

Can zebrafish be autistic?

Philip Washbourne Ph.D.
Institute of Neuroscience
University of Oregon

What is autism?

- Range of disorders characterized by:
 - Abnormal/decreased social interaction
 - Repetitive Behavior (stereotypies, compulsive behavior, resistance to change, self-injury)
 - Can also involve:
 - Sensory hyper/hyposensitivity
 - Intellectual Disability
 - Seizures
 - Schizophrenia
 - Gastrointestinal symptoms

Incorrect stereotype:



Autism Epidemic?

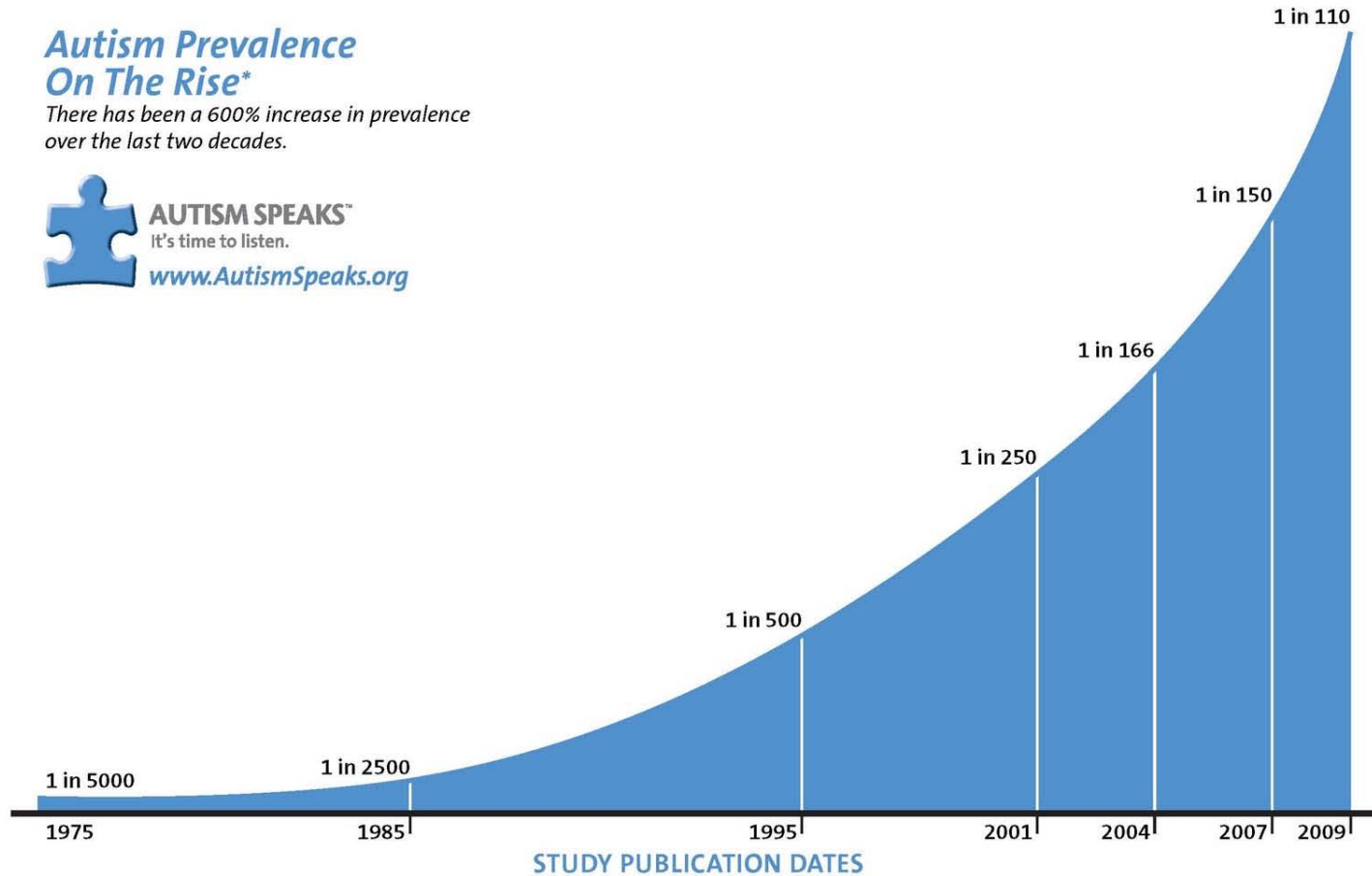
Autism Prevalence On The Rise*

There has been a 600% increase in prevalence
over the last two decades.



AUTISM SPEAKS™
It's time to listen.

www.AutismSpeaks.org



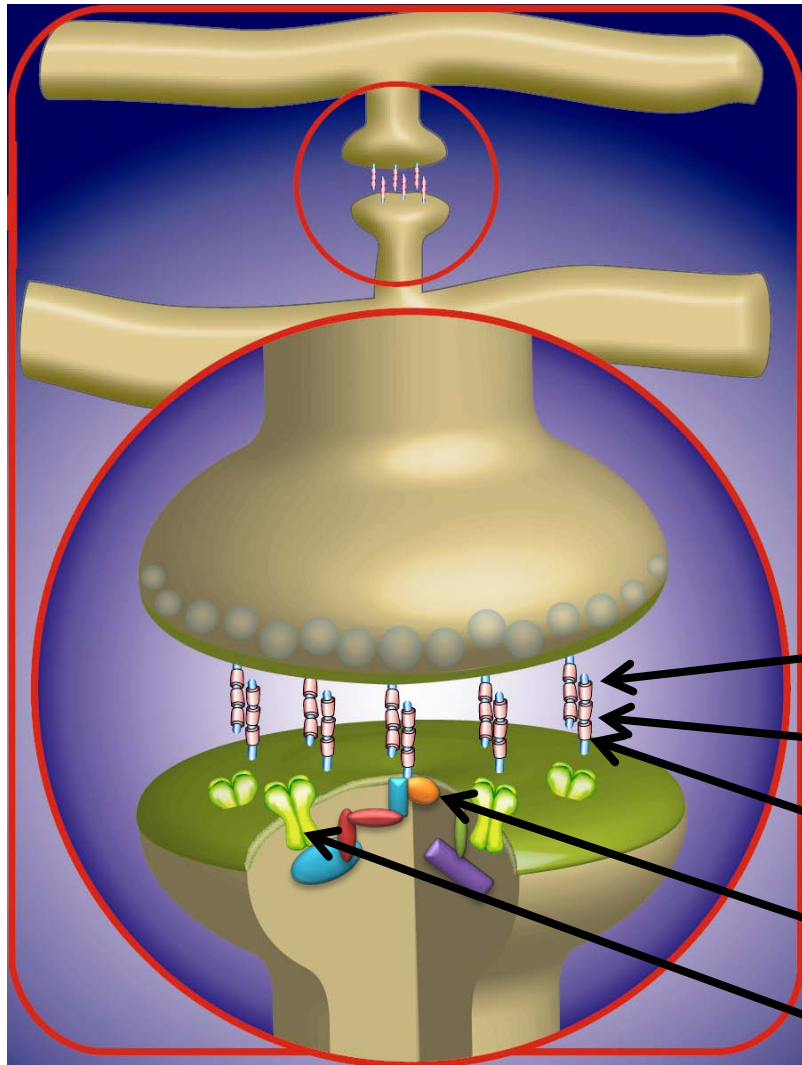
*Recent research has indicated that changes in diagnostic practices may account for at least 25% of the increase in prevalence over time, however much of the increase is still unaccounted for and may be influenced by environmental factors.

