

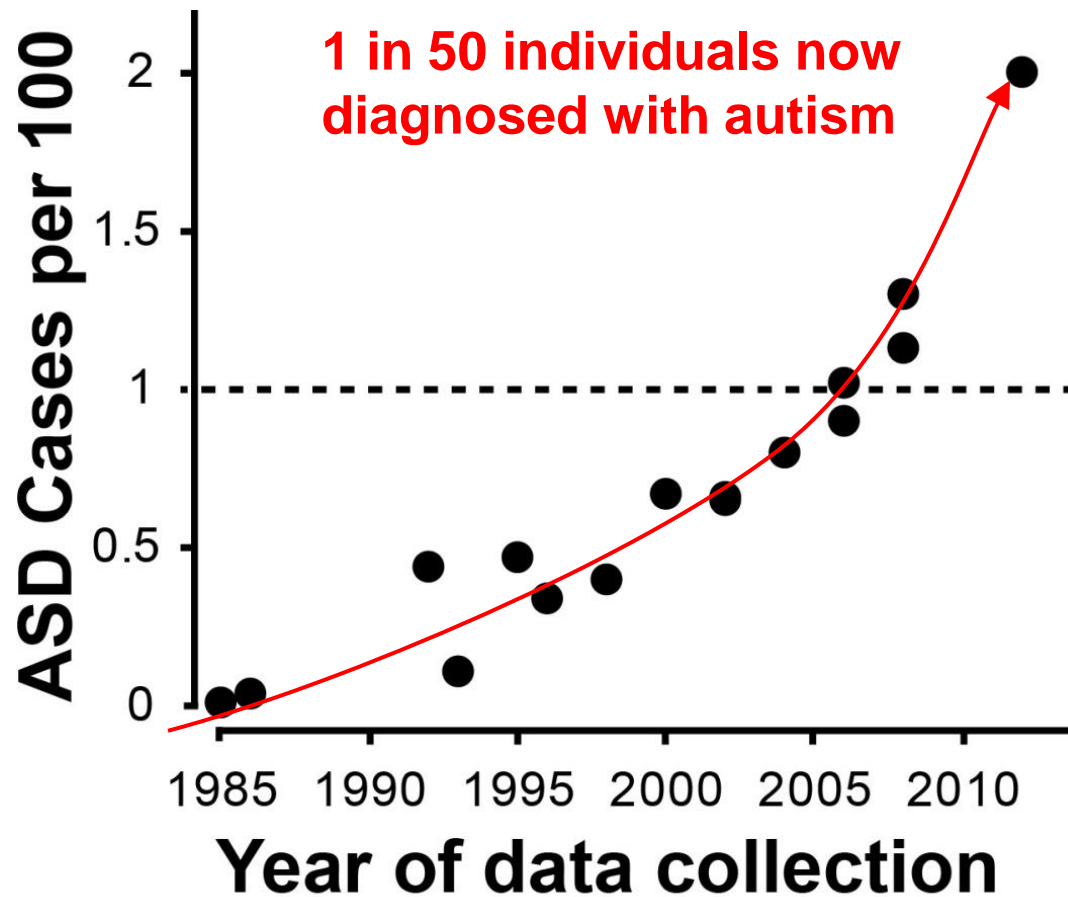
Reducing the biomedical burden of autism



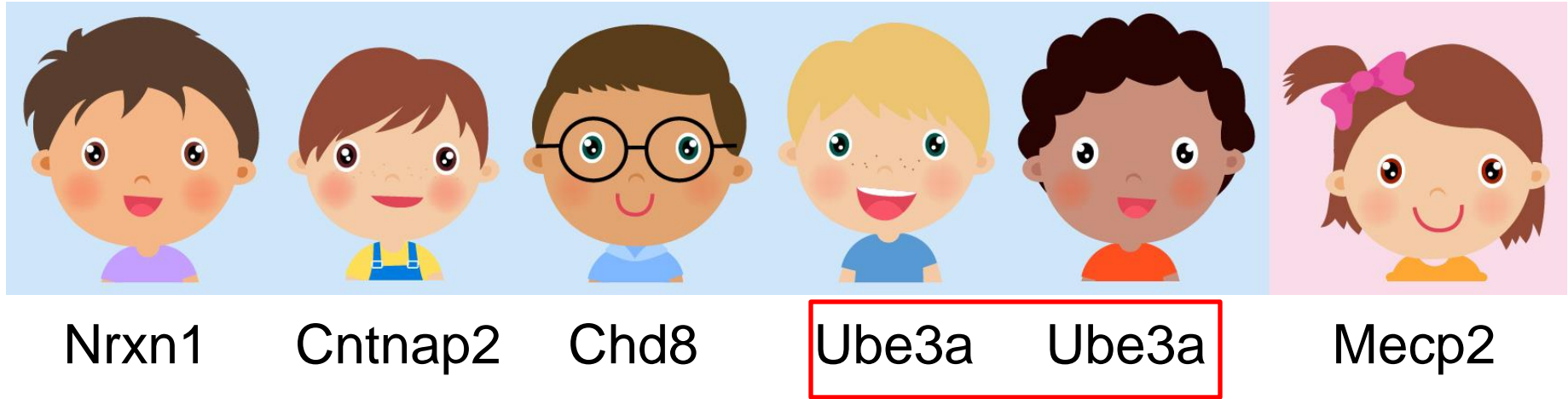
Ben Philpot, Ph.D. & Mark Zylka, Ph.D.

