Extracellular vesicle-based drug delivery for synergistic therapy

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Extracellular vesicles (EVs), including exosomes, microvesicles, and apoptotic bodies, are cell-derived vesicles that display specific properties and functions associated with their parent cells. Meanwhile, they show great potential in the drug delivery owing to their outstanding biocompatibility and the nanosized diameter. Our group focuses on developing smart systems that can synergize the drug delivery function with the inherent biology properties of EVs so as to achieve potent therapy effects for different diseases.

EVs of M2 macrophages are loaded with FDA-approved hexyl 5-aminolevulinate hydrochloride (HAL). Owing to the inflammation-tropism of M2 EVs, the prepared HAL@M2 EVs can accumulate in the inflammatory atherosclerosis areas, where effective anti-inflammation effects are achieved through the cooperation of the anti-inflammatory cytokines released from M2 EVs and the anti-inflammatory carbon monoxide and bilirubin generated from the intrinsic biosynthesis and metabolism of HAL. In view of the fact that the photosensitizer PpIX, the production of the haem biosynthetic pathway by using HAL as the material, is likely to excessively accumulate in the mitochondria of tumor cells. We encapsulated HAL and 3-bromopyruvic acid (3BP) into EVs of tumor cells. The developed HAL/3BP@X-MP can specifically target and recognize tumor cells, where the accumulation of PpIX and increased oxygen supply in mitochondria lead to the sufficient generation of ROS, resulting in significantly improved PDT outcomes. By replacing 3BP with 3-methyladenine (3MA), we prepared a HAL/3MA@X-MP system that can simultaneously synergize the mitochondrial damage, mitophagy inhibition and anti-tumor immunity, resulting in effective therapeutic efficacy without obvious side-effects. The bacterial outer membrane vesicles (OMVs) are also used to construct therapeutic system in our study. By loading UNC2025 into OMVs and modifying the surface with maleimide (Mal), a system that can not only inhibit the efferocytosis but also boost the following antitumor immunity is prepared to prevent the growth, metastasis and recurrence of tumors in mice. These smart systems show great potential as new candidates for disease treatment.

References:

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