Flying to the clinic: Drug repurposing for CTNNB1

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Personalized medicine is having its day

Caroline Seydel

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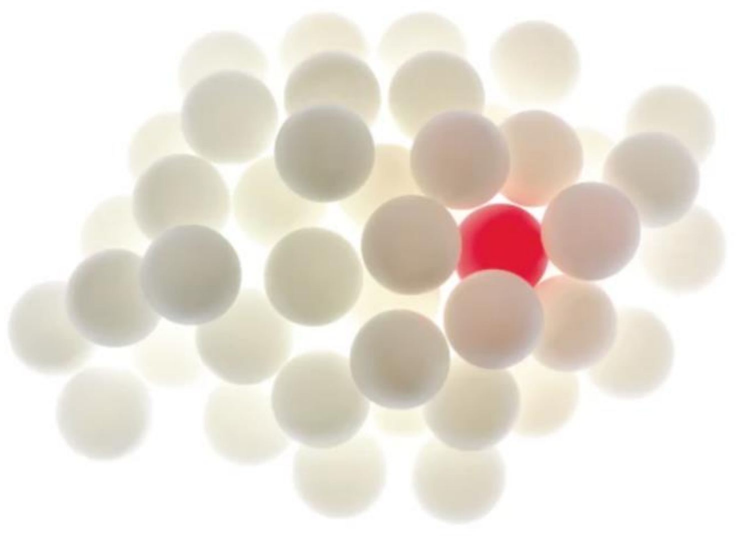
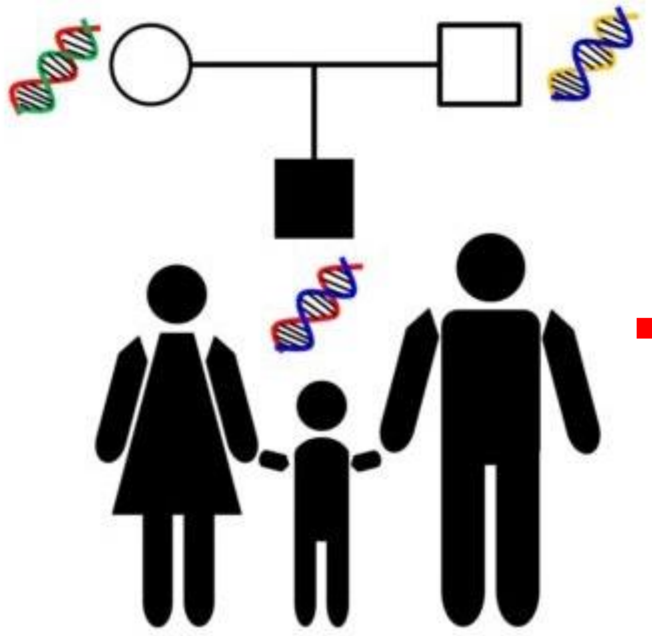
From made-to-order genetic therapies to model organisms engineered to be 'patient avatars', the technology exists right now to save patients with rare diseases.



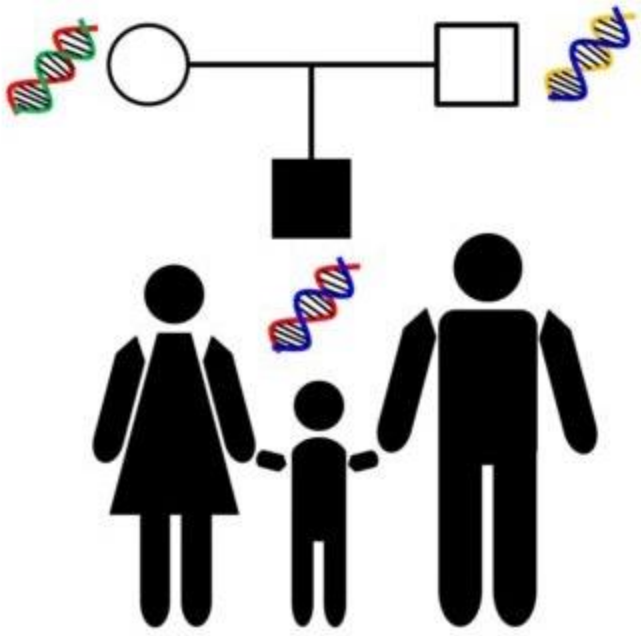
Personalized drug screens in the lab



Fast models

Efficient screens

Drug repurposing



Physician/patient partnerships

Why fruit flies?

