

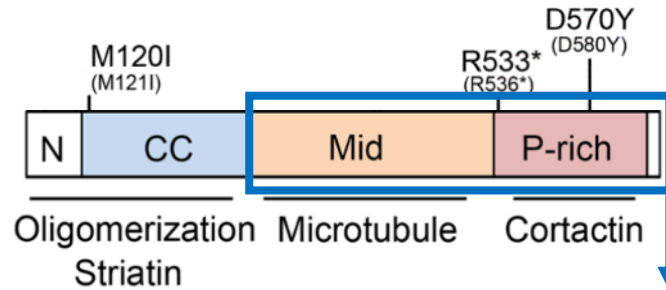
Phase separation and zinc-induced transition modulates synaptic distribution and association of autism-linked CTTNBP2 and SHANK3

Yu-Lun Fang
2023/10/28

CTTNBP2 encoded by an autism causative gene undergoes phase separation

ASD-linked mutations:

CTTNBP2 structure:

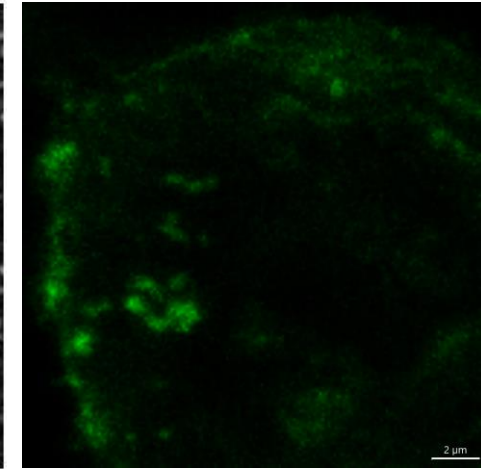
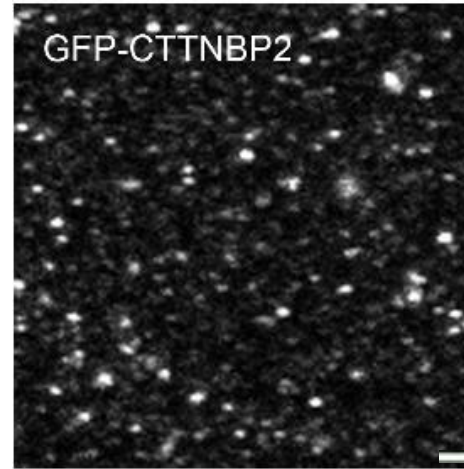


