A label-free characterization of extracellular vesicles on a unique multiplexed biochip by a multimodal & multiscale analytical platform

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Recent advances in the clinical extracellular vesicles (EVs) field highlight their potential as biomarkers for various pathologies, in addition to their therapeutic applications. However, due to their high complexity in size, composition, and cell origin, the characterization of EVs subpopulations from complex media remains challenging. To achieve this goal, we established a nanobioanalytical platform (NBA) which allowed original investigations of various type of EVs based on a combination of multiplexed biosensing methods based on Surface Plasmon Resonance with metrological and morphomechanical analyses by Atomic Force Microscopy [1-2]. At present, the NBA platform investigates EVs in medical fields as cancer research, wound healing, toxicology ...
For the last 3 years, we have been working on implementing this platform with additional analytical modules and performances, in order to improve the discriminative characterization of coexisting components presents in a complex biological sample. For that, our particular strategy is especially to rethink & optimize the substrate at the core of this analytical platform, to make it compatible with the different techniques [3]. The phenotype of the different EVs subsets is obtained by Surface Plasmon Resonance Imaging, followed by Raman spectroscopy that gives a deeper & broader molecular signatures and Atomic Force Microscopy to address metrology of the EVs, size distribution and the morpho mechanical information of the different subsets. By combining machine learning algorithm, we accurately identified whether the spectra came from the treated cells derived EVs or the control ones [4]. The nanomechanical mapping highlighted noticeable difference in the Young's modulus between different EV subpopulations, some of which containing mitochondria [5]. Lastly, we increased the throughput and speed of the EVs subets analysis through nanospotting of numerous ligands on the biochip. These new multiplexed chips will be used for multi-scale detection of the main active compounds (cytokines and extracellular vesicles) in different secretomes from M1 and M2 macrophages which have demonstrated anti-fibrogenic and pro-fibrogenic properties, respectively. The EVs and molecules identified could lead to the development of an innovative drug (or drug product).

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