Emerging drug delivery systems of anticancer agents: exosomes

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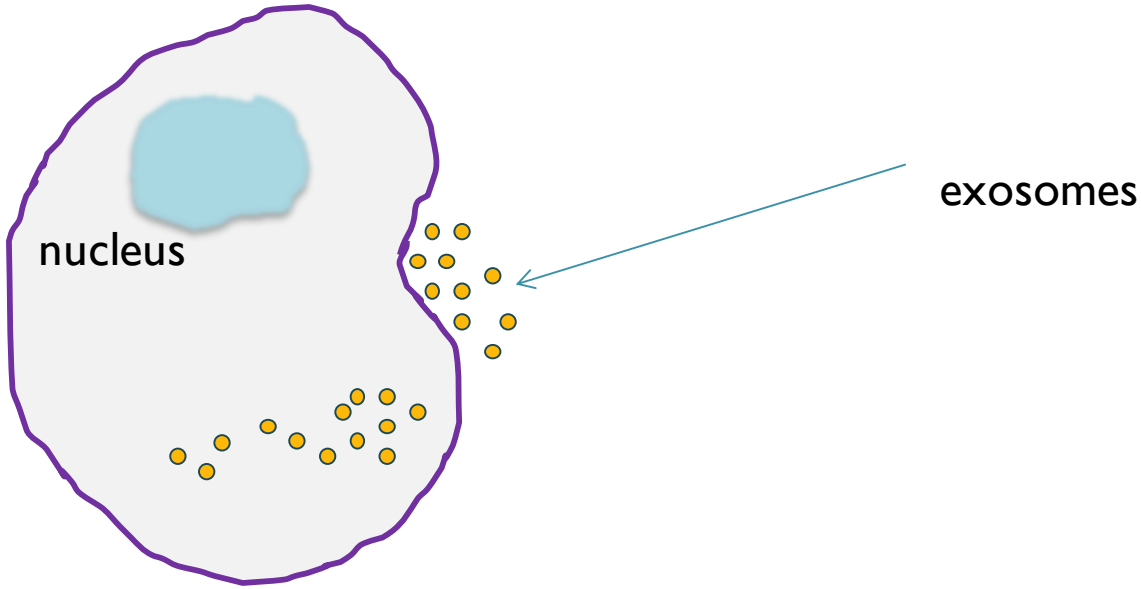
What are exosomes?

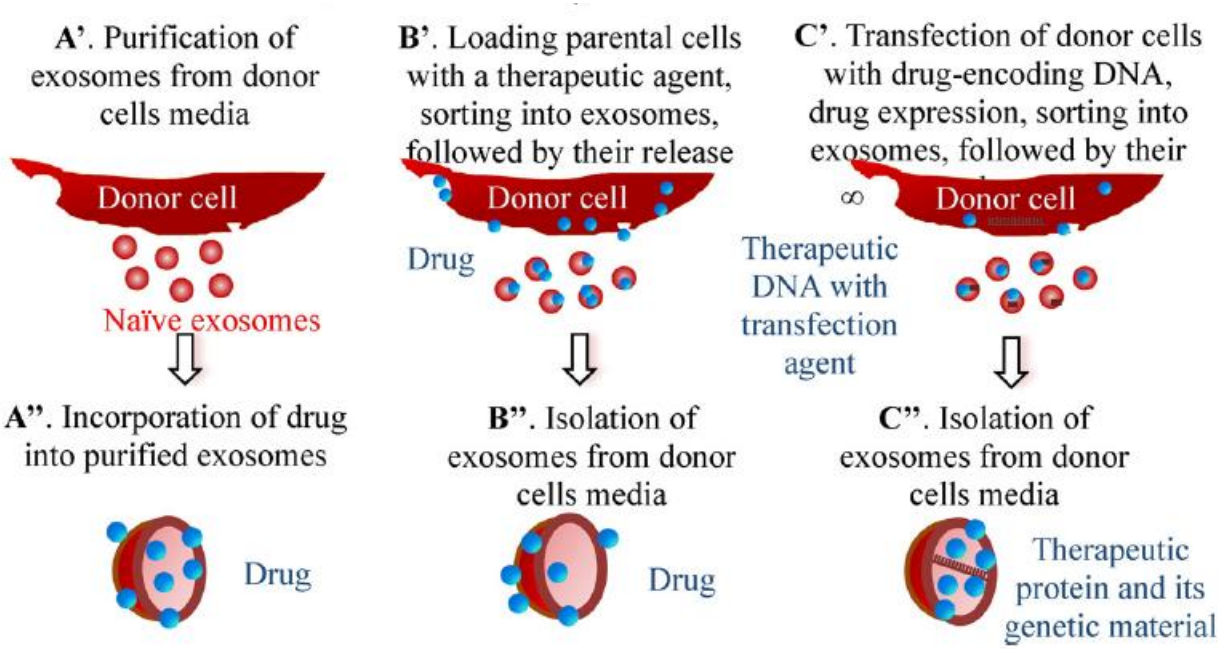
- Endocytous membrane vesicles that range from 30-120 nm.
- Formed from the plasma membrane
- Involved in cell – cell communication and signaling, specific membrane functions, various roles in the immune system



