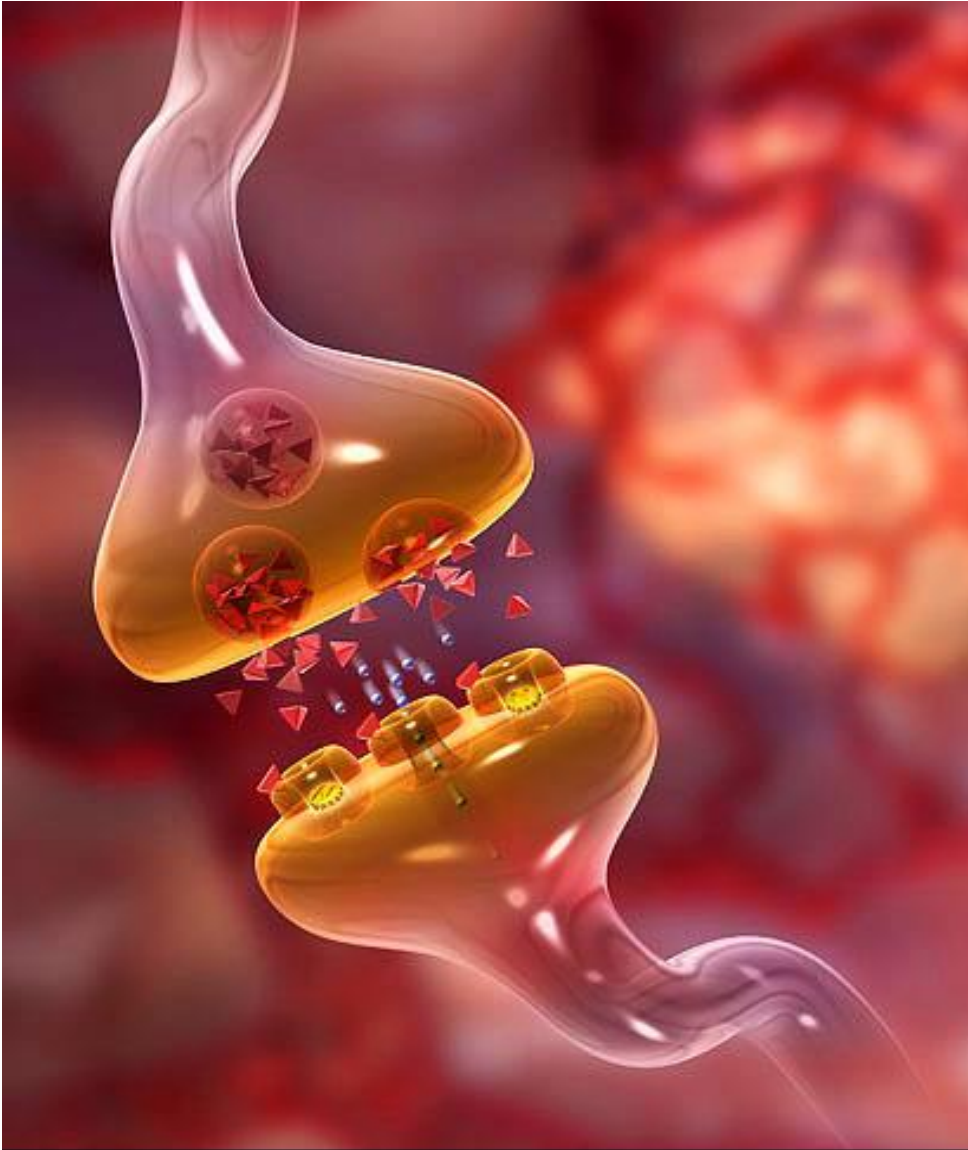


Anxiety and the GLO1 gene



By Emma Baar

University of Wisconsin-
Madison

What is an anxiety disorder?