Department of Cell Biology and Physiology, Carolina Institute for Developmental Disabilities,
UNC Neuroscience Center

Autism is a major health problem



Hundreds of genes are linked to autism



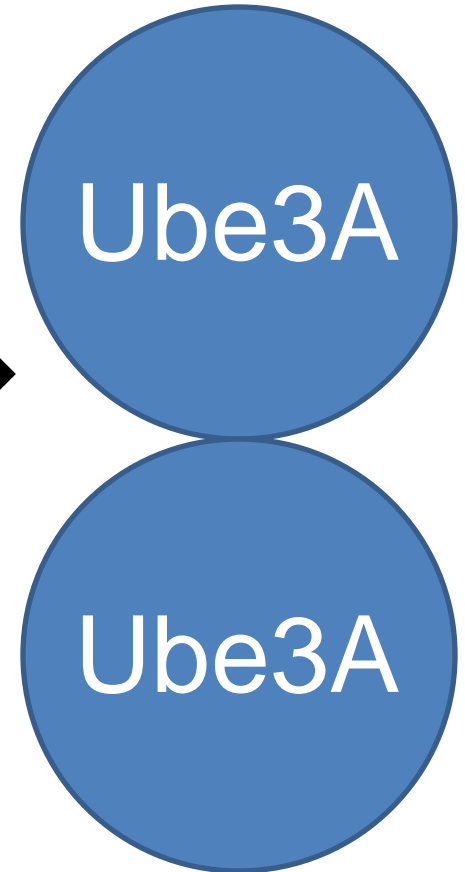
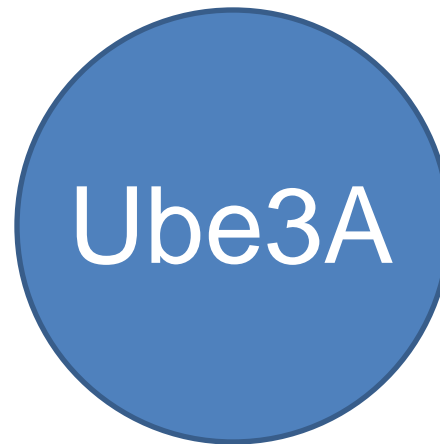
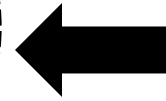
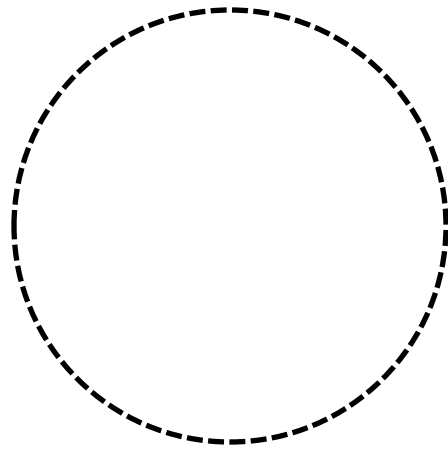
- No drugs treat the core symptoms of autism.
- No way to identify chemicals that cause autism.