- Functions of condensates in cell

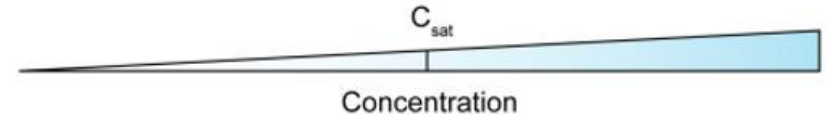
- Forming condensates via LLPS

In vitro

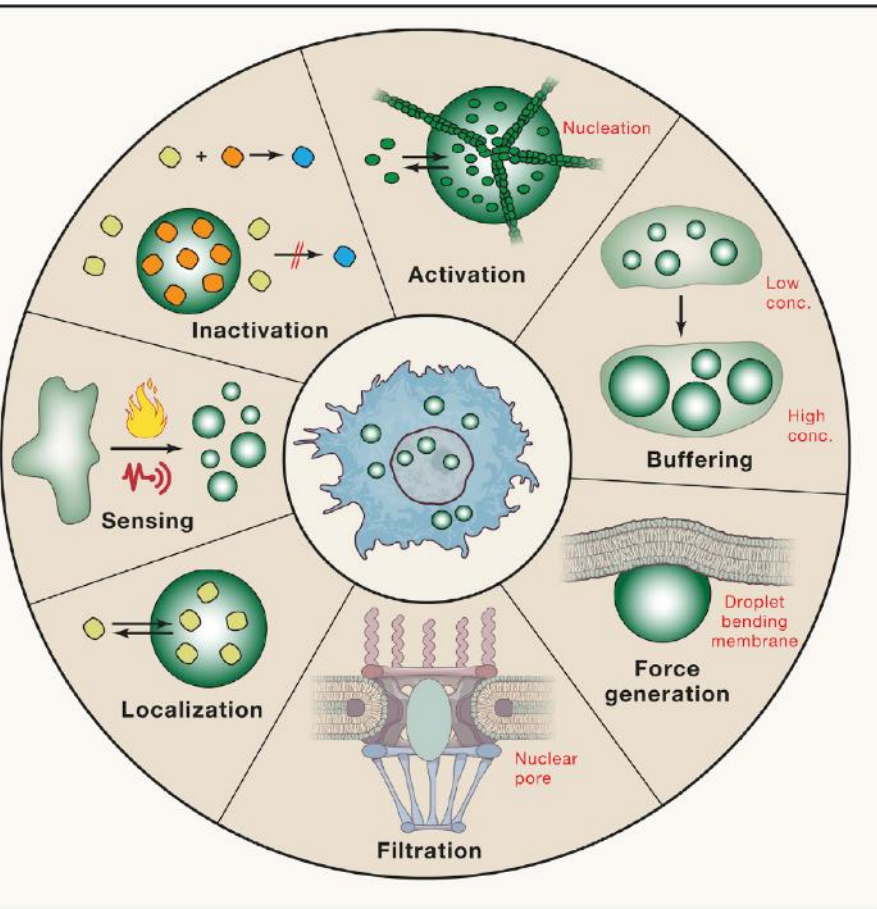
In HEK293T



Liquid condensate



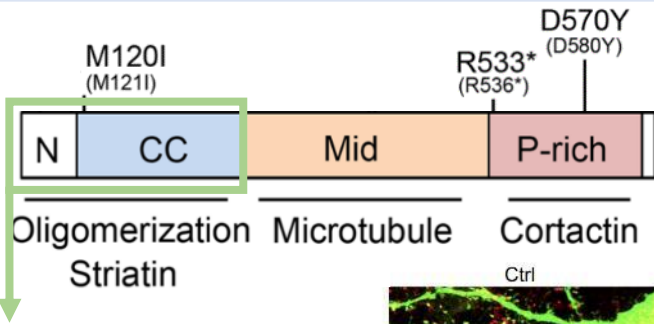
Concentration



Zinc induces high-order multimerization and enhances synaptic retention of CTTNBP2

