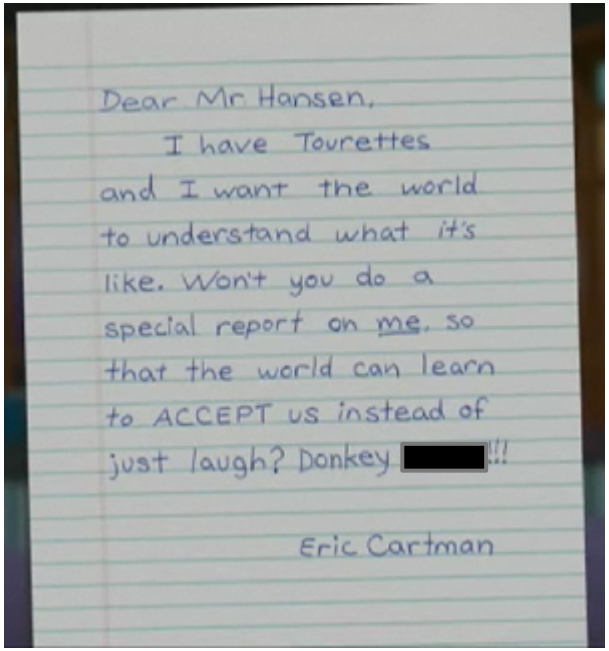
TOURETTE SYNDROME & THE HDC GENE

Ellen Siefkes

In the media



Coprolalia

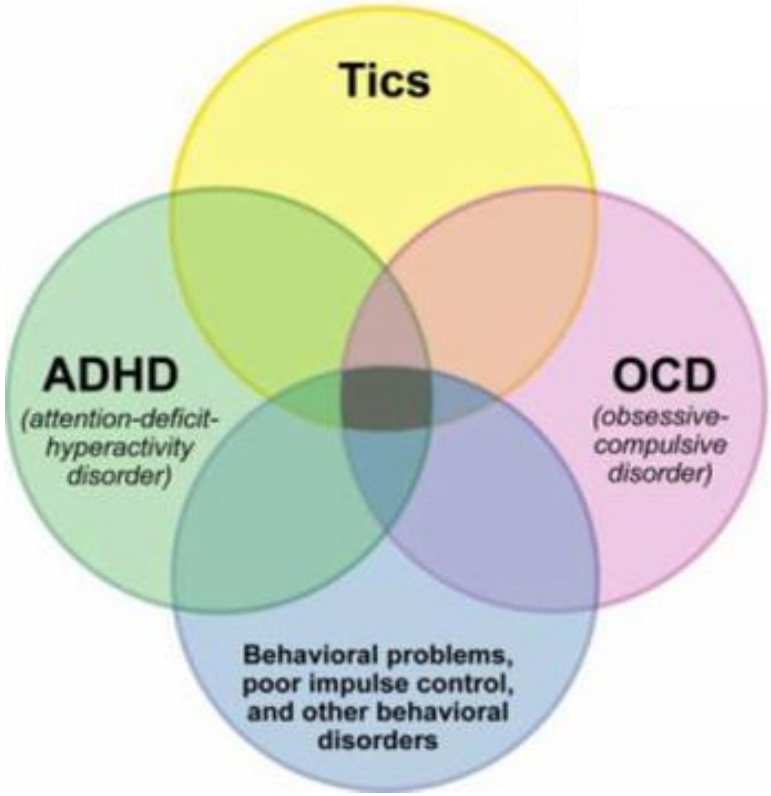
10-15%

What is Tourette Syndrome?