Imbalance of Ube3a causes two forms of autism

Angelman
Syndrome

Unaffected
Individual

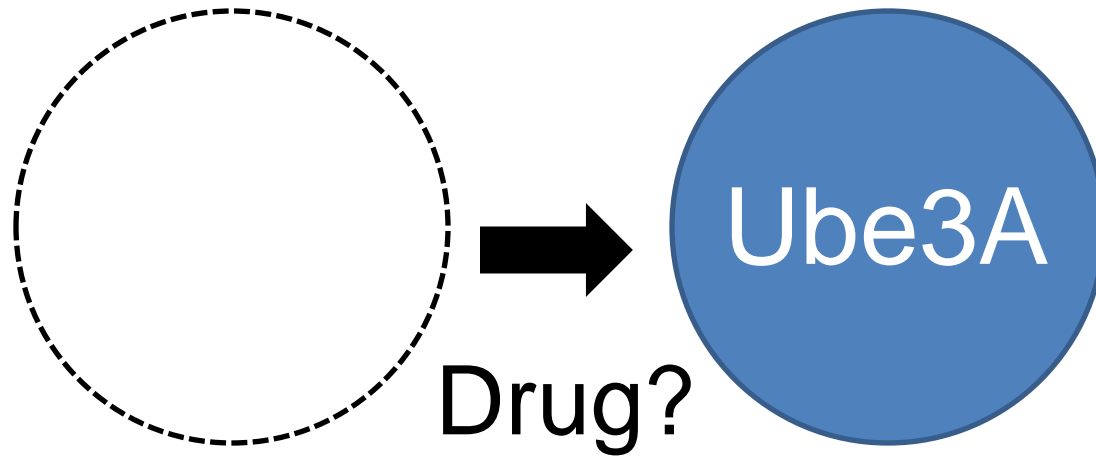
Duplication
Syndrome



Perform screen to find drugs that increase Ube3a

Angelman
Syndrome

Unaffected
Individual

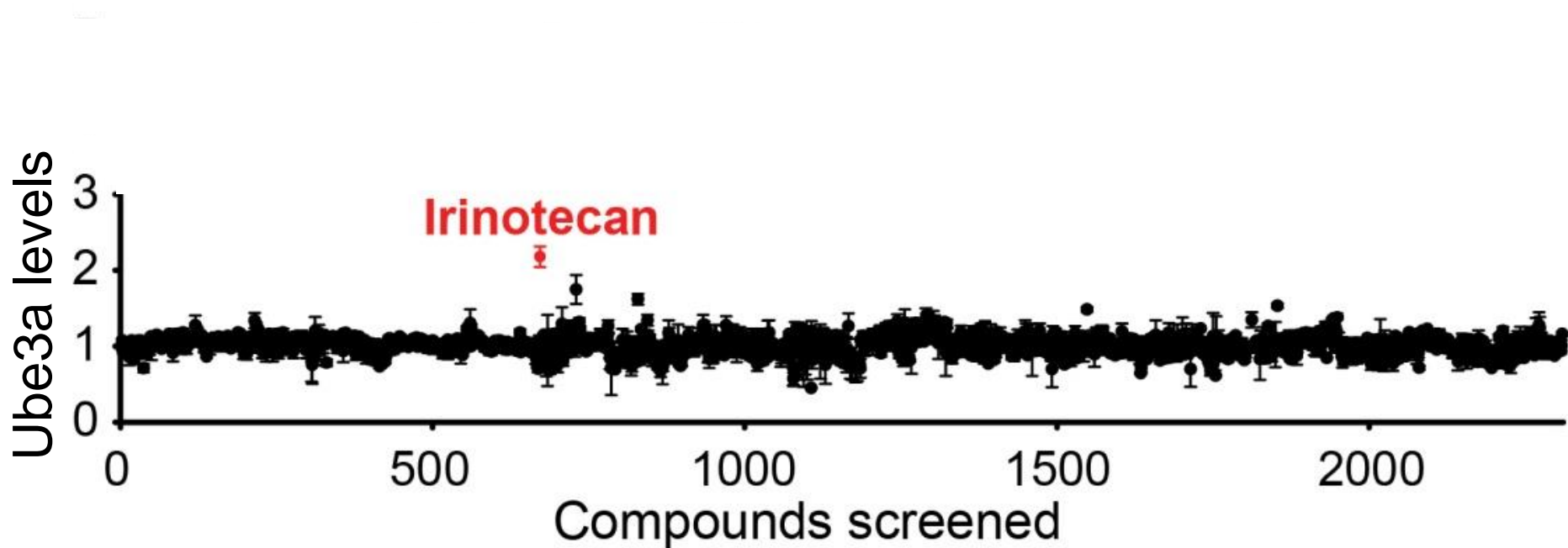


