TARGETING AN OLD STORY WAITING FOR SOLUTIONS

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The attractive feature of nanoparticles is indeed in their capacity to load therapeutics, to protect the loading from degradation, and to anchor targeting ligands such as antibody, peptides and proteins to increase their penetration in tumors. However, despite the engineering of the nanocarriers with possible targeting units the efficient delivery in specific organs or tumors is very limited.

Here we will discuss what are the possible strategies using different biomolecules able to recognize antibodies or proteins and nove approaches inspired by nature, using extracellular vesicles, EVs.

In particular despite the use of the entire EV more recently our group is aiming to implement the EV membrane as a cover of organosilica porous particles with the aim of targeting tumors and lung metastasis, while avoiding systemic effects and accumulation of the nanoparticles in undesired organs.

The tissue-specific fingerprint provided by the EVs-derived membranes from e.g. melanoma B16-BL6 cells provides preferential uptake into the tumor and selective targeting of lungs. The ability of the EVs hybrid systems to behave as the natural EVs was demonstrated *in vitro* and *in vivo* in two different tumor models. As proof of concept, the loading and release of doxorubicin drug, was investigated using breakable organosilica porous nanoparticles coated by the EV's membrane.

Advantages and disadvantages of the strategies will be discussed using literature data.

Key words: *targeting, nanoparticles, extracellular vesicles, exosomes*

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