Experimental report

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Proposal: 8-04-969 **Council:** 4/2023

Title: Effects of extracellular vesicles on model plasma membranes dynamics

Research area: Biology

This proposal is a new proposal

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Samples: extracellular vesicles
DMPC phospholipid

Instrument	Requested days	Allocated days	From	To
IN15	6	5	08/11/2023	13/11/2023

Abstract:

Extracellular vesicles (EVs), nanosized vesicles produced by all cells, are widely studied for their key role in mediating intercellular communication and for being responsible for the spreading of diseases as cancer. Still, their internalization mechanisms as their effects on target cells membrane are not widely explored. We are studying EVs extracted from neuroblastoma N2a cells comparing their properties to EVs isolated from the same cells after treatment with the OligoGM1 saccharide, found to have neuroprotective functions to neuronal cells. The treatment with OligoGM1 is found to affect also EVs-mediated cell-cell communication and EVs effects on target plasma membranes properties: complementary DLS, AFM, NR, SANS, FT-IR measurements show differences in the two EVs structural properties and on their mecahnisms of interaction with model membranes. DSC shows that they differently affect target membrane thermotropic behaviour and phase transition cooperativity. To shed light on EVs effects on target membrane dynamics, linked to EVs physiological function, we propose neutron spin-echo experiments on DMPC liposomes before and after interaction with the two kinds of EVs.

Scientific background and objectives

Extracellular vesicles (EVs) play an important role in intercellular communication, but their effects on the dynamic properties of target cell membranes remain poorly understood. Previous experiments using complementary biophysical techniques demonstrated that EVs can interact with lipid membranes and modify their structural and thermotropic properties, with effects depending on both EV origin and membrane composition.

The aim of this experiment was to investigate whether EVs derived from neuroblastoma N2a cells (Ctrl EVs) and from N2a cells treated with the neuroprotective OligoGM1 oligosaccharide (Oligo EVs) differently affect the dynamics of model lipid membranes. Neutron spin-echo (NSE) spectroscopy was employed to probe membrane fluctuations and bending dynamics.

Samples and measurements

DMPC large unilamellar vesicles were investigated alone and after incubation with Ctrl or Oligo EVs. Measurements were performed at 17 °C and 37 °C, corresponding respectively to temperatures below and above the main phase transition of DMPC, in order to compare membranes in the gel and fluid states.

The intermediate scattering functions were measured by NSE to investigate membrane dynamics and their possible modification upon interaction with the two EV populations.

Preliminary results

The measurements performed on the lipid model membranes showed the expected temperature-dependent changes in membrane dynamics, confirming the sensitivity of the experiment to changes associated with the different physical states of the lipid bilayer.

However, under the experimental conditions investigated, no significant differences in membrane dynamics could be resolved following the addition of either Ctrl or Oligo EVs. In particular, no measurable EV-induced modification of the membrane bending dynamics could be identified within the accessible experimental window. Therefore, although previous structural and thermotropic investigations had demonstrated interactions between these EVs and lipid membranes, these interactions did not result in detectable changes in membrane dynamics by NSE under the conditions explored in the present experiment.

Outcome and perspectives

The experiment confirmed the capability of NSE to detect changes in the dynamic properties of the lipid model membranes, as demonstrated by the expected temperature-dependent response. However, no significant effect associated with the investigated N2a-derived EVs could be resolved.

Interestingly, subsequent experiments performed with EVs of different cellular origin revealed detectable differences in their effects on membrane dynamics. These observations suggest that the ability of EVs to modify the dynamic properties of target membranes is not a general feature of extracellular vesicles, but strongly depends on their biological origin and, consequently, on their molecular composition.

Future NSE investigations will therefore focus on comparing EVs from different cellular sources under equivalent experimental conditions, with the aim of identifying the compositional features responsible for their different effects on target-membrane dynamics.