Altered immune activity of plasmatic extracellular vesicles derived from Parkinson's Disease patients

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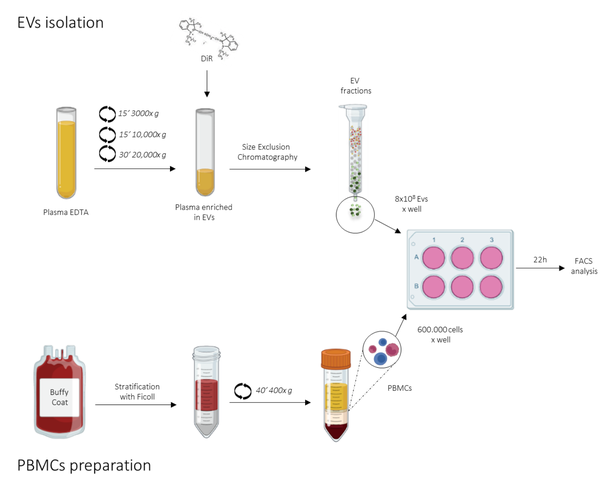
Background

There is extensive and growing evidence about the role of inflammation in Parkinson's disease (PD). In addition to neuro-inflammatory processes occurring in the brain, elevated levels of pro-inflammatory factors are also present in the plasma of PD. Extracellular vesicles (EVs), secreted membrane particles involved in cell-to-cell communication, carry important information on immunity and its regulations. Thus, we hypothesize that in PD, plasmatic EVs may have a functional role in disease initiation and progression.

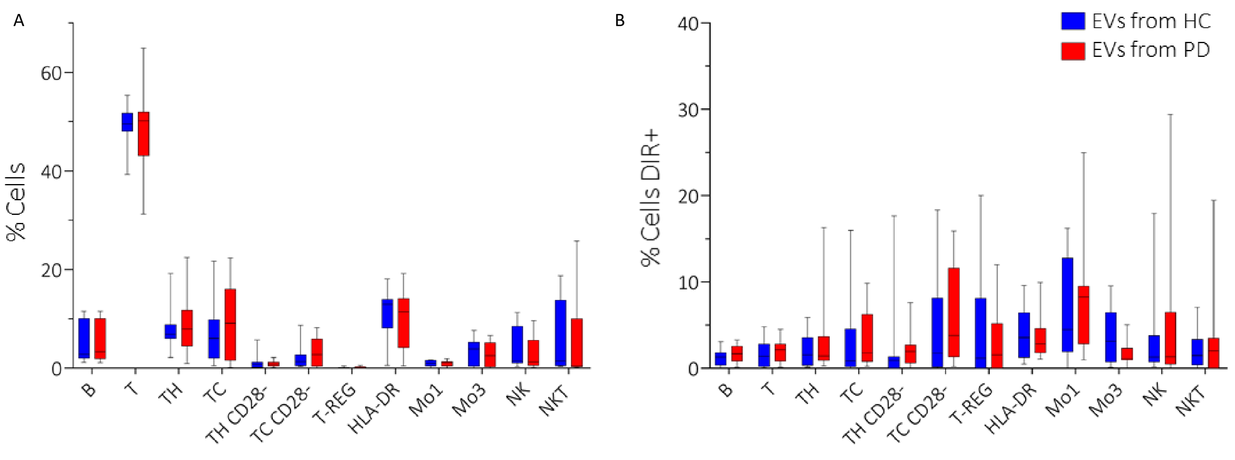
Methods

Plasmatic EVs derived from PD or healthy subjects (HC), previously labeled with the lipophilic dye DiR, were incubated for 22 hours with peripheral blood mononuclear cells (PBMC) from healthy donors. A panel of 14 specific antigens was used to identify more than 12 subpopulations of PBMCs by FACS analysis. For each subpopulation, we analyzed EV internalization and immune activation. Cytokine secretion by PBMCs exposed to PD vs. HC-derived EVs was also evaluated.