Why are exosomes potential DDSs

- They are derived from membrane: can be regarded as natural liposomes
- Endogenous origin
- Reduced side effects
- Possible targeted action
- Can carry different type of cargos (RNA, DNA, proteins, various therapeutically active substances)

Approaches of drug loading into exosomes*



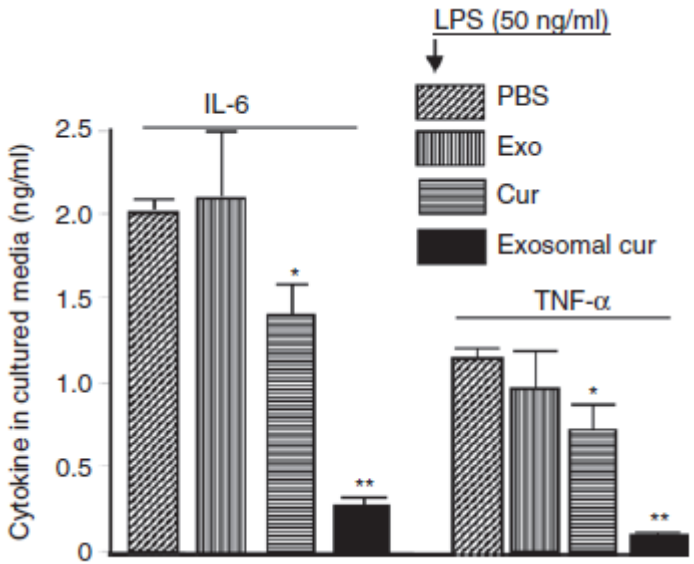
* Batrakova, E.V. and Kim, M. S. Using exosomes, naturally-equipped nanocarriers, for drug delivery. Journal of Controlled Release, 2015, 219:396-405.

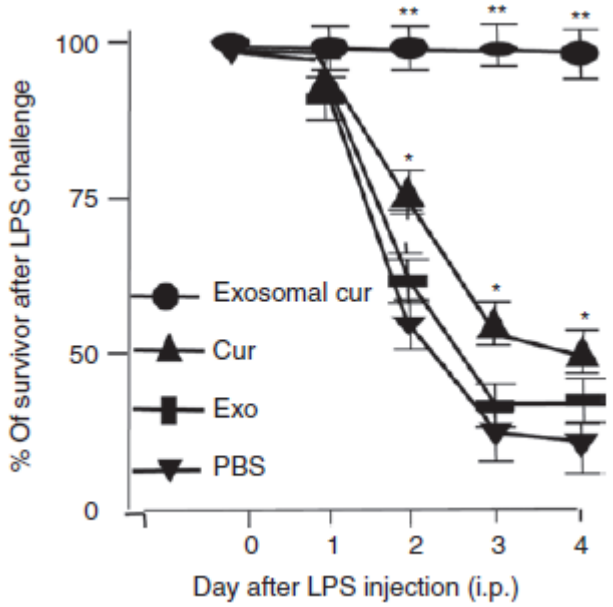
Curcumin-loaded exosomes*

- Curcumin loaded to EL-4-derived exosomes with simple mixing
- Increased stability and bioavailability of curcumin