Motor & Vocal Tics

Co-morbid

3X more prevalent in males



The *Hdc* gene

Histidine decarboxylase

W317X

G-to-A

Peridoxal_deC

active domain

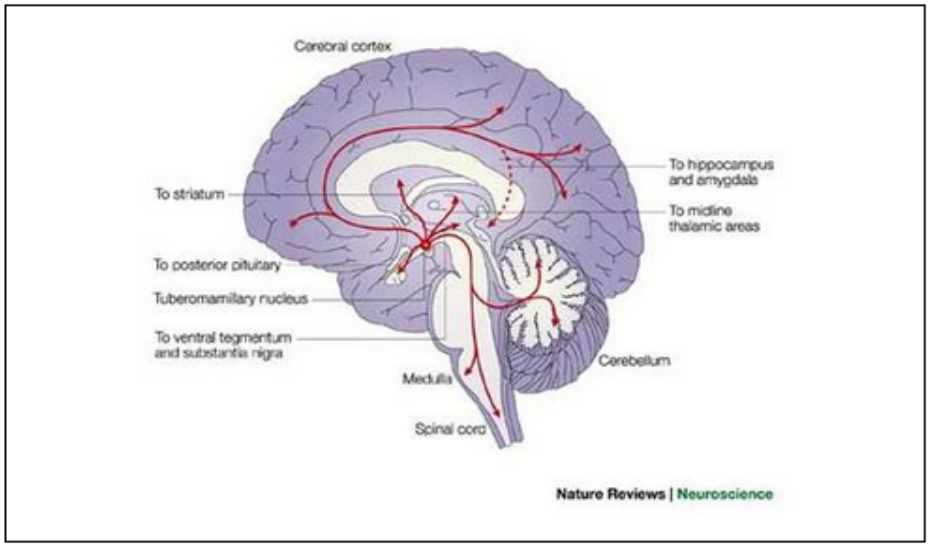
The HDC protein – histamine

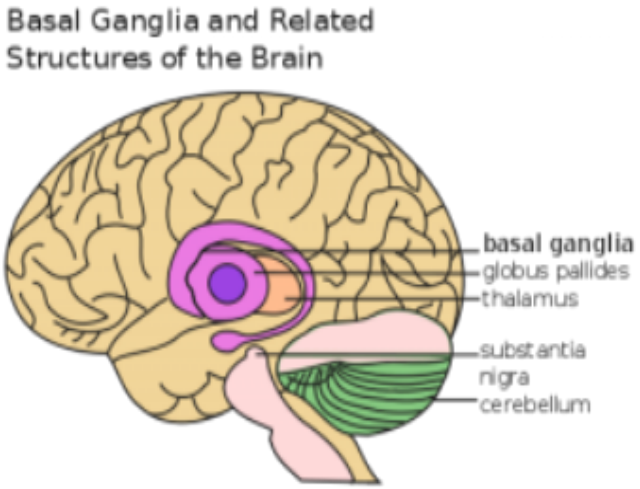
Arousal, cognitive functions, hormone secretion

