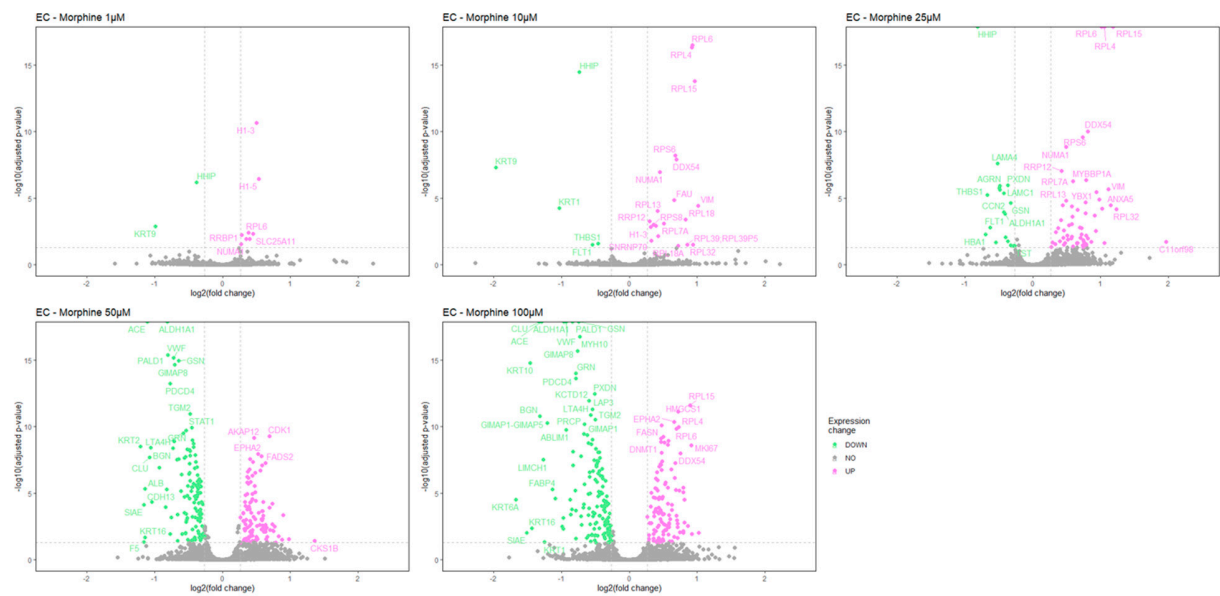
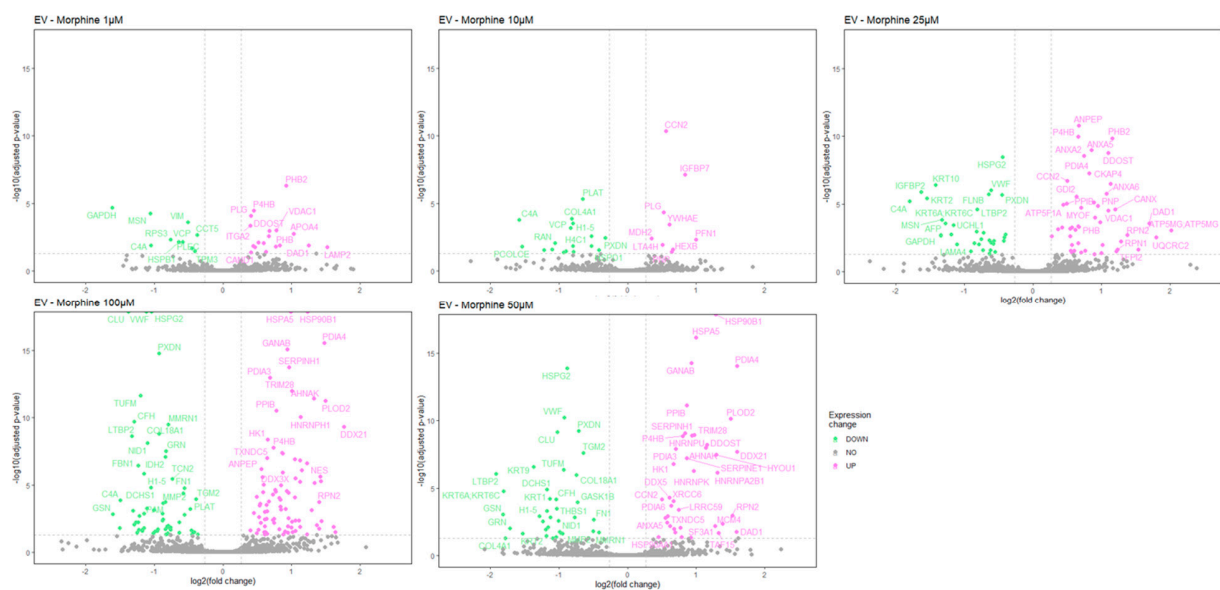


