In vivo imaging of alkynylated drug using surface-enhanced Raman scattering

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KEY WORDS: Raman scattering, surface-enhanced Raman scattering, SERS, drug imaging

Raman scattering provides molecular information of the analyte by reflecting chemical vibrations. We have developed Raman imaging techniques and combined with surface-enhanced Raman scattering (SERS) spectroscopy to develop biological applications by introducing metallic nanoparticles into live cells and tissues for the enhancement of sensitivity in molecular detection[1-3].

In this research, we developed a technique to observe a distribution of small drugs in a brain tissue by utilizing alkyne-tag Raman imaging [4]. Alkyne has a Raman peak around 1900-2300 cm^{-1} which is distinct from the Raman peaks of typical biological molecules[5]. We observed a distribution of an alkyne-terminated drug, which works as a selective serotonin reuptake inhibitors for antidepressants in brain. We incorporated an alkynyl group by replacing the nitrile group at the C-5 position of the 1,3-dihydroisobenzofuran ring and chemically synthesized alkynylated. We confirmed that alkynylated S-citalopram levels in the brain were not significantly different from S-citalopram levels using liquid chromatography-tandem mass spectrometry and brain microdialysis. We then tested whether alkynylated S-citalopram can be detected with SERS *in vitro*. Alkynylated S-citalopram showed a strong Raman peak in the silent region and was detected with a sensitivity of 400 pM. Finally, we performed SERS imaging on coronal mouse brain sections and successfully visualized alkynylated S-citalopram in a part of the brain; dorsal raphe nucleus, using a home built slit scanning Raman microscopy(Figure 1)[6].

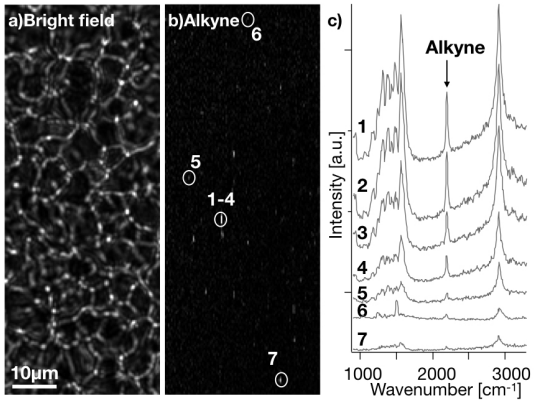

Figure 1: a)Bright field image of the brain tissue b)SERS spectra of the drug. c)Spectra indicated at b).

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