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Extracellular vesicles of human glial progenitor cells exhibit neuroprotection by modulating the PI3K-Akt pathway in glutamate excitotoxicity

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RUDN biomedhub

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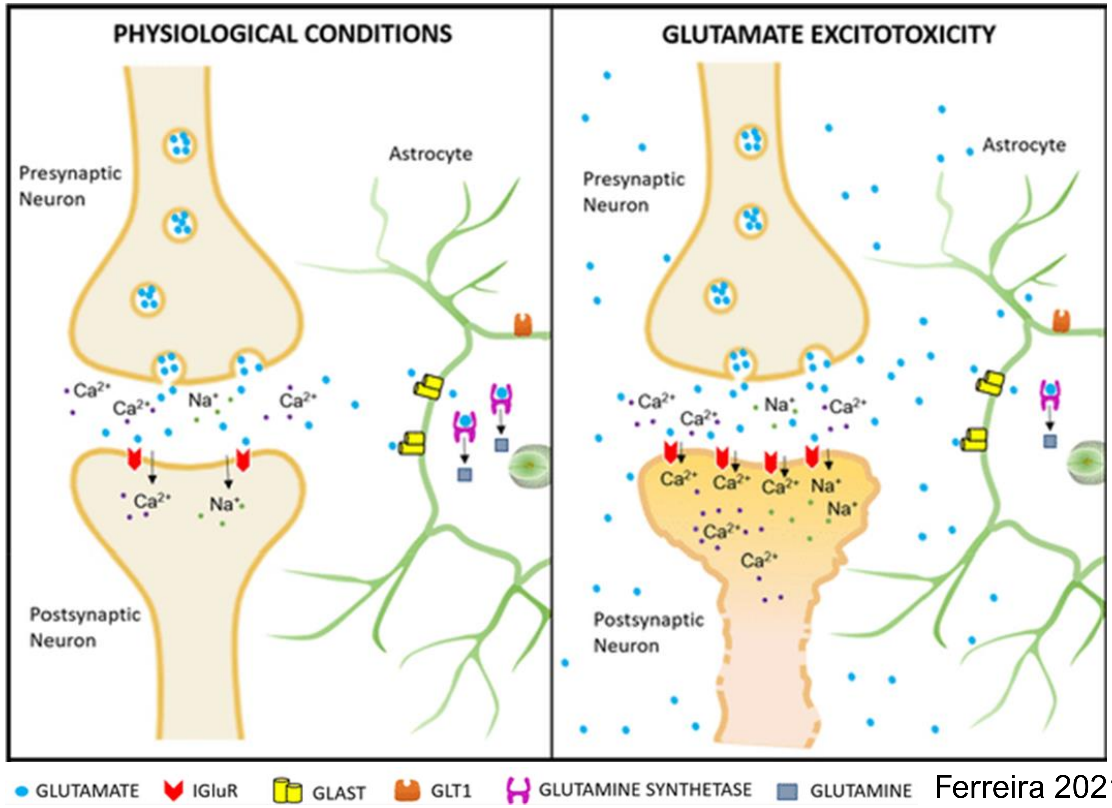
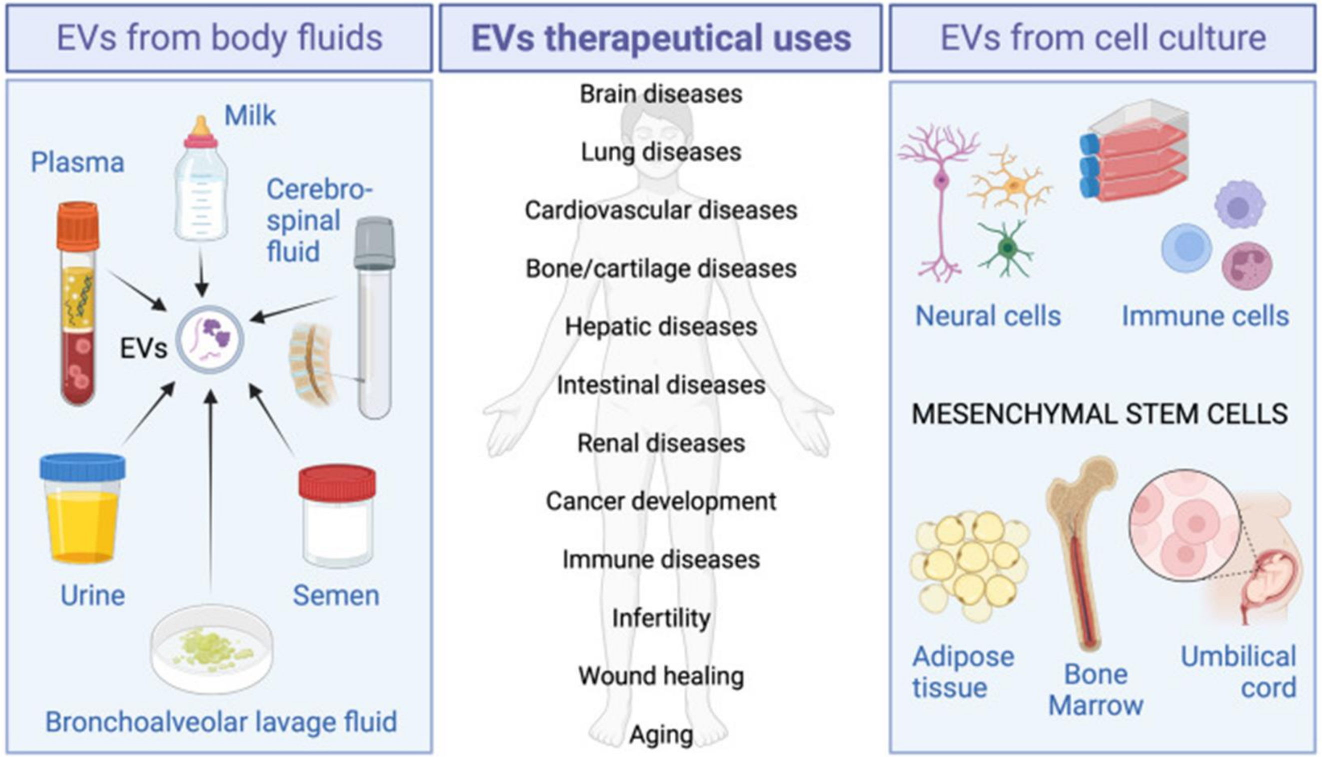
Motivation and Aim



