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PROJECTE DE DOCTORAT INDUSTRIAL EXPEDIENT 2014 DI 051

DADES DE L'EMPRESA I DE L'ENTORN ACADÈMIC

Títol del projecte

Detection of DNA lesions and mutations by Surface-enhanced Raman Scattering (SERS) Spectroscopy

Empresa

Medcom Advance, SA

Responsable de l'empresa

Carlos Villanueva Leal

Universitat

Universitat Rovira i Virgili – Centre Tecnològic de la Química de Catalunya (CTQC)

Director/a de tesi

Ramon Angel Alvarez Puebla

Treballador/a de l'empresa i doctorand/a

Judit Morlà Folch

BREU DESCRIPCIÓ DEL PROJECTE DE RECERCA

The prime objective for every life form is to deliver its genetic material, intact and unchanged, to the next generation. To ensure the high-fidelity transmission of genetic information, cells have evolved mechanisms to monitor genome integrity. An inability to respond properly to, or to repair, DNA damage leads to genetic instability, which in turn may enhance the rate of cancer development. Importantly, these mutations can also influence how the tumor will respond to therapy. Gaps in our knowledge may be responsible for the failure to produce consistent and definitive results when applied to understanding the role of DNA damage in disease, highlighting the need for further studies.

Nowadays, the exploring of the genetic information carried by DNA has become a major scientific challenge, finding a vast set of applications in different fields, such as medical diagnostics, genomic screening, drug analysis, forensic and bioterrorism. The vast majority of current DNA detection methods involves the use of (i) amplification strategies, such as polymerase chain reaction (PCR), which however produce inaccurate end point quantification due to the difficulty in maintaining linear, and (ii) fluorescent reporters as part of the signal transduction, which require costly chemicals and complex chemistry.

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In the broad field of plasmonics, Surface-enhanced Raman Scattering (SERS) spectroscopy has arisen as a powerful analytical tool in the detection and structural characterization of biomolecules. SERS combines the intrinsic structural specificity and high flexibility of Raman spectroscopy with an extremely high sensitivity resulting from the amplification of the optical signal by localized surface plasmon resonances occurring at noble metal nanostructured surfaces (mostly silver or gold) when analytes adsorb near/at such surfaces. Recently, studies carried out in our group show that appropriate modification of the surface chemistry of colloidal silver nanoparticles with positively charged molecules promotes the fast adsorption of double stranded DNA (dsDNA) structures and the formation of nanoparticle clusters where the biomolecules reside at the interparticle junctions. As a result, highly reproducible and intense SERS spectra of dsDNA in the nanomolar regime can be acquired.

In the first step of his/her project, the student will synthesize and fully characterize positively charged silver nanoparticles (AgNPs) which will be employed as the SERS substrate both in their original colloidal suspension and included into hybrid plasmonic microparticles consisting of a microscopic bead of silica covered with an external dense shell of interacting AgNPs. These substrates will then be exposed to buffered solutions of synthetic dsDNA systems and their modified forms (i.e. single-base mistmaches, double-helix breakages, oxidative lesions, adducts with cancer-causing chemicals etc.). This will serve as control experiments, providing the spectroscopic tools to interpret the results with genomic DNA isolated from eukaryotic cells cultured in our lab. Subsequently, the student will isolate dsDNA from unhealthy cells, or model cells for a disease, carrying a mutation (knock out cells) which will be investigated by SERS and compared to their healthy counterpart (wild type cells). Finally, healthy cells will be exposed to exogenous stress (i.e. UV irradiation, human-made mutagenic chemicals etc.) and their DNAs analyzed by SERS upon isolation. Ultrasensitive, precise and fast detection of genetic modifications, as well as disclosure of unknown DNA lesions, would represent a breakthrough advance towards the understanding of the complex cancer process and the development of effective treatments.