2-O-B3-3 Oral Sessions**The effect of σ_1 R agonist/wildtype σ_1 R on abnormal insoluble feature and toxicity of σ_1 R ALS mutant (E102Q)**

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Mutations in sigma-1 receptor (σ_1 R) gene are found in ALS. The σ_1 R forms oligomers that are regulated by its ligands. However, little is known about the effect of mutations. Here, we transfected motor neuronal NSC-34 cells with σ_1 R-mCherry (mCh), σ_1 R^{E102Q}-mCh or untagged forms to assess detergent solubility and subcellular distribution by immunostaining and FRAP. The oligomeric state was assessed using crosslinker. Wildtype σ_1 Rs were soluble to detergents, but the mutants were enriched in the insoluble fraction. In the soluble fraction, distribution of mutants appeared in higher sucrose density fractions. Mutants formed aggregates that were co-stained with p62, ubiquitin, and p-PERK, and which had lower recovery in FRAP. Acute treatment with σ_1 R agonist SA4503 failed to improve recovery, prolonged treatment (48 h) reduced σ_1 R^{E102Q}-mCh insolubility and inhibited apoptosis. While σ_1 R-mCh formed monomers/dimers, σ_1 R^{E102Q}-mCh also formed trimers/tetramers. SA4503 reduced the four types in the insoluble fraction but elevated monomers in the soluble fraction. Co-expression of σ_1 R-mCh reduced σ_1 R^{E102Q} insolubility. These results suggest that the agonist and wildtype σ_1 R can modify the detergent insolubility, toxicity, and oligomeric states of σ_1 R^{E102Q}. Pharmacological and genetic approaches may be promising to treat σ_1 R-related ALS.