**A.**



**B.**

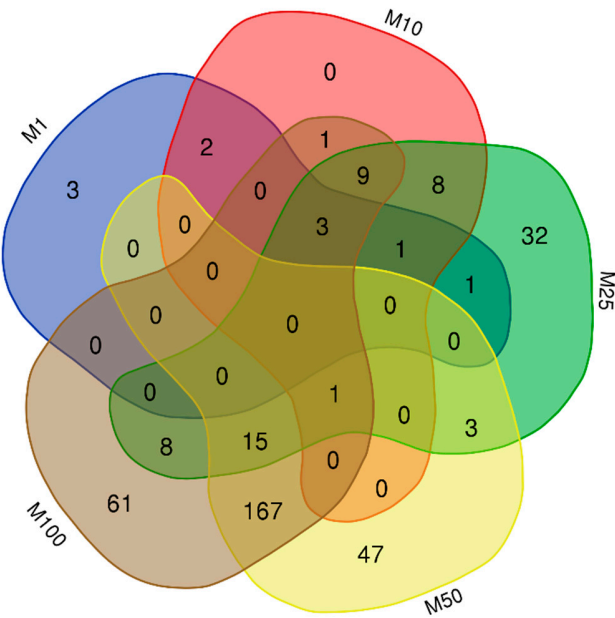


**Figure S1. Volcano plots.** (A) Volcano plots displaying quantified proteins from morphine-treated human brain endothelial cells at 1, 10, 25, 50 and 100 $\mu$ M and (B) from EVs released by morphine-treated human brain endothelial cells. Grey dots correspond to proteins which

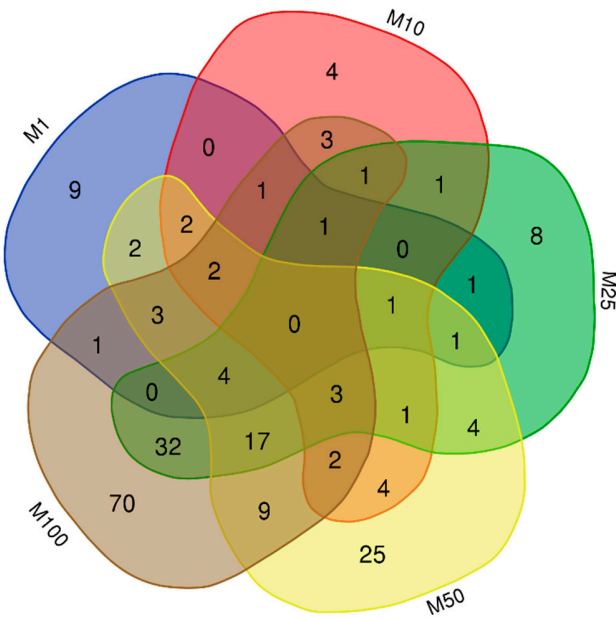
are not differentially expressed. Green dots correspond to downregulated proteins. Pink dots correspond to upregulated proteins. Horizontal dot line represents cut at  $-\log_{10}(p\text{-value}) = 1.33$  as  $p\text{-value} = 0.05$ . Vertical dot lines represent cut at  $\log_2(\text{fold-change}) = -0.26$  and  $0.26$  as fold change is set at 1.2.

Supplemental Figure S2

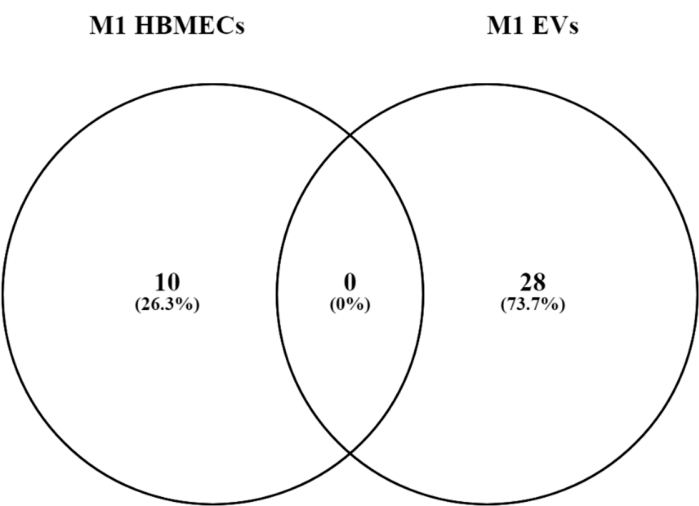
A.



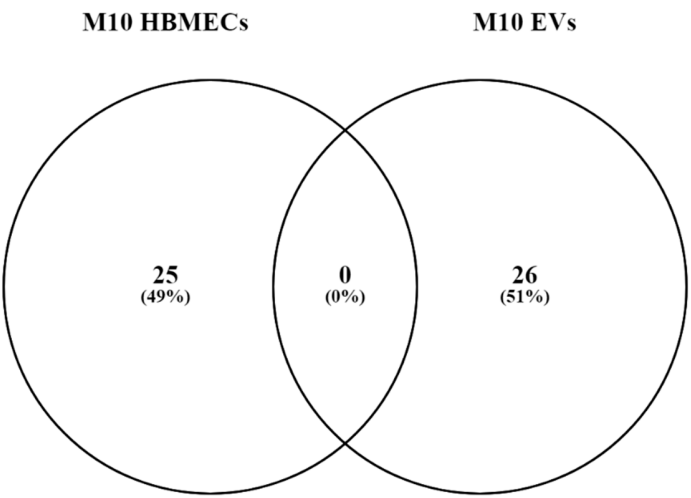
B.



