Asesora: Dra. Tzarara López Luke

Co - Asesor: Dr. Elder de la Rosa Cruz

Sinodales: Dra. Valeria Piazza
(Sinodal Interna, Secretaria)

Dr. Arturo Ponce Pedraza
(Sinodal Externo – University of Texas at San Antonio, Vocal)

Dra. Tzarara López Luke
(Asesora de Tesis, Presidenta)

Tesis: **"STUDY OF INTERACTION EFFECTS OF QUANTUM DOTS AND GOLD NANOPARTICLES WITH CELLS BY RAMAN SPECTROSCOPY AND ADVANCED MICROSCOPY"**

Resumen:

At present quantum dots and gold nanoparticles are widely used in bio-applications due to their size and highly efficient optical properties. The present work is focused on the study of the interactions of these materials at a cellular level. The results of this research show the way of internalization and adsorption of thioglycolic acid (TGA) capped CdTe quantum dots (TGA@CdTe QDs) into human and plant cells together with a systematic Raman spectroscopy study of their interaction with cellular molecules. Raman spectroscopy is carried out through the use of gold nanoparticles as nanosensors for SERS biomolecule detection. Naked gold nanoparticles are used to assess the interactions of the TGA@CdTe QDs with the cells whereas the SERS activity of Au/SiO2 clouds in powder is studied for tissue applications. The localization and interaction of TGA@CdTe QDs within the extracellular matrix (ECM) of Haematococcus pluvialis (Chlorophyceae) microalgae (HPM) after an incubation period of five minutes is presented. Changes in the Raman spectrum of HPM induced by the adsorption of the TGA@CdTe QDs are successfully found by using naked gold anisotropic structures as nano-sensors for the SERS effect. Raman spectroscopy results show that TGA@CdTe QDs interact with the biomolecules present in the ECM. Sample preparation and characterization by complementary techniques such as confocal and electron microscopy are also used to confirm the presence and localization of the nanoparticles in the algae.

Stressed Haematococcus Pluvialis Microalgae (SHPM) are used as control sample since they do not present an ECM. Compared with the HPM samples, a small amount of TGA@CdTe QDs is observed on the outside of the secondary cell wall of SHPM. Therefore, it is proposed that the secondary wall prevents or reduces the interaction of QDs with the cells. The internalization mechanisms of QDs for the variety of freshly extracted, not

cultivated human cells and their specific molecular interactions remains an open topic for discussion. In this study, we also assess the internalization mechanism of TGA@CdTe quantum dots (3 nm) into non cultivated oral epithelial cells obtained from healthy donors. Naked gold nanoparticles (20 nm) are successfully used as nanosensors for surface-enhanced Raman spectroscopy to efficiently identify characteristic Raman peaks, providing new evidence indicating that the first interactions of these QDs with epithelial cells occurred preferentially with aromatic rings and amine groups of amino acid residues and glycans from trans-membrane proteins and cytoskeleton. Using an integrative combination of advanced imaging techniques, including confocal microscopy, ultra-high resolution SEM, high resolution STEM coupled with EDX spectroscopy together with the results obtained by Raman spectroscopy, it is determined that TGA@CdTe QDs are efficiently internalized into freshly extracted oral epithelial cells only by facilitated diffusion, distributed into cytoplasm and even within the cell nucleus in three minutes. This research shows new evidence on early accumulation of QDs in plant and human cells and would further improve our understanding about their environmental impact. In addition,

Au/SiO2 powder and gold nanoparticles in colloidal solution are synthesized and their morphology, optical, and the SERS properties have been characterized. In tissues breaded with Au/SiO2 powder, several characteristic peaks frequently used for the diagnosis of adenocarcinoma in breast tissue and carious dental tissue in the range of the Amide III are successfully enhanced. The SERS activity of Au/SiO2 is attributed to the properties of the silica powder structures to interact with tissue components, particularly its propensity to rehydrate in contact with the tissues promoting the formation of clusters of gold nanoparticles and also allowing the adsorption and interaction with biomolecules. Sample preparation and characterization by complementary techniques such as electron microscopy are also used to confirm the attachment of the Au/SiO2 powder and image their locations on the tissues. As an additional part to this research a focused ultrasound system for cellular sonoporation experiments is designed, built and tested. By means of this system it is expected that future experiments to conduct a controlled internalization of nanomaterials in cells can be made..