The dichotomy of exosomes in cancer: targets and treatment vehicles

Exosomes are extracellular vesicles released by all cell types that mediate intercellular communication. Exosomes exist in healthy as well as pathological conditions, but it is in cancer research that they are gaining increasing attention. Exosomes released by cancer cells are said to be involved in most of the processes associated with cancer initiation and tumor progression. Recent evidence demonstrates the specificity of action of cancer exosomes targeting specific cells in vivo, ultimately supporting tumor progression. If on one hand exosomes' role in different hallmarks of cancer has been widely described, highlighting the urge to understand the potential to target them for cancer treatment, on the other hand, exosomes stability and tumor-targeting capacity shows their applicability in the delivery of anti-cancer molecules. This dichotomy associated with exosomes has sparked our recent review.

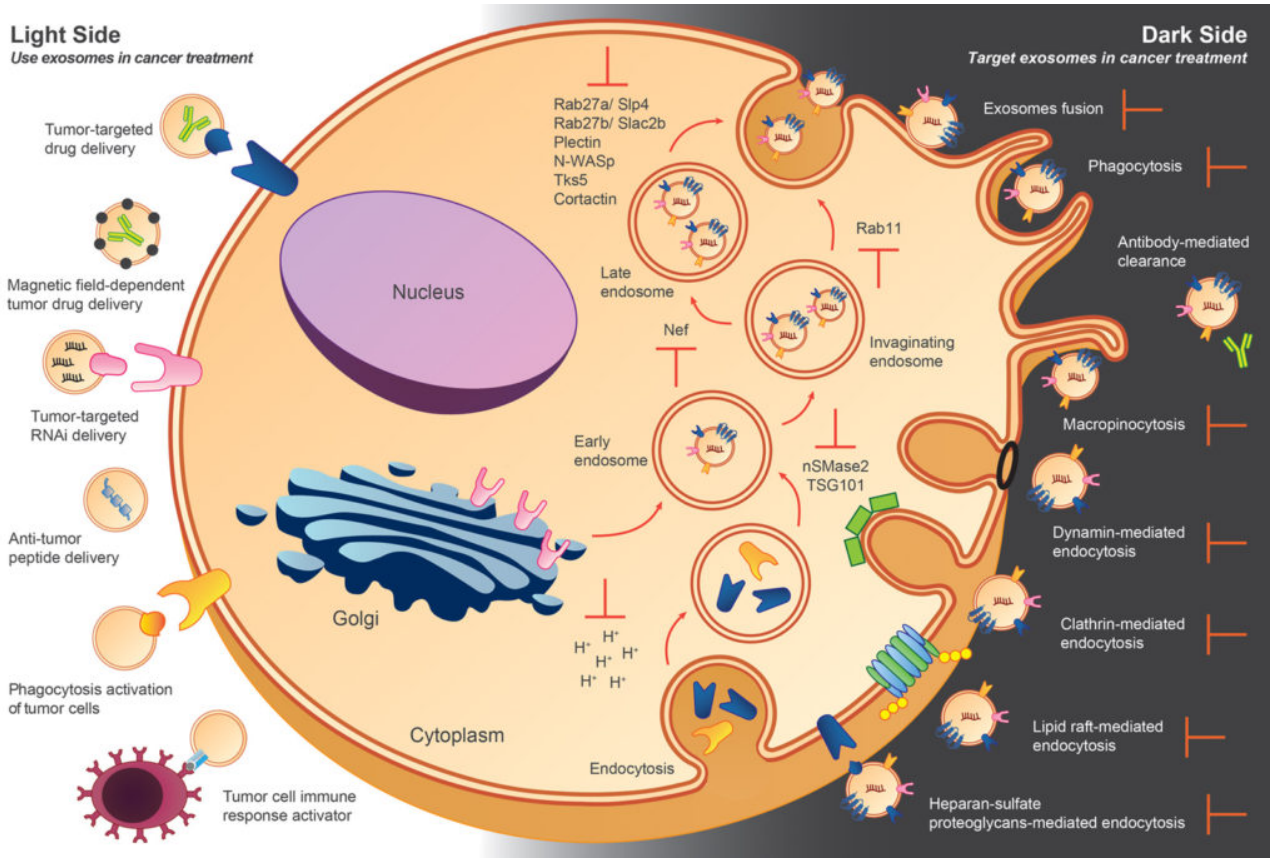

Fig. 1.

Exosomes are derived from the endocytic pathway and are released to the extracellular space

upon fusion of late endosomes with the plasma membrane. During this process Rab proteins are involved in all stages of exosomes biogenesis, what makes them potential targets to inhibit exosomes release by cancer cells and in this way interfere with intracellular communication in cancer mediated by extracellular vesicles. So far, the genetic targeting of Rab27a and Rab27b, proteins involved in the late stages of the endocytic pathway, has been the most widely used strategy in cancer to downregulate exosomes exocytosis. However exosomes biogenesis is a complex process with a multitude of parallel mechanisms involved, compromising the effect of this targeting strategy. Overall further studies are necessary to fully understand the role of cancer exosomes during all stages of disease progression, ultimately so they can be validated as a potential new therapeutic target in cancer.

On the other side of the spectrum, the use of exosomes in the treatment of cancer has made large advances in the recent years. Due to their high stability in circulation, low immunogenicity and engineering ability, exosomes-based therapy possesses great promise either alone or in combination with current treatment strategies. So far, exosomes have demonstrated the ability to increase the specificity of action of different chemotherapeutic agents, the efficacy of RNAi molecules and anti-tumor peptides in the treatment of cancer using them as delivery vehicles. Additionally, exosomes loaded with tumor-associated antigens have proven to be efficient in triggering the immune response against tumor cells.

Clinical trials are currently ongoing in order to validate the potential of this new therapeutic approach. However, exosomes production, isolation and loading still represent major challenges in their use in the clinic.

We have recently highlighted the current developments and strategies used to enhance the potential of exosomes in the treatment of cancer and discuss what is still missing in order to bring exosomes to the clinic to improve patient survival.

Nuno Bastos[1,2], ***Sonia A. Melo***[1,2,3]
[1]*Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Portugal (i3S), Porto, Portugal*
[2]*Institute of Molecular Pathology & Immunology of the University of Porto (IPATIMUP), Porto, Portugal*
[3]*Medical Faculty of the University of Porto (FMUP), Portugal*

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