Detection of the Metabolite of Molecular Targeted Agent in Colon Cancer Cells by Label-free Imaging

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In the last decade several methods were established to extend and support the chemotherapeutic treatment of cancer. Targeted cancer therapies block cancer growth and spread using small molecules interfering with tumor growth and progression. Many molecular targets for epidermal growth factor receptor (EGFR) selectively compete with the adenosine triphosphate-binding site of its tyrosine kinase domain. Detection of molecular targeted agents and their metabolites in cells/tissues by label-free imaging is attractive because dyes or fluorescent labels may be toxic or perturbative. Obtaining detailed information of uptake and metabolization allows improving the transport mechanisms of drug uptake and the development of new drugs. In our studies colon cancer cells were incubated with erlotinib (Tarceva) and investigated with Raman microspectroscopy (532 nm Nd:YAG Laser). It shows that the molecular targeted agent erlotinib is internalized and metabolized to its demethylated derivative in colon cancer cells. This observation was confirmed by fluorescence measurements in which the EGFR was labeled. We recognized that the erlotinib C≡C vibration is an excellent label-free marker for Raman imaging. This study provides new insights into drug uptake and intracellular targeting mechanisms, and demonstrates the potential of Raman microspectroscopy as a non-invasive label-free technique to investigate pharmacokinetics.