The role of natural nanovesicles in drug and nanomaterials delivery

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Extracellular vesicles (EVs) are released by almost all cells, involved in numerous biological networks, whose may vary from micro to nano. Preclinical studies demonstrated that these nanovesicles can act as physiological low immunogenic liposomes and can be engineered to carry target molecules (mRNA, siRNA, drugs), supporting the possible future use of EVs as potential delivery systems in cancer immunotherapy and in drug and RNA interference therapies. EVs can deliver fully active drugs, such as cisplatin, curcumin and Doxorubicine. Interestingly, EVs-associated drugs showed an increased delivery at the tumor site as compared to liposomes loaded with the same molecules. Moreover, EVs can naturally deliver biological molecules as well. EVs could then represent a natural nanodelivery system for biological and/or chemical therapeutic molecules, possibly exploited in the future strategies based on cell-free therapies against cancer, neurological diseases and regenerative programs. Nanomedicine is one of the most important and innovative field of Research in Medicine, focusing on the use of nanoparticles for diagnosis, therapy and toxicology in health and disease. Being EVs nanovesicles able to shuttle various molecules, EVs may represent ideal candidates in the field of Nanomedicine. Considering that EVs can deliver cytotoxic molecules more efficiently than liposomes, to test the ability of EVs in shuttling a series of therapeutic agents with antitumor activity, with the aim to improve their biological efficacy at the tumor site has been hypothesized; and at least demonstrated in pre-clinical settings. Our studies have also shown that the acidic tumor microenvironment induce a marked increase in exosome release by tumor cells. Moreover, it appears conceivable that exosomes may have an acidic content, inasmuch as they derive from cytoplasmic vesicles with a variable acidic content. Therefore, acidophilic molecules might be ideal to be charged in these nanovesicles to act as therapeutic agents for neoplastic conditions. At the same time exosomes are considered a source of tumor biomarkers and probably the circulating levels of exosomes may represent a valuable marker as well; in order to detect the presence of a tumor or a tumor relapse, being the exosomes plasmatic levels in tumor patients always higher than in healthy individuals. Recently, in our Lab the levels of circulating exosomes and their biomarkers' make-up were investigated using the implementation of three different methodological approaches including immunocapture-based ELISA, nanoscale flow cytometry and NTA, providing significant results.