

## Gain's STAR compounds show neuroprotective properties in cell-based models of Alzheimer's disease

### GCCase and Alzheimer's Disease

- GCCase levels and activity are decreased in sporadic AD
- Overexpression of GCCase promotes lysosomal degradation of A $\beta$ 1-42<sup>1</sup>
- Hyperphosphorylated and oligomeric Tau is thought to be downstream of A $\beta$ 1-42 in the pathological cascade, and to underlie neurodegeneration and cognitive impairment
- Increasing GCCase activity may be a potential therapeutic option for the treatment of AD

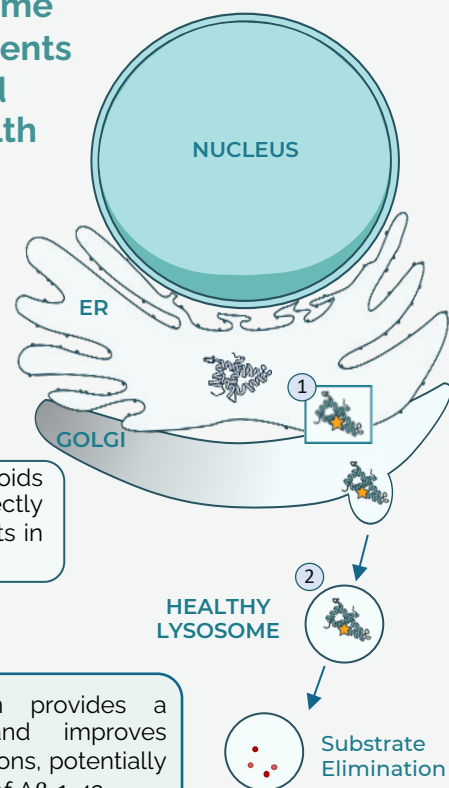
<sup>1</sup>Choi et al., 2015 doi: 10.1371/journal.pone.0143854.

### STARs restore enzyme function, which prevents cell damage and improves cell health

1 STAR compound binds to GCCase and allows it to fold correctly

2 Correctly folded GCCase avoids degradation, traffics correctly to the lysosome, and results in more lysosomal GCCase

Restoring GCCase function provides a neuroprotective effect and improves lysosomal autophagic functions, potentially promoting the degradation of A $\beta$ -1-42



### Increase of Neuronal Survival after A $\beta$ -1-42 Injury

STAR compound increased neuronal survival which was assessed by MAP2 immunostaining and quantification in rat cortical neurons injured with A $\beta$ -1-42



### Increase of Neurite Network after A $\beta$ -1-42 Injury

STAR compound increased the neurite network which was assessed by MAP2 immunostaining and quantification in rat cortical neurons injured with A $\beta$ -1-42



### Reduction of Hyperphosphorylated Tau after A $\beta$ -1-42 Injury

STAR compound reduced hyperphosphorylation of Tau which was assessed by AT-100 immunostaining and quantification in rat cortical neurons injured with A $\beta$ -1-42



### Reduction in Human Tau Oligomer-Induced Neurotoxicity

STAR compounds reduced human Tau oligomer-induced neurotoxicity as assessed by the MTT assay in rat hippocampal neurons