EVs as tools for enhanced imaging: insights from preclinical studies

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Nano- and micro-sized extracellular vesicles (EVs) are naturally occurring cargo bearing packages of regulatory macromolecules, responsible of physiological intercellular communication. Cancer cell-derived EVs show a marked tropism for tumors, as extensively demonstrated by *in vivo* studies. The encapsulation of cancer cell-derived EVs with fluorescent molecules or contrast agents represent an attractive strategy for cancer therapy. By labelling plasma-derived EVs with indocyanine green (ICG) or contrast agents and following their biodistribution by *in vivo* and *ex vivo* imaging, we demonstrated the existence of nanoparticles with a highly-selective cancer tropism in the blood of colorectal cancer (CRC) patients, but not in healthy volunteers. In CRC patients-derived xenograft (PDX) mice, we have shown that transplanted EVs can recognize the tumor from the cognate nanoparticle-generating individual, allowing the precise labelling of cancer cells with fluorescence or contrast agents for magnetic resonance and computed tomography, thus enhancing the signal-to-noise ratio of these medical imaging systems. The application of EVs to diagnostic drug delivery could open the way to advanced medical imaging techniques, including the precise localization of metastases, the delivery of contrast agents to brain tumors, as well as the intraoperative imaging with autologous EVs in cancer patients.

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