Anti-inflammatory activity of exosomal curcumin *in vitro*, *RAW* 264.7 cells

Exibited protection in LPS-induced septic shock model in female C57BL/6j mice





*Sun D, Zhuang X, Xiang X et al. A novel nanoparticles drug delivery system: The anti-inflamatory activity of curcumin is enhanced when encapsulated in exosomes. Molecular Therapy, 2010 ; 18(9): 1606-1614

Curcumin-loaded exosomes*

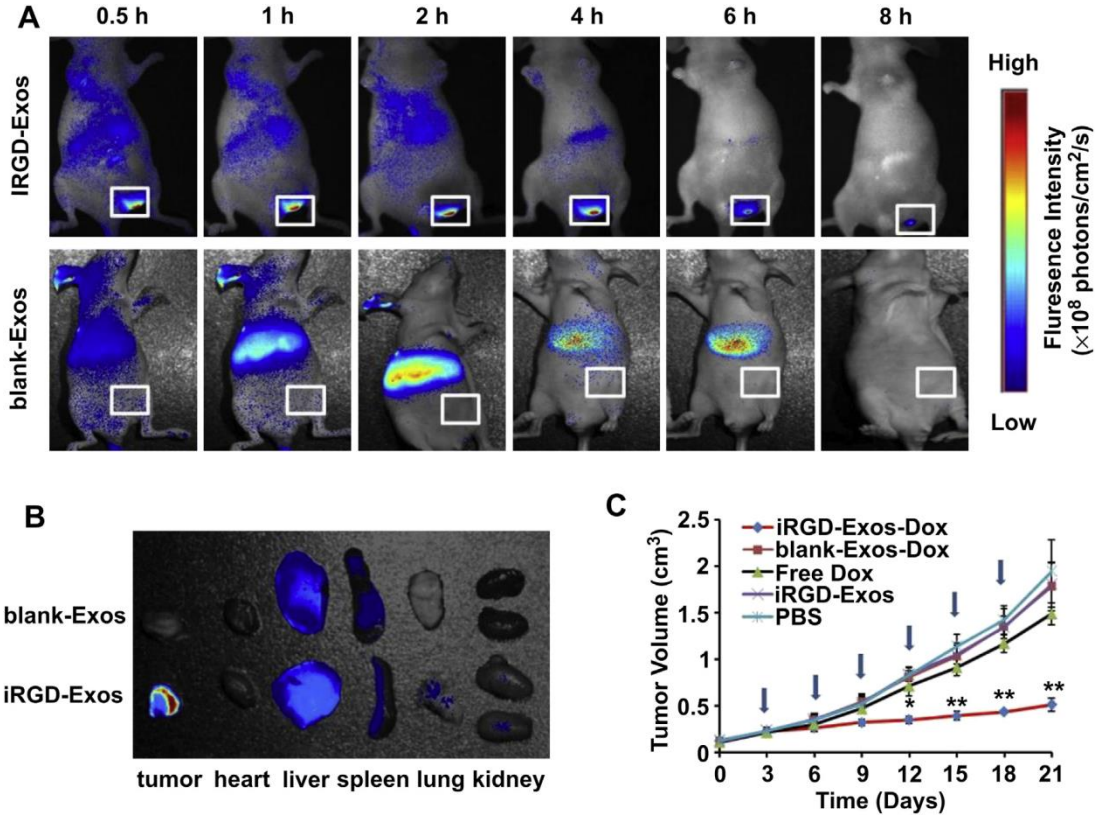
Proven advantages over nanosystems:

- exosomes (dendritic and tumor cell–derived), exhibit strong tendencies to regulate immune responses and tumor progression (unlike liposomes)
- exosomes can carry multiple therapeutic drugs
- exosomes can modulate the activity of multiple pathways in the same targeted cells

*Sun D, Zhuang X, Xiang X et al. A novel nanoparticles drug delivery system: The anti0inflamatory activity of curcumin is enhanced when encapsulated in exosomes. Molecular Therapy, 2010 ; 18(9): 1606-1614

