Live cell assay using SERS

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Technology Overview:

In order to overcome current spatial and temporal resolution of the live cell Raman imaging techniques, the near-infrared (NIR)-sensitive SERS-active nanoparticles that can selectively target specific intracellular organelles are introduced. The use of highly SERS-sensitive nanoparticles can greatly decrease acquisition time per pixel and allow us to obtain the intracellular particle distributions for specific subcellular organelles. Further, the great multiplexing capability from narrow Raman signature opens new biomedical directions.

Biomedical application potential:

We reported a method to achieve high speed and high resolution live cell Raman images using small spherical gold nanoparticles with highly narrow intra-nanogap structures responding to NIR excitation (785 nm) and high-speed confocal Raman microscopy. The three different Raman-active molecules placed in the narrow intra-nanogap showed a strong and uniform Raman intensity in solution even under transient exposure time (10 ms) and low input power of incident laser (200 μW), which lead to obtain high-resolution single cell image within 30 s without inducing significant cell damage. The high resolution Raman image showed the distributions of gold nanoparticles for their targeted sites such as cytoplasm, mitochondria, or nucleus. The high speed Raman-based live cell imaging allowed us to monitor rapidly changing cell morphologies during cell death induced by the addition of highly toxic KCN solution to cells. These results suggest that the use of SERS-active nanoparticle can greatly improve the current temporal resolution and image quality of Raman-based cell images enough to obtain the detailed cell dynamics and/or the responses of cells to potential drug molecules.

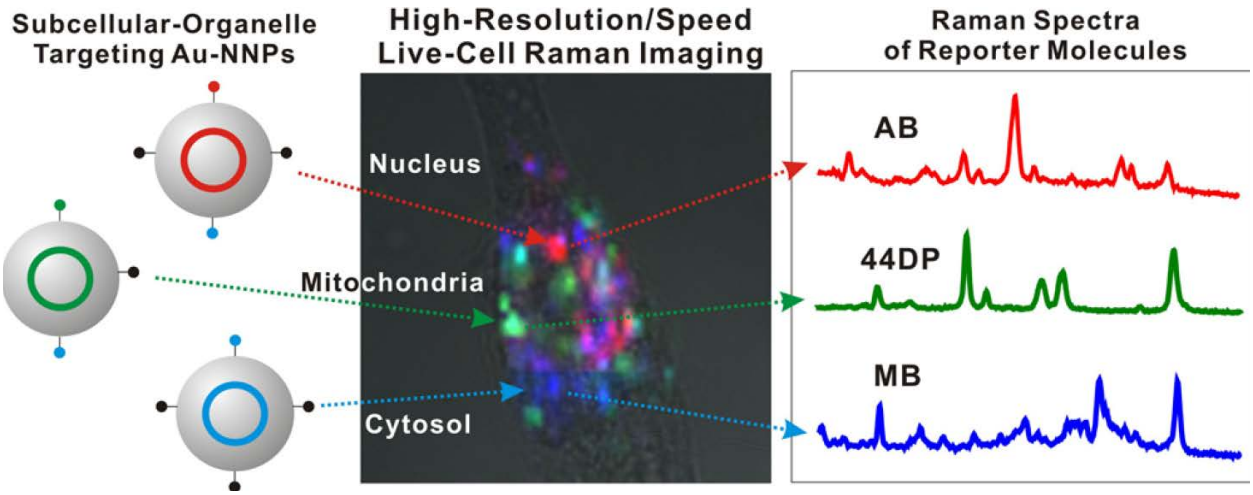
Circulating biomarkers have emerged as promising non-invasive, real-time surrogates for cancer diagnosis, prognostication and monitoring of therapeutic response. Emerging data, however, suggest that single markers are inadequate in describing complex pathologic transformations. Architecting assays capable of parallel measurements of multiple biomarkers can help achieve the desired clinical sensitivity and

specificity while conserving patient specimen and reducing turn-around time. In addition to offering extensive multiplexing capability, SERS immunoassay provides higher sensitivity than conventional immunoassays and demonstrates exquisite specificity owing to selective formation of conjugated complexes and fingerprint spectra of the Raman reporter. We envision that clinical translation of this assay may further enable asymptomatic surveillance of cancer survivors and speedy assessment of treatment benefit through a simple blood test.