Drosophila melanogaster

Tissue specific tools allow flexibility

Drug repurposing is key

Established use

New use in rare disease

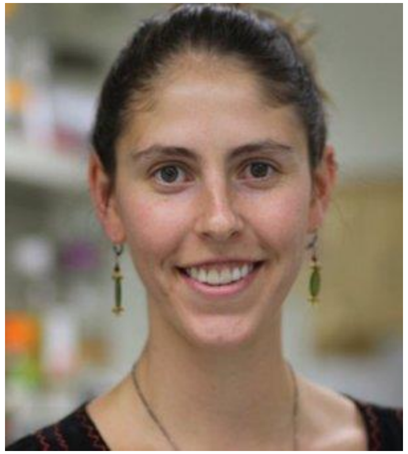

FDA approved drugs
What we think we know
What we don't know
POTENTIAL

The Team

Kate Beebe, Ph.D.

Caroline Massey

Sydney Peterson



Emily Coelho

Delaney Baratka

Bench to Bedside
Rare Disease Partnerships

FCDGC

Frontiers In Congenital
Disorders Of Glycosylation
U54NS115198

Perlara

CTNNB1
CONNECT AND CURE

Intermountain
Primary Children's Hospital
100

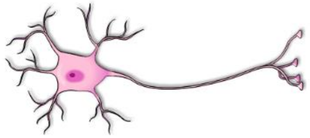
Bench to Bedside
Rare Disease Partnerships

