput analysis of microtumors.

We present a spectroscopic imaging system that allows rapid quantitative measurements of multiple fluorescent viability markers simultaneously by using a liquid crystal tunable filter to record fluorescence and transmittance spectra. As a proof of concept, 16 microtissues composed of ovarian cancer cell line TOV112D were trapped in a microfluidic system, stained with a live cell marker (CellTrackerTM Green or Orange) and a dead cell marker (propidium iodide), and imaged. System response, background noise and autofluorescence were removed. Fluorescence intensity was normalized by the white-light spectrum at excitation to isolate the markers' intrinsic fluorescence from tissue absorption and scattering. Spectral un-mixing was applied to separate each fluorophore's contribution. We have demonstrated that rapid and simultaneous viability measurements on multiple microtissues can be achieved, which will have a significant impact to predict a tumor's response to multiple treatment options as well as in drug discovery to assess the potential of a drug candidate directly on human primary tissue.

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