DOCTORATS INDUSTRIALS

EL PLA DE DOCTORATS INDUSTRIALS

PROJECTE DE DOCTORAT INDUSTRIAL
EXPEDIENT 2015 DI 015

DADES DE L'EMPRESA I DE L'ENTORN ACADÈMIC

Títol del projecte
Surface-Enhanced Raman scattering (SERS) spectroscopy of RNA.

Empresa
Medcom Advance, SA

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BREU DESCRIPCIÓ DEL PROJECTE DE RECERCA

Among several analytical techniques, Surface-Enhanced Raman scattering (SERS) spectroscopy has emerged as a rapid and effective method for identifying unknown species, finding direct application in biomedical analysis, forensics, art and cultural heritage and homeland security. In the very recent years, we have witnessed an upsurge of interests in the direct SERS analysis of DNA boosted by the efforts from several groups addressing the reproducibility issues associated with the DNA interaction with negatively charged colloids. Our group instead developed an alternative approach based on the fabrication of positively-charged silver nanoparticles coated with spermine molecules (AgNP@Sp). Spermine molecules attached to the metal surface promote the electrostatic adhesion of the phosphate groups onto the NPs resulting in the formation of highly SERS active and stable clusters in suspension and the generation of highly reproducible SERS spectra at nanogram levels. On the other hand, a surprisingly scarce number of papers describe the direct SERS analysis of RNA, which was also limited so far to microRNA structures or, more often, to simple homopolymeric or bipolymeric single strand sequences.

Recently, the central roles of RNAs become one of the most dynamic and fast growing field. In particular, mature microRNAs (miRNAs) are a class of evolutionally conserved, single-stranded, small (approximately 19–23 nucleotides), endogenously expressed, that play critical regulatory roles in a vast range of biological processes including early development, cellular differentiation, proliferation, apoptosis, developmental timing etc. Thus, alterative expression of miRNAs has been associated with a number of diseases. Tremendous observations have been

made in linking the aberrant expression levels of miRNAs to the initiation and development of human diseases, genetic disorders, and altered immune system function. Therefore, miRNA expression profiles can be used as biomarkers for the onset of disease states.

In this project, the student will develop a direct SERS-based in vitro detection method for miRNA expression and quantification of miRNA biomarkers for molecular diagnostic applications in colon cancer.

In the first step of his/her project, the student will synthesize and fully characterize positively charged silver nanoparticles (AgNPs). The student will also investigate the possibility to improve the synthetic protocol to yield positively charged nanoparticles with better size monodispersity and as improved sensitivity for miRNA detection.
These substrates will then be exposed to buffered solutions of synthetic miRNAs. The SERS experiments with controlled synthetic RNA will serve both as control experiments and to acquire the necessary database, providing the spectroscopic tools to interpret the results with miRNAs extracted from unhealthy cells using commercial extraction kits. In addition to the direct vibrational analysis, the SERS spectra will be classified using partial least squares discriminate analysis (PLS-DA), an established and statistically robust method for objective and blind data classification. Training spectra of known origin will be used to build a PLS-DA model with a class reserved for each miRNA sequence. The SERS-based detection strategy will be finally combined with a microfluidic device able to manipulate and analyze small volumes of sample in a rapid and continuous way.