Ferreira 2021

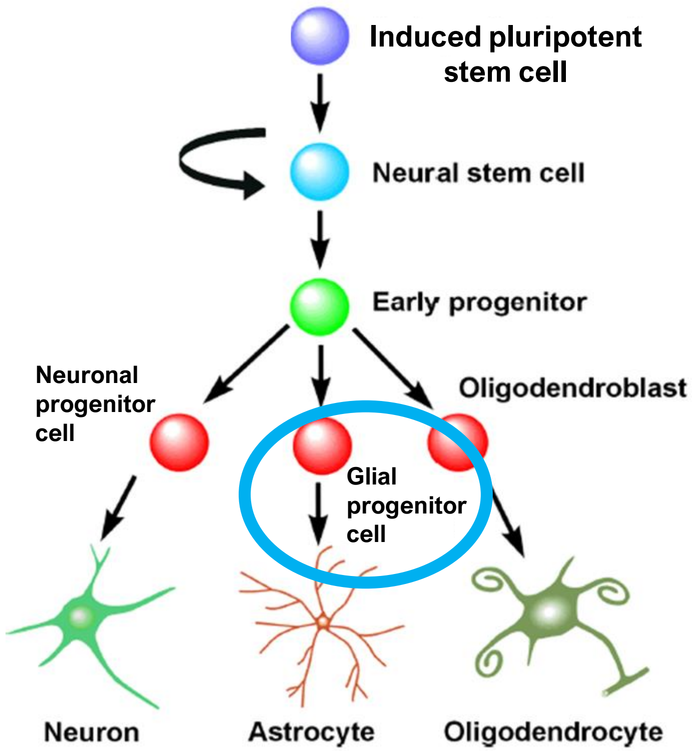


Sanz-Ros 2023

- Glutamate excitotoxicity is a short-term increase of glutamate's concentration in the synaptic cleft to toxic levels, that is a factor of many brain diseases
- Extracellular vesicles (EVs) are vesicles that are secreted by cells and contain specific cargo: proteins, RNAs, peptides etc.