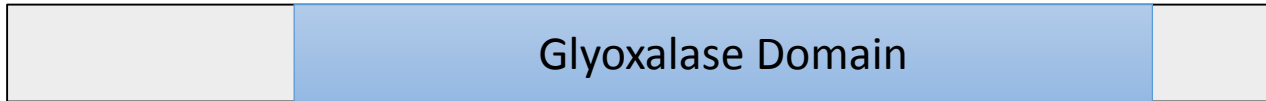


Current treatments: Therapy/Medication

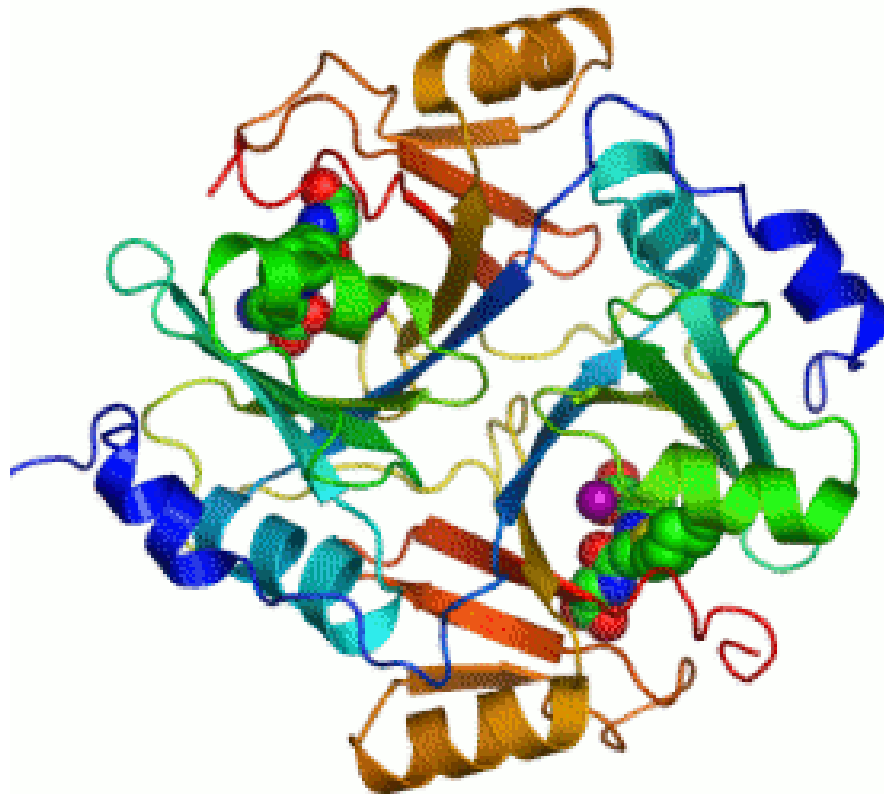


The GLO1 Gene

Human GLO1



184aa



What does GLO1 do?

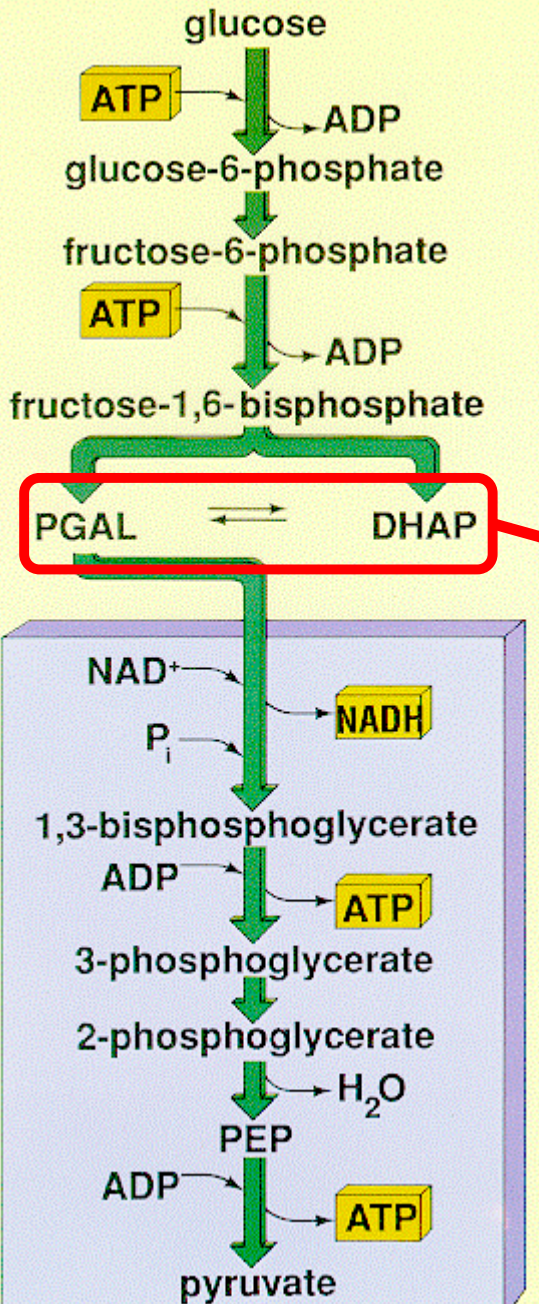
Methylglyoxal
(MG)