dopamine

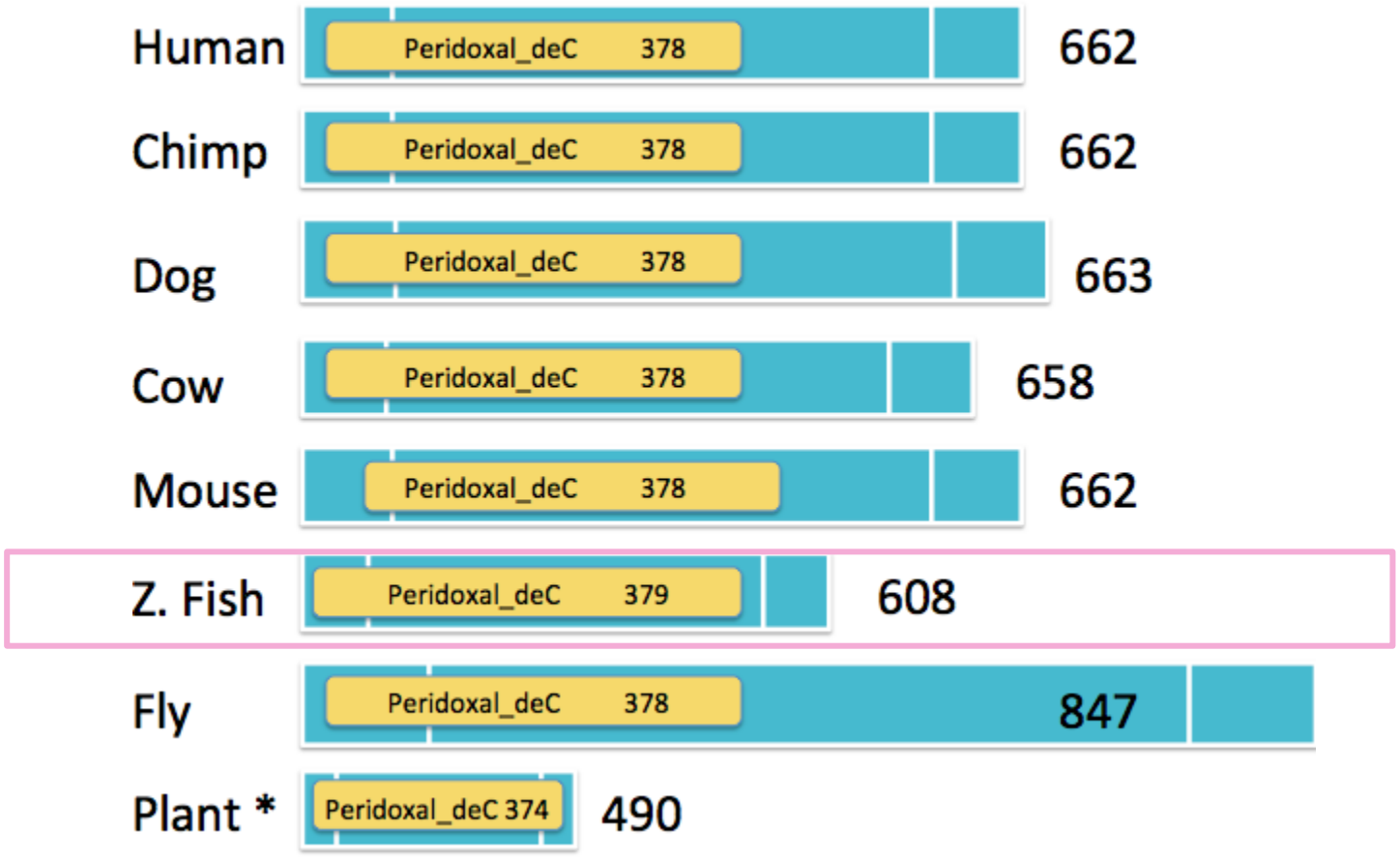
Low histamine levels

convulsions and seizures





Conservation



Mutation & domain are well conserved

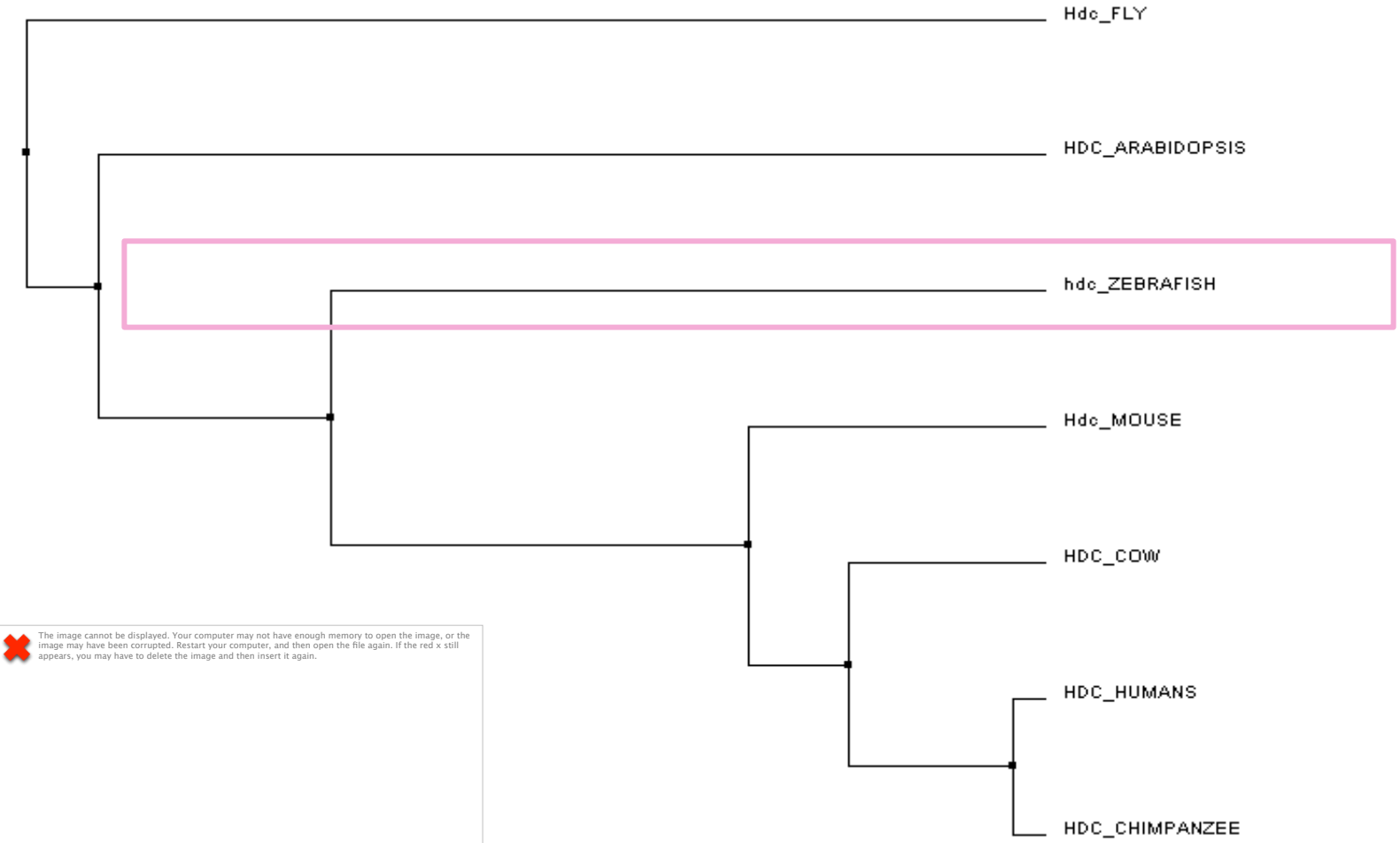