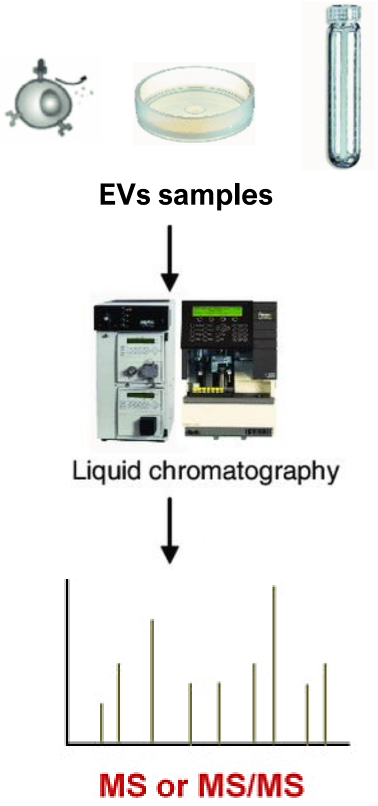
Materials and methods

Our specific source of EVs



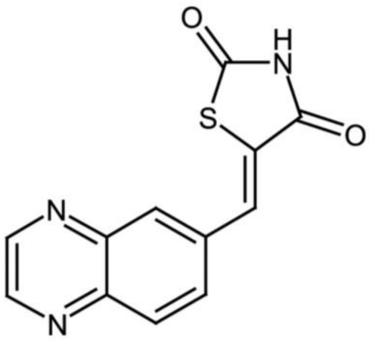
Ultracentrifugation

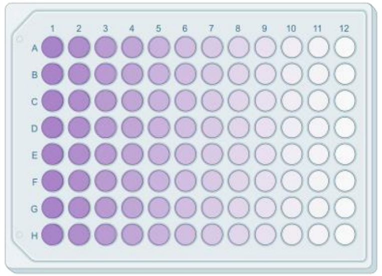
Proteomic analysis



Inhibitor analysis

AS605240





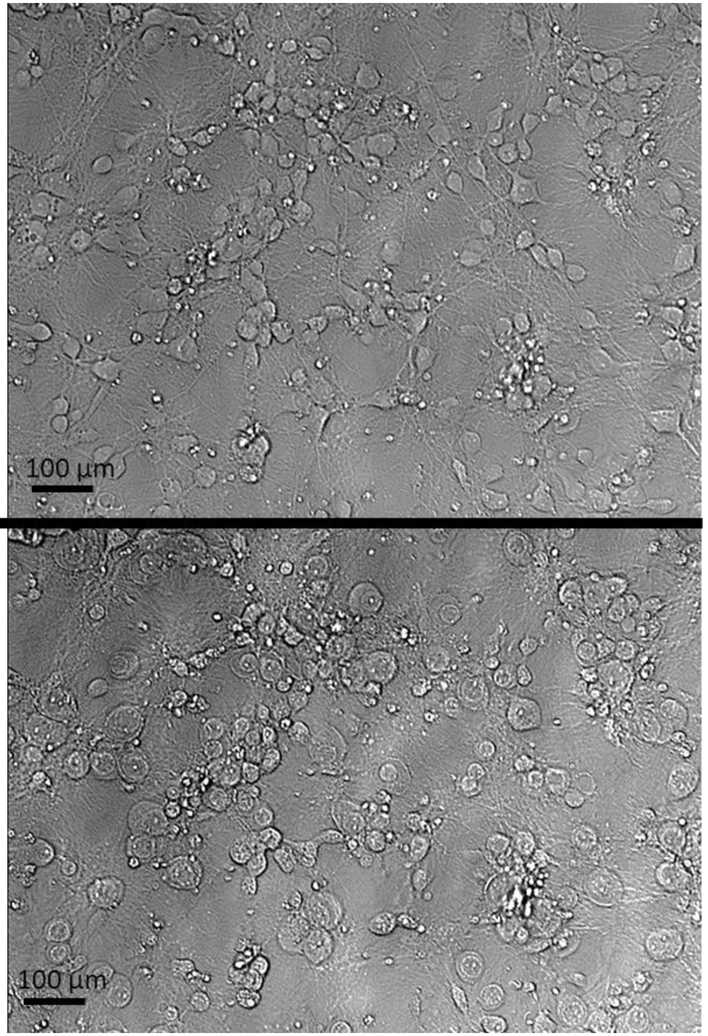