Family or
Foundation
Contact

Can we do a screen? Search for a phenotype

Survival

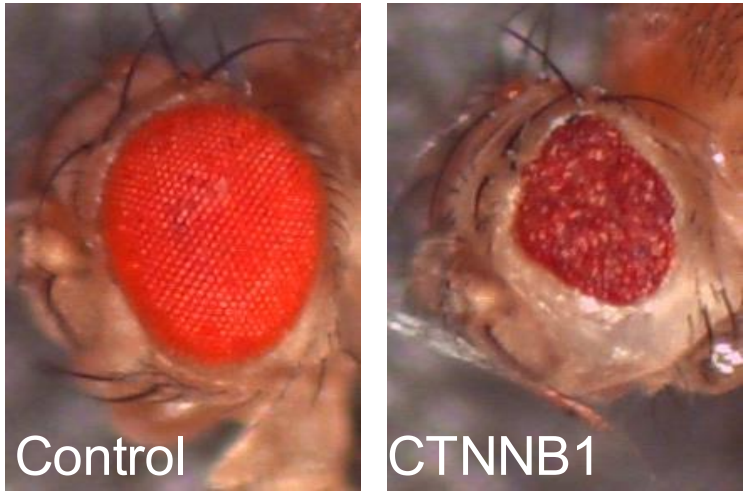
Shape and Size

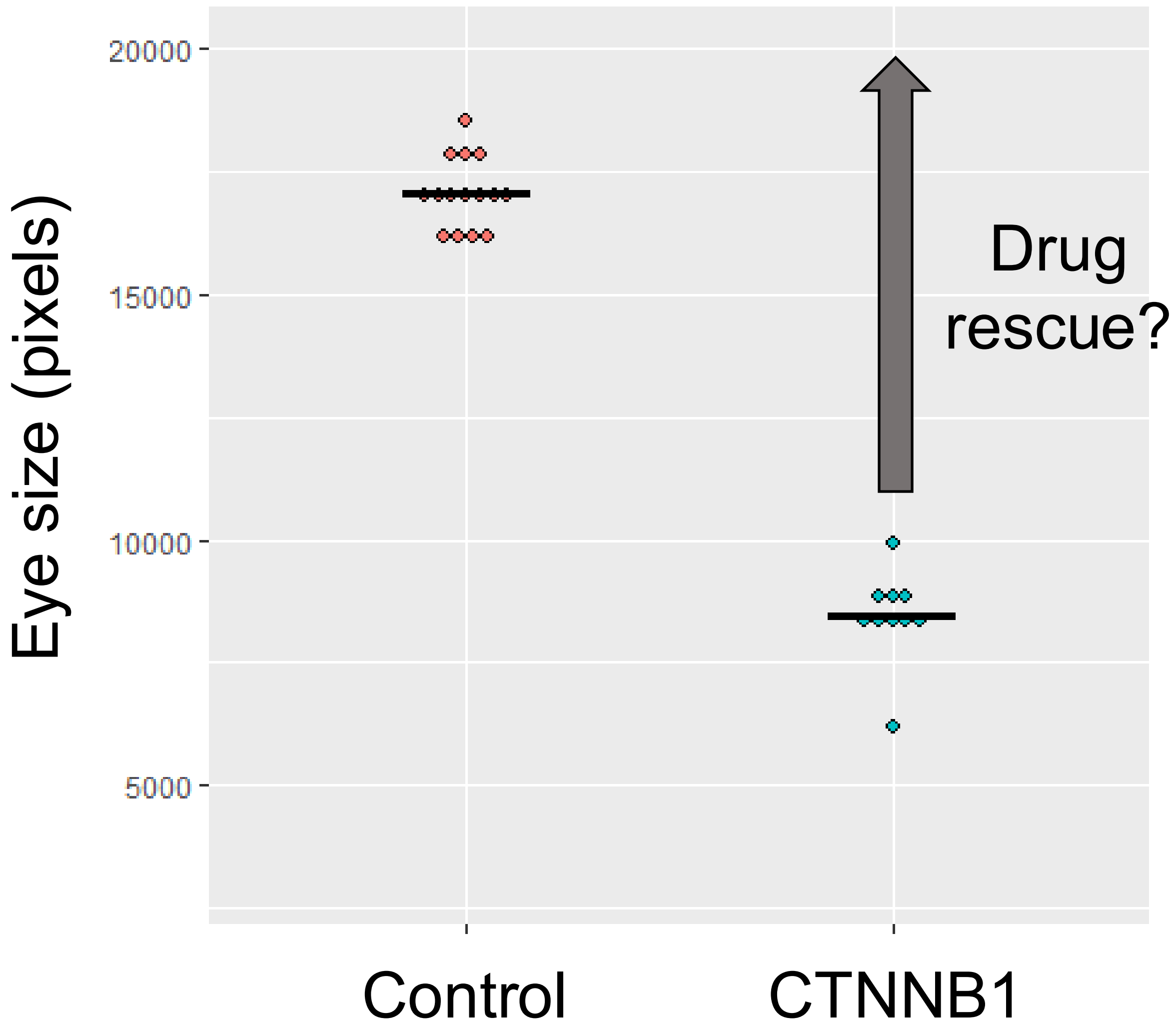


Behavior or Survival

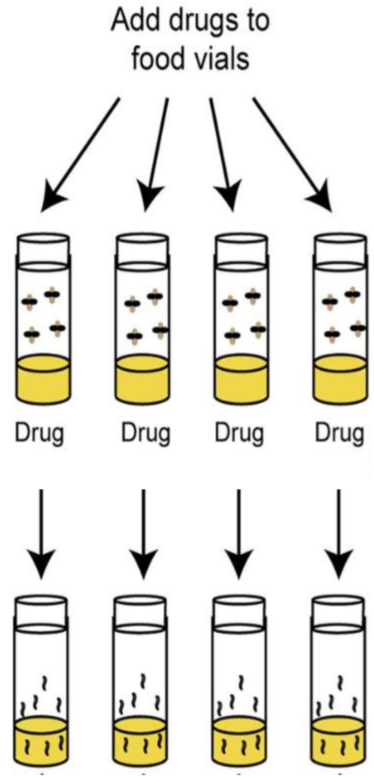
Behavior or Survival

Eye-based CTNNB1 drug screen





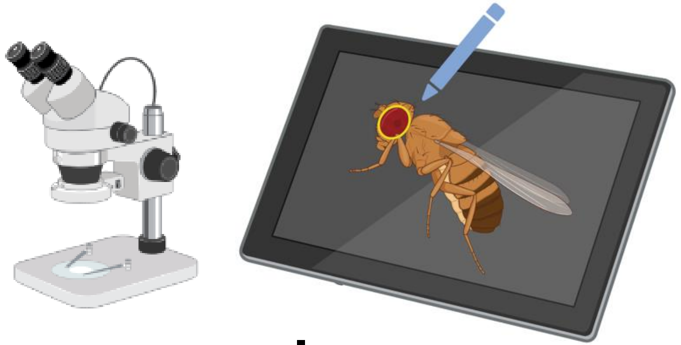