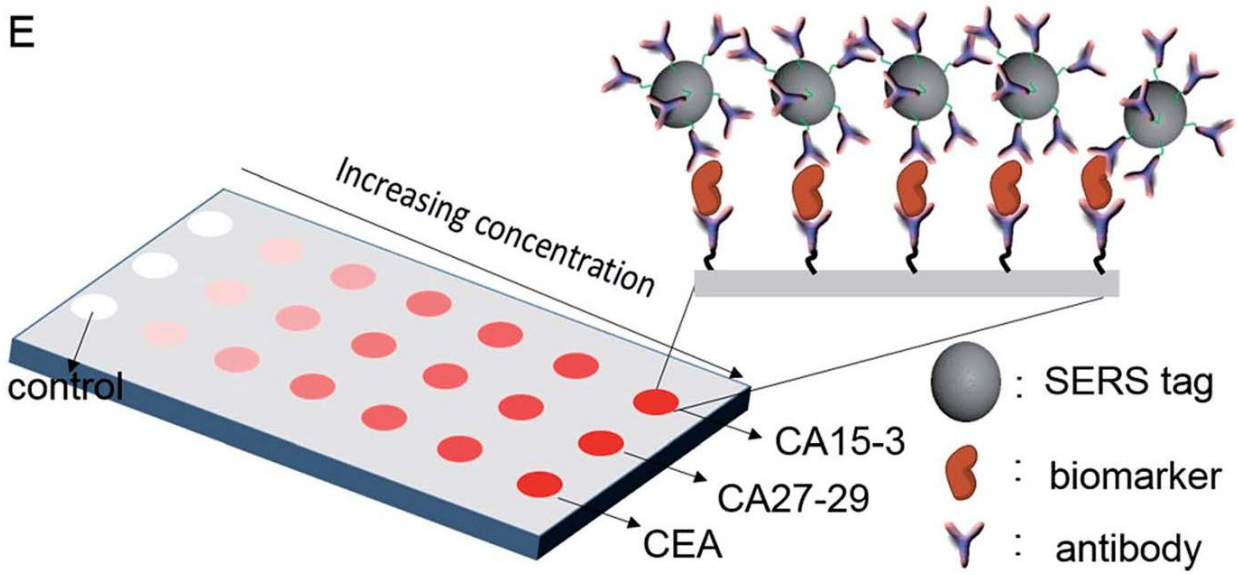
Ongoing project:

High resolution live cell imaging using SERS nanoparticles.

Multiplexed detection of cancer markers with SERS immunoassay



Multi-color live cell images with SERS particles targeting nucleus, mitochondria and cytosol.



Schematic illustration of SERS assay for multiplex detection of biomarkers

Background Publications

1. Lim DK, Jeon KS, Kim HM, Nam JM, Suh YD. Nanogap-engineerable Raman-active nanodumbbells for single-molecule detection. Nat Mater. 2010; 9(1):60-7.
2. Lim DK, Jeon KS, Hwang JH, Kim H, Kwon S, Suh YD, Nam JM. Highly uniform and reproducible surface-enhanced Raman scattering from DNA-tailorable nanoparticles with 1-nm interior gap. Nat Nanotechnol. 2011; 6(7):452-60.
3. Li M, Zhang J, Suri S, Sooter LJ, Ma D, Wu N. Detection of adenosine triphosphate with an aptamer biosensor based on surface-enhanced Raman scattering. Anal Chem. 2012; 84(6):2837-42.
4. Li M, Cushing SK, Zhang J, Suri S, Evans R, Petros WP, Gibson LF, Ma D, Liu Y, Wu N. Three-dimensional hierarchical plasmonic nano-architecture enhanced surface-enhanced Raman scattering immunosensor for cancer biomarker detection in blood plasma. ACS Nano. 2013; 7(6):4967-76.

Center Publication

1. Li M, Kang JW, Dasari RR, Barman I. Shedding light on the extinction-enhancement duality in gold nanostar-enhanced Raman spectroscopy. Angew Chem. 2014; 53(51):14115-9
2. Kang JW, So PTC, Dasari RR, Lim DK. High Resolution Live Cell Raman Imaging Using Subcellular Organelle-Targeting SERS-Sensitive Gold Nanoparticles with Highly Narrow Intra-Nanogap. Nano Lett. 2015; 15(3):1766-72.
3. Li M, Kang JW, Sukumar S, Dasari RR, Barman I. Multiplexed detection of serological cancer markers with plasmon-enhanced Raman spectro-immunoassay. Chem Sci. 2015; 6(7):3906-3914.