MTT-test Survival

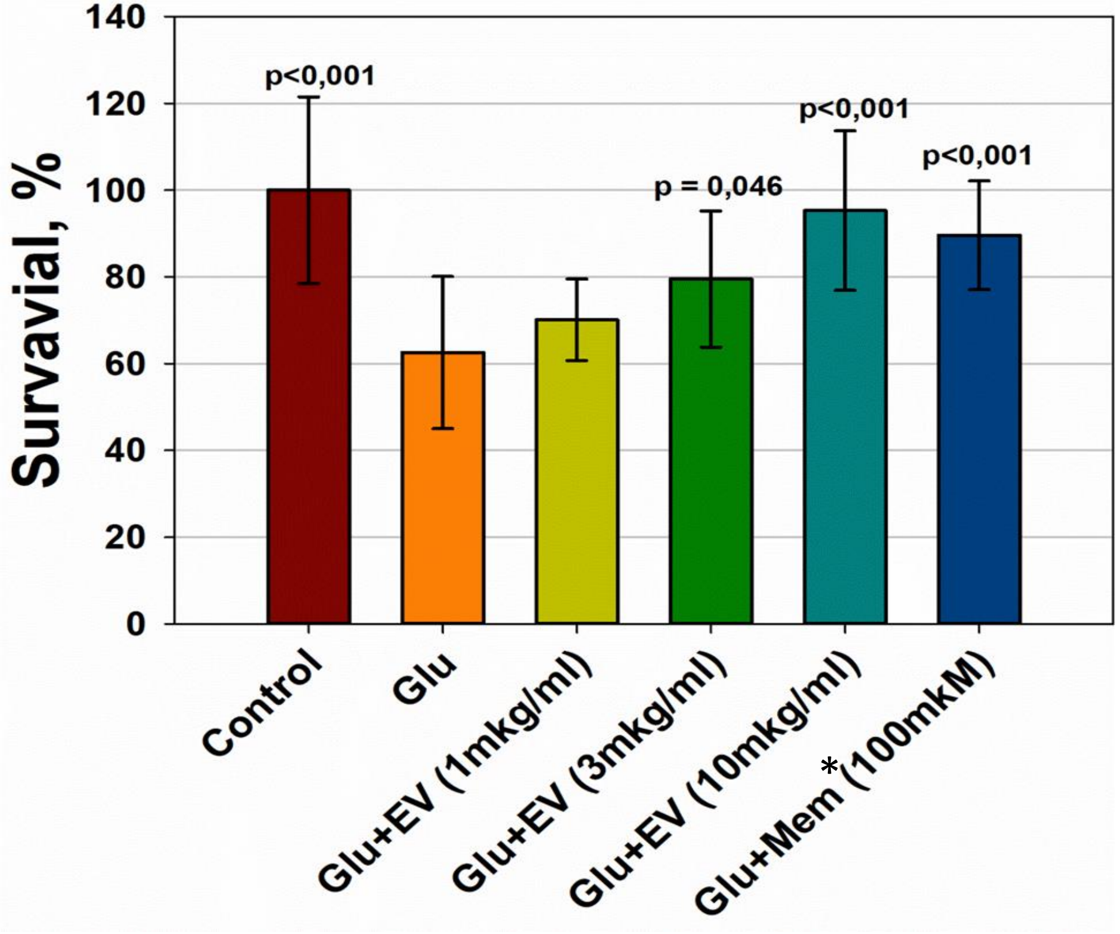
- Our **<u>unique</u>** source of EVs is **<u>glial progenitor cells derived from human iPSCs</u>**
- EVs were obtained by ultracentrifugation
- EVs were analyzed by proteomic analysis
- The obtained protein data were confirmed by inhibitor analysis