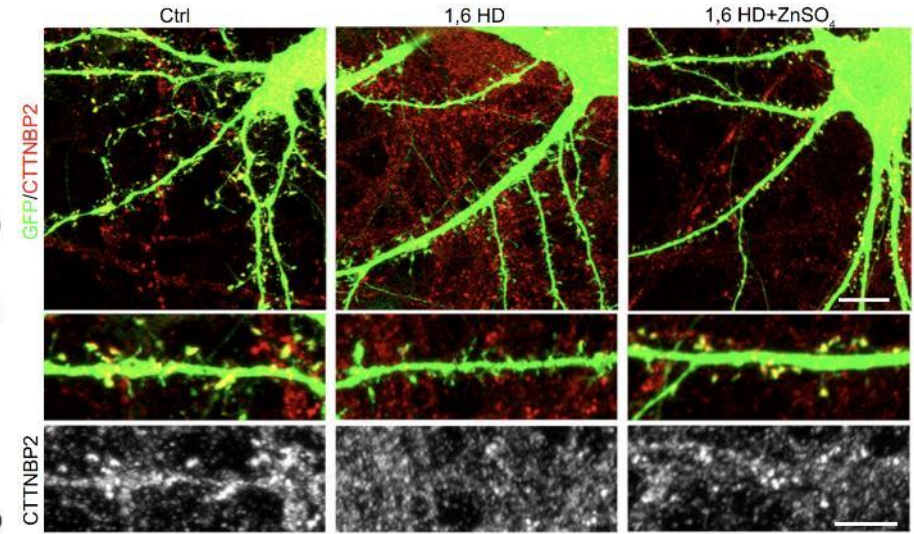
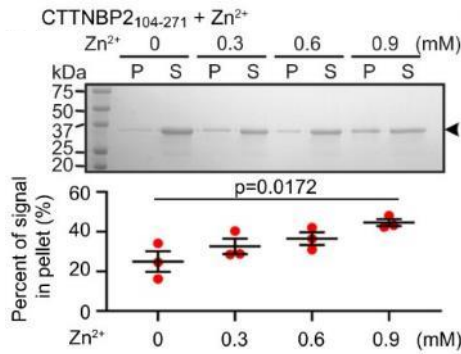
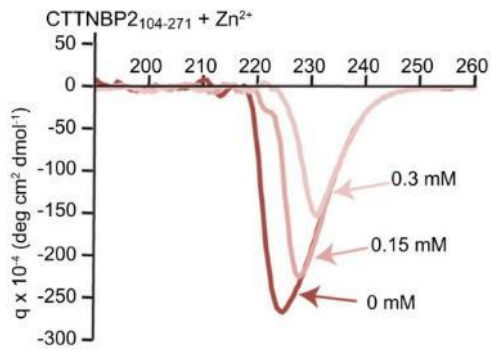
ASD-linked mutations:

CTTNBP2 structure:

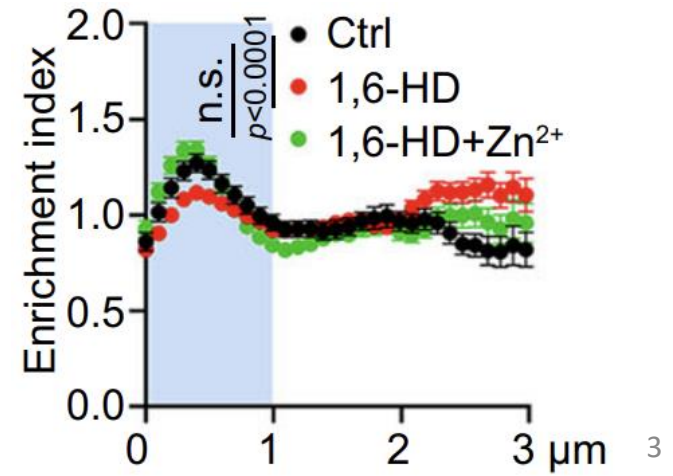
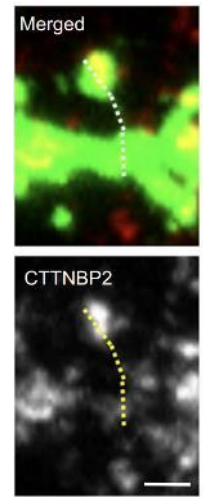
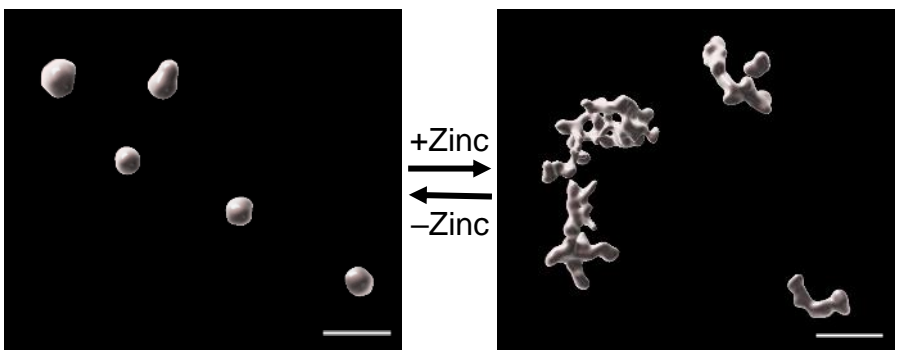


