

Biomimetic bilayers designed for nanoparticles-membrane interactions and proteins transport studies

Joel Chopineau

Biological membranes carry out the essential function of a natural barrier that separates the cell from the outside environment. To study, in controlled conditions, the biological events occurring at the cell membrane interface, we recently develop biomimetic devices based on supported biomembranes.

A solid supported biomimetic membrane was developed to study *in vitro* the translocation process of a bacterial toxin, the adenylate cyclase (CyaA) from *Bordetella pertussis*. The membrane was assembled over a calmodulin (CaM) layer and exhibits the fundamental characteristics of a biological membrane separating two *cis* and *trans* compartments. The activation of the catalytic activity of CyaA by the tethered CaM was used as a probe of its translocation across the bilayer. This work constitutes the first *in vitro* demonstration of protein translocation across a tethered lipid bilayer.

Biomimetic assemblies are also important tools for the study of the interaction of mesoporous silica nanoparticles (MSN) with membranes. We have developed synthetic routes to achieve the production of gold loaded radial mesoporous silica nanoparticles (Au-MSN) and MSN@Fe₃O₄ materials incorporating magnetic and fluorescent properties as multifunctional platforms. The size of particles was checked by dynamic light scattering while zeta potential measurements reflect their surface charge. The particles morphology was characterized by transmission and scanning electron microscopies. Their textural properties, specific surface area and pore size, were determined from N₂ adsorption.

The gold metallic nanoparticles embedded in the pore channels of Au-MSN are responsible for a plasmonic activity. The coating with phospholipid bilayers of Au-MSN particles provided a biofunctional device with plasmonic properties relevant for biosensing. For this purpose different model systems have been investigated, direct adsorption of bovine serum albumin or molecular recognition events between a biotin receptor, integrated in the supported lipid bilayer, and avidin molecules. The obtained results demonstrate the plasmonic sensitivity of the bare Au-MSN particles or coated lipid bilayer Au-MSN devices.

We investigate MSN@Fe₃O₄ cell membrane interactions depending on nanoparticle surface coverage, to study MSN@Fe₃O₄ behavior in biological fluids. The dispersibility of MSN@Fe₃O₄ materials (pristine, lipid or polyethylene glycol coated) was largely dependent on medium composition and nanoparticle coating. A biomimetic membrane model was used to investigate MSN@Fe₃O₄ – cell membrane interactions. The presence of a -80mV transmembrane potential applied in *trans* side seems to increase MSN@Fe₃O₄ interaction with the membrane. Dispersion media, MSN@Fe₃O₄ coating and transmembrane potential appeared as major factors influencing MSN cell membrane interactions.

References

- Rossi, C., Doumiati, S., C. Lazzarelli, D., Davi, M., Meddar, F., Ladant, D. and **Chopineau, J.** (2011) "A tethered bilayer assembled on top of immobilized calmodulin to mimic cellular compartmentalization" *PLoS ONE* 6(4): e19101.
- Veneziano, R., Derrien, G., Tan, S., Brisson, A., Devoisselle, JM., **Chopineau, J.**, and Charnay, C. (2012) "One step synthesis of gold loaded radial mesoporous silica nanospheres and supported lipid bilayers functionalization: towards bio-multifunctional sensors" *Small*. **8**, 3674-3682.
- Allouche, M., Pertuiset, C., Robert, J.L., Martel, C., Veneziano, R., Henry, C., Dein, O.S., Saint, N., Brenner, C., **Chopineau, J.** (2012) "ANT-VDAC1 interaction is direct and depends on ANT isoform conformation *in vitro*" *Biochem Biophys Res Commun*. **429**, 12-17.
- Subrini O, Sotomayor-Pérez AC, Hessel A, Spiaczka-Karst J, Selwa E, Sapay N, Veneziano R, Pansieri J, **Chopineau J**, Ladant D, Chenal A. (2013) "Characterization of a membrane-active peptide from the *Bordetella pertussis* CyaA toxin" *J. Biol. Chem*. **288**, 32585-98.
- Veneziano R, Rossi C, Chenal A, Devoisselle JM, Ladant D, **Chopineau J.** (2013) "*Bordetella pertussis* adenylate cyclase toxin translocation across a tethered lipid bilayer" *Proc Natl Acad Sci U S A*. **110**(51),

20473-8.

- Damiani S1, Zayni S, Schrems A, Kiene E, Sleytr UB, **Chopineau J**, Schuster B, Sinner EK. (2015) "Inspired and stabilized by nature: ribosomal synthesis of the human voltage gated ion channel (VDAC) into 2D-protein-tethered lipid interfaces". *Biomater Sci.***3** (10):1406-13.