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Extracellular vesicles (EVs)' journey in recipient cells: from recognition to cargo release

Key words: extracellular vesicles (EVs); exosomes; endocytosis; uptake; release

Research Summary

This review summarizes the current understanding of the molecular mechanisms of EVs' biological journey in recipient cells, from recognition to uptake and cargo release.

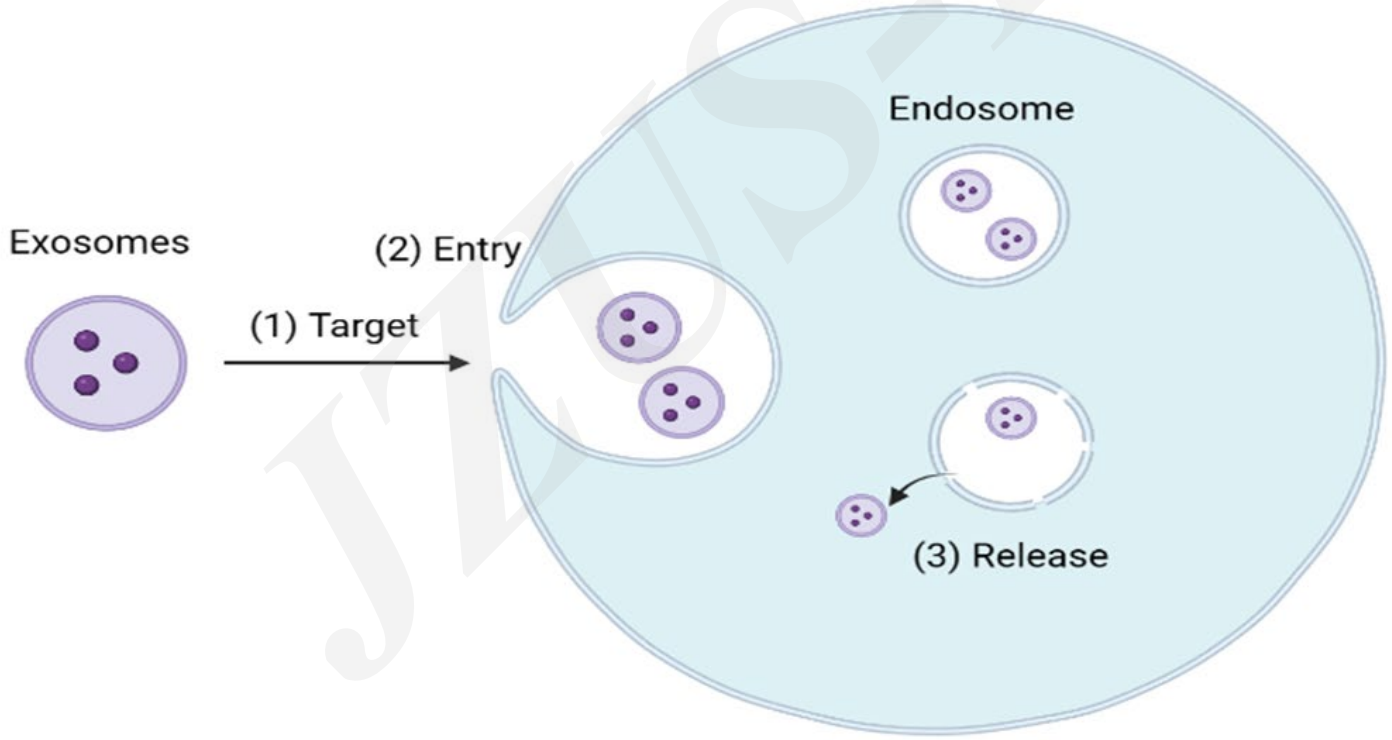


Figure 1

Innovation points

- **Introduction** of the entire process of EVs from recognition, uptake to cargo release.

- **Summary** of current research on the shortcomings of EV recognition and uptake mechanisms.

- **Emphasis** of the value of EVs as delivery vehicles and the focus of future research directions.

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Innovation points

We created a table summarizing the components that have been shown to be involved in the recognition and uptake of EVs.

Table 1 | Components involved in the identification and uptake of EVs.

Table 1. Components involved in the identification and uptake of EVs.

EVs or exosomes surface recognition molecules		Donor cells	Recipient cells	target molecules on Recipient cells surface	Function	Action mechanism	Potential application	Ref.
Molecular type	Specific molecule							
Tetraspanins	CD9	Melanoma cells (FEMX-I, A375 and C8161 cells) and mesenchymal stromal cells	Melanoma cells (FEMX-I cells)	unknown	Participates in the uptake of EVs by recipient cells.	unknown	Divalent CD9 Ab could cross-link CD9 proteins associated with host cells and EVs to stimulate the endocytosis on EVs which may favor tissue/organ repair.	(Santos et al., 2019)
		Colorectal carcinoma cell (Colo-320 cells)	Colorectal carcinoma cell (Colo-320 cells)	unknown	Resulting in reduced adhesion and uptake of exosomes by recipient cells.	By inhibiting the interaction between the ligand ADAM17 on exosomes and the receptor integrin α5β1 on cells	CD9 may be a promising therapeutic targets to inhibit peritoneal carcinogenesis in colorectal cancer.	(Cardenes et al., 2021)
	CD81	Human cervical cancer cells (Hela cells)	Liver carcinoma cells (Huh-7 cells) and gastric carcinoma cells (NCI-N87 cells)	Laminin	Promotes the binding and uptake of EVs by recipient cells.	CD81 interacts with laminin.	Taking advantage of the feature that Laminin binding CD81 enhances cellular uptake of EVs, recombinant expression of CD81 on the surface of EVs enables EV-mediated specific delivery to various cells and tissues.	(Vogt et al., 2021)
	TSPAN8 / CD151	Human breast cancer cells (T-47D cells)	Human breast cancer cells (T-47D cells) and human fetal lung fibroblasts (MRC-5 cells)	unknown	Promotes sEV attachment to recipient cells and uptake in vivo.	Increasing the attachment efficiency and reducing the evasion frequency	TSPAN8-sEV promotes cancer cell motility and invasion and may serve as an important direct or indirect therapeutic target.	(Wang et al., 2021a)