Robotics-assisted drug screen



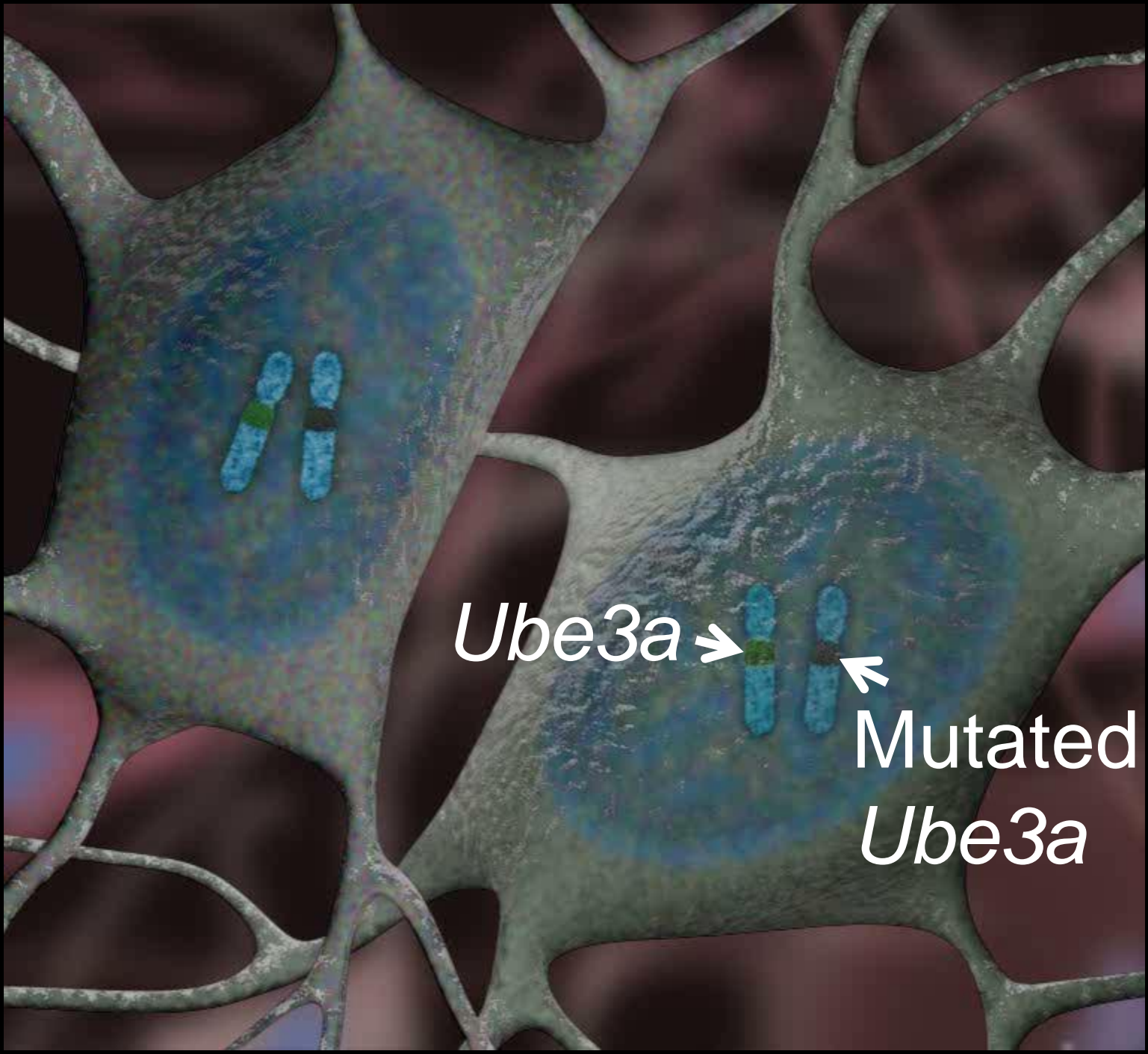
Done in collaboration with Bryan Roth @ UNC

A topoisomerase inhibitor turns on Ube3a



Huang, Allen et al., *Nature* 2011

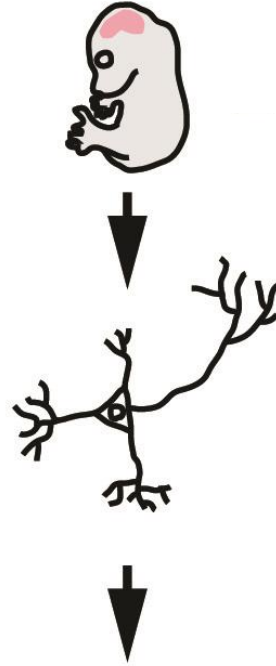
Topoisomerase inhibitors are FDA-approved to treat cancer