1,6-HD: 1,6-hexanediol, an aliphatic alcohol that disrupts weak hydrophobic protein-protein interactions

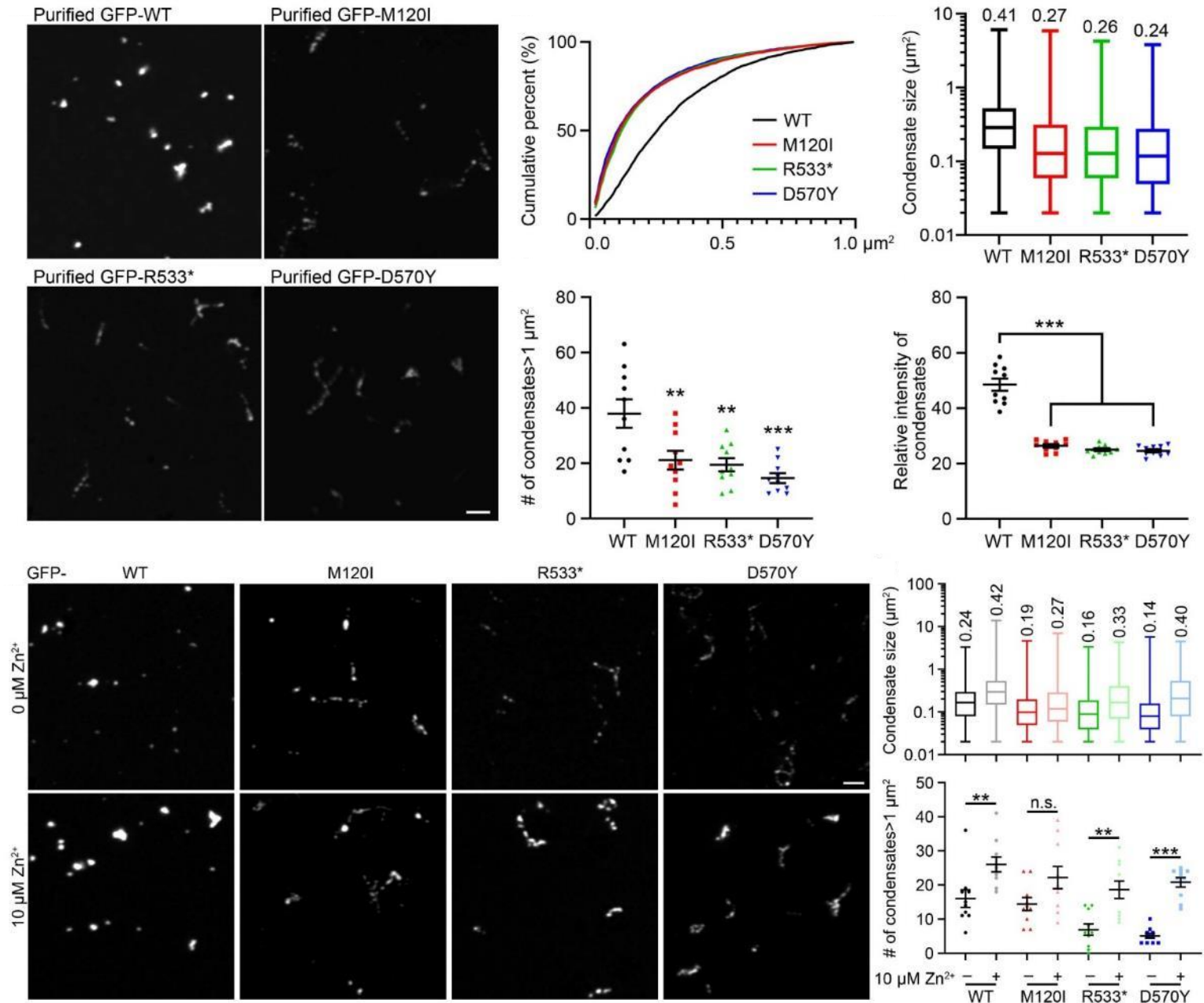
- Binding zinc and inducing high-order multimerization