Drug repurposing workflow



1520 drugs
Prestwick Chemical Library

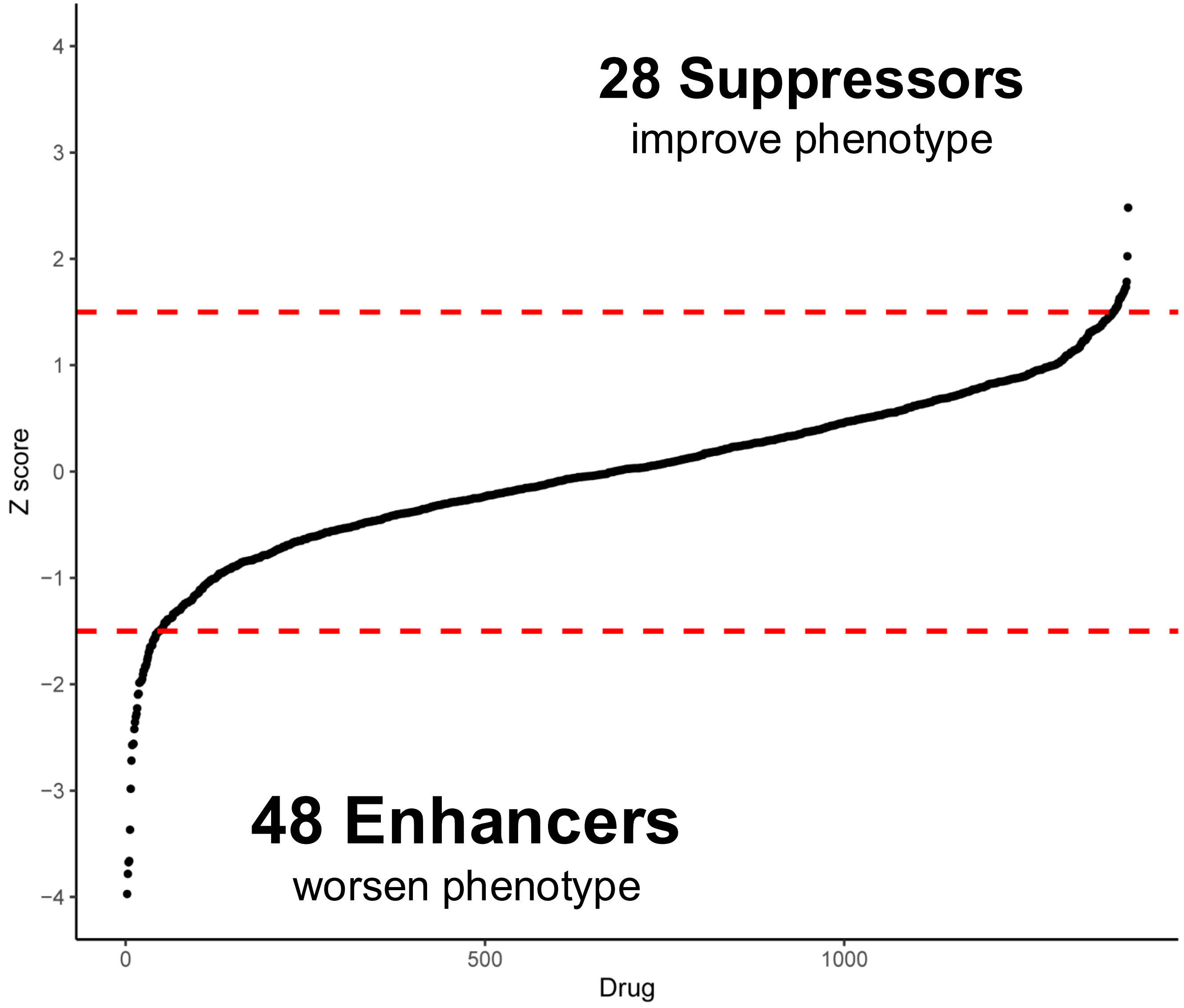
Collect flies
≥5 per drug tube

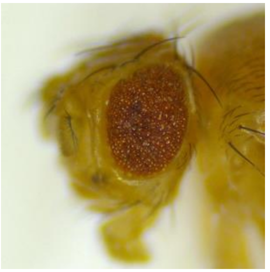
Image and measure eyes



Calculate Z-score
for each drug

CTNNB1 drug screen results overview

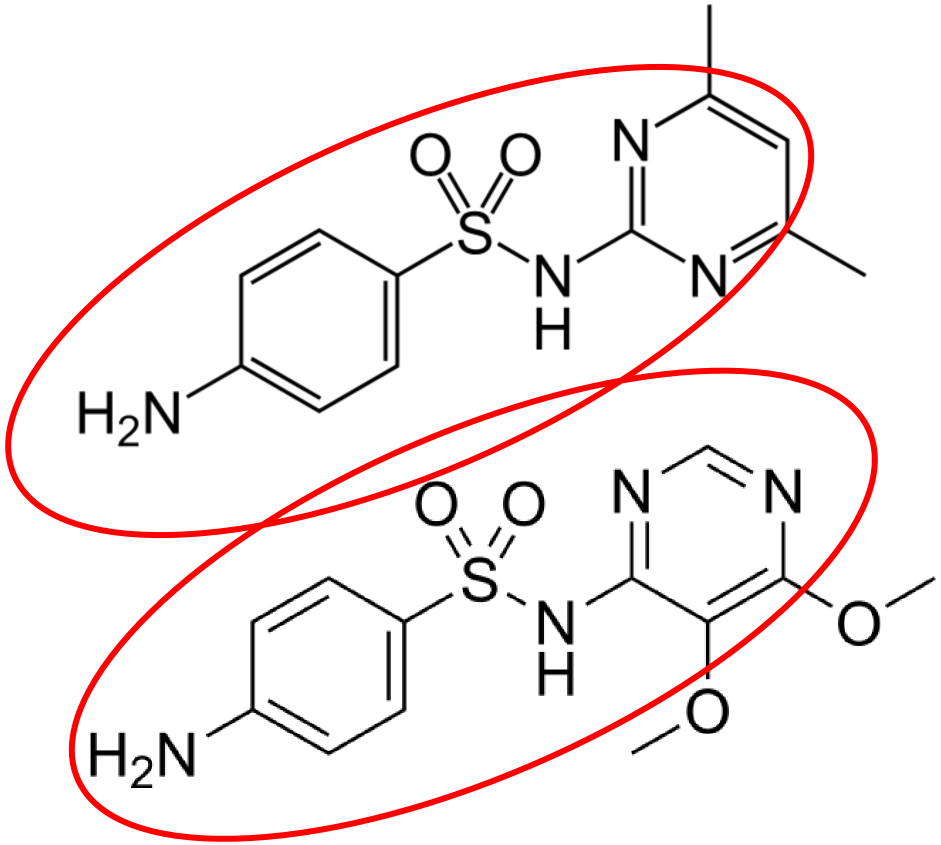