Ube3a →

←
Mutated
Ube3a

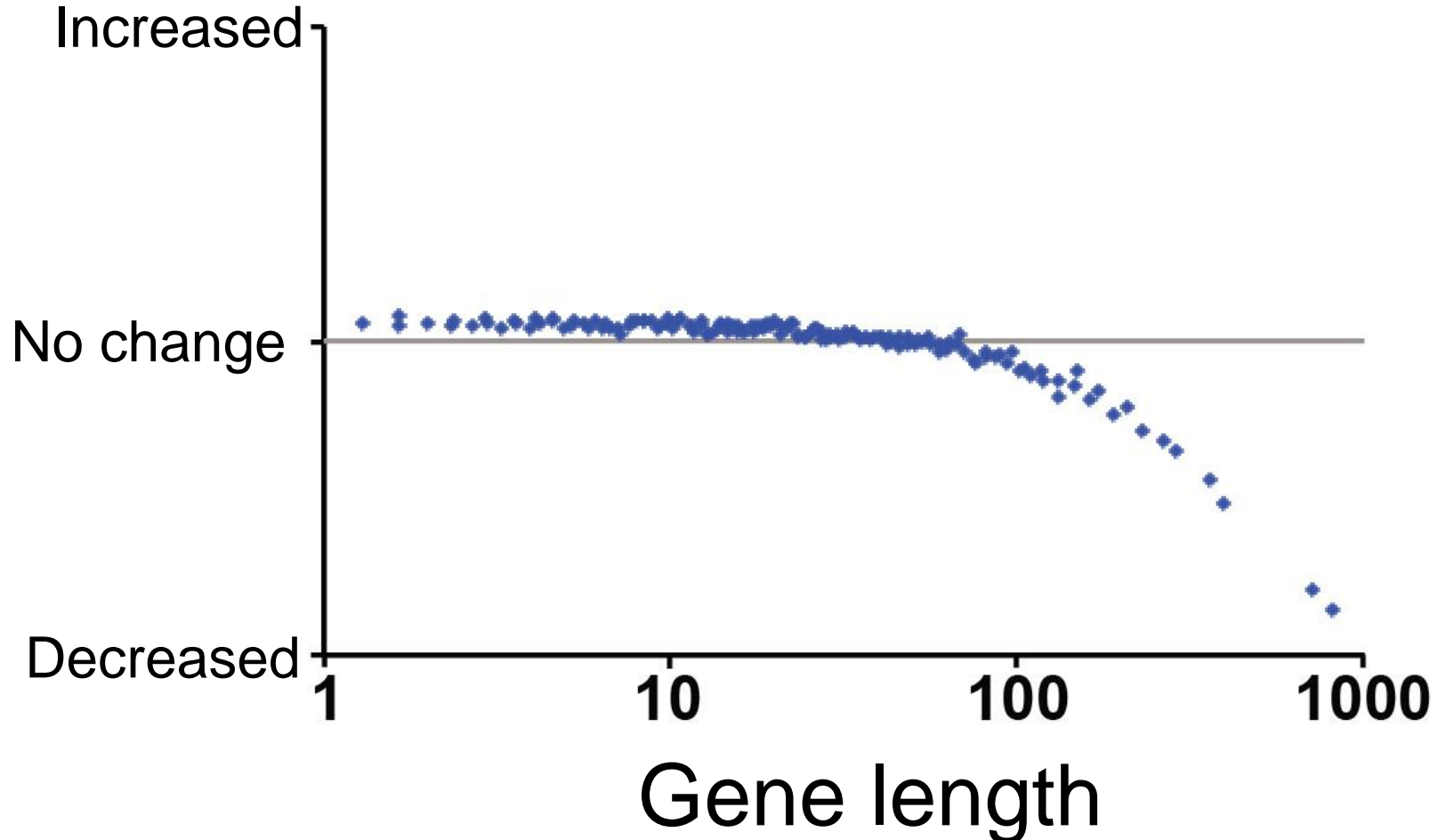
Do topoisomerase inhibitors affect additional genes?



**Treat with topoisomerase inhibitor,
measure levels of all genes**

Topoisomerase inhibitors reduce the levels of long genes

Gene Levels



Many autism genes are extremely long...