- Now: 3.4 in 1000 children between 3 and 10 years (NIMH)
- 15-fold increase in autism incidence since 1990
 - Broadening of diagnostic criteria
 - New diagnostic tools
 - Awareness
 - Special educational services
 - Reduced stigma

Genetics and Autism

- Autism is the most genetic of neuropsychiatric disorders:
 - ~77% concordance in monozygotic male twins
 - ~30% concordance in dizygotic male twins
- Environmental factors explain about 55% of liability for autism
- Autism is prevalent in boys (4:1) suggesting mutations in X-linked genes as possible causes

Autism and Synapses

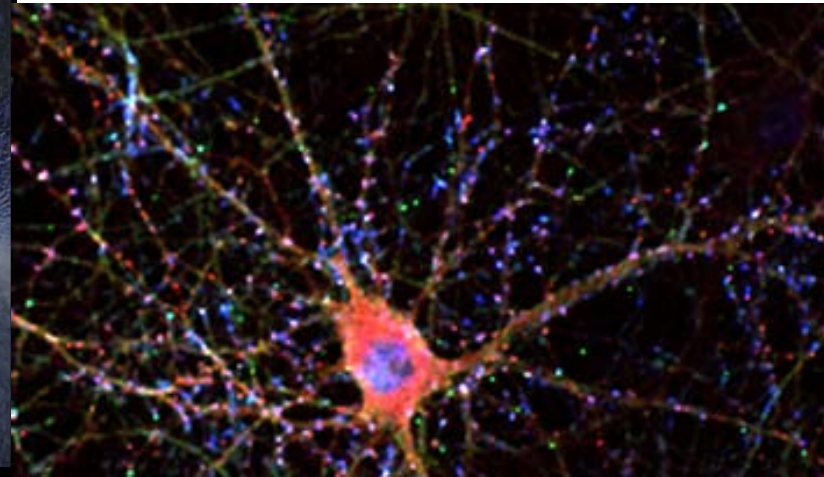


- Many of the genes with mutations found in families with autism have synaptic functions:

- Neurexins
- Neuroligins
- SynCAMs
- SHANKs
- GRIK2

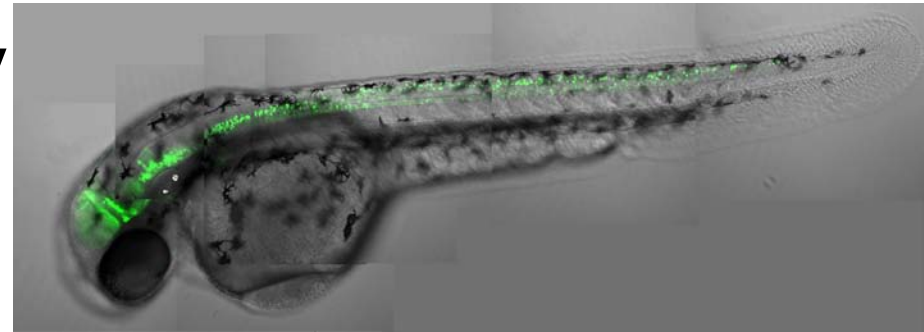
What is a synapse?

- Site of communication between neurons
- Signaling occurs in one direction
- A chemical transmits the signal, e.g. glutamate, dopamine
- Some synapses are “excitatory”, whereas others are “inhibitory”
- “Computation” occurs by adding signals from all of the synapses on a single neuron



