Label-Free Monitoring of Cancer Cell Response to Chemotherapy Drugs Using Raman Spectroscopy

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Raman spectroscopy has being increasingly used for the analysis of biological specimens because of its unique ability to acquire information of their molecular content at the subcellular level without requiring exogenous labels, extensive sample preparation, or sample perturbation and destruction\cite{1}. The ability to use the intrinsic Raman fingerprint of cells to identify different cell phenotypes, such as cancerous and normal cells or different strains of bacteria cells, has been demonstrated. In addition to cell identification and discrimination, another attractive application of Raman spectroscopy is in monitoring cell dynamics since the Raman signals, unlike traditional fluorescence signals from exogenous dyes, do not photobleach.

Recent efforts in our laboratory have focused on applying Raman spectroscopy and microscopy to study the cellular response of cancer cells to chemotherapy drugs\textsuperscript{2}. This research is motivated by the need for new single cell analytical methods that can accurately predict the behavior of cells to different drugs for drug screening and discovery, patient treatment monitoring, and pharmacokinetics studies. Using laser tweezers Raman spectroscopy (LTRS)\textsuperscript{3} and line scan Raman imaging systems in our lab, we have studied the biochemical response of T lymphocytes to the cancer drug doxorubicin. We have investigated the Raman spectral changes that occur as a function of exposure time and drug concentration and have quantified the cell-to-cell reproducibility and the classification sensitivity and specificity of the Raman results. In addition, we are studying the effects of using local (subcellular) and global (total cell) Raman fingerprints on the detection sensitivity for monitoring drug induced cellular changes. Our findings indicate that local and global Raman fingerprints provide different information about the biochemical changes happening in a cell. These changes can be overlooked when relying on only one or the other. These results have important ramifications on the future implementation of Raman spectroscopy for single cell applications.

\begin{itemize}
\item \cite{1} Chan et al., Laser Photonics Rev, 2 (5), 325-349 (2008)
\item \cite{2} Moritz et al., Biomedical Optics Express, 1 (4), 1138-1147 (2010)
\item \cite{3} Chan et al., J. Biophotonics, 6 (1), 36-48 (2013)
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