Chemoresistance assessment of ovarian cancer microtumors trapped in a microfluidic chip using a spectroscopic imaging system

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ABSTRACT

In recent years, the microfluidic community has put a lot of effort in developing on-chip bioassays to measure cell response to a given set of stimuli. Our group has developed a chip to keep submicroliter spheroids or mouse xenografts in culture on-chip and perform *in vitro* chemoresistance assays. Current methods to analyze chemoresistance involve marking the microtumors with fluorescent live/dead cell markers and measuring their viability after drug treatment. While confocal and two-photon microscopy provides spatial information, and flow cytometry provides molecular information, they provide limited ways to assess cell population viability using multiple fluorophores on-chip and at multiple time-points non-destructively.

We present a liquid crystal tunable filter-based spectroscopic imaging system that can record fluorescence and transmittance spectra of samples located in the large field of view (36 mm^2). Two high-grade serous ovarian cancer cell lines, OV1946 (chemosensitive) and OV90 (chemoresistant), were transfected with green fluorescent protein (GFP) and red fluorescent protein (RFP), respectively, and used in different ratios to form co-culture spheroids. Their chemoresistance to carboplatin was followed by quantifying the GFP and RFP fluorescence after treatment. Each fluorescence image was normalized to the integration time and gain, and background noise, system response, and autofluorescence were removed. Spatial intensity variations were corrected. Spectral unmixing was then applied to separate each fluorescent protein's contribution. Building upon the results presented at Photonics West 2016 (96894E), multiplexed and simultaneous quantitative imaging of co-culture spheroids is demonstrated here opening the way to chemoresistance assays on-chip where multiple molecular tags can be used simultaneously.

SUMMARY

Our group has developed a microfluidic chip to keep submicroliter spheroids or mouse xenografts in culture on-chip and perform *in vitro* chemoresistance assays by marking the microtumors with fluorescent live/dead cell markers after drug treatment. Using a custom-built spectroscopic imaging system with a large field of view, chemoresistance assays on spheroids made from two ovarian cancer cell lines (OV1946, chemosensitive, green fluorescent protein-transfected, and OV90, chemoresistant, red fluorescent protein-transfected) were performed. Multiplexed and simultaneous quantitative imaging of co-culture spheroids is demonstrated here, opening the way to chemoresistance assays on-chip where multiple molecular tags can be used simultaneously.