GLO1

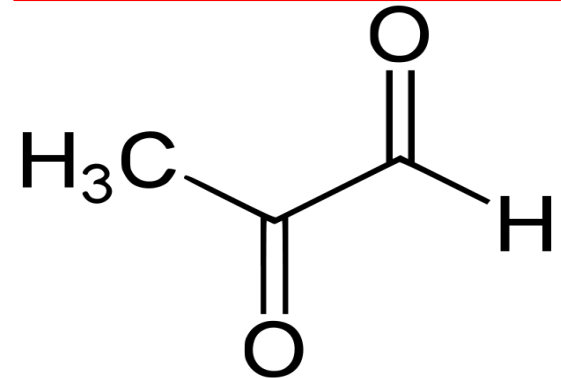


D-lactate



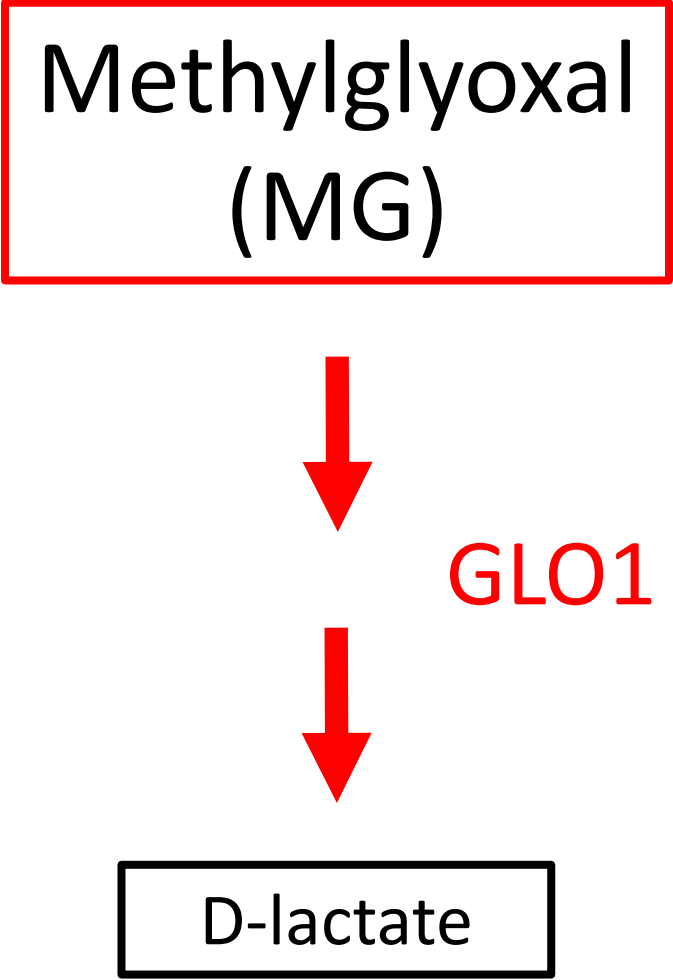
MG is a byproduct of glycolysis

Methyglyoxal (MG)



What does GLO1 do?

