Detection of mutations in hTERT gene promoter sequence without DNA amplification by novel SERRS sensor for cancer diagnostics

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Recently developed liquid biopsy analysis based on circulating tumor DNA (ctDNA) released by tumor cells in body liquids significantly enhanced non-invasive molecular diagnostics of cancer as ctDNA contains all mutations generated in the tumor. For example, mutations in the promoter of telomerase catalytic subunit (TERT) gene are highly specific for multiple cancers, including bladder cancer. Thus, selective determination of such mutations can improve early diagnostics of cancer and monitoring of cancer progression and treatment. Main limitations for existing methods of ctDNA detection in body fluids are: a) a low portion of tumor DNA in comparison to wild type circulating DNA that results in poor sensitivity, especially in case of preliminary DNA amplification and b) high fragmentation of cell free DNA that complicates DNA purification. In this regard, novel approaches without DNA isolation and amplification for specific detection of tumor DNA are of unmet medical need.

Spectroscopy Resonance Raman Scattering (SERRS) allows detection of target molecules in multicomponent complex mixtures without isolation at fM concentrations due to the resonant enhancement of the signal. To apply this approach, we developed SERS-active colloids based on silver nanoparticles deposited on planar sensor surfaces. Short oligonucleotide probes were immobilized on silver nanoparticles using anchor sequences. As a result, we were able to detect DNA with TERT promoter sequence from femtomolar to micromolar concentration with the linear response of SERRS signal.

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Biography

Zvereva M has her expertise in investigation of telomerase as molecular target for anticancer drug development and base of new molecular tests for diagnostics of oncogenic process. Her research group was concentrated on understanding of telomerase functioning and regulation using biochemical and bioengineering approaches for model organisms. They optimized the telomerase activity tests and used it in different ways (Biochemie, 2013; Mol Cell Biol., 2014; and etc.), created two novel classes of telomerase inhibitors for future anti-cancer therapy development (J Med Chem. 2014; Nucleic Acids Res., 2014) and one of them could be used possibly for diagnostics (Biochemistry (Moscow), 2015, review). The screening of telomerase activation in clinical samples and assessing the potential role of splicing events during activation of telomerase was done for cervical cancer and pre-cancerous lesion (Biochimie, 2010). As a scientist of IARC she participated in development of method for detection of mutations in hTERT gene promoter sequence for bladder cancer diagnostics (EBiomedicine, 2019).

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