



Supplementary Figure S1. Proteomics Links Melanoma Brain Metastasis and Neurodegeneration. **A-E**, 10-230 paired STCs intracardiac injection in mice (9-10 NSG mice per group). **A**, Representative IVIS images at 35 days post-intracardiac injection in mice. **B**, Quantified brain/body luminescence ratio on day 35. 10-230 NBM vs. BM (* p<0.05). **C-D**, Representative pictures of skulls revealing leptomeningeal metastasis. **E**, Quantification of NuMA+ metastatic cells in mouse livers. 10-230 NBM vs. BM (**** p<0.00005). **F-H**, WM-4071 STC pair intracardiac injection in mice (n=9-10 NSG mice per group). **F**, Representative images of FFPE brain slides with metastatic cells stained by anti-NuMA immunohistochemistry. **G-H**, Quantification of NuMA+ metastatic cells in mouse brains (**G**), WM-4071 NBM vs. BM (** p<0.005), and livers (**H**), WM-4071 NBM vs. BM (**** p<0.00005). **I-J**, WM-4257 STC pair intracardiac injection in mice (n=11-12 nude mice per group). **I**, Representative images of FFPE brain slides with metastatic cells stained by anti-NuMA immunohistochemistry. **J**, Quantification of NuMA+ metastatic cells in mouse brains. WM-4257 NBM vs. BM (**** p<0.00005). **K-L**, Western blot analysis of STC pairs for differentially expressed proteins identified by proteomics. **M-R**, Seahorse metabolic analysis of STC pairs (4-6 biological replicates per group). 12-273 NBM vs. BM oxygen consumption (**M**, **** p<0.00005) and H⁺ production (**P**, **** p<0.00005), 10-230 NBM vs. BM oxygen consumption (**N**, ** p<0.005) and H⁺ production (**Q**, ** p<0.005), WM-4071 NBM vs. BM oxygen consumption (**O**, * p<0.05) and H⁺ production (**R**, ** p<0.005).