

## **Cancer EVs and their potential in diagnosis and therapy**

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Mammalian cells release different types of extracellular vesicles (EVs) into the extracellular space. The function of EVs is to mediate intercellular communication in physiological or pathological processes by trafficking biologically active molecules (proteins, nucleic acids and lipids) from secreting to recipient cells, and even to remote sites via circulation through bodily fluids, including blood. The composition of the complex cargo of EVs reflects that of the generating cell, and it is readily and easily accessible via sampling of biological fluids (liquid biopsies). EV-based liquid biopsy highlights their potential utility in diagnosis and in determining the prognosis, disease progression and response to therapy by a multicomponent analysis of EVs. To this aim, we are trying to develop a simple screening analyzing, by ultra-resolution microscopy, a small pool of selected cancer biomarkers (6-8 markers) in EVs isolated from plasma of patients with prostate, lung and colorectal tumors, in order to be able to translate the evidences obtained from the long and expensive high throughput proteomic analyzes (RPPA) into clinical practice. Moreover, in the context of cancer, EVs are considered as important vehicles that assist the intercellular communication and the development of the microenvironment where tumors develop, preparing the so called "pre-metastatic niche". Recent studies reported the involvement of HERVs (human endogenous retro-virus) in cancer progression and metastasis formation. HERVs' sequences, that cover the 8% of human genome, are mostly silenced in normal cells, but recent studies reported a re-activation of HERVs in different tumors. We want to explore whether the EV cargo can be involved in such HERVs reactivation during intercellular communication, analyzing their expression in recipient healthy cells (fibroblasts) receiving EVs isolated from tumor cells presenting high levels of HERVs expression.