



**Additional File 11. wtSOD1 aggregates activate membrane perturbation and dextran uptake in iPSC derived human motor neurons.** (A) The induction of fluid phase uptake was measured using fluorescently labelled dextran. Laser scanning confocal micrographs of dextran-Alexa647 uptake in treated motor neurons were quantified using ImageJ of dextran uptake in the treated neurons. A minimum of 100 cells per treatment were scored. Results shown as means  $\pm$  SD of 3 experiments \*\*\*  $p < 0.001$  \*\*. Laser scanning confocal micrographs of treated cells stained with the membrane dye FM1-43FX were used to measure membrane perturbation and fluorescence intensity quantification using ImageJ. A minimum of 100 cells were scored per treatment. Results shown are means  $\pm$  SD of three experiments, \*\*\*  $p < 0.001$  \*\*. (C) Laser scanning confocal micrographs of aggregated SOD1 internalized by motor neurons in the presence or absence of a pre-incubation step with macropinocytosis inhibitors EIPA, Rottlerin and rac1 inhibitor W56 were quantified by imageJ. Data are mean fluorescence intensity per cell of a minimum of 100 cells  $\pm$  SD, \*\*\*  $p < 0.001$ . Data shown is from experiments performed on cells derived from one fibroblast line and represents experiments performed on cells from 2 individuals.