Doxorubicin-loaded exosomes*

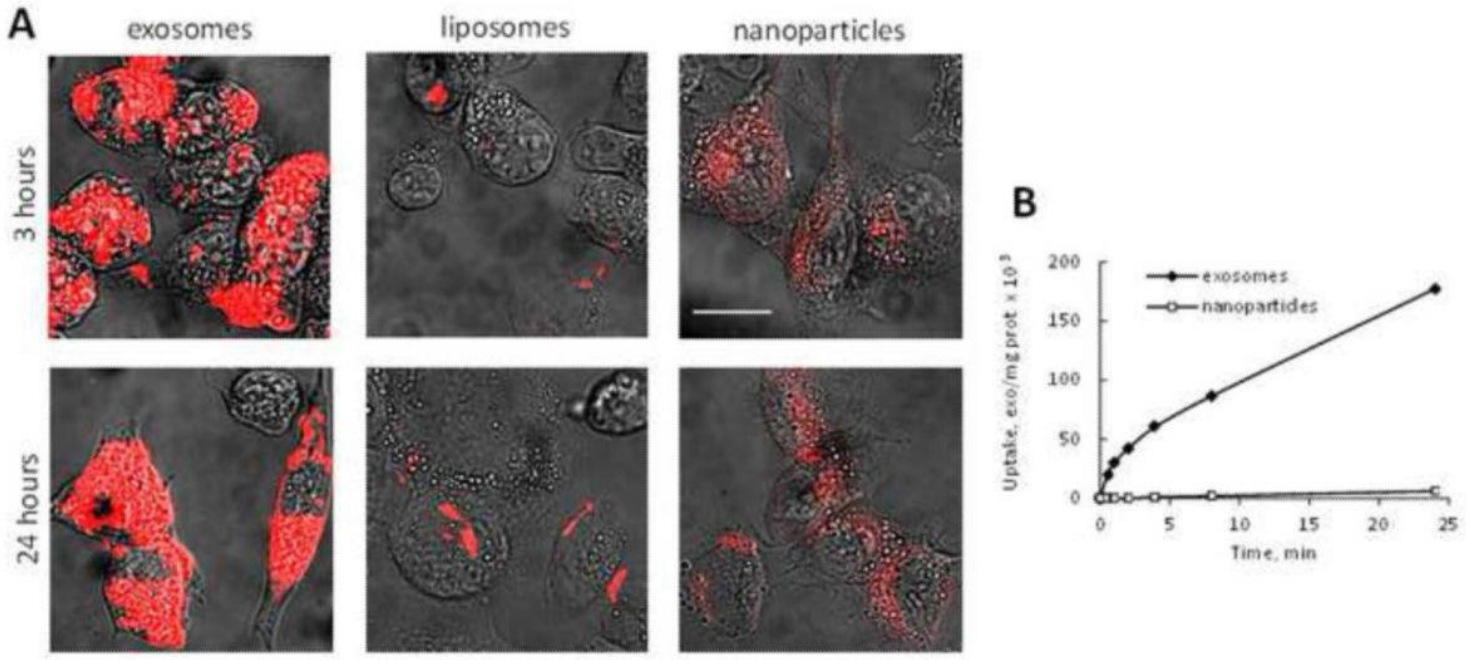
- Exosomes produced from immature dendritic cells (imDCs), engineered to tumor targeting capability
- Doxorubicin loaded to exosomes via electroporation
- In vivo antitumor efficacy in female BALB/c nude mice bearing MDA-MB-231 breast cancer



* Tian Y, Li S, Song J, Ji T, Zhu M, Anderson GJ, et al. A doxorubicin delivery platform using engineered natural membrane vesicle exosomes for targeted tumor therapy. Biomaterials. 2014; 35(7):2383–90.

