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Glial-neuronal interactions

Shortcut:	**PS III - 09**
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Room:	**Archive Hall,D. Maria Hall,Despachantes Hall,Infante Hall,Noble Hall**
Session type:	**Poster**

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T09-088C

The serine shuttle sustains neuronal D-serine synthesis and regulates NMDAR synaptic activity (#743)

I. Radzishevsky[1], S. Neame[1], H. Safory[1], J. - M. Billard[2], H. Wolosker[1]

T09-089C

Axo-glial interplay in oligodendrocyte specification and myelination: role of JNK1 (#745)

M. Lorenzati[1], E. Boda[1], T. Borsello[2], A. Buffo[1], A. Vercelli[1]

T09-090C

Ultrastructural and molecular characterization of astrocyte-derived extracellular vesicles from nigrostriatal brain regions: implications for dopaminergic neuroprotection (#502)

L. Leggio[1], F. L'Episcopo[2], S. Vivarelli[1], C. Tirolo[2], N. Testa[2], S. Caniglia[2], C. Bastos[3], N. Faria[3], M. J. U. Navas[5], J. M. G. Verdugo[5], S. Pluchino[4], B. Marchetti[1], N. Iraci[1]

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Content

Astrocytes (AS) are key players in the regulation of dopaminergic (DA) neuron homeostasis both in health and disease. Parkinson's disease (PD) is a chronic neurodegenerative disorder characterized by the progressive degeneration of DA cell bodies in the subtantia nigra pars compacta of the ventral midbrain (VM) and their terminals in the striatum (Str). Our previous work identified a crucial role of AS-neuron crosstalk and underscored AS key contribution to DA neuroprotection in preclinical models of PD. Specifically, chemokine-activated AS, such as Ccl3, were shown to exert robust DA neuroprotection against the PD neurotoxin, MPTP, but the mechanism(s) underlying this complex intercellular signalling remain elusive.
Recent experimental evidences suggest that extracellular vesicles (EVs) are important players in the cell-to-cell communication. EVs are released by virtually all cells in the microenvironment and include exosomes, microvesicles and apoptotic bodies, different for size and biogenesis.
We herein characterized AS-derived EVs from both the VM and Str, and addressed the effect of the Ccl3 vs. degenerative conditions (MPP^+).
EVs have been characterized for their dimension and concentration by electron microscopy and nanoparticle tracking analysis. We observed that the basal EV secretion rate is specific for each brain area, with VM releasing more EVs than Str. Moreover, Ccl3 treatment affects both AS morphology and their EV secretion, in absence of any influence on cellular viability and proliferation. In fact, Ccl3-treated AS show much more membrane protrusions that reflect an increased secretive activity, as confirmed by the higher number of EVs released by AS after Ccl3 treatment. The amount of EVs resulted increased also after MPP^+ treatment, especially in the Str. The appearance of MPP^+-EVs differs from Ccl3-EVs suggesting the presence of different class/cargoes in response to specific stimuli.
In particular, we found an enrichment of EVs in the size range of exosomes (~100 nm). Also, several exosomal markers (Cd63/9, Alix1) have been analysed by WB and confirmed the enrichment of exosomes in the AS-derived EVs. Finally, the presence of mRNAs and miRNAs has been evaluated by qPCR, finding both of them associated with AS-derived EVs. These findings suggest a possible involvement of EVs in the horizontal transfer of RNAs in the context of glia-neuron communication. This in-depth characterization was preliminary to our next steps of investigation that aim to evaluate, *in vitro* and *in vivo*, the impact of AS-EVs on PD target cells.

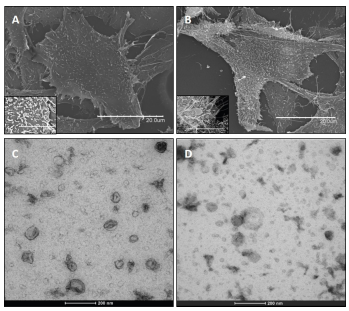

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Figure 1. Ultrastructural characterization of astrocyte-derived exosomes

Scansion Electron Microscopy of astrocytes in basal (A) and after Ccl3 treatment (B); Transmission Electron Microscopy on astrocyte-derived EVs in basal (C) and after Ccl3 treatment (D).

Keywords: Astrocytes, Parkinson's disease, Vesicle trafficking, endo- and exocytotic processes

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