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## Biomimetic interfaces to unveil the cell internalization mechanisms of extracellular vesicles

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Biomacromolecules, when approaching cell surface, can see different exposed chemical groups with a variety of possible spatial organization, depending on local plasma membrane composition and on intra- and extracellular environmental conditions. We develop experimental biomimetic interfaces in the form of dispersed aggregates in solution or of single supported bilayers, mimicking different cellular interfaces, suitably to be investigated by complementary scattering and reflectometry of neutrons and X-rays, calorimetry and FT-IR, to study their thermotropic behavior and structure upon interaction with incoming molecules. Lately, following our previous investigation [1][2][3], we could deepen the molecular details of plasma membrane interaction of extracellular vesicles (EV) of different origin. EV are nanosized vesicles secreted from all kind of cells, responsible of cell-cell communication [4]; there are widely investigated for diagnostic purposes, since their molecular cargo is specific of the originating cells, but their mechanisms of interaction with the plasma membrane of recipient cells are still hotly debated and hard to disentangle [5]. Our study reveals that the interaction extent, details at the molecular level, kinetics and the effects on target membrane lipid mobility are strictly dependent on EV origin as well as on the target membranes composition. Our approach has clear implications on the possibility to intervene and modulate EV internalization routes by targeting specific domains at the plasma cell membrane and, as a consequence, on the development of EV-based therapies.

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