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Model membrane systems to elucidate cell-membrane processes: from signalling proteins to extracellular vesicles interaction.

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Cell signalling, strongly involves plasma cell membranes, is at the basis of any cell communication process: errors in signalling interactions cause the development of diseases. The number of complex and dynamical interactions between the molecules involved is huge. Therefore model systems are required to reduce such complexity.

In order to mimic lipid and protein organization of cellular membranes, we have developed artificial lipid bilayers that simulate the organization of lipid rafts, functional microdomains that act as signalling platforms. These systems are either planar, supported lipid bilayers, or lipid vesicles. We use here atomic force microscopy (AFM), a powerful tool to study the morphology of macromolecular assembling and molecular interactions in physiological environment, complemented with x-ray and neutron scattering techniques (SAXS, SANS) and infrared spectroscopy, to study the interaction of artificial lipid membranes with alpha synuclein aggregates and extracellular vesicles (EVs) produced in disease conditions. Alpha synuclein is the main protein of Parkinson's disease (PD). The key hallmark of the pathology is the aberrant misfolding and aggregation of this presynaptic protein, which culminates in
the formation of amyloid fibrils. We demonstrated the ability of iron to induce aggregation of the protein and a functional change of its binding to the membrane that might be associated with the disease. Then, we studied the interaction of EVs extracted from healthy and diseased cell lines, with model membranes systems. EVs are nanometer-sized cell-derived vesicles ensuring transport of molecules between cells and throughout the body, optimal candidates as therapeutic agents in immune therapy, vaccination, regenerative medicine, and drug delivery. The characterization of biophysical and biochemical properties of EVs and of their interaction with the membrane of recipient cells is fundamental to assess their role. AFM and scattering
measurements indicate a strong interaction of EVs with artificial vesicles mimicking lipid rafts pointing out the importance of rafts-like structure in the uptake processes.

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