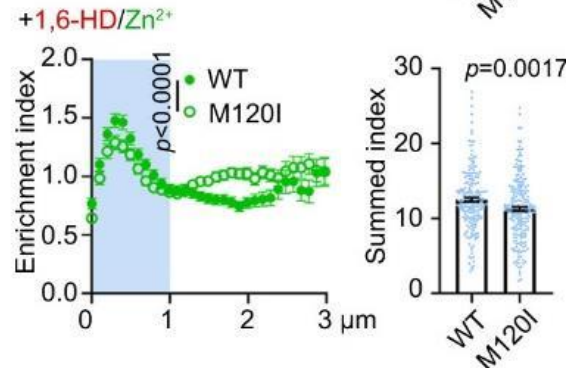
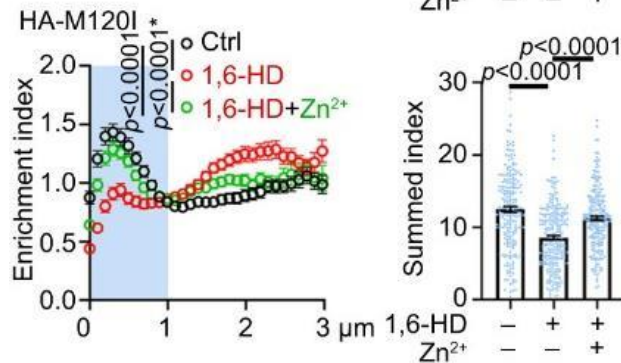
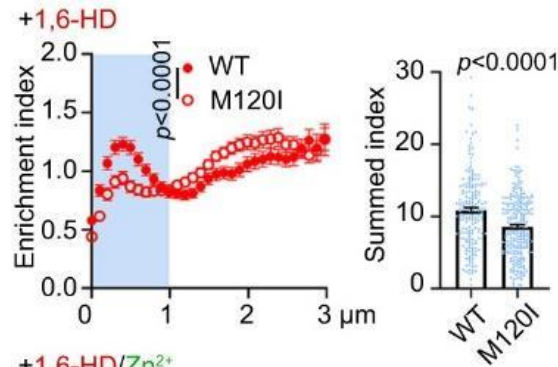
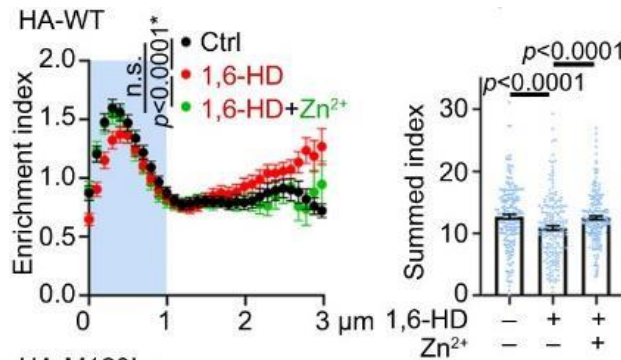
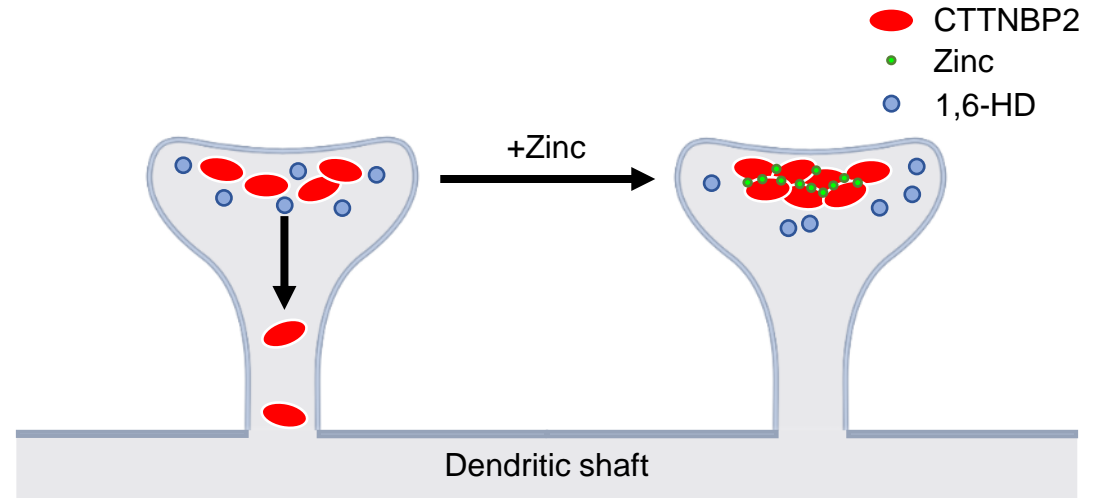
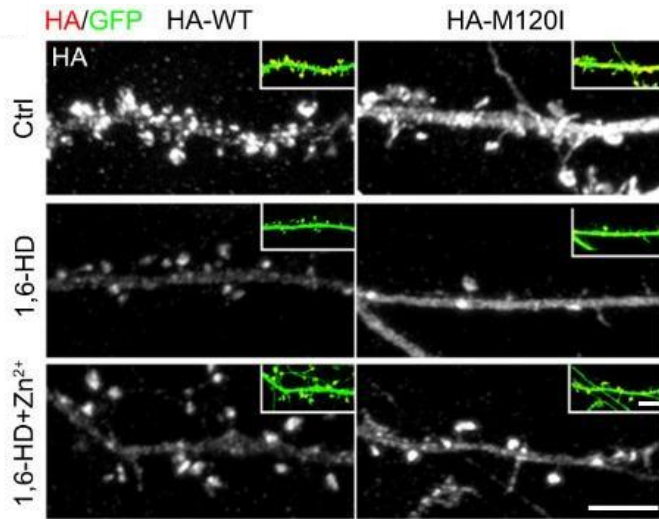
Purified GFP-CTTNBP2



