Experimental report

16/02/2017

Proposal: 8-03-892 **Council:** 4/2016

Title: Exosomes: structural characterization and interaction with gold nanoparticles

Research area: Biology

This proposal is a new proposal

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Samples: exosomes

Instrument	Requested days	Allocated days	From	To
D11	2	2	16/09/2016	18/09/2016

Abstract:

Exosomes are cell secreted vesicles involved in cell signaling, trafficking and, in general, intercellular communication phenomena. In this view, they are of great interest as biological targets for therapeutics and diagnostics. Moreover, they can be useful platforms for biophysical studies on cell-related phenomena, bridging the complexity of cells and the simplicity of synthetic cell membrane model systems. However, despite these extremely promising features, fundamental studies on exosomes are still lacking. After a pilot experiment where we were able to measure a SANS spectrum on a prototypical exosomal sample, we plan to use SANS to obtain a structural characterization of exosomes and of their interaction with nanosystems.

Exosomes: structural characterization and interaction with gold nanoparticles

Exosomes are nanosized vesicles (30-150 nm) engineered by the cellular secretory machinery for multiple, long-distance intercellular communication. The information is encoded in their content – proteins, nucleic acids and lipids – while their surface is tailored for circulation in biological fluids and selective recognition. The tremendous potential of exosomes in translational (nano)medicine has been recently recognized. In addition, exosomes are an unexplored natural model for biological membranes, bridging the complexity between synthetic and cell membranes. However, notwithstanding these promising features, effective application of the exosomes is blocked by the fact that their structural and colloidal properties, from a physicochemical point of view, has never been systematically explored. In our recent research we are characterizing exosomes with two main aims: first, as biomedical nanodevices and tools (e.g. for drug delivery applications), characterized by unsurpassed biocompatibility and intrinsic capacity to interfere in the machinery of a host of specific biological functions (e.g. signaling and trafficking) of living organisms. Second, we foresee exosomes as profitable natural model membranes (especially for nanotoxicology and nanomaterial-lipid membrane interaction studies), with intermediate complexity between real cells and artificial lipid vesicles.

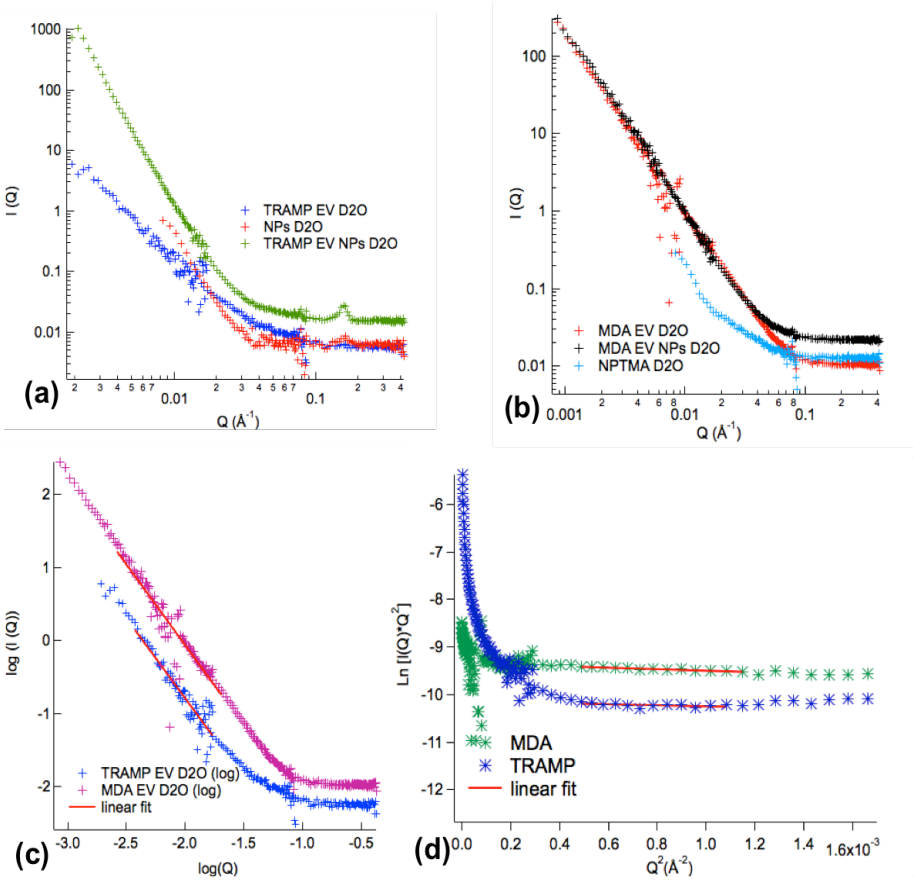

Figure 1 *SANS profiles of (a) TRAMP and (b) MDA exosomes in D2O, before and after interaction with (a) hydrophobic and (b) hydrophilic cationic SPIONs, compared to SANS curves obtained for the bare nanoparticles; (c) LogI vs LogQ plot and (d) intermediate Guinier plot of SANS curves measured for the two*

In this light, the aim of our SANS study was dual: first, the characterization of the exosomes as colloidal smart objects, from a physicochemical and structural point of view, second, the investigation of their interaction with inorganic nanoparticles. In Figure 1a and 1b representative SANS profiles of the two types of exosomes investigated (exosomes from transgenic adenocarcinoma of the mouse prostate (TRAMP) and from human breast adenocarcinoma (MDA)) acquired in D_2O before and after incubation with two different types of nanoparticles, hydrophobic and hydrophilic cationic SPIOs. In Figure 1c the Porod plot of the two SANS curves, measured for the two types of exosomes is reported: as expected for vesicles, a slope equal to 2 is obtained for both samples; in Figure 1d an intermediate Guinier plot of the two SANS curves is reported, to

determine the thickness of the bilayer in the two cases, that was estimated as 44 Å and 38 Å, for MDA vesicles and TRAMP vesicles, respectively.

Concerning the interaction of the exosomes with the nanoparticles, interestingly enough, a different effect is observed concerning the interaction of TRAMP vesicles with hydrophobic SPIONs and of MDA vesicles with cationic SPIONs.

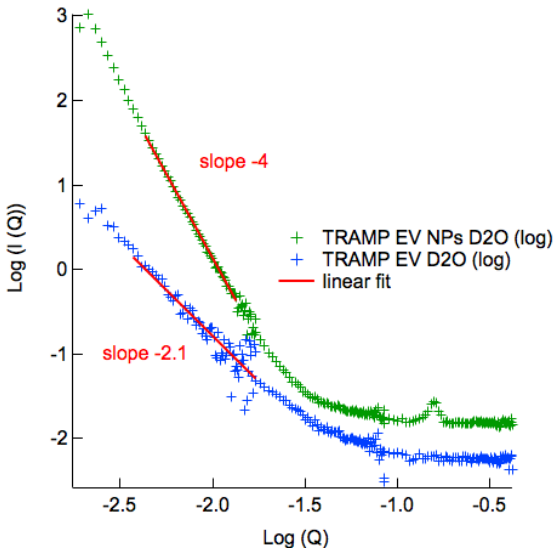

Figure 2 SANS analysis on the interaction of TRAMP vesicles with hydrophobic SPIONs.

As displayed in Figure 2, the LogI vs LogQ of TRAMP vesicles in the absence and in the presence of the SPIONs highlights a change in the slope from -2 to -4 in the power low, that is attributable to the aggregation of the vesicles induced by the NPs. Conversely, as clearly shown in Figure 1b, for MDA vesicles no significant variation of the SANS profile is observed upon interaction with hydrophilic nanoparticles.