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ORIGINAL PAPER

# A SHORT EDITORIAL VIEW ON THE RELEVANCE OF EXOSOMES IN SOME NEUROPSYCHIATRIC MANIFESTATIONS - MODEL STUDIES

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**Abstract.** Exosomes are a class of extracellular vesicles derived from cells of endosomal origin and typically have a diameter between 40 to 100 nm, being the smallest type of extracellular vesicle. Although in recent years, the use of exosomes in experimental studies has increased, currently there are few studies that have as a research subject the neurobehavioral changes that exosomes have on model organisms. For this reason, our group is further looking to develop and apply the methodology regarding the neurobehavioral changes that exosomes have on zebrafish (*Danio rerio*). Thus, we present here a short editorial view on the relevance of exosomes in some neuropsychiatric manifestations-models studies, as wel as some of our future plans in this new area of reearch.

**Keywords:** exosomes, neuropsychiatric , zebrafish studies.

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## Introduction

Exosomes are a class of extracellular vesicles derived from cells of endosomal origin and typically have a diameter between 40 to 100 nm, being the smallest type of extracellular vesicle (Edgar, 2016; Koga et al., 2005). They have a lipid bilayer, being released into the extracellular environment containing a complex cargo of contents derived from the original cell, including proteins, lipids, messenger ribonucleic acid (mRNA), micro ribonucleic acid (miRNA), and deoxyribonucleic acid (DNA) (Carretero-González et al., 2018; Melo et al., 2014).

In the nervous system, exosomes play a role in intercellular communication, maintain the myelin sheath and remove waste. Similarly, exosomes found in the brain may play a role in CNS diseases, the most common being: Alzheimer's disease (AD) and Parkinson's disease (Liu et al., 2019).

Although in recent years the use of exosomes in experimental studies has increased, currently there are few studies that have as a research subject the neurobehavioral changes that exosomes have on model organisms. For this reason, our group is further looking to develop and apply the methodology regarding the neurobehavioral changes that exosomes have on zebrafish (*Danio rerio*).

In the past decade, zebrafish have been an excellent model to study normal development and congenital malformations due to the knowledge of their genetics. Also, its analogy with the human genome makes it an increasingly used model to model human diseases and to analyze the formation and functions of cell populations in organs. Thus, it generated new models of human disease and began to identify potential therapeutics, including chemicals that protect organs from disease.

We aim to use zebrafish as a relevant vertebrate model organism to study in vivo the neurobehavioral potential of exosomes for neurodegenerative diseases , based on the data already published by our research group in which we use zebrafish as a model for behavioral neuroscience.

However, the use of exosomes as drug-delivery vehicles presents a number of research challenges. The aim of the project is to address these challenges so that exosomes can be engineered for production at an appropriate scale and quality.

We aim to pursue the following four objectives, our research group consists of experts for using the fish as model organisms in neurodegenerative disease. To establish the relevance of our model we propose the following objectives: we will chronically administer exosomes to zebrafish, intraperitoneally, in different concentrations, thus we will establish the administration dose at which behavioral effects will be signaled. Thus we will perform behavioral tests, such as the aggression test, novel tank test, the sociability test, the swimming performance test.

Also, we will analyze the parameters obtained from the behavioral tests between the control group and the groups that were administered exosomes, such as total distance moved, swimming velocity, maximum swimming acceleration, minimum swimming acceleration, rotation frequency, left arm cumulative duration, right arm cumulative duration, center arm cumulative duration. We will also be able to evaluate the evolution of the parameters throughout the duration of their exposure.

In addition we will evaluate if the administration dose has effects on the biochemical parameters, as wel as establishing the administration protocol for exosomes, respectively for substances with effects on the nervous system (rotenone-for PD model, valproic acid-for autism model, mercury, pentylenetetrazole etc).

**Conclusions**

In this way, the completion of this project will highlight the contribution of zebrafish as a reference model in the use of exosomes as biomarkers and to evaluate their effectiveness as therapeutic vectors in neurodegeneration. On this basis, we will evaluate the characteristics and potential of exosomes in the study of neurodegeneration, as we can strengthen the relevance of zebrafish, in order to test therapeutic exosomes in vivo.

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