

## **LIPID CONTENT OF HUMAN TUMOR EXOSOMES MAY EXPLAIN THEIR RESISTANCE IN BIOLOGICAL FLUIDS**

1)Accattatis F.. 2)Ferro S.. 3)De metrio S.. 4)Granata A.. 5)Corsini A.. 6)Huber V.. 7)Arnaboldi L..

*Dipartimento di Scienze Farmacologiche e Biomolecolari*

Exosomes are cell-derived nanovesicles involved in intercellular cross-talk through the transfer of nucleic acids, proteins and lipids. In cancer, they are involved in the modulation of tumor microenvironment, angiogenic processes, evasion of immune surveillance, multi-drug resistance, invasion and metastasis. Exosomes can be abundantly found in biological fluids including blood, milk, saliva and urines, suggesting a resistant structure able to cope with adverse biochemical conditions. Since lipids may play a key role in these features, we characterized lipid profiles of three different tumor cell lines and related exosomes, respectively myelogenous chronic leukemia (K562), adenocarcinoma human alveolar basal epithelial cells (A549) and human melanoma (Mel501).

The fatty acids (FA) composition of total lipid extracts and of two phospholipid classes, namely Phosphatidylcholine (PC) and Phosphatidylethanolamine (PE) were characterized as phospholipids are the main species in exosomes membrane, while PC and PE are the most abundant ones and contain relevant amount of plasmalogens. The latter are of interest because, due to their unique biochemistry, may lead to changes in membrane fluidity, fusion, vesicle trafficking and protein folding. Moreover, they also render membrane more lipophilic, thanks to the ether in sn-1, perpendicularly arranged to the membrane, and more rigid and thicker because of the closer packaging of the proximal regions of the sn-1 and sn-2 chains.

We showed that, despite each cell line is characterized by a unique lipid profile, exosomes present a common increase in stearic and palmitic acids, counterbalanced by a decrease in palmitoleic and oleic acids. Changes in the ratio of saturated/monounsaturated (SFA/MUFA) may lead to changes in membrane fluidity, making exosomes more rigid than parental cells. We found that in A549 exosomes, SFA raised from 30.2% to 50.1%, whereas MUFA decreased from 42.6% to 23.2%, compared to parental cells. The same trend was found in K562 exosomes, where SFA increased from 35.7% to 36.6%, while MUFA dropped from 40.8% to 33.9%. Finally, in Mel501 SFA increased from 36.2% to 43.4%, while MUFA decreased from 54,9% to 39,8%. These differences were also evident in PC and PE. Relative % in exosomes content of plasmalogens ranged from 6.90 to roughly 10% of the total lipids extract, but changes between exosomes and parental cells were not significant. Altogether these data lead to the conclusions that exosomes membrane is more rigid compared with parental cell membrane.