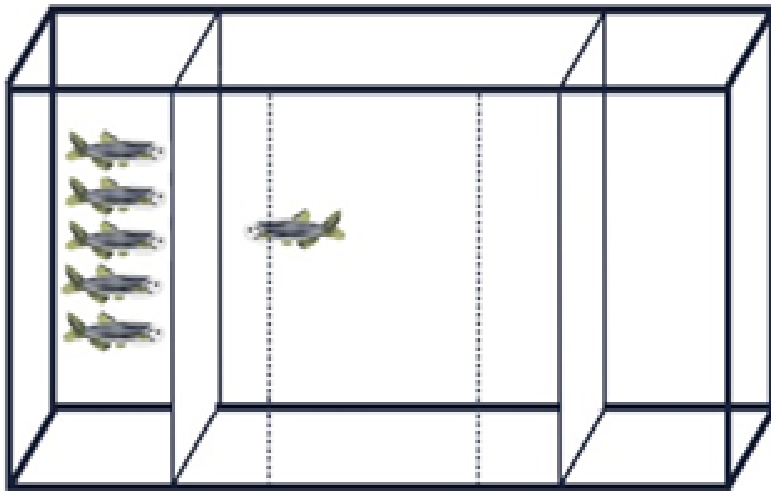
Why study autism in zebrafish?

- Easier access to study molecular/cellular events during development
- Highly homologous genes to mammals
- Small animals with large numbers of offspring

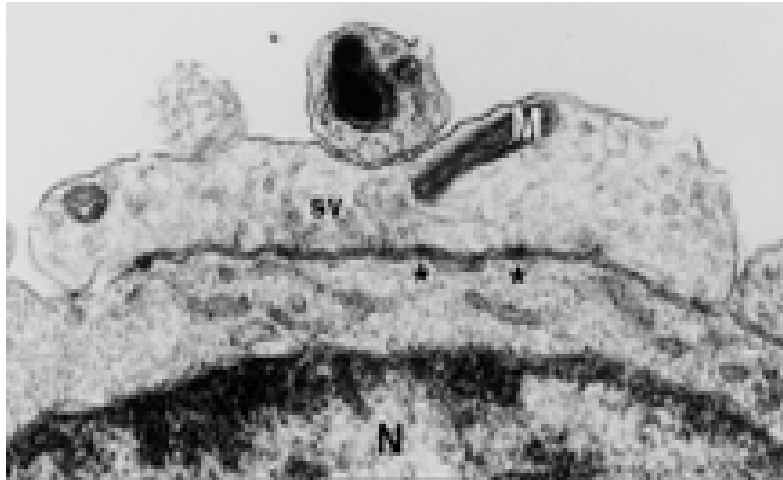


Why study autism in zebrafish?

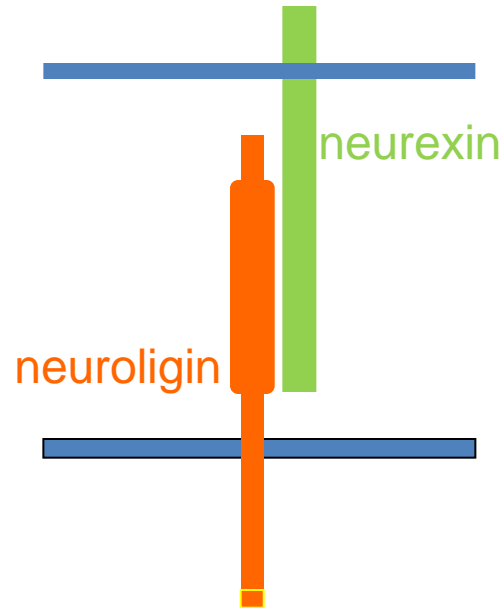
- Behaviors relevant to autism?
 - Shoaling (social swimming)
 - Startle response (sensory reflexes)



Neuroigin genes in autism



From Scheiffele et al. Cell (2000)



Mutations of the X-linked genes encoding neuroiginins NLGN3 and NLGN4 are associated with autism