Results: EVs protect cortical neurons cultures from glutamate excitotoxicity

Before Glutamate 100 mkM

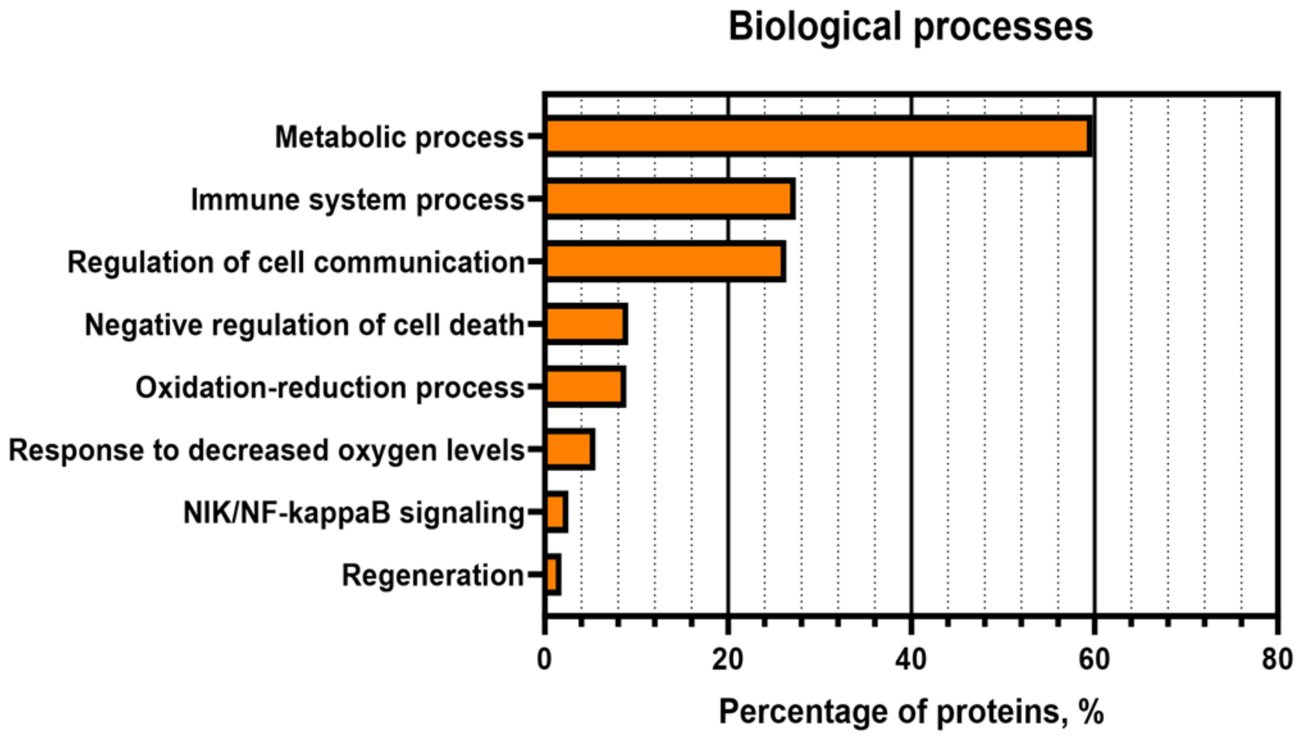
After 1 hour of Glutamate 100 mkM

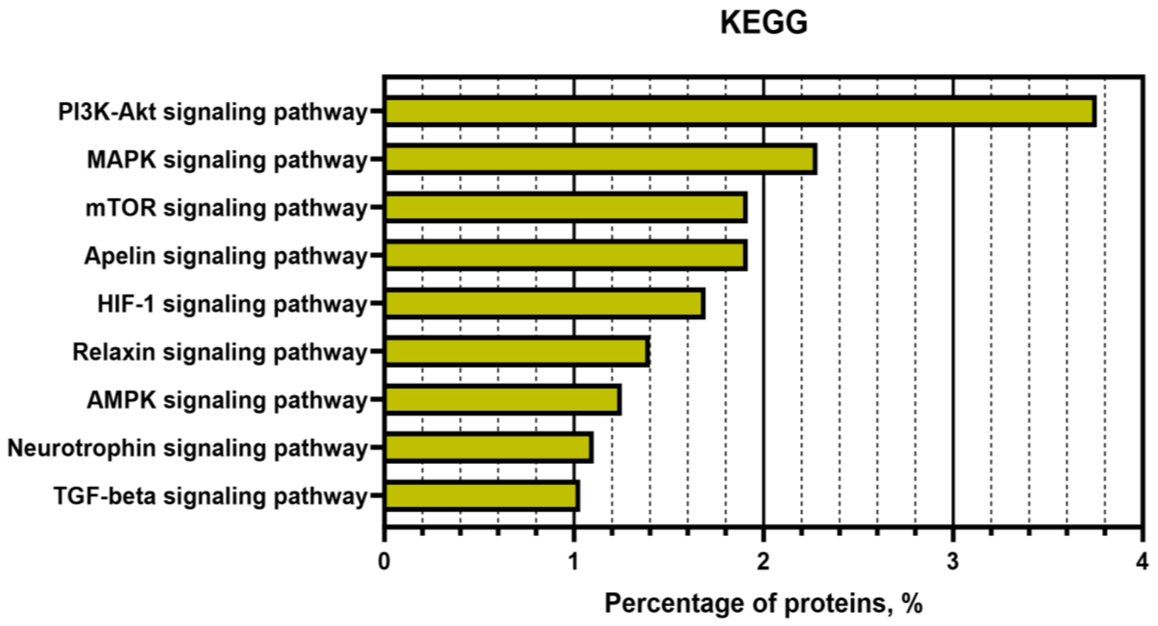




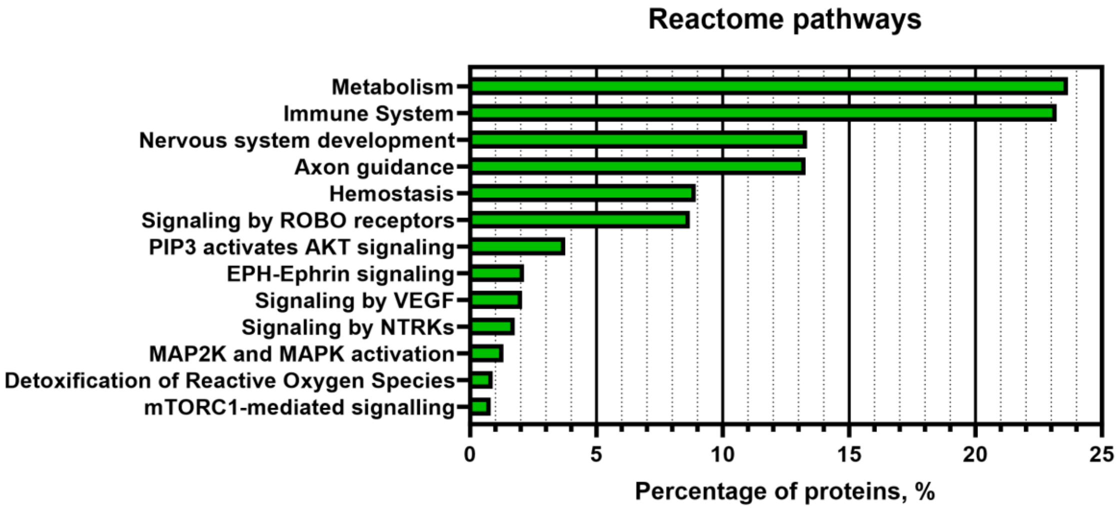
* Memantine (Mem) – positive control

Results: Proteomic analysis of EVs

