Salivary exosomes as carriers of novel biomarkers in pancreatic cancer

Silvia Rocchiccioli[1], Elisa Ceccherini[1], Antonio Morlando[1], Lucia Piazza[1,2], Rossella Mosca[2], Annalisa Comandatore[3], Luca Morelli[3], Giovanni Signore [1,2]

[1] Institute of Clinical Physiology, CNR, Pisa, Italy

[2] Biochemistry Unit, Department of Biology, University of Pisa, Pisa, Italy

[3] General Surgery Unit, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Pancreatic ductal adenocarcinoma cancer (PDAC) is an aggressive malignancy with a 3-year survival rate of 1%. Symptoms only manifest in advanced stages and tardive diagnosis significantly impact on the outcome. Discovery of biomarkers for early detection of PDAC remains a significant challenge. Liquid biopsies such as saliva offer further advantages including easy-collection and non-invasiveness. Exosomes carry a panel of factors that represent the molecular fingerprint of the source cells. This study aims at detecting biomarkers in the saliva of PDAC patients through a novel method for the high-quality collection and omics analyses.

Saliva of PDAC patients and healthy donors was collected and processed through an innovative, patented filtering device (Patent Number 102023000023502). Purified exosomes were characterized by transmission electron microscopy, dynamic light scattering and western blotting. Bottom-up proteomics analysis of exosomal constituents were performed to identify potential cancer biomarkers.

Collected exosomes show a small variety in size and low grade of impurity. Proteins identified by proteomic analysis include classic exosomal biomarkers (CD9 tetraspanin), biomarkes primarily linked to salivary exosomes (DPP IV/CD26), and other 24 proteins already found in exosomes according to ExoCarta database. 12 proteins were found differentially expressed (5 upregulated, 7 downregulated, $p<0.05$) in PDAC vs. control samples. A functional analysis of identified Exocarta proteins performed with WikiPathways associates 6 proteins to PDAC-related pathways.

Proteomics analysis of ultra-purified saliva-derived exosomes provides a powerful strategy for the identification of potential PDAC biomarkers with intriguing translational potential.