



Proteomic analysis of exosomes extracted from the medium of cell cultures derived from patients with schizophrenia and controls

Danielle Gouvêa-Junqueira*, Verônica M. Saia-Cereda, Juliana M. Nascimento, Daniel Martins-de-Souza.

Abstract

Exosomes are cell-derived nano vesicles that play multiple roles as mediate cellular communication, elimination of undesirable components and transport of molecules such as RNAs and proteins. Misfolded proteins associated to the development of pathologies may be also transported by exosomes. This study aims to perform a quantitative proteome analysis of exosomes collected from cell cultures derived from patients with schizophrenia and mentally healthy controls, in order to find differentially expressed proteins possibly associated to the disease.

Key words:

Exosomes, proteome, proteomics, schizophrenia.

Introduction

Schizophrenia is a complex psychiatric disorder, which is influenced by genetic and environmental factors¹. The disease manifest through several symptoms as hallucinations, cognitive problems and social withdraw, which are generally managed by antipsychotic drugs. Proteomics is one of the tools which have been employed in order to better understand schizophrenia from the molecular point of view. The proteome corresponds to the set of proteins expressed in an individual under certain physiological conditions². And by proteomic analysis it is possible to identify proteins and relate them to the metabolic pathways in which they operate³.

In diseases affecting the central nervous system, such as schizophrenia, cell-derived vesicles are released. These can transport molecules and proteins which might be associated with the development of pathology. The exosomes are nano-vesicles present in various body fluids, working on communication and cell signaling, transfer of molecules and elimination of unwanted proteins^{4,5}. This study aims to analyze for the first time the proteome of exosomes obtained from the cell culture medium of cells derived from patients with schizophrenia and controls, in order to identify possible proteins expressed differently associated to schizophrenia.

Before that, we are testing the separation of exosomes and the extraction of their proteins.

Results and Discussion

Here we are comparing the separation of exosomes using two different techniques: differential centrifugation and sucrose gradient size exclusion chromatography. Proteins were then extracted, digested and subjected to nano ultra performance liquid chromatography – tandem mass spectrometry (nUPLC-MS/MS). With the data obtained, we identified and quantified the proteins present using the software Progenesis. Next, we analyzed and correlated the proteins with the metabolic pathways in which they operate, through a process of enrichment analysis tool (GO term analysis, Ingenuity Pathway Analysis and String database analysis).

Conclusions

This work wasn't finished at the time of submission to this congress, and the data generated will be presented in the poster.

¹ Sullivan PF, Kendler KS, Neale MC. Schizophrenia as a Complex Trait Evidence From a Meta-analysis of Twin Studies. *Arch Gen Psychiatry*. 2003;60:1187–92.

² Martins-de-Souza D. Proteomics as a tool for understanding schizophrenia. *Clin Psychopharmacol Neurosci*. 2011;9(3):95–101.

³ Nascimento JM, Martins-de-Souza D. The proteome of schizophrenia. *npj Schizophr* [Internet]. 2015;1(October 2014):14003. Available from: <http://www.nature.com/articles/npjSchz20143>.

⁴ Wood MJ, O'Loughlin AJ, Lakkhal S. Exosomes and the blood-brain barrier: implications for neurological diseases. *Ther Deliv*. 2011;2(9):1095–9.

⁵ Frühbeis C, Fröhlich D. Emerging roles of exosomes in neuron – glia communication. 2012;3(April):1–7.