

**Suppl. Fig 1 EVs derived from macrophages fail to promote complete OPC differentiation**. (A) Histograms showing the mean fluorescence intensity (MFI) for the pre-oligodendrocyte marker CNPase and the percentage of CNPase positive cells in OPCs exposed to i-EVs or IL4-EVs, or not treated (control). (B) Histograms showing the MFI for the mature oligodendrocyte marker GST-Pi in OPCs exposed to the same conditions. One replicate was analyzed for each condition.

## Suppl. Fig.1



### Suppl. Fig 2 Raman spectra of EVs released from macrophages versus microglia

Raman spectra of intact EVs derived from macrophages (A) and microglia (B) in absence of stimuli (untreated cells) or polarized towards different activation states. Spectra show that the molecular composition of macrophages-derived EVs largely differs from that of microglia-derived EVs and reveal differences and similarities between the four conditions.

### Suppl. Fig.2



#### Suppl. Fig.3 2-AG and AEA in plasma EVs

Histograms represent 2-AG and AEA content in total EVs or IB4+ EVs isolated from 1 ml plasma obtained from a pool of three patients affected by relapsing remitting Multiple Sclerosis. pg=picograms

# Suppl. Fig.3