Extracellular vesicles (EVs) including exosomes and microvesicles are secreted by all cells on the body in order to communicate with nearby or distant cells, and to modify their environment contributing to tissue homeostasis. They carry a particular cargo that depends on the cellular status and cell type of origin, and include proteins, different biotypes of nucleic acids, lipids and metabolites. By applying “omics” technologies, including metabolomics, proteomics and transcriptomics, as well as, specific biochemical tools, our group has studied EVs for more than a decade, especially in the field of cancer and metabolic diseases. Along these years, we have moved through different methodologies and experimental models that have provided a repertoire of low invasive candidate markers for cancer and metabolic diseases. The group put special emphasis in the application of methodology that could accelerate the translation into the clinic. Remarkably, EVs are not only carriers of molecules, they are also active nano-machines that contain functional enzymes that modify their environment and influence different patho-physiological processes including endothelial function, cancer and metabolic disorders.