Goal

1 to 10 in every 1,000

Non-debilitating

Treatments safe for children

Zebrafish



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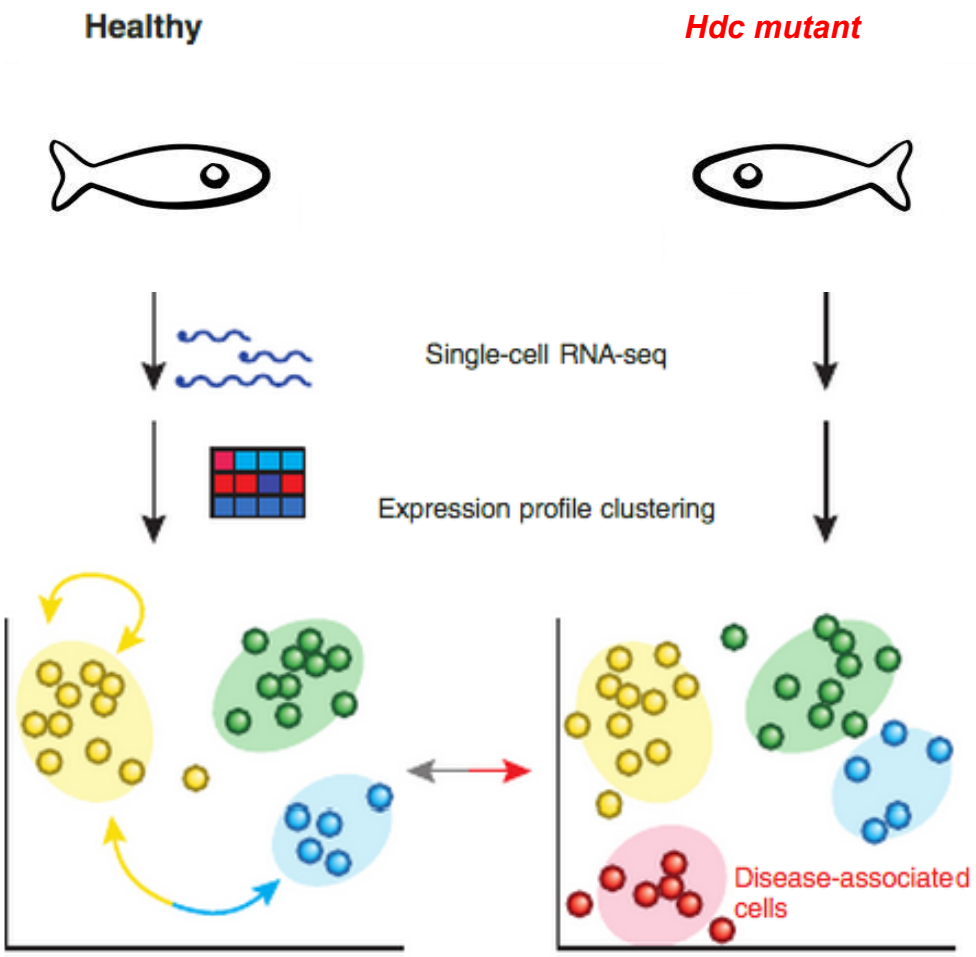
Clustal Omega