Average gene

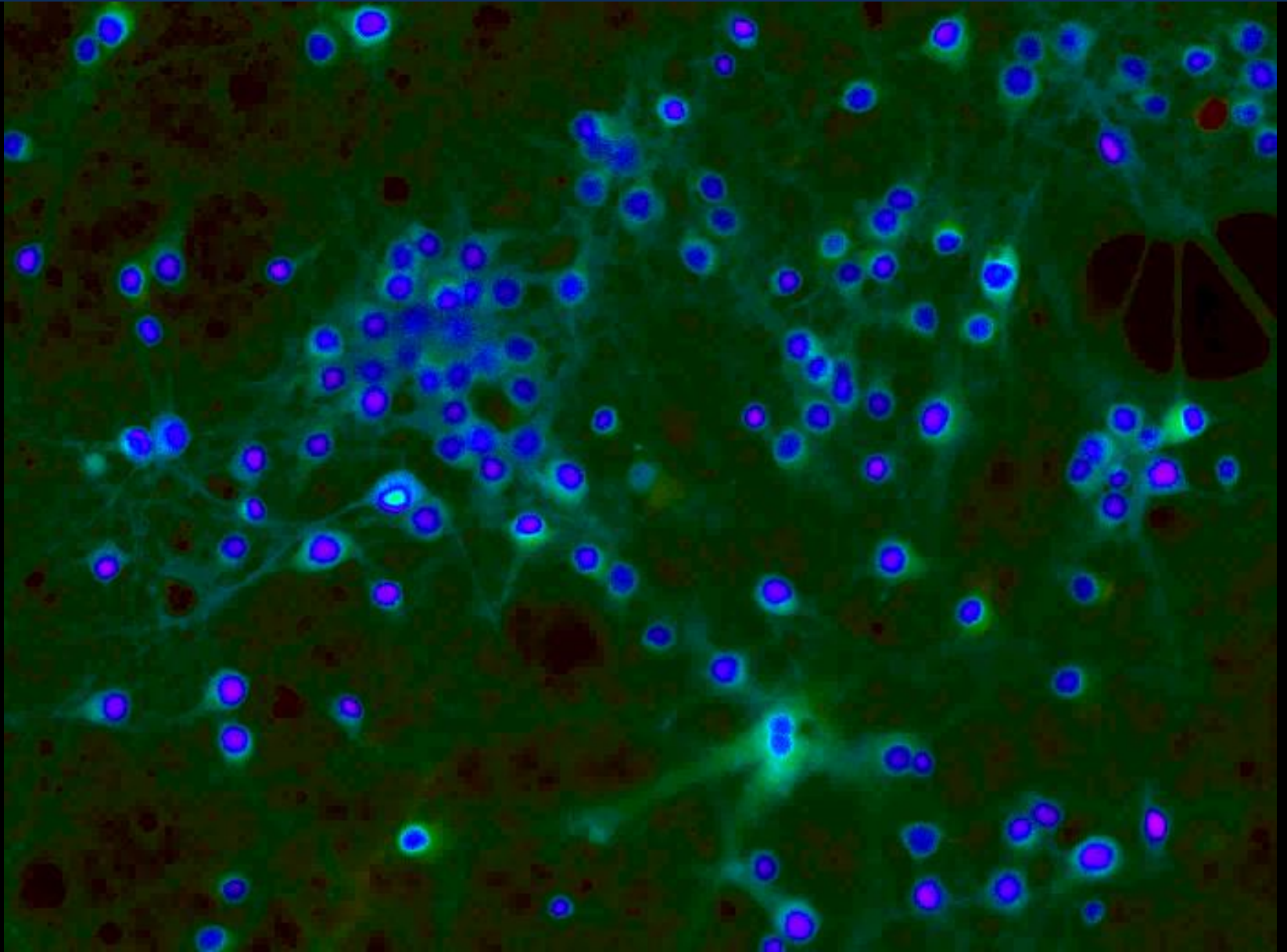


Autism gene
(25x longer)