Paclitaxel-loaded exosomes*

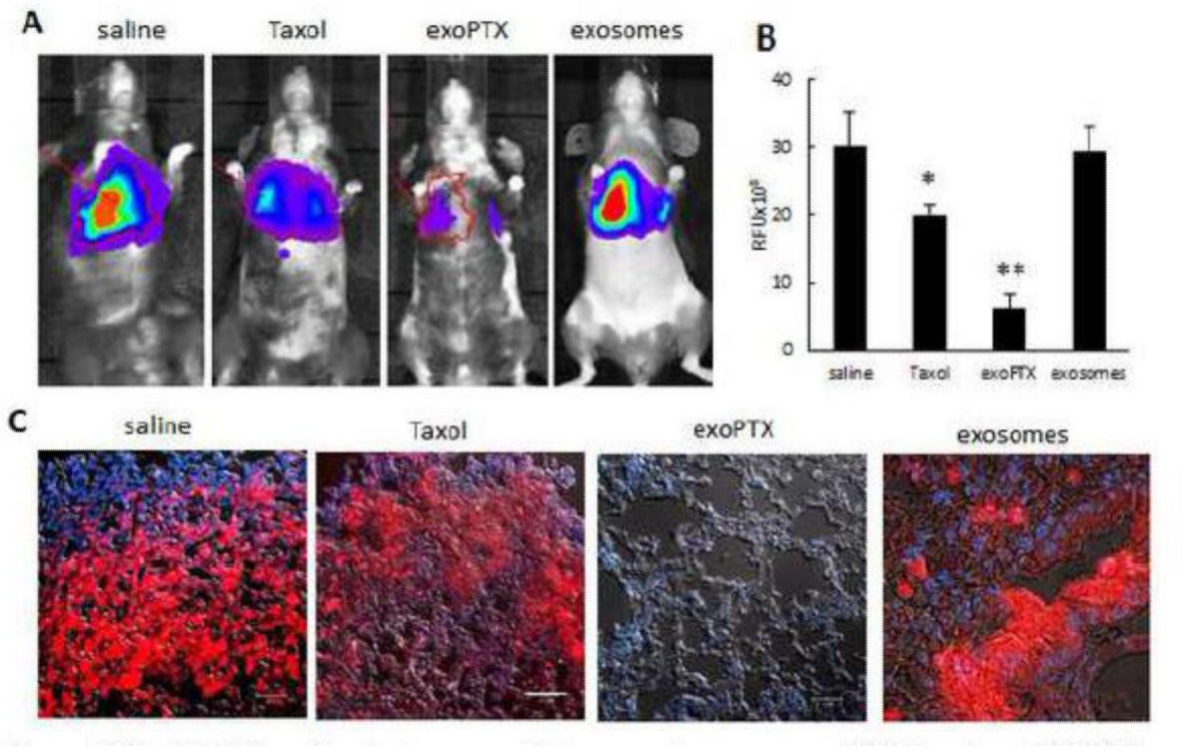
- Different methods (incubation, electroporation, sonication) of loading exosomes released by macrophages with paclitaxel
- anticancer effects of exoPTX were evaluated in a resistant MDR cells expressing the drug efflux transporter, Pgp (MDCKMDR1), and their sensitive counterparts (MDCKWT)



Kim MS, Haney MJ, Zhao Y, et al. Development of exosomes encapsulated paclitaxel to overcome MDR in cancer cells. Nanomedicine : nanotechnology, biology, and medicine 2016;12:655-64.

Paclitaxel-loaded exosomes*

- Efficacy shown in mouse model of pulmonary cancer (C57BL/6 mice were injected with 8FlmC-FLuc-3LL-M27 cancer cells)



Kim MS, Haney MJ, Zhao Y, et al. Development of exosomes encapsulated paclitaxel to overcome MDR in cancer cells. Nanomedicine : nanotechnology, biology, and medicine 2016;12:655-64.

Conclusion

- Exosomes as DDSs have big potential to be considered in the development of new anticancer drugs, but also in improving bioavailability of other compounds, mainly of antiinflammatory nature
- Exosomes present many advantages over other nano-sized delivery systems
- Further studies are needed in order to assess the applicability of different types of exosomes in clinical terms

- Exosomes derived from plants, loaded with curcumin have been included in one clinical trial to-date, in order to assess their efficacy as dietary supplement in colon cancer

Thank you