Cancer cell morphology and dynamics classification based on label-free quantitative phase microscopy

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I review our latest advances in quantifying morphology and dynamics of cancer cells, followed by automatic classification of the cell metastatic potential. Detecting and monitoring cancer in its early curable stages is a clear and critical unmet need. Late stage metastatic forms of cancer are almost always fatal. We develop methods for characterizing cancer cells without exogenous cell labeling. Using such labeling might cause cytotoxicity by perturbing the cell environment, by influencing its behavior over time and its viability, and eventually damaging the accuracy of the test or prohibiting further clinical use of the cells. In addition, suitable exogenous markers might be not available for certain cell types, or might be difficult to use. We use interferometric phase microscopy implemented by clinic-ready compact modules, which are external to the imaging system, and thus are easy to use even in harsh environments. These modules provide the dynamic quantitative phase profiles of the cells, indicating the cell dry masses and volumes, parameters that are not available in conventional imaging. In Ref. [1], we used this approach, together with machine learning, for automatically classifying between cancer cells of different metastatic potential, originated from the same patients. In Ref. [2], we further developed this method, taking into account the temporal nanometer-scale fluctuations of the cells. Stiffness of cancer cells changes during cancer progression, which can be measured without labeling via the cell fluctuation profiles based on dynamic quantitative phase imaging. In Ref. [3], we classified blood cells and cancer cells of different metastatic potential during fast flow as a model for detecting circulating tumor cells in blood. The proposed techniques can yield powerful tools for cancer detection and monitoring, as well as tools for examining possible cancer therapeutic approaches.

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3. N. Nissim, M. Dudaie, I. Barnea, and N. T. Shaked, "Real-time stain-free classification of cancer cells and blood cells using inteferometric phase microscopy and machine learning," *Cytometry A*, Vol. 99, Issue 5, pp. 511-523, 2021.

Short Resume: Natan T. Shaked is a Professor and the head of the Department of Biomedical Engineering at Tel Aviv University, Israel. He is the coauthor of more than 90 refereed journal papers and 160 conference papers. He is chairing the SPIE Label-Free Imaging and Sensing (LBIS) Conference in SPIE Photonics West, San Francisco, USA. He is a Fellow in OPTICA (previously OSA) and a Fellow in SPIE. In 2015, he received the HORIZON2020 ERC grant.