DOCTORATS INDUSTRIALS

EL PLA DE DOCTORATS INDUSTRIALS

PROJECTE DE DOCTORAT INDUSTRIAL EXPEDIENT 2014 DI 052

DADES DE L'EMPRESA I DE L'ENTORN ACADÈMIC

Títol del projecte
Control of intracellular ion homeostasis is essential for all cellular organisms.
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BREU DESCRIPCIÓ DEL PROJECTE DE RECERCA

Control of intracellular ion homeostasis is essential for all cellular organisms. Eucaryotic cells regulate numerous reactions by continuously exchanging ions between the inside and the outside environment but also inside the cells between the different organelles. Many pathological situations like liver insufficiency, infection, diabetic ketoacidosis, hypercatabolism, fibrosing disorders, sickle cell anemia, or cystic fibrosis are associated with a defective regulation of the ion concentrations. Often such an alteration affects more than one ion specie at the same time. Nowadays the concentration of some ions inside different organelles is not known yet. Furthermore, the dynamics of ions flux under physiological and pathophysiological conditions cannot be determined due to the lack of appropriate techniques. So far most of the techniques employed make use of electrodes, fiber-based optodes or are based on a microanalysis. These techniques either work well for solutions but not for living organisms or are destructive. For subcellular (intracellular) analyte detection smaller noninvasive sensors are required, especially if long term measurements in live cells are envisaged. One possibility towards this direction is the use of nano/microparticles as carrier matrix for analyte-sensitive molecules. The sensors allow for the transduction of chemical concentration information into a read-out signal. Mostly optical signals are used as read-out because of their ease of detection. Optical sensing can be performed with fluorophores but also with plasmonic nanoparticles. The highest limitation of organic fluorophores beside the low selectivity for the target ligand or their finite response, is their multiplexing abilities. The response of different dyes is detected if the emission wavelengths are spectrally separated, thus the number of analytes detected is linked to the spectral resolution of the fluorescent signals. A way of overcoming these limitations is by using plasmonic nanoparticles as carriers for analyte-sensitive molecules. Metal nanoparticles like Au, Ag and Cu have their plasmon peak (i.e. the collective oscillation of the surface electrons upon light irradiation) in the visible region. Au is an inert material and an ideal candidate to work with living organisms. If excited with light matching the plasmon absorbance, these materials are able to enhance the Raman signal of a nearby molecule. In an effect called surface enhanced Raman scattering (SERS) we take the advantage of using the molecular signature provided by the Raman spectrum and the extraordinary enhancement of the electromagnetic field provided by the nanoparticle to increase the selectivity and sensitivity of the system to detect ions even at low concentrations while allowing multiplexing.

Within the context of this PhD, plasmonic nanocapsules consisting of porous silica bearing gold nanoparticles conjugated with different ion sensing molecules will be used. The shell is permeable allowing for the free diffusion of ions that can then specifically interact with the capturing molecule. Upon interaction, the vibrational spectrum of the capturing molecule will change and due to the close proximity to the surface of the plasmonic nanoparticle, the specific Raman signal will be enhanced so that the presence of the analytes can be detected. By coupling different capturing molecules to the gold nanoparticles inside the nanocapsules, different physiologically relevant ions will be sensed in parallel and since the Raman signal is unique for each molecule, multiplexing should be possible to perform. Furthermore, the enhancement is of several orders of magnitude allowing for very low detection limits. Eucaryotic cells will be exposed to the sensing nanocapsules for the first demonstration of parallel sensing within living organisms. Further functionalization of the nanocapsules surface with targeting moieties will allow the sensor to be directed to specific organelles where ion concentrations need to be determined. These approach will allow to create a system for the ultrasensitive and selective detection of ions inside living cells at the subcellular level to monitor ion homeostasis.