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Oncogene-induced senescence modify lipid composition of exosomes released from H-RasV12 expressing cells

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Cell proliferation induced by oncogene activation is restrained by cellular senescence, which acts as barriers in pre-neoplastic lesions. Senescent cells show proliferation arrest, flat morphology, activation of senescent associated β -galactosidase and acquisition of a specific secretory phenotype. Exosomes, 30-100 nm extracellular vesicles derived from the endosomal system, have been recently implicated in a variety of biological processes including the transfer senescence signals to surrounding cells. Similar to proteins and miRNA, lipid species enriched in exosomes are different to those of parental cells. A detailed analysis of exosomal lipid composition could be useful to understand the role of lipids in the functional response of target cells resulting in a senescent phenotype. In this study, lipid profile of human fibroblasts transfected with H-RasV12 and their released exosomes was analyzed by LC-MS/MS and GC-MS, and compared to mock transfected cells and their released exosomes. Results showed alteration in cell lipid composition during senescence. Relative quantification and comparison of exosomes versus the corresponding cell lipid profiles reveals an enrichment of lysophosphatidylcholine, ether-phosphatidylcholine (PCether) and sphingomyelin (SM). Furthermore, remodeling and changes in the amount of specific lipid species of diacyl-PC, PCether and SM in exosomes released by senescent cells were detected. Overall results confirmed that lipid composition of exosomes is distinct from parental cells. Moreover, an increased release of exosomes with specific lipid composition was shown to be associated to H-Ras-induced senescence, suggesting a specific role of exosomal lipids in the spreading of senescence signals to surrounding cells.

Biography

Sandra Buratta is a permanent researcher at the Department of Chemistry, Biology and Biotechnology, University of Perugia, Italy. In the last decade her research focused on several aspects of phospholipid metabolism, with the main aim to define the role of enzymes involved in the biosynthesis and replacement of membrane phospholipids in several cellular processes. Particular attention has dedicated to the role of phosphatidylserine and of the enzymes of its metabolism in signal transduction and apoptosis. Her present research focus on cellular effect associated to drug-induced phospholipidosis and on the role of lipids in exosomes fate and bioactivity.

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