Methylglyoxal
(MG)



```
graph TD; MG[Methylglyoxal (MG)] -- GLO1 --> DL[D-lactate];
```

GLO1

D-lactate

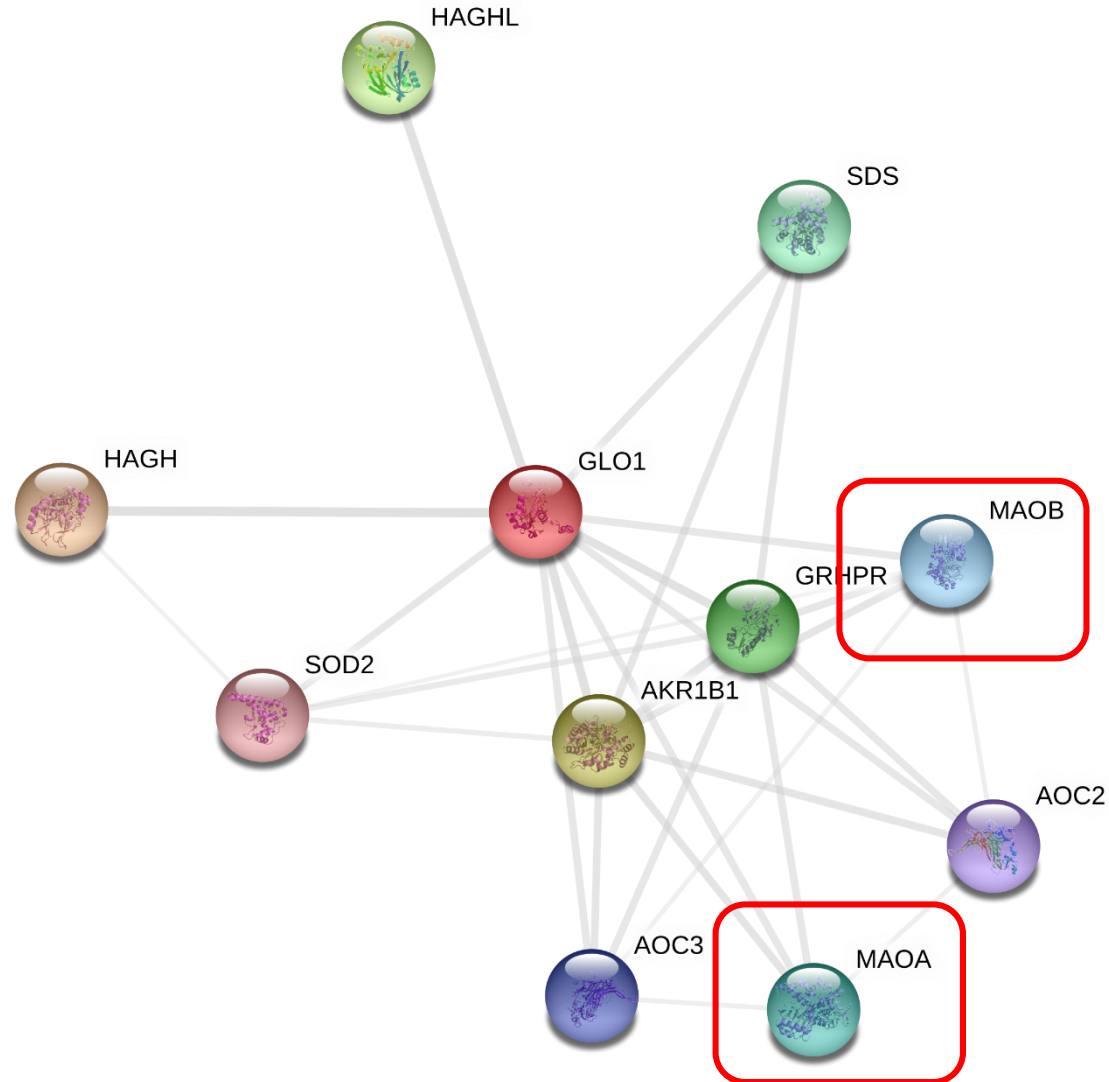
GLO1 substrate works like anti-anxiety medication



