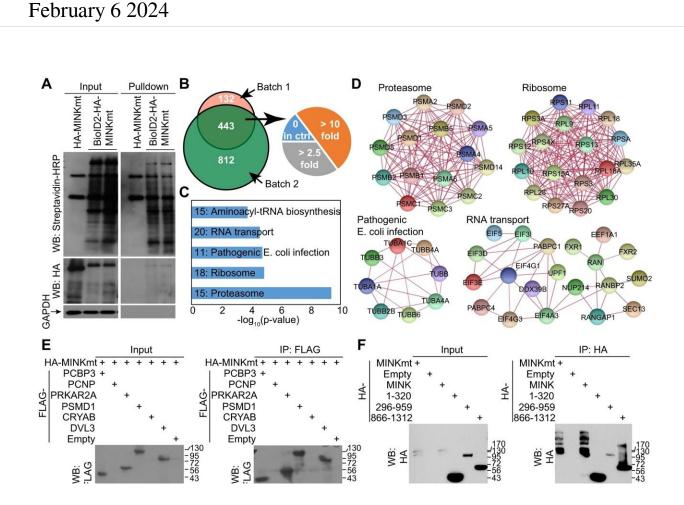


## Experimental compound extends life in amyotrophic lateral sclerosis mouse model



MAP4K interactome and the effect on RANGAP1 subcellular distribution. A Western-blotting analysis of proteins after proximity labeling in ALS1-hiMNs at 10 dpi. **B** Venn diagram of proteins from two batches of samples analyzed by Mass Spectrometry. With a cutoff of 2.5-fold enrichment, 443 proteins were common to these two sets of data, including proteins with no expression in control group (0 in ctrl), proteins with over 2.5-fold changes, and proteins with over 10-fold changes. **C** The top 5 KEGG pathways. **D** STRING analysis of association networks of proteins in the top 4 KEGG pathways. **E** Validation of



protein associations in HEK293T cells by co-immunoprecipitations (co-IP) and western blots. **F** co-IP assays in HEK293T cells showing association of MINK1mt with RANGAP1 or RAN. **G** Confocal images showing subcellular distribution of RANGAP1 or RAN in ALS1-hiMNs at 52 dpi. Arrows indicate aggregated cytoplasmic RANGAP1 foci. Scale bar, 10  $\mu$ m. **H** MINKmt improves nuclear/cytoplasmic (Nuc/Cyt) ratios of the indicated proteins in ALS1-hiMNs at 52 dpi (mean ± SEM; *n* = 30 neurons per group; \*\*\**p* 

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