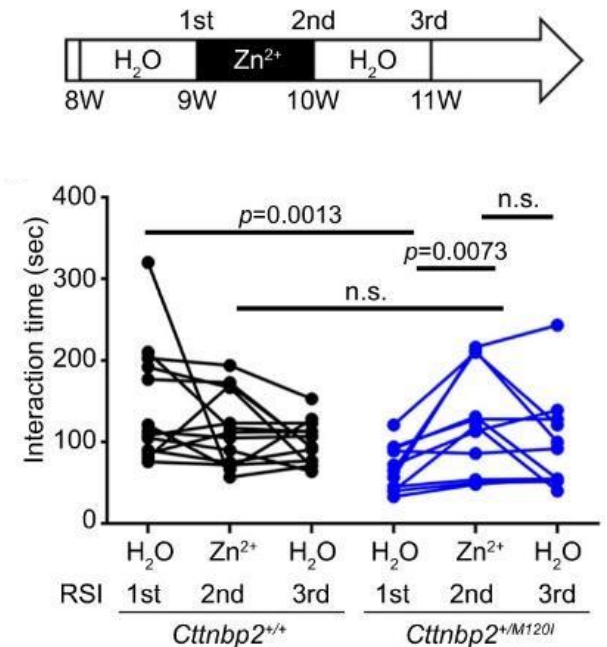
ASD-linked mutations result in the impairment of phase separation of CTTNBP2, which is ameliorated by zinc



ASD-linked mutation impairs the synaptic distribution of CTTNBP2 and social behavior, which are rescued by zinc



- Behavior test-Reciprocal social interaction



Take Home

