4D SERS IMAGNG OF ALKYNE-TAGGED SMALL MOLECULES IN LIVING CELLS

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Although fluorescence labeling is a powerful technique to highlight target molecules during optical imaging of biological samples, it has been difficult to be applied for observation of small molecules because labeling small molecules by fluorescent probes often alter their chemical properties. Recently, we proposed the use of alkyne as a tag for imaging small molecules [1]. Since alkyne exhibits a Raman peak that does not overlap with those from endogenous molecules, observation by Raman microscopy provides the distribution of the tagged molecules by detecting Raman scattering from alkyne. The technique has been utilized to image nucleic acids, lipids, drugs, and organelles [1-4]. However, the small scattering cross-section of Raman scattering hinders the application of imaging low-concentration molecules.

In this research, we demonstrate the use of surface-enhanced Raman scattering (SERS) to detect alkyne-tagged molecules in living cells. With introducing gold nanoparticles into a cell, the enhancement of the Raman signal at the surface of gold nanoparticle allows us to detect intracellular molecules at a low concentration. To examine the effectiveness of SERS in detecting drugs in living cells, we tagged a drug by alkyne and observed the entry of the drug into living cells by using slit-scanning Raman microscopy [5]. Gold nanoparticles with a diameter of 50 nm were introduced into the cells by endocytosis so that we can detect the entry of the drug into lysosome or endosome. The cells were scanned in 3D at a temporal resolution of about 20 sec/volume with using 660nm light for SERS excitation. The time-lapse imaging allowed us to monitor the drug uptake into the cells, which can be used to evaluate the efficiency of drug administration to cells.

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