



Neurogenetics Lab

Genetic strategies to study ASD

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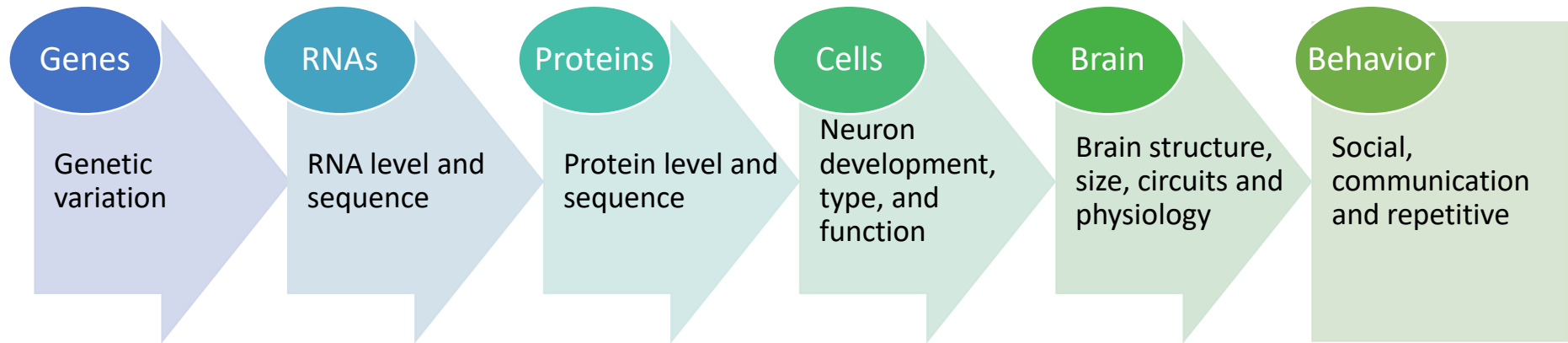


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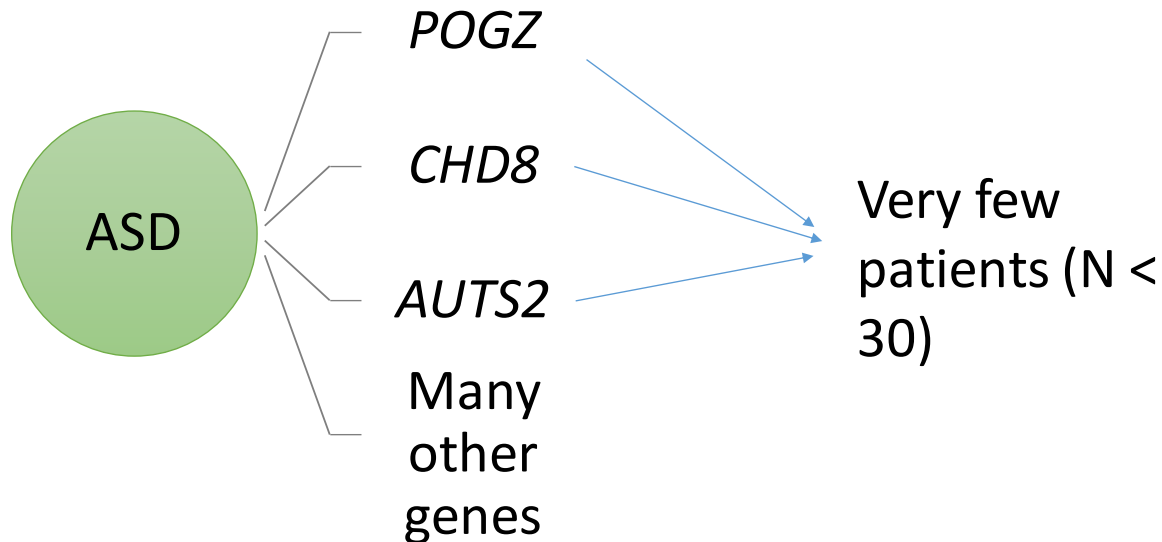
From genes to behavior



Main observations and questions

(1) Genetic variation in hundreds of genes contribute to ASD

What are the shared pathways or processes?