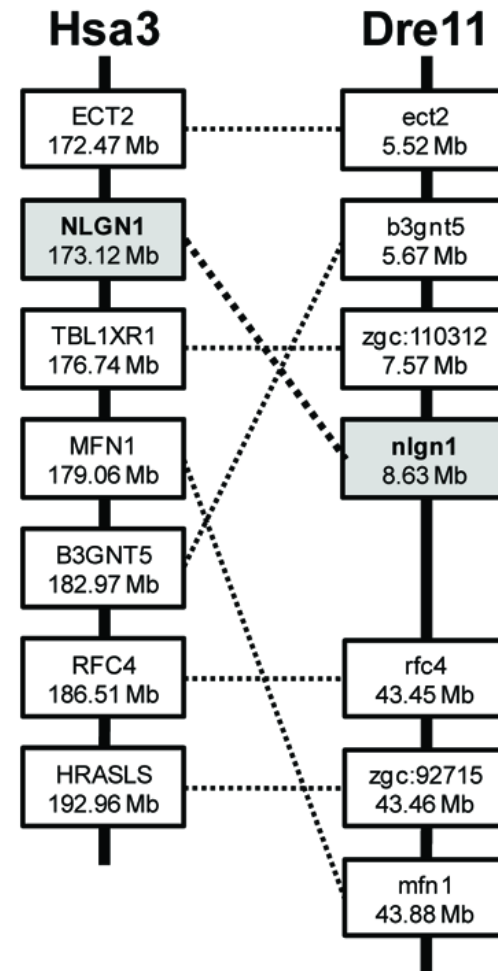
Published online 31 March 2003; doi:10.1038/ng1136

Many studies have supported a genetic etiology for autism. Here we report mutations in two X-linked genes encoding neuroiginins NLGN3 and NLGN4 in siblings with autism-spectrum disorders. These mutations affect cell-adhesion molecules localized at the synapse and suggest that a defect of synaptogenesis may predispose to autism.

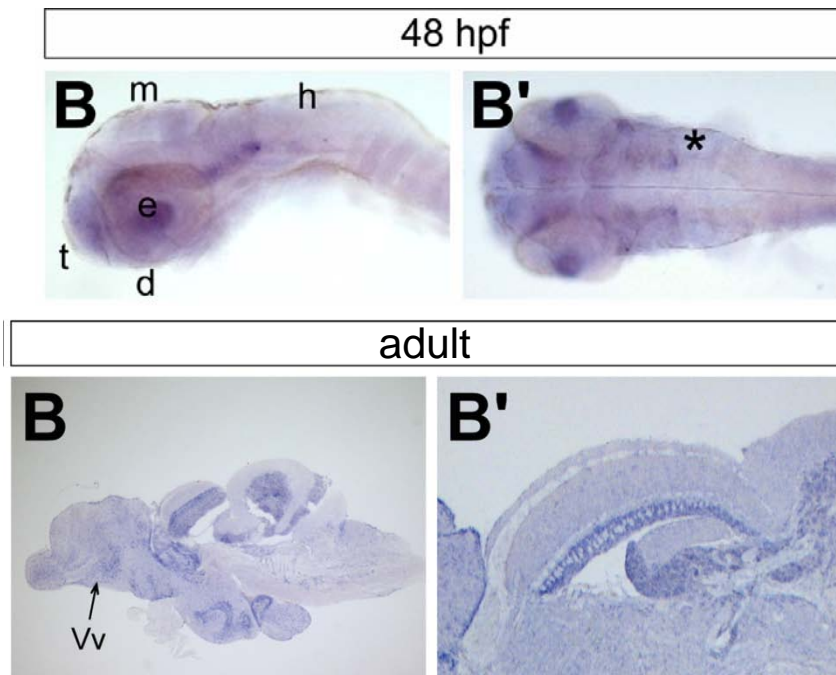
Neuroligins in zebrafish

- 5 genes in humans
 - (1,2,3,4X, 4Y)
- 7 genes in zebrafish
- Only 1 *nlgn1* gene
- Broad neural expression in larva and adult for *nlgn1*

Nlgn1



Davey et al. 2009



Thanks:

- Sarah Stednitz
- Raluca McCallum
- Victoria Norton
- Alexandra Tallafuss
- Washbourne Lab
- Eisen Lab
- UO Zebrafish Facility