AIM 1: To determine targets of *Hdc* in healthy and *Hdc* mutant models

RNA seq & GSEA analysis



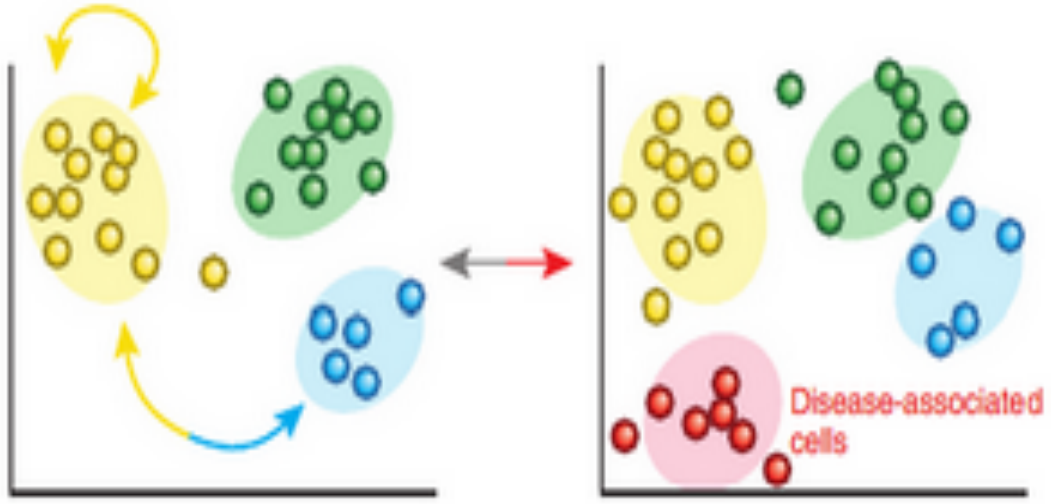
New genes discovered that can also regulate neurotransmitter levels