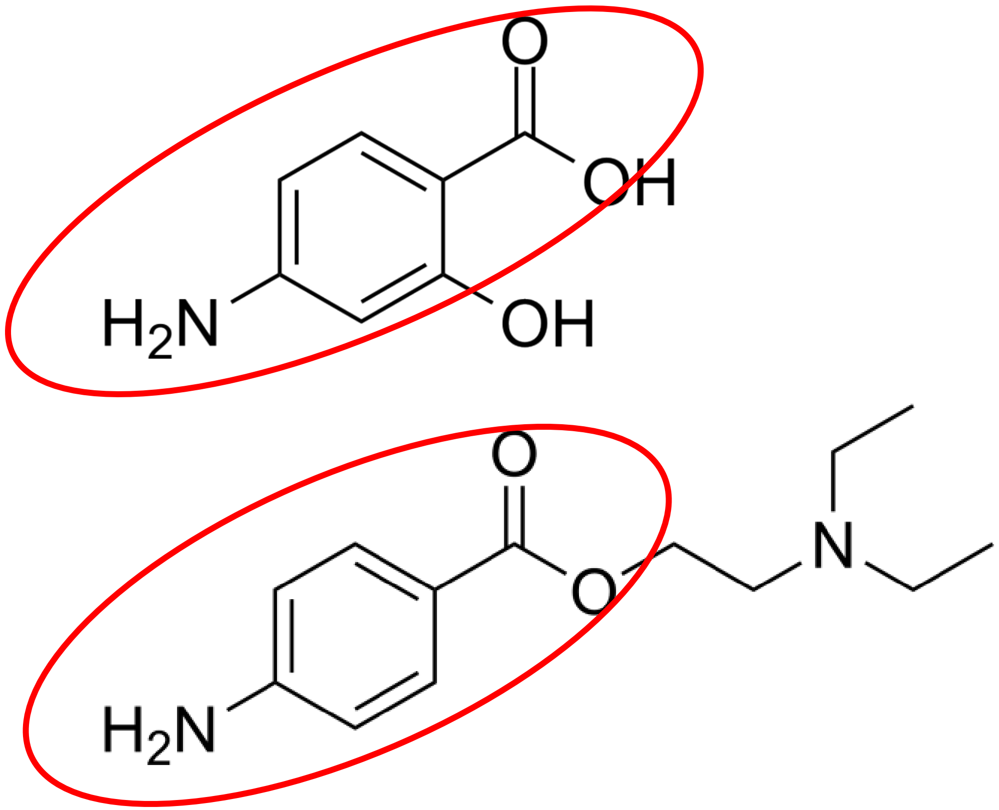


- Serotonin
- Histaminergic
- Antimalarial
- Sodium channels

- >1/3 Wnt/β-catenin inhibitors
- NSAIDS
- PPARα activators
- EGFR inhibitors

Common structures and common functions





Hit validation

- Prioritize
  - Mechanism of action
  - Availability
  - Pediatric safety

3 drugs are OTC
- Allergy
- Heartburn
- Antifungal

- Retest with new drug source
- Multiple concentrations (dose curve)
- Eye phenotype
- Other phenotypes

HOPE

Acknowledgements

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UNIVERSITY OF UTAH HEALTH SCIENCES

CTNNB1 CONNECT AND CURE

Contact us:

How flies help rare disease