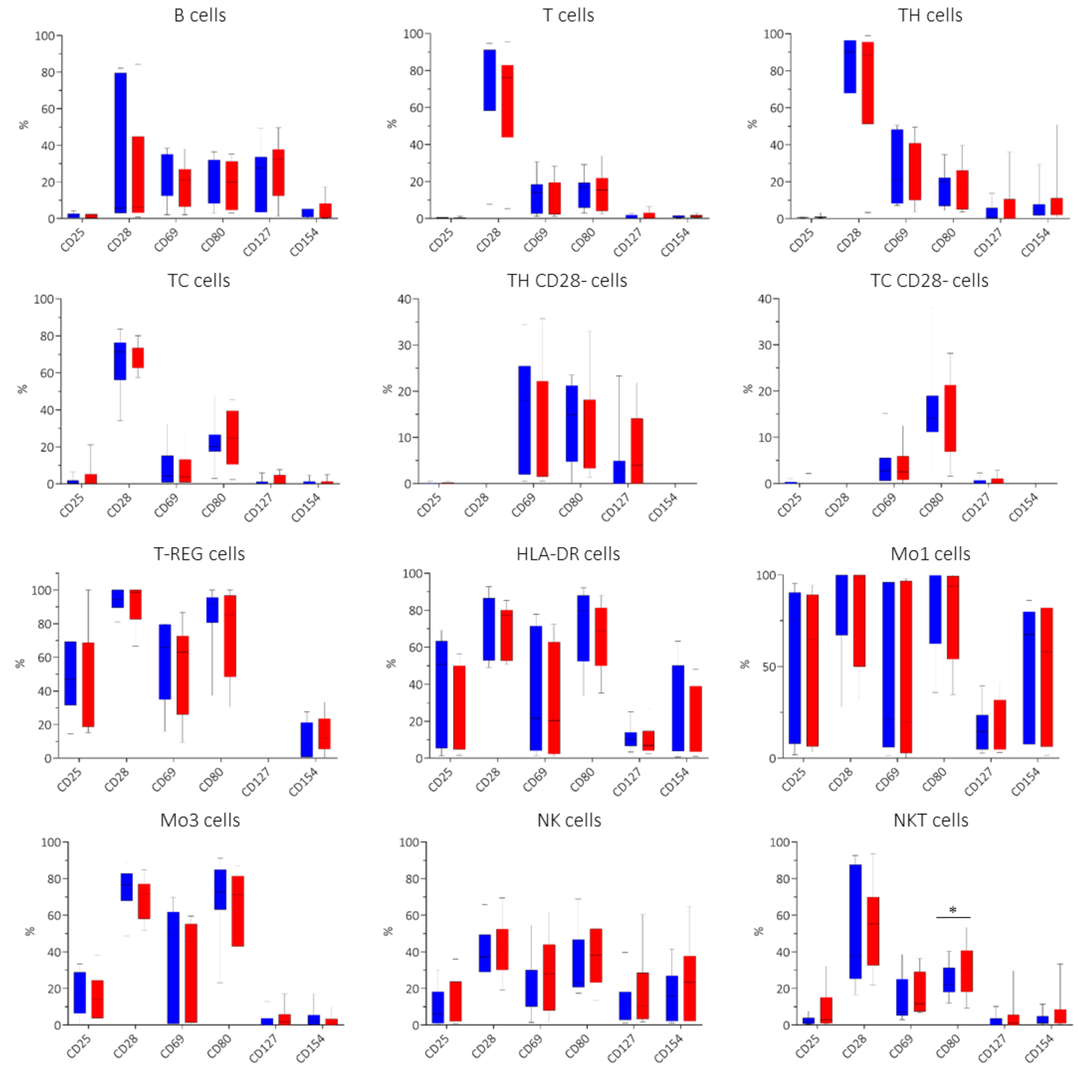
Results

1. PBMCs subpopulation and internalization of EVs



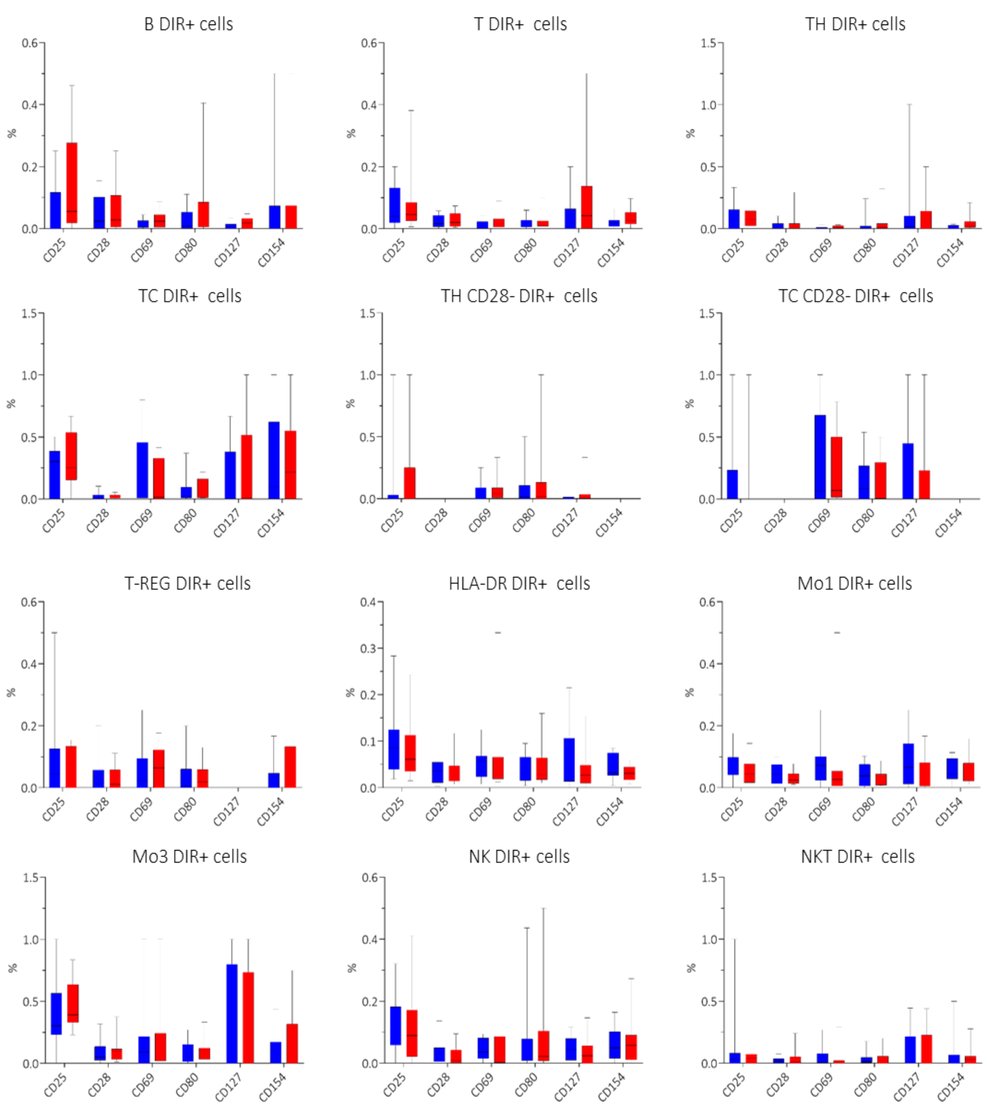
A) Evaluation of the percentage of PBMCs' cell subpopulations after 22h exposure to EVs from HC (blue) or PD (red).
B) Internalisation of EVs (DiR+) from HC (blue) or PD (red) in PBMCs subpopulations.

2. Activation Markers



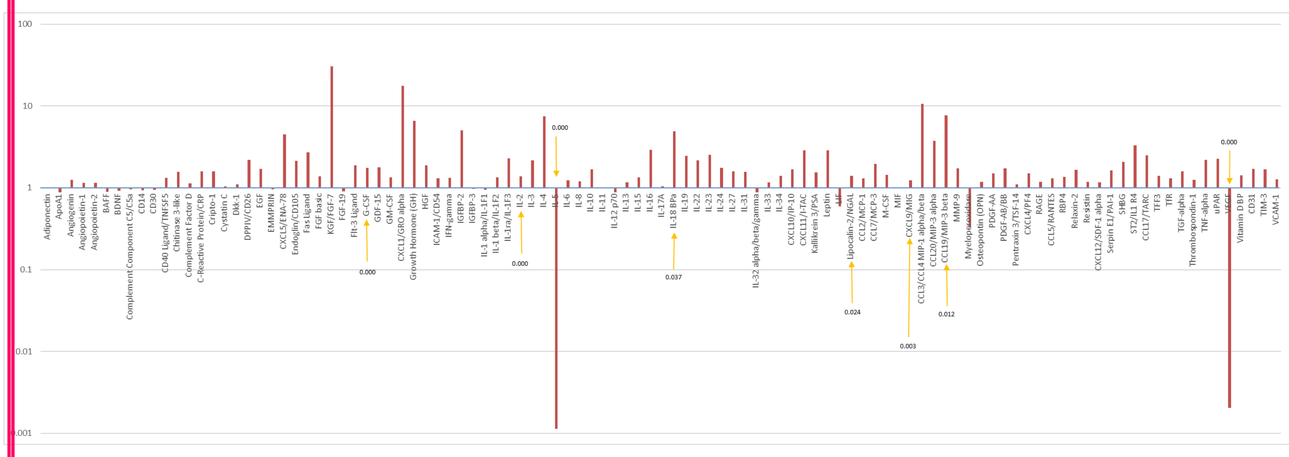
Differential activation of PBMCs subpopulations (analyzed with 5 different activation markers) after receiving EVs from HC (blue) and PD (red).

3. Internalization of EVs



Differential internalization of EVs (DiR+) from HC (blue) or PD (red) in PBMCs cell subtypes.

4. Cytokine array



Differential secretion of human cytokines in PBMCs receiving EVs from PD (red columns) compared to cells receiving EVs from HC (blue line).

Conclusions

We found an increase in NKT CD80+ cells in PBMCs treated with EVs from PD patients. In addition, a differential cytokines secretion by PBMCs exposed to PD-derived EVs was observed. Further analysis of EV content is warranted to dissect novel mechanisms of disease.

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