Results -Find *Hdc* interactions & pathways

Histidine metabolic processes

Biosynthetic pathways of neurotransmitter production

Binding/communication pathways



New focus

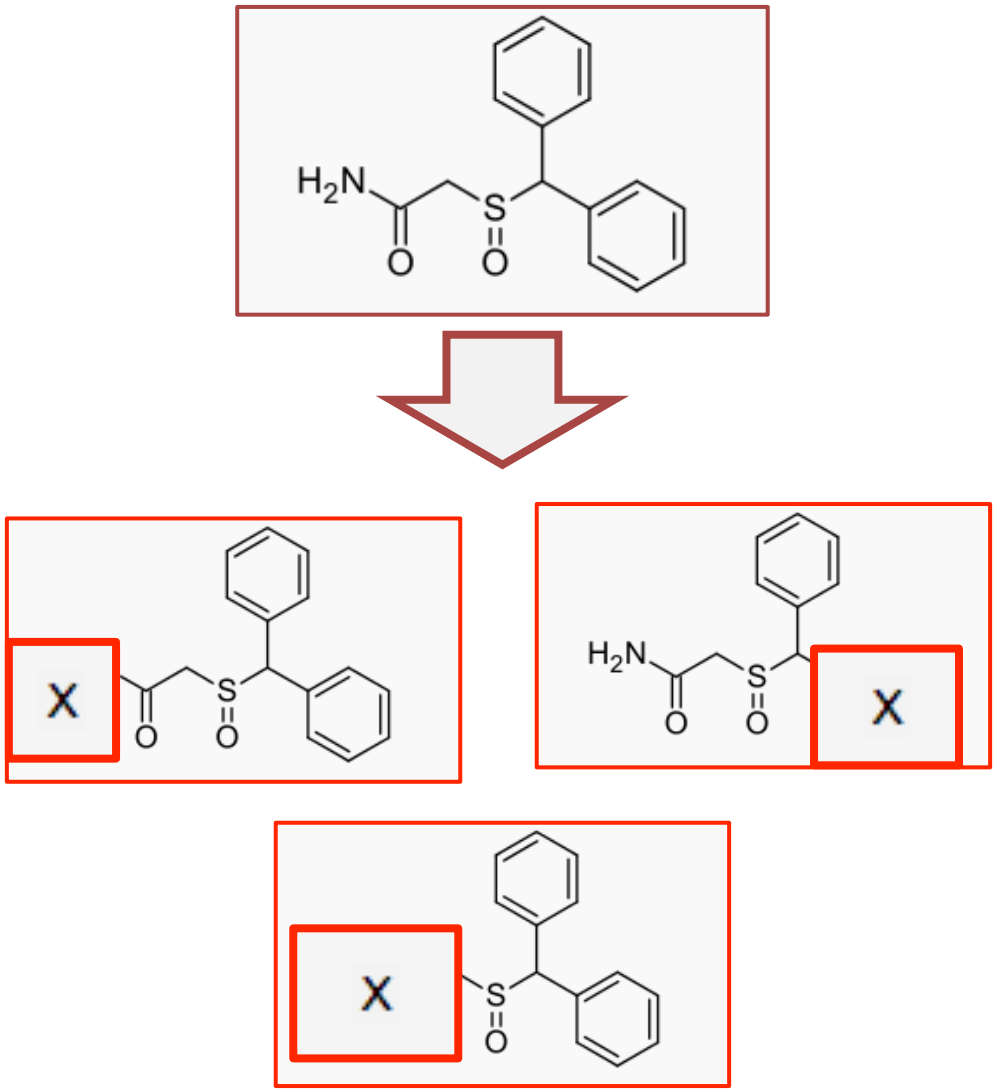
Directly affected by *Hdc*

AIM 2 – Identify new chemical compounds that regulate *Hdc*

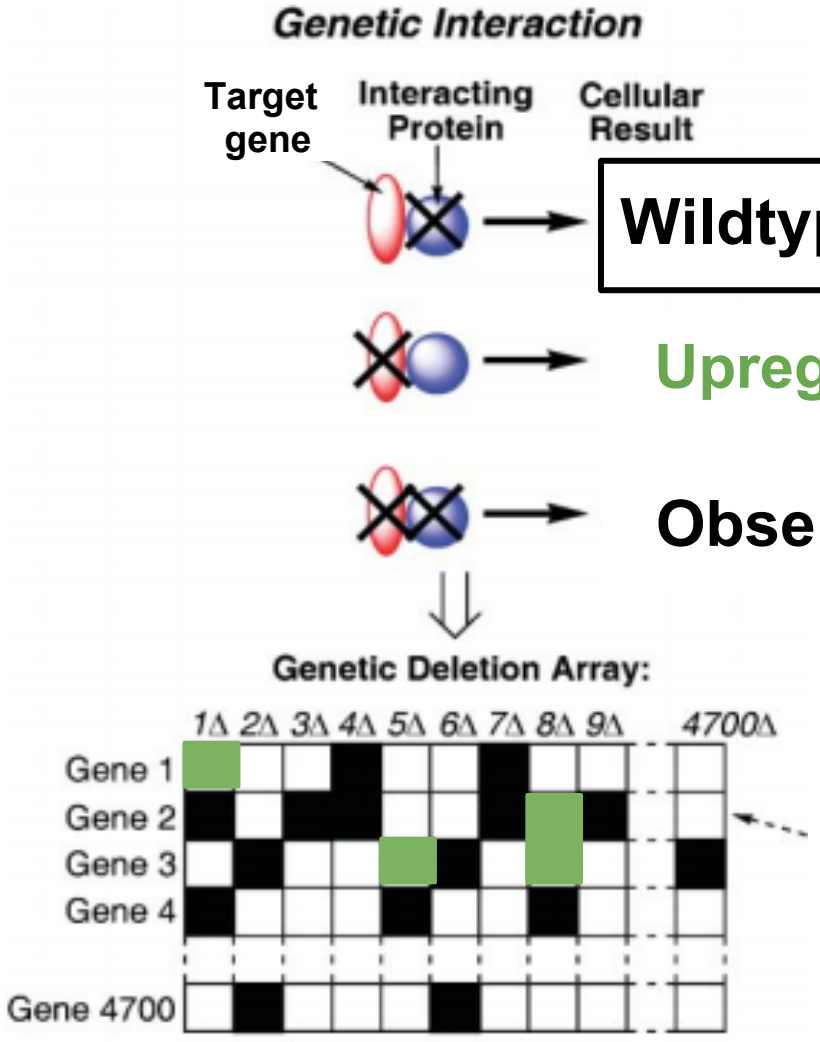
Focused library

Modafinil

Use: Narcolepsy
"Wakefulness"



Screen to find increased neurotransmitter levels



Wildtype phenotype

Upregulate neurotransmitter production

