Séminaire externe

"Extracellular vesicles as a bio-camouflaged nanocarrier for therapy and imaging ."

Introduction: Extracellular vesicles (EVs) are multifaceted subcellular entities that may represent a new generation of bio-camouflaged drug/ nanoparticle delivery system. **Methods**: In a top-down procedure, our group has engineered nanoparticle/drug-loaded EVs from precursor cells previously loaded with this cargo. For this purpose, parent HUVEC cells or THP1 macrophages were first incubated with the desired payload and allowed to internalize it. Starvation stress was employed to induce the release of vesicles high-jacking the cargo from their precursor cell. **Results**: By this method, EVs could encapsulate a set of nanoparticles regardless their chemistry or shape, such as iron oxide nanoparticles, iron oxide nanocubes, gold/iron oxide nanodimers, gold nanoparticles and quantum dot. Different hybrid nanovesicles were designed: magnetic, magnetic-fluorescent and magnetic-metallic vesicles, either single component or multicomponent. These hybrid vesicles were able to generate heat when submitted to an alternating magnetic field and could be monitored by fluorescence imaging or MRI. Dual drug/nanoparticle EV loading was also feasible by this method. We demonstrated that vesicles from THP-1 cells could be loaded with iron oxide nanoparticles and different therapeutic agents irrespective to their molecular weight, hydrophobic, hydrophilic and amphiphilic character. Thereby, magnetic vesicles were loaded with a chemotherapeutic drug (doxorubicin), anticoagulant protein (tissue-plasminogen activator (t-PA)), or two photosensitizer (disulfonated tetraphenylchlorin (TPCS2a) or meta-tetra(hydroxyphenyl) chlorin (mTHPC). The theranostic potential of mTHPC-loaded magnetic EVs was tested *in vivo* in a murine tumoral model. Vesicles could be tracked *in vivo* by dual-mode imaging, combining optical imaging and MRI. The engineered EVs were found to induce an efficient photodynamic action, as evidenced by tumor growth curves and histological analysis. **Summary/conclusion**: In brief, we succeeded in customizing EV by engineering them to display several nanoparticle/drug cargoes featuring therapeutic and imaging properties both *in vitro* and *in vivo*.

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Invitée par Chantal Pichon

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Salle de conférence du CBM