Experimental evolution to probe gene networks underlying cognition in Drosophila

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What is the goal of genetics?

- uncovering of the relationships between genotype and phenotype.
 - identification of the genetic variation that underlies phenotypic variation (e.g. in human disease)
 - understanding HOW a given genetic variant impacts phenotype



















A new approach to use selective breeding to uncover mechanisms of non-linear gene interaction

- novel insight I-- Constrain genetic variability to a set of 23 informative loci with known impact on the phenotype
 - Vastly reduces complexity to an upper limit of 3²³ possible combinations.
 - Provides an opportunity for high throughput genotyping of multiple individuals
 - yields a data set that is amenable to sophisticated computational methods
- **novel insight II -- Mechanistic Anchor point** by using the selective breeding to ameliorate the phenotype of a specific gene of interest
 - provides a cell biological `anchor-point' that places gene interactions into a mechanistic context





The Constrained Genetic Variability: A collection of mutations that also disrupt memory! typical FI progeny															
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The Constrained Genetic Variability:													
starter strains													
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9	0	0	2	0	0	0	0		0	I	0	0	Aa=1
10	0	0	2	0	0	0	0		0	I	0	0	AA=2
11	0	0	2	0	0	0	0		0	I	0	0	
12	0	0	2	0	0	0	0		0	1	0	0	
13	0	0	0	2	0	0	0		0	0	0	0	
14	0	0	0	2	0	0	0		0	0	0	0	
15	0	0	0	0	2	0	0		0	0	0	0	
16	0	0	0	0	2	0	0		0	0	0	0	
17	0	0	0	0	2	0	0		0	0	0	0	
18	0	0	0	0	0	2	0		0	0	I	0	
19	0	0	0	0	0	2	0		0	0	I	0	
20	0	0	0	0	0	2	0		0	0	I	0	
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Conclusions

 Our approach combines the strengths of selective breeding and "suppressor screens" to uncover gene interactions capable of suppressing the learning deficit of rutabaga.
Identified 8 alleles predicted to explain the response to selection.
-validated prediction: 3 of 6 tested improve memory of rutabaga mutants.
-provides entry points for mechanistic cell biological investigation

•This data set provides a unique opportunity to investigate the landscape of higher order gene interactions.

-28 di-allele combinations among 8 alleles

-6561 total combinations

• The data output from this approach provides an opportunity to bring computational methods to bear on classical but formerly theoretical genetic notions

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Collaborators

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