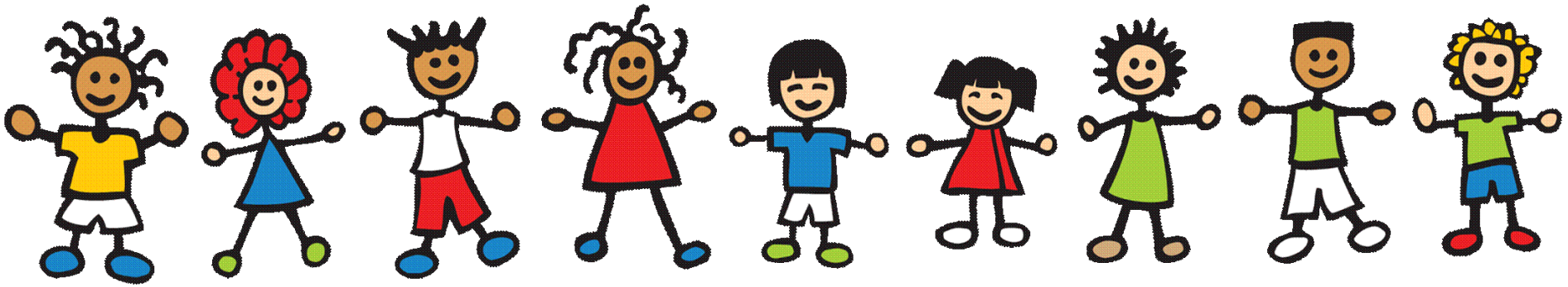
Observable phenotype

New safe treatments for children

HDC function restored

-increasing dopamine and histamine

-increase cell sensitivity to low amounts

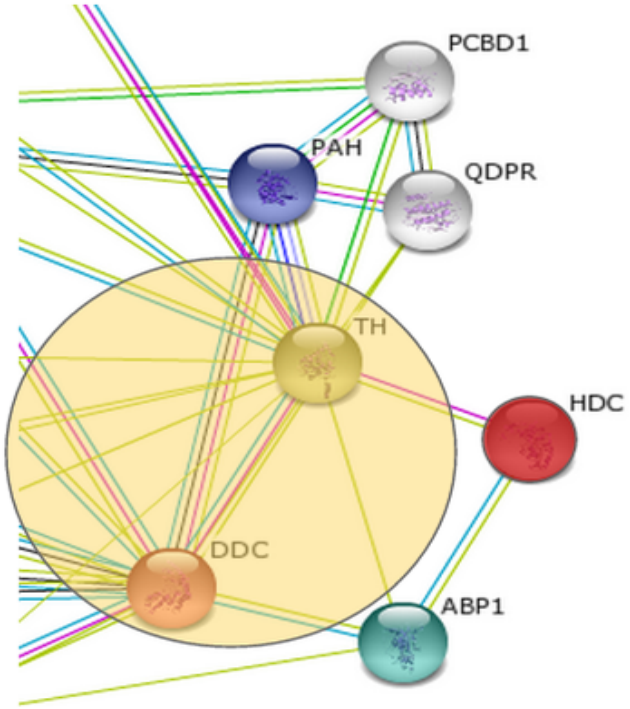


Future Directions

Phase I trials

mimic experiment in other model organisms

Experimental focus on protein domains



DDC

Peridoxal_deC

Biosynthetic process of dopamine and serotonin synthesis

Questions?

REFERENCES

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