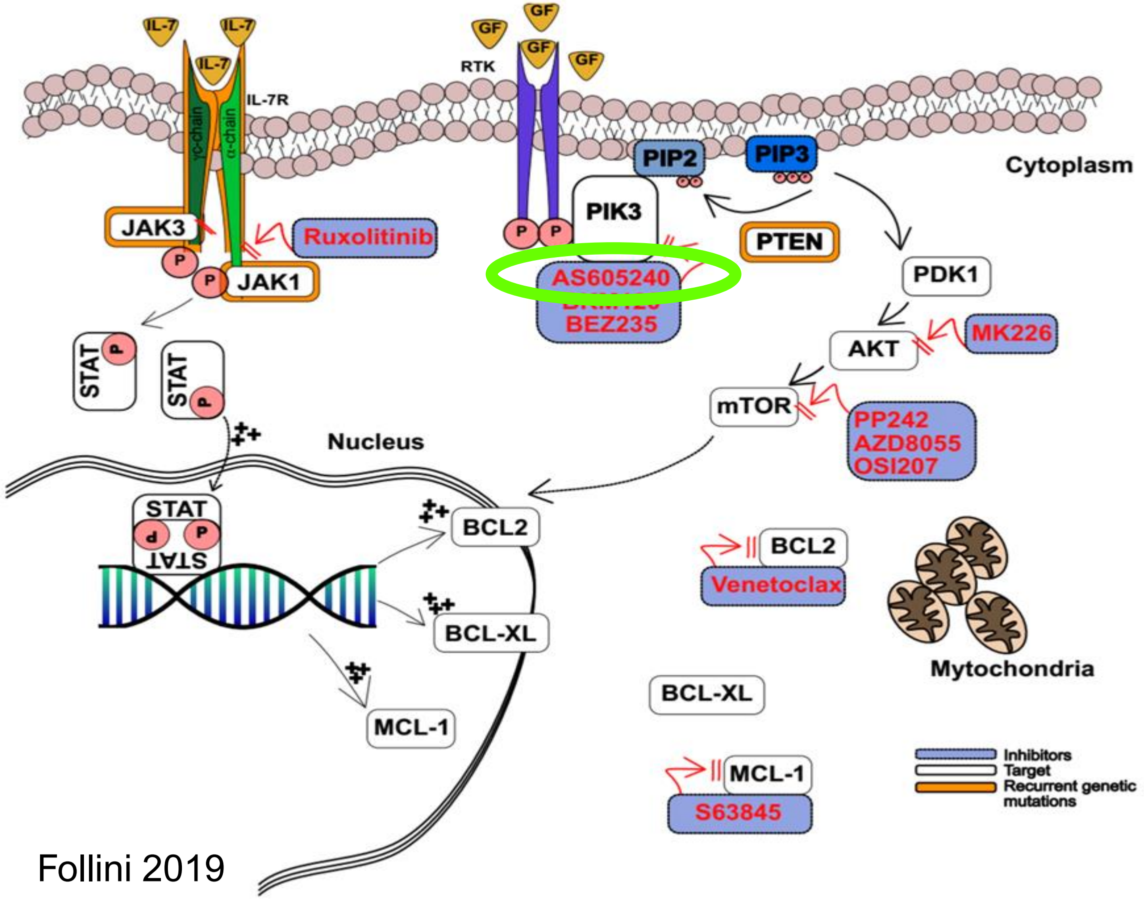




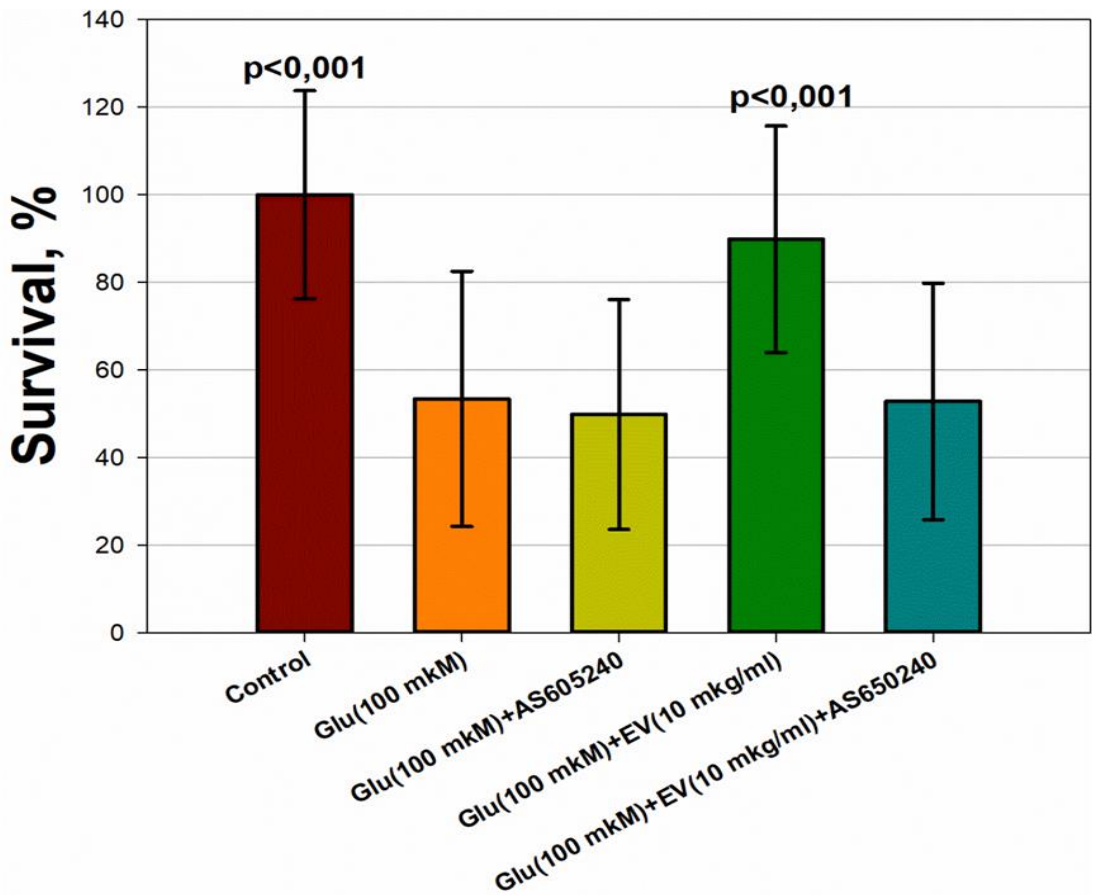
Proteins were categorized according to their involvement in biological processes and against KEGG and Reactome pathways databases



Results: Inhibition of PI3K-AKT pathway by AS605240 offsets neuroprotective effects of EVs



Follini 2019



- According to the KEGG database, EVs activate the PI3K-AKT pathway
- It was confirmed using a PI3K inhibitor - AS605240

Conclusion

The results obtained indicate that EVs from glial progenitor cells have a neuroprotective effect in glutamate excitotoxicity because of the proteins they contain that reduce neuronal death through various mechanisms and signaling pathways, among which the involvement of the PI3K-Akt signaling pathway was confirmed. These data suggest that EVs from glial progenitor cells may become a new type of therapeutic drug to treat neurological diseases.

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