Extracellular Vesicles: new frontiers for modern delivery of therapeutics

Mariangela Garofalo

Università degli Studi di Padova

The use of oncolytic viruses (OVs), able to selectively infect, replicate in and kill cancer cells, is one of the most encouraging approach to treat cancer. Even though promising efficacy has been observed in in vitro and in vivo preclinical studies, the OV therapeutic approach is mainly restricted to neoplasia amenable to direct local administration of viral particles, thus, the possibility of a systemic delivery would extend the OV application to the treatment of metastatic tumors. Extracellular vesicles (EVs) are naturally occurring cargo delivery agents able to shuttle biological molecules, such as OVs, even over longer distances. We initially showed that EVs could be used for the systemic delivery of OVs and chemotherapy drugs such as paclitaxel (PTX), leading to enhanced anti-tumor effects in nude mice. Then, by using in vivo and ex vivo imaging technologies, as a detection system for the characterization of the whole-body biodistribution of EV formulations, we evaluated, at the same time, the biodistribution and the effects of EV-formulations carrying OVs and PTX on the immune system. Moreover, in vivo imaging of NFκB activation in an immunocompetent reporter mouse model allowed to demonstrate the selective ability of EVs to induce tumor-associated inflammatory reactions, which are characterized by immunogenic cell death and CD3+/ CD4+/CD8+ T-cell infiltration. Altogether, our findings strongly support the systemic administration of anticancer agents encapsulated into EVs as a safe and efficacious strategy for the selective delivery of diagnostic/therapeutic agents to solid tumors.