

Investigation of human plasma depletome from patients with schizophrenia

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Abstract

The proteome of blood plasma is an interesting source of biomarkers and a potential way to improve treatment outcomes in psychiatric disorders. Respire that, its wide dynamic concentration range makes reducing its complexity necessary. Thus, in proteomic studies, a few of the most abundant proteins are depleted and normally discarded. This high-abundance fraction, called the depletome, however, is a source of potential biomarkers due to nonspecific bindings with low abundance proteins. In this work, we aimed to characterize the high-abundance fraction using a shotgun mass spectrometry approach. These proteins show the importance of studying depletome proteins in the quest for biomarkers.

Key words:

Schizophrenia, biomarkers, proteomics

Introduction

The proteome of the blood plasma is an interesting source of biomarkers. A potential way to improve treatment outcomes in psychiatric diseases is the discovery and clinical application of biomarkers for the diagnosis and prognosis of such disorders. The wide and dynamic concentration range of blood plasma proteins, on the other hand, makes its complexity reduction necessary. In proteomic studies, a few most abundant proteins are depleted and discarded, with the intent of leaving a fraction of less abundant and generally more interesting proteins. The discarded fraction, called depletome, however, is a source of potential biomarkers due to nonspecific bindings with low abundance proteins^{1,2}. In this work, we aimed to characterize the depletome using shotgun mass spectrometry approach.

Results and Discussion

The depletome from 20 antipsychotic-free patients was obtained by MARS-14 immunodepletion system and digested to peptides by trypsin. The peptides were injected in a 2D-RP/RP Acquity UPC M-Class System coupled to a Synapt G2-Si Mass Spectrometer using ion mobility. Data independent .analysis method was used and a fragmentation spectrum was obtained by MSE analysis. The identification of proteins was executed by Progenesis software. Finally, systems biology in silico was performed to characterize proteins.

The resulting data set comprised 83 identified proteins, with stringent identification by a minimum of two distinct peptides detected at least in >70% of samples. Most of these proteins have unknown biological processes and molecular functions. Among the depletome proteins, immune response, complement pathway, protein metabolism and transport are some of the biological processes identified (Image 1).

The immune system plays an important role in the etiology of psychiatric diseases. Patients with schizophrenia may have increased levels of immune system proteins, affecting the functioning of neurotransmitters through hypothalamic axes. Some antipsychotic medications may be associated with an immunomodulatory role^{3,4}. Aside from that, transport processes proteins, which may be linked to the

distribution of medication in the body, were found in the depletome⁵.

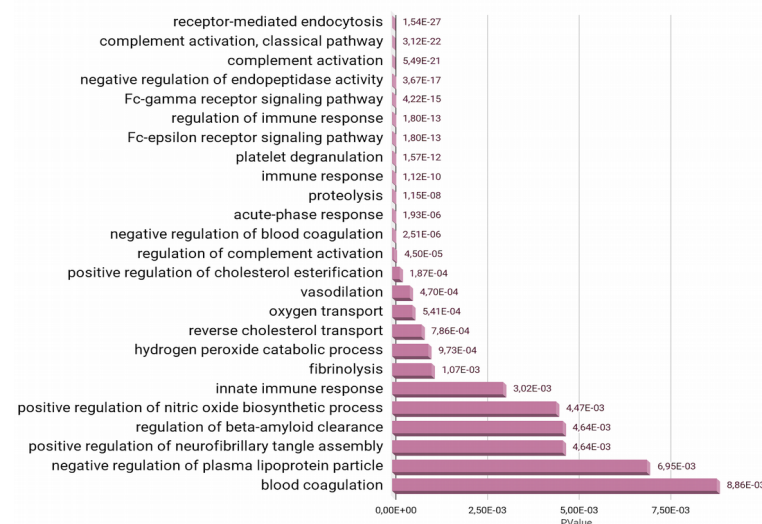


Image 1. Depletome proteins participate of many different biological processes

Conclusions

Depletome characterization from patients with schizophrenia demonstrates the importance of investigating this fraction, considering the intrinsic potential of plasma to participate in and exhibit changes related to endogenous and exogenous stimuli. In addition, the high-abundance fraction of human blood plasma, usually neglected, carries proteins involved in the most diverse biological processes, making this material a possible source of potential biomarkers for positive response to medication.

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