FEATURES

Fish, frogs, flies and other fauna in scientific firsts

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Over the past century, scientists have used a variety of animal models to advance their understanding of the developing brain and autism. Here's a chronology of some of the landmark discoveries involving uncommon autism models.

1916

Notch up:

Biologist Thomas Hunt Morgan identifies a fruit fly gene called **NOTCH** that affects wing maturation and is part of a pathway later linked to nervous system development in people.

1920

Heart to heart:

Austrian scientist Otto Loewi observes parallel activity in two frog hearts suspended in saline, theorizing that a **chemical messenger** he dubs ‘vagusstoff’ traveled through the solution — the first identified neurotransmitter.

1962

Pluripotent possibilities:

English zoologist John Gurdon replaces the nucleus of a frog egg with a nucleus from an intestinal cell. The resulting embryo **successfully develops** into a tadpole, demonstrating that mature cells contain all the information needed to create any cell type and kicking off research in induced pluripotent stem cells.

1971

Fly time:

Biologist Seymour Benzer and a colleague demonstrate that mutations in a fruit fly gene dubbed PER disrupt the **fly's circadian rhythm**, launching *Drosophila melanogaster* as a model for the study of how genes control behavior.

1986

Worm wiring:

Scientists publish the complete wiring diagram of the ***Caenorhabditis elegans* nervous system**, paving the way for the extensive use of roundworms in studies of nervous system development.

1990

Elegans experiment:

Studies show that *C. elegans* is **capable of habituation**, a simple form of learning that may be disrupted in autism.

2007

Mouse milestone:

Researchers debut a single-gene **mouse model of autism**: mice with a mutation in the gene NLGN3.

2010

Inching forward:

Scientists create one of the first invertebrate models of autism: a strain of *C. elegans* with a faulty version of the roundworm's **neuroligin gene NLG1**.

2012

Fish tale:

A zebrafish study shows that multiple genes in the **16p11.2 chromosomal region**, which may be deleted or duplicated in autism, play roles in brain development.

2015

Social space:

Researchers report that fruit flies in an enclosure tend to keep a **reliable amount of space** between them, an observation that can be used to investigate how mutations in autism-linked genes affect social behavior.

2015

Eight is enough:

The **complete genome sequence** of the California two-spot octopus (*Octopus bimaculoides*) is published, revealing striking similarities to people in genes involved in nervous system development and function.

2016

Sedated swimmers:

Zebrafish larvae lacking the autism-linked gene CNTNAP2 are **hyperactive at night**, but adding estrogen-like compounds to their tank calms the fish — demonstrating a use for the animals in screening potential autism treatments.

2018

Two to tango:

A study of gene expression in the developing fly eye reveals the importance of interactions between **genes in the 16p11.2** region during neurodevelopment.

2018

Social circuits:

Researchers identify **neurons in the forebrain** of zebrafish that support their social interactions, suggesting that zebrafish can be used to probe social brain circuitry.

2019

Picking priorities:

An analysis of 20 autism-linked mutations in roundworms **flags 10 autism** candidate genes as worthy of further study, because of their impact on the worm.

2019

Gut feeling:

Scientists find that food moves **through the gut** slowly in zebrafish larvae with SHANK3 mutations, providing a clue to the roots of digestive problems associated with autism.

2019

Habit forming:

The behavior of fruit flies with mutations in autism-linked genes suggests that dozens of these mutations lead to **impairments in habituation**.

2019

Stranger danger:

Like their mouse counterparts, zebrafish lacking the autism-linked gene RELN show little interest in socializing with unfamiliar fish, supporting use of the fish as a **model for social difficulties** in autism.

2020

Roundworm rodeo:

A study of more than 27,000 roundworms with mutations in the worm versions of 98 autism-linked genes hints at the **function of these genes**; many of them affect habituation.

2020

Sound check:

Zebrafish larvae lacking FMR1, the gene altered in fragile X syndrome, are **hypersensitive to sound**, suggesting that zebrafish can be used to study sensory processing differences in autism.

2021

Show stopper:

Reducing the expression of the autism-linked gene FOXP1 in a particular brain region in songbirds

impairs the birds' ability to memorize songs they hear from their fathers, suggesting a specific role for this gene in language learning.

2021

Fly by night:

Fruit flies lacking a gene akin to the autism-linked genes CHD7 and CHD8 have **fragmented sleep**, a problem researchers corrected using an adapted form of 'sleep restriction,' an insomnia treatment.

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