Exosomes are nanovesicles naturally released by almost all the cells of our body that—in both physiological and pathological settings—deliver several molecules including proteins, lipids and nucleic acids to target cells. They are able to interact with target cells located in the close proximity or at distance using different mechanisms, including ligand-receptor interactions1,2 and plasma membrane fusion, leading to the transfer of their contents to the target cell cytoplasm.3 Thus, exosomes appear as a vectorized signaling system operating between the cytoplasm of a donor cell and either the extracellular compartment or potentially all the internal compartments of a target cell. These observations place exosomes at the center of current interests in translational research and point to exosomes as potential self-nanovectors for future nanomedicine approaches. Moreover, exosomes are attracting great consistent attention as tools for the identification of novel disease biomarkers. In fact, new tests offering the possibility to simultaneously characterize and quantify exosomes in human body fluids have been recently developed.4 Such a dual potential of exosomes suggest that they might consistute an ideal tool for “theranostic.” This new discipline of nanomedicine focuses on a multi-disciplinary research approach to build new systems for various nano-biomedical applications, ranging from the medical use of nanoplateform-based diagnostic agents to the development of therapeutic interventions, alone or combined to each other (therapy + diagnostic = theranostic).

We have recently shown that human natural killer (NK) cells release exosomes that express both NK-cell markers and cytotoxic molecules. Similar results were obtained with circulating exosomes from human healthy donors. Both NK-cell derived and circulating exosomes exerted a full functional activity and killed both tumor and activated immune cells. These findings indicate that NK-cell derived exosomes might constitute a new promising therapeutic tool.

Keywords: exosomes, natural killer, nanomedicine, perorin, theranostic

NK cell-released exosomes
Natural nanobullets against tumors

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We have recently reported that human natural killer (NK) cells release exosomes that express both NK-cell markers and cytotoxic molecules. Similar results were obtained with circulating exosomes from human healthy donors. Both NK-cell derived and circulating exosomes exerted a full functional activity and killed both tumor and activated immune cells. These findings indicate that NK-cell derived exosomes might constitute a new promising therapeutic tool.
exosome-associated perforin may constitute a new target for the development of therapies against cancer and other diseases. In this context, it should be noted that the tumor microenvironment is acidic, which, on one hand, may impairs the effectiveness of chemotherapeutics and possibly of the antitumor immune response, but, on the other hand, may favor the accumulation and delivery of exosomes, as they are attracted by low pH and these conditions promote membrane fusion. Thus, paradoxically, differences in the electrostatic charges between exosomes and the plasma membrane of tumor cells might be more important than the specificity of ligand-receptor interactions. This said, based on the different mechanisms through which exosomes may interact with target cells, it is likely that NK cell-derived exosomes may interact with target cells with either a exosome-to-membrane fusion or a receptor-to-ligand interaction (Fig. 1).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.



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