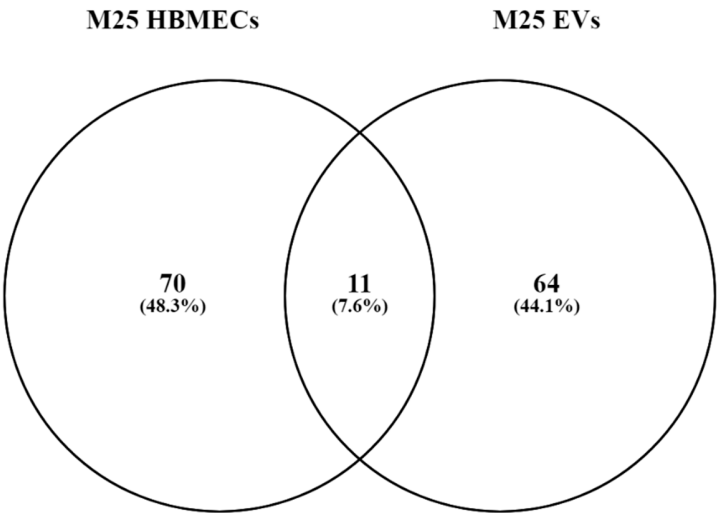
C.



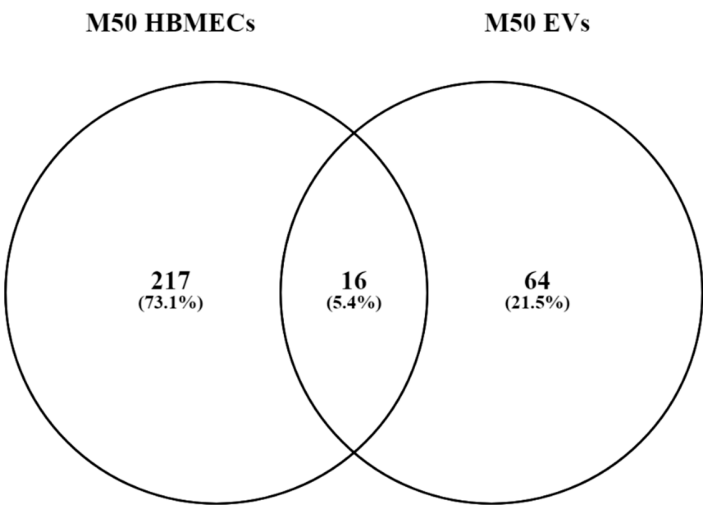
D.

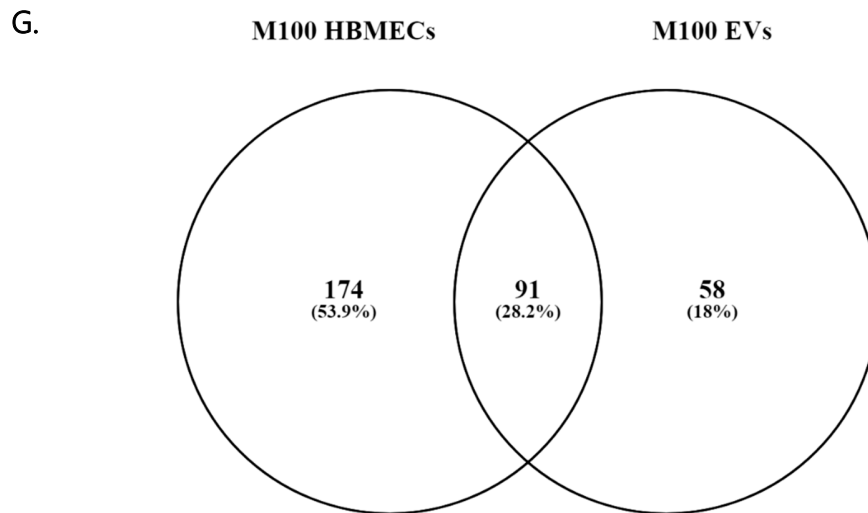


E.



F.





**Figure S2.** Venn diagrams of quantified proteins in **(A)** in HBMECs for morphine condition at 1, 10, 25, 50 and 100  $\mu\text{M}$ , **(B)** derived EVs for morphine condition at 1, 10, 25, 50 and 100  $\mu\text{M}$ , **(C)** HBMECs and derived EVs for morphine condition at 1  $\mu\text{M}$ , **(D)** at 10  $\mu\text{M}$ , **(E)** at 25  $\mu\text{M}$ , **(F)** 50  $\mu\text{M}$  and **(G)** at 100  $\mu\text{M}$ . Venn diagrams were created with <https://bioinfogp.cnb.csic.es/tools/venny/index.html> and <https://bioinformatics.psb.ugent.be/webtools/Venn/>.