... and are found at synapses

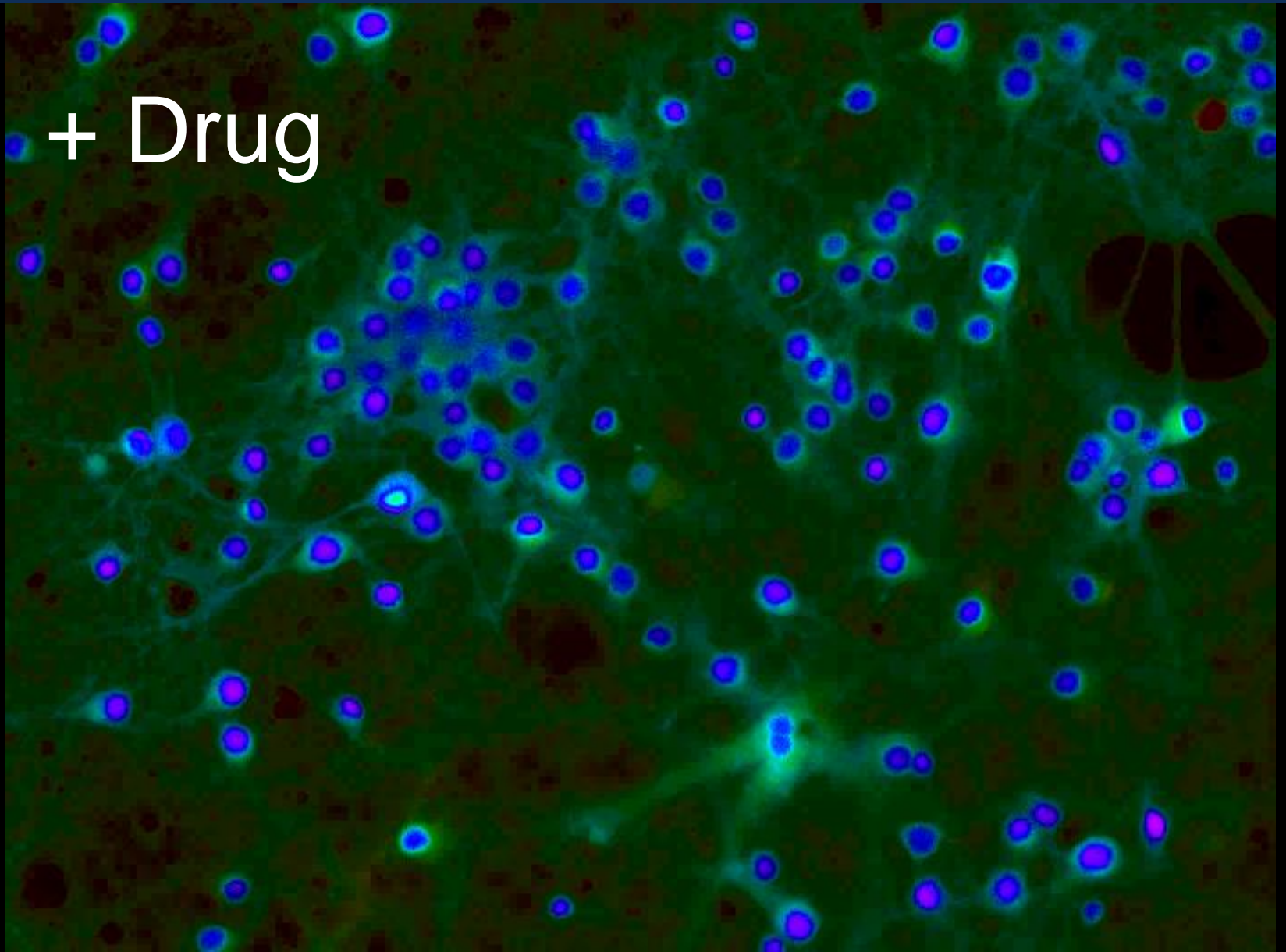


Visualizing synaptic activity



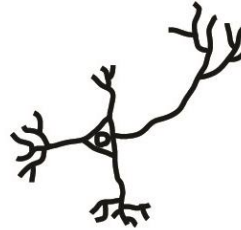
Visualizing synaptic activity

+ Drug



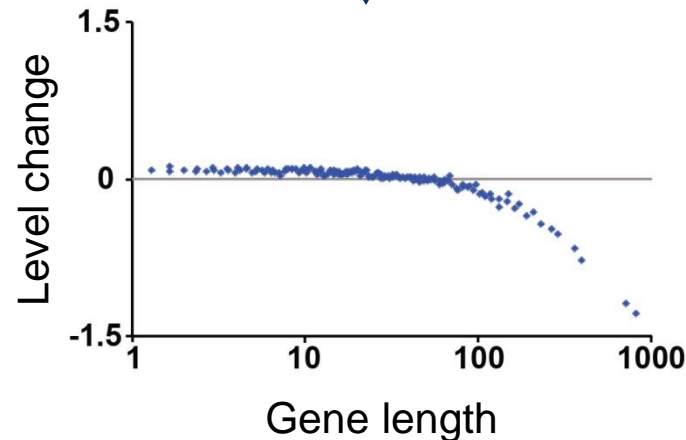
Identify additional chemicals that reduce the levels of long autism genes

