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TITLE

Profiling Alternative Splicing in Breast Cancer Cells by Surface-Enhanced Raman Spectroscopy

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Alternative pre-mRNA splicing takes place during the development, progression, and metastasis of breast cancer. To elucidate the role of alternative splicing in tumorigenesis and to explore the possibility of using the alternative splicing profile as a breast cancer marker, a sensitive detection platform that can monitor multiple targets simultaneously and provide reliable quantitative estimation is highly desirable. With its superb multiplexing capability, single-molecule sensitivity, photostability and a wide choice of labels, surface-enhanced Raman scattering (SERS) based detection is very promising to meet the requirements.

We designed and fabricated a SERS based DNA probe to covalently attach both the DNA probe molecules and the nonfluorescent Raman tags to the surface of gold nanoparticles (DNA-AuP-RTag). Simultaneous identification of up to eight DNA-AuP-RTag probes in a mixture was demonstrated. Then we developed an array platform on a gold-coated glass slide to detect multiple DNA targets simultaneously through sandwich structures utilizing these DNA-AuP-RTag probes. A four-plex detection was demonstrated for DNA sequences specific to four alternative splice variants of breast cancer susceptibility gene 1 (BRCA1) including Δ(11q) (the last 3309 nt deleted from exon 11), Δ(9, 10) (exon 9 and 10 deleted), Δ(5) (exon 5 deleted) and Δ(5q, 6) (the last 22 nt of exon 5 and the entire exon 6 deleted). Detection sensitivity of up to 1 fM was achieved. Furthermore, we employed a strategy comprising DNA/RNA hybridization, S1 nuclease digestion, and alkaline hydrolysis to obtain two DNA targets specific to two alternative splice variants of BRCA1, Δ(9, 10) and Δ(5), from MCF-7 and MDA-MB-231 breast cancer cells. These targets were detected simultaneously using the SERS array platform and their expression levels were determined quantitatively by using the inherent plasmon-phonon mode of the SERS substrates as a self-referencing standard. The analytical methodology developed can be extended to other nucleic acid based diagnostics.

Biography

Dr. Lan Sun has received her PhD in Biological Engineering from Purdue University in 2008. Currently, she is a postdoctoral researcher with Sandia National Laboratories working at Joint BioEnergy Institute. She has published several research papers in highly reputed peer-reviewed journals in the area of nanobiosensing and hyperspectral imaging. She is a member of the American Chemical Society and the American Institute of Chemical Engineers. She is serving as a reviewer for several journals in the area of bio & chemical sensing and nanotechnology.