Main observations and questions

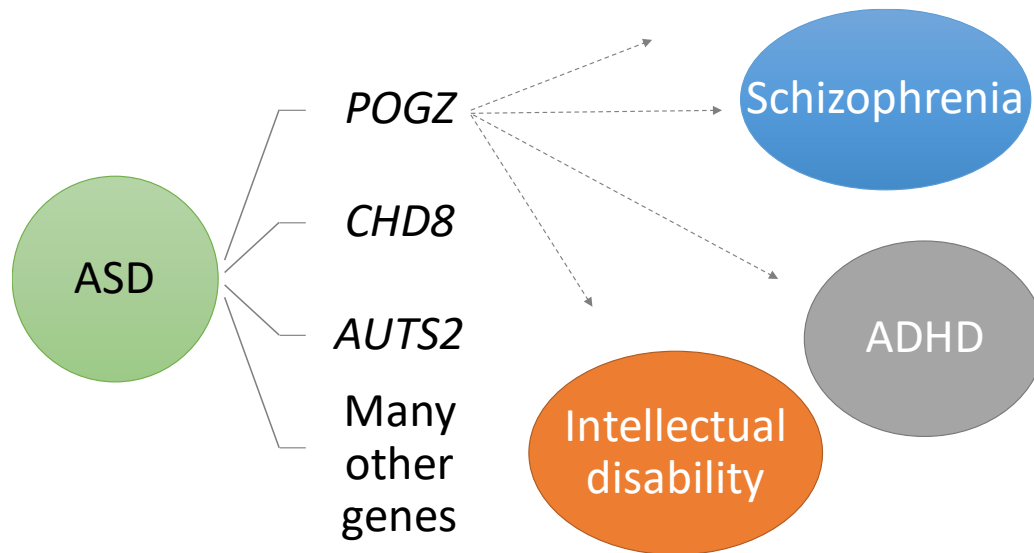
(2) Convergence on chromatin regulators that are active during brain development

How the alteration in chromatin regulators causes the deficits observed in ASD?

Main observations and questions

(3) Significant genetic overlap between different neurodevelopmental disorders

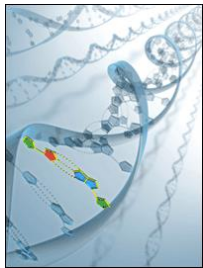
How mutations in the same gene can lead to different disorders?



How do we study ASD?

Systems to genes (top-down)

Genetic variations



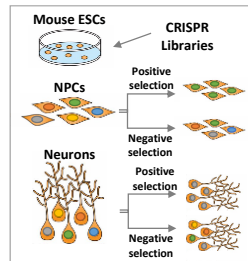
Computational analysis

Human Brain



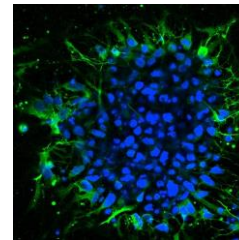
High-throughput genomics

CRISPR screens



Genes to systems (bottom-up)