Brain neurons

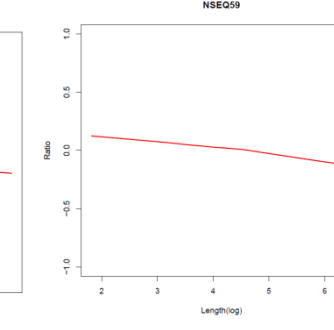
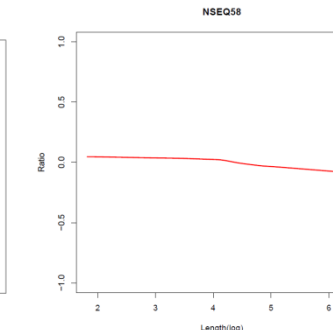
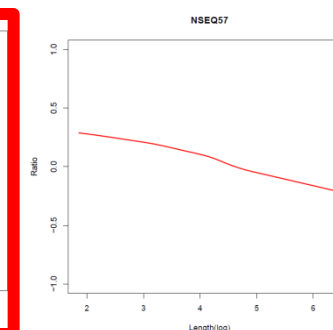
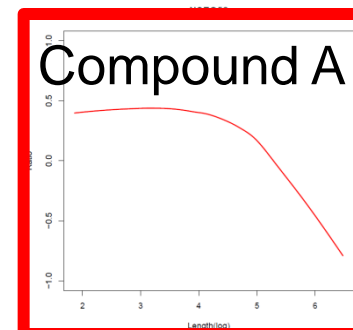
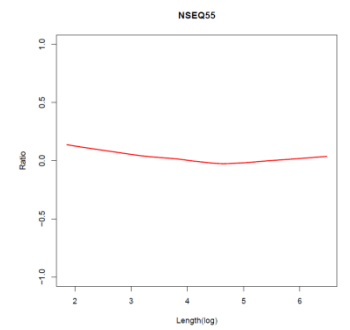
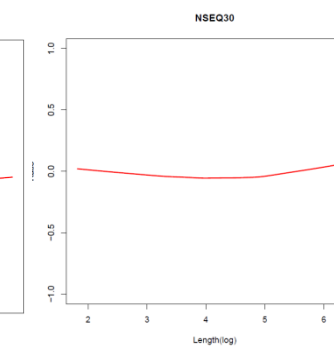
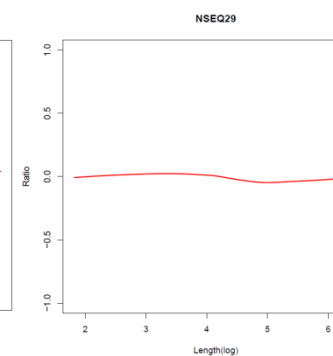
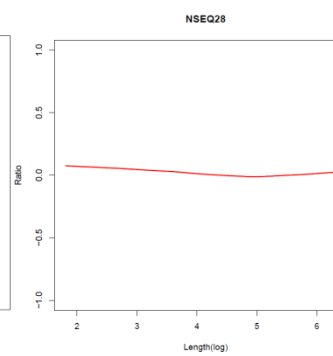
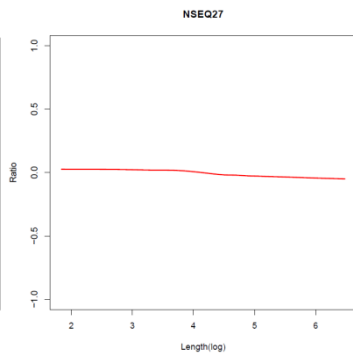
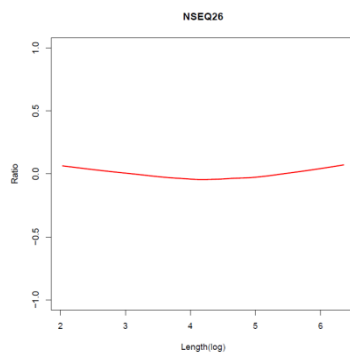
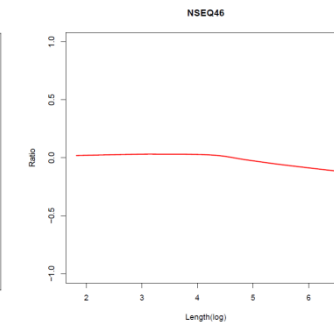
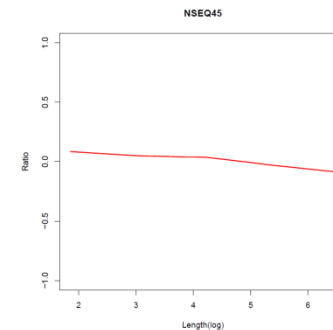
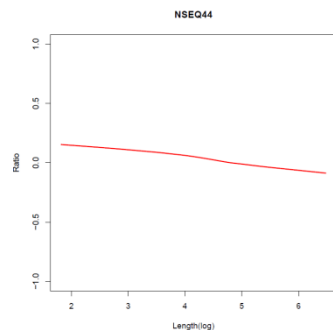
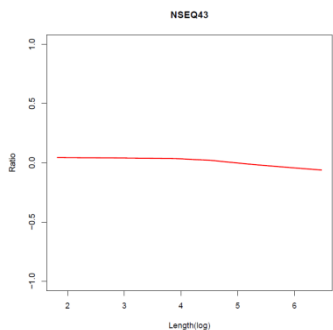
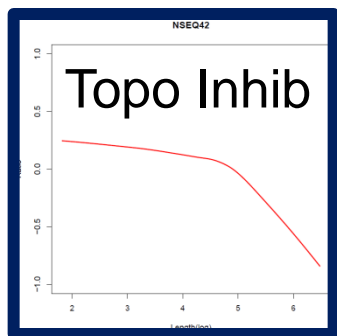


Drugs, pesticides,
herbicides, fungicides

Gene Sequencing



Additional compounds have been found



Towards preventing and treating autism

- Identify chemicals that cause autism so they can be avoided by mothers and babies
- Test if topoisomerase inhibitors can be therapeutic for Angelman syndrome



UNC Angelman Syndrome Clinic



UNC
CAROLINA INSTITUTE FOR
DEVELOPMENTAL DISABILITIES

- UNC is ranked 2nd in WORLD for autism research
- Goal: Become the leading institution in autism research