

Quantitative Proteomics of Exosomes in Small Cell Lung Cancer.

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Received: 01-Jan-2022, Manuscript No. AASBPR-22-54622; Editor assigned: 03-Jan-2022, PreQC No. AASBPR-22-54622(PQ); Reviewed: 17-Jan-2022, QC No. AASBPR-22-54622; Revised: 18-Jan-2022, Manuscript No. AASBPR-22-54622(R); Published: 25-Jan-2022, DOI:10.35841/aasbpr-3.1.104

Abstract

Small cell lung cancer (SCLC) requires very reliable markers for early identification. Evidence is mounting that extracellular vesicles convey tumour cell-specific cargo that could be used as cancer protein markers. Quantitative proteome analysis of circulating microvesicles and exosomes can be used as a high-throughput platform for finding new molecular insights and potential indicators. In order to improve early detection, this study looked into the proteome dynamics of plasma-derived microvesicles and exosomes in newly diagnosed SCLC patients. Microvesicles and exosomes produced from plasma were extracted from healthy subjects and patients using either high-speed or ultracentrifugation. Proteins extracted from these extracellular vesicles were measured using label-free mass spectrometry, with the goal of discovering significantly different protein expressions between SCLC patients and healthy controls. Furthermore, functional enrichment analysis was performed on significantly expressed proteins to uncover molecular pathways involved in SCLC pathogenesis. Several differently expressed proteins were discovered when SCLC patients and healthy people were compared. This is the first study to indicate that circulating extracellular vesicles may contain specific proteins with potential diagnostic properties for SCLC, potentially paving the way for new non-invasive indicators.

Keywords: Proteomics, Exosomes, Lung cancer, SCLC, Microvesicles, Extracellular vesicles.

Introduction

Lung cancer is the leading cause of cancer-related deaths, as well as the second and third most common cancers in men and women in Europe. Small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) are the two primary histological subtypes of lung cancer (NSCLC). SCLC is a type of neuroendocrine carcinoma that accounts for around a quarter of all lung malignancies and is characterised by rapid development to early metastases. Currently, the diagnosis is predicated on a computed tomography (CT) scan and cytology acquired from a suspected lesion via fine-needle aspiration (FNA) biopsy [1]. FNA is connected with a risk of complications, but CT scans have a high sensitivity and low specificity due to a high false-positive rate. SCLC patients have a poor prognosis in part due to late diagnosis, as two-thirds of patients have advanced tumour stages at the time of diagnosis. As a result, better diagnostic processes are required to reduce diagnostic delays and increase patient safety [2]. Efforts have been made throughout the years to develop conveniently accessible, cost-effective, and non-invasive biomarkers for lung cancer. NSE and ProGRP are two proteins that have been shown to be useful in distinguishing between NSCLC and SCLC, and it has been suggested that a panel that includes both markers could enhance diagnosis. Despite extensive research, the perfect diagnostic biomarker for SCLC has yet to find a position in clinical practice [3].

Extracellular vesicles (EVs), a rapidly growing field, have revealed a fresh technique to studying SCLC. Because EVs are released by nearly all cells, including cancer cells, and are found in a variety of bodily fluids, they can be used as non-invasive liquid biomarkers. Exosomes (small EVs) and microvesicles (MVs or giant EVs) are two types of EVs that are continuously released under healthy and pathological situations. The vesicles contain a specific payload, which includes lipids, proteins, and genetic material from the parent cell. As a result, the content of EVs may mirror the molecular profiles of the source cells to some extent [4]. As a result, the use of EVs could be a game-changing technique for researching SCLC in a clinical environment. Proteomic analysis combined with discovery-based mass spectrometry (MS) is a relatively recent method for identifying potential biomarker candidates in a variety of malignancies. This method of profiling EV proteomes has led to the discovery of new diagnostic biomarkers in malignancies like as ovarian and prostate cancer. Exosomal biomarkers with diagnostic potential in NSCLC patients employing MS have been discovered in recent research. The goal of this work is to look at the proteome dynamics of plasma-derived exosomes and MVs from SCLC patients in order to find proteins that are significantly expressed and can help with lung cancer biology and early detection. This is the first study to use quantitative proteomics to investigate the potential relevance of circulating MVs and exosomes in SCLC diagnosis [5].

Citation: McDonald A. *Quantitative Proteomics of Exosomes in Small Cell Lung Cancer. J Syst Biol Proteome Res. 2022; 3(1):104*

Conclusions

To our knowledge, this is the first study to use an untargeted quantitative proteomic technique to identify specific proteins (CFHR4 and F13A1) and a panel of proteins as possible candidates for SCLC diagnosis. In contrast to NSCLC and other malignancies, we found altered expression of proteins involved in inflammation, coagulation, complement activation, haematological dysfunction, lipid metabolism, and hydrogen peroxide catabolism. Validation studies to confirm these proteins as possible markers in SCLC are, however, required.

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