Cellular models



Molecular biology

Animal models



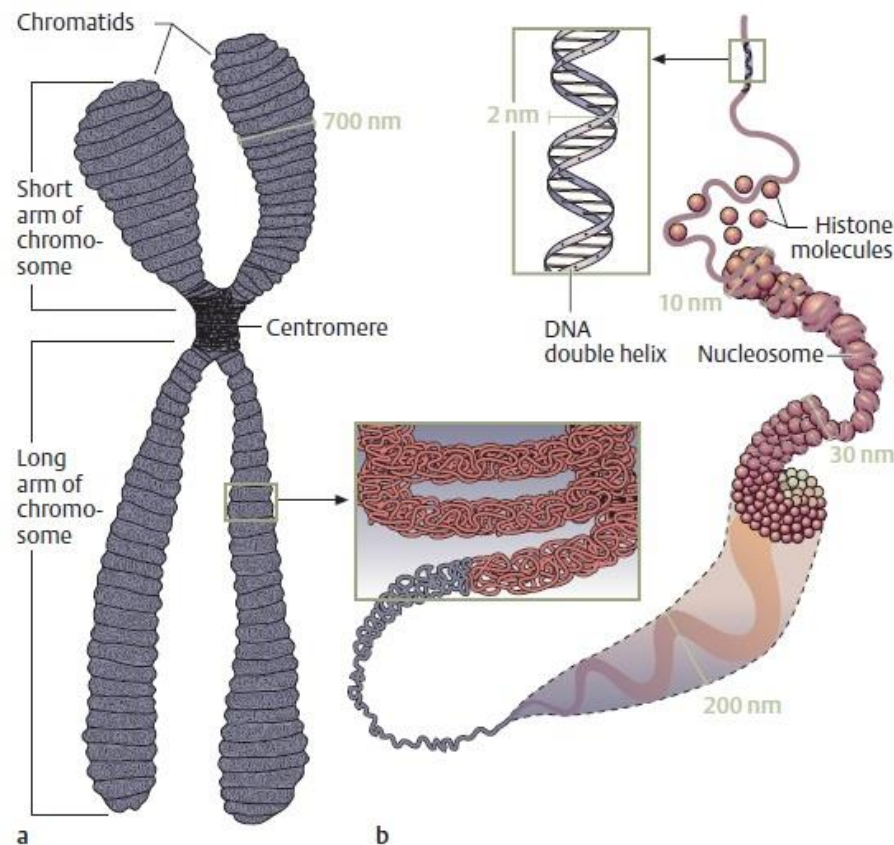
Behavior and physiology

What are the shared processes that are affected by multiple ASD-associated genes?



Eyal Ben-David

A significant proportion of *de novo* mutations alter proteins that involved in chromatin regulation during brain development



What causes divergence between different disorders?

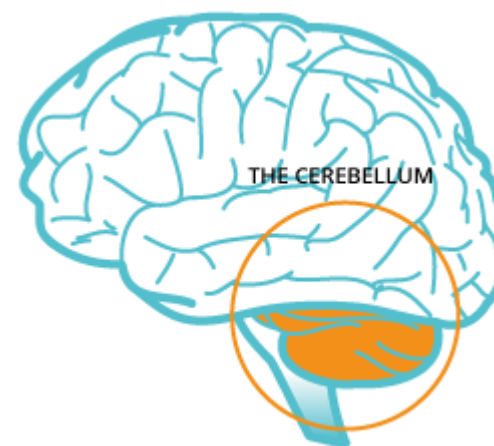
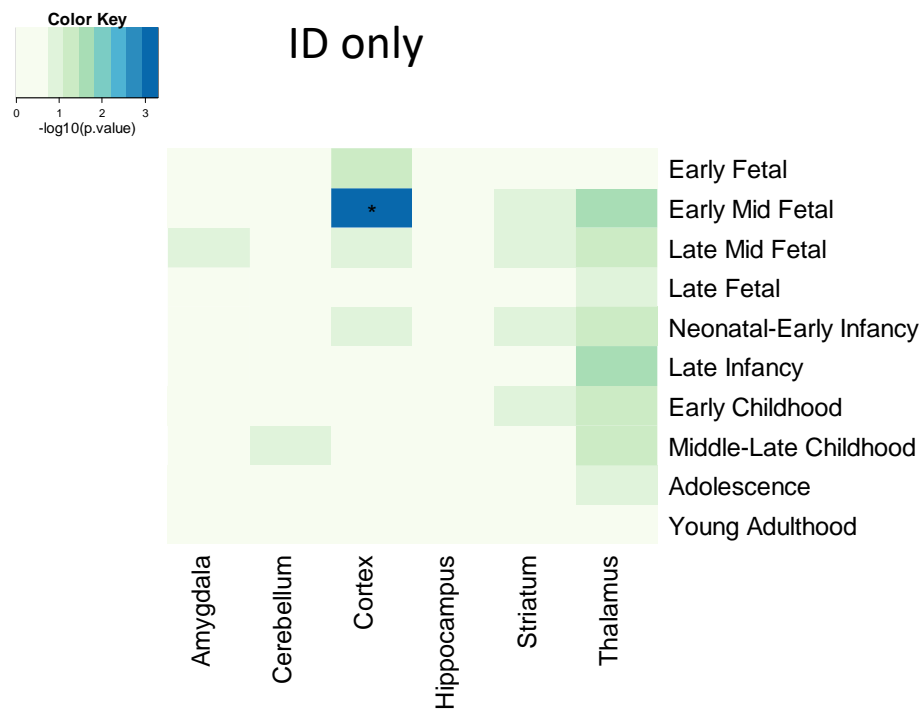


Shahar Shohat



- Intellectual disability (**ID**)
- Autism spectrum disorders (**ASD**)
- Schizophrenia (**SCZ**)
- Normally developing individuals

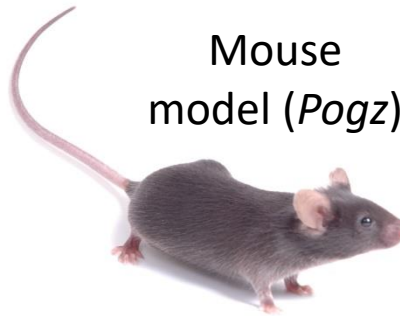
Genes disrupted by mutations in ID and ASD are enriched in developing cortex



How does the alteration in chromatin regulators cause the deficits observed in ASD?

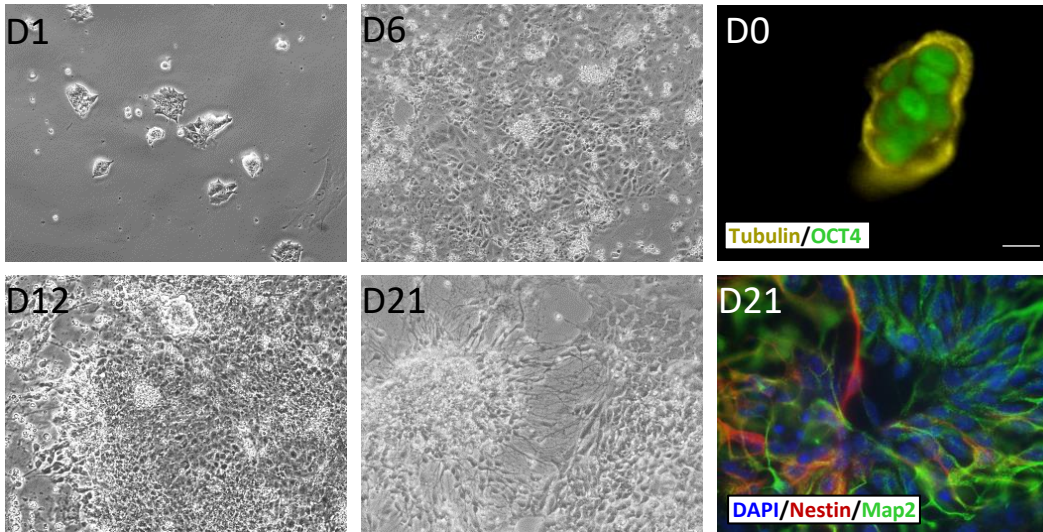


Reut Suliman



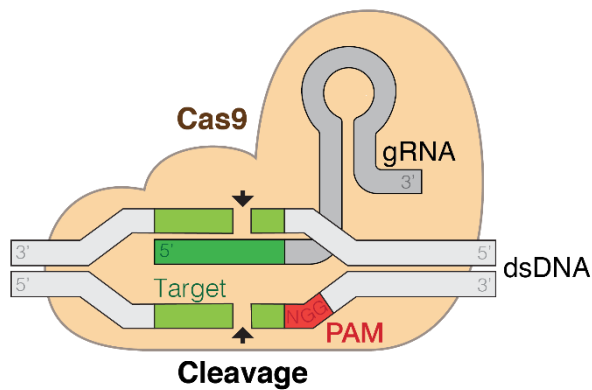
Ben Title

Effect of chromatin regulators during *in vitro* corticogenesis

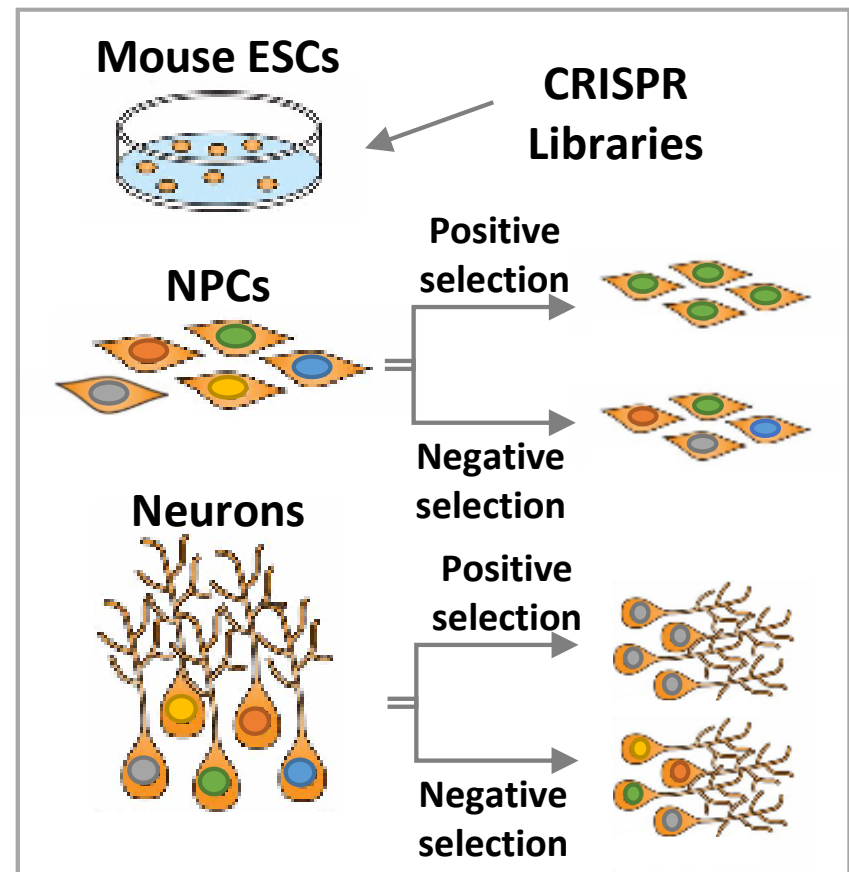


Galya Rothkoff

Experimental approach to study essential genes for brain development



- CRISPR/CAS9 pooled library
- 19,674 coding genes
- 4 gRNA per gene
- 1000 control gRNA
- 8, 11, 15 and 18 DIV



Thanks!

- Reut Suliman (Suli)
- Ben Title
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- Alana Amelan
- Ethel Vol

Yosef Yarom
Guo-Jen Huang
Jonathan R Keller
Bjorg Gudmundsdottir
Kristbjorn O. Gudmundsson

