Detection of Cancer Cells Response to EGFR Inhibitors by Raman Spectral Imaging

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Targeting epidermal growth factor receptor (EGFR) is one of the major strategies in cancer therapy. EGFR is overexpressed, dysregulated or mutated in many malignancies. The inhibitors of EGFR showed a promising therapeutic potency. They can be classified according to their inhibition mechanism into (1) the monoclonal antibodies that block the extracellular domain of the receptor to prevent ligand binding, and (2) small-molecule EGFR tyrosine kinase inhibitors that blocks the ATP acceptor site. Therefore, they disrupt downstream signaling cascade, which is responsible for tumor growth and progression. Confocal Raman microspectroscopy showed a promising capability towards human cell imaging and spectral characterization of the different cellular compartments without the need of labeling. Furthermore, it offers high resolution and great reproducibility. In the present study we have implemented the confocal Raman microscopy in detecting the response of cancer cells to EGFR inhibitors. Raman spectral datasets of cells were acquired with a pixel size of 500 nm. The data were analyzed by hierarchical cluster analysis (HCA). The clusters that contain the spectral data are then normalized, rearranged, and merged according to the spectral similarity. Eventually the mean spectra for the cell membrane, cytoplasm, and nucleus are then obtained and the difference spectra between untreated and drug-treated cells were calculated. The difference spectra of cell compartments showed obvious spectral changes. Consequently, these results show the changes of the biochemical composition of treated cells. This can be attributed to the therapeutic effect of EGFR inhibitors. These interacted agents can prevent autophosphorylation of different downstream pathways and trigger the apoptotic state.