Fishing for Neural Health and Disease in the Evolutionary Gene Pool

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We can decode any genome using DNA sequencing

DNA “sequence”

http://www.ashg.org/education/everyone_1.shtml

By comparing genome sequences to each other, we can identify “variants” that differ between people

Person 1
ATGGCTTT

Person 2
AAGCCT

Person 3
ATTCCT

Person 4
GTCCTT

http://www.ashg.org/education/everyone_1.shtml
Variants have been identified in children with autism and epilepsy

Thousands of variants in hundreds of genes identified!

But not all variants actually cause disease...

How can we test if a variant actually leads to dysfunction of the brain?

Zebrafish
Wait, we can use zebrafish to test the function of human genes?

Humans and fish share 70% of their 20,000 genes!

Why zebrafish?
Why zebrafish?

- Produce many babies
- Grow quickly

https://www.youtube.com/watch?v=hSMgt5gV-8s

First 18 hours of development

Many thousands of fish can be housed in a small laboratory
Inject “CRISPR” into eggs to create human variants in zebrafish genes

How do we test for changes in zebrafish brains?
Test for seizures in our fish by tracking their motion

DanioVision
5 day old larvae treated with PTZ drug

Stage 1
Sudden hyperactivity and burst movements

Stage 2
“Whirlpooling”

Stage 3
Loss of posture and periodic spasms

Test variants of SYNGAP1 gene found in children with autism and epilepsy
Measure body features using imaging

Gene variants unique to humans have led to changes in our brains and behavior

Brain size

Neural networks

Reading

Complex language
Test variants of *SRGAP2* gene that might be important in larger brains in humans

*SRGAP2* "mutant" larvae have more neurons
Earlier diagnoses

Possible treatments

What makes us human

Dennis lab
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Many awesome undergrads!

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Pamela Lein
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Bruce Draper
Gerald Quon

Funding
R00 NS083627 (NIH/NINDS) DP2
OD025824 (NIH/OD/NIMH)
Alfred P. Sloan Foundation
UC Davis IDDRC pilot grant
Generous faculty startup funds

NIH National Institute of Neurological Disorders and Stroke
NIH National Institute of Mental Health