ABSTRACT

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Role of extracellular vesicles in cancer-specific interactions between tumour cells and the vasculature.

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Cancer progression impacts and exploits the vascular system in several highly consequential ways. Among different types of vascular cells, blood cells and mediators that are engaged in these processes, endothelial cells are at the centre of the underlying circuitry, as crucial constituents of angiogenesis, angiocrine stimulation, non-angiogenic vascular growth, interactions with the coagulation system and other responses. Tumour-vascular interactions involve soluble factors, extracellular matrix molecules, cell-cell contacts, as well as extracellular vesicles (EVs) carrying assemblies of molecular effectors. Oncogenic mutations and transforming changes in the cancer cell genome, epigenome and signalling circuitry exert important and often cancer-specific influences upon pathways of tumour-vascular interactions, including the biogenesis, content, and biological activity of EVs and responses of cancer cells to them. Notably, EVs may carry and transfer bioactive, oncogenic macromolecules (oncoproteins, RNA, DNA) between tumour and vascular cells and thereby elicit unique functional changes and forms of vascular growth and remodeling. Cancer EVs influence the state of the vasculature both locally and systemically, as exemplified by cancer-associated thrombosis. EV-mediated communication pathways represent attractive targets for therapies aiming at modulation of the tumour-vascular interface (beyond angiogenesis) and could also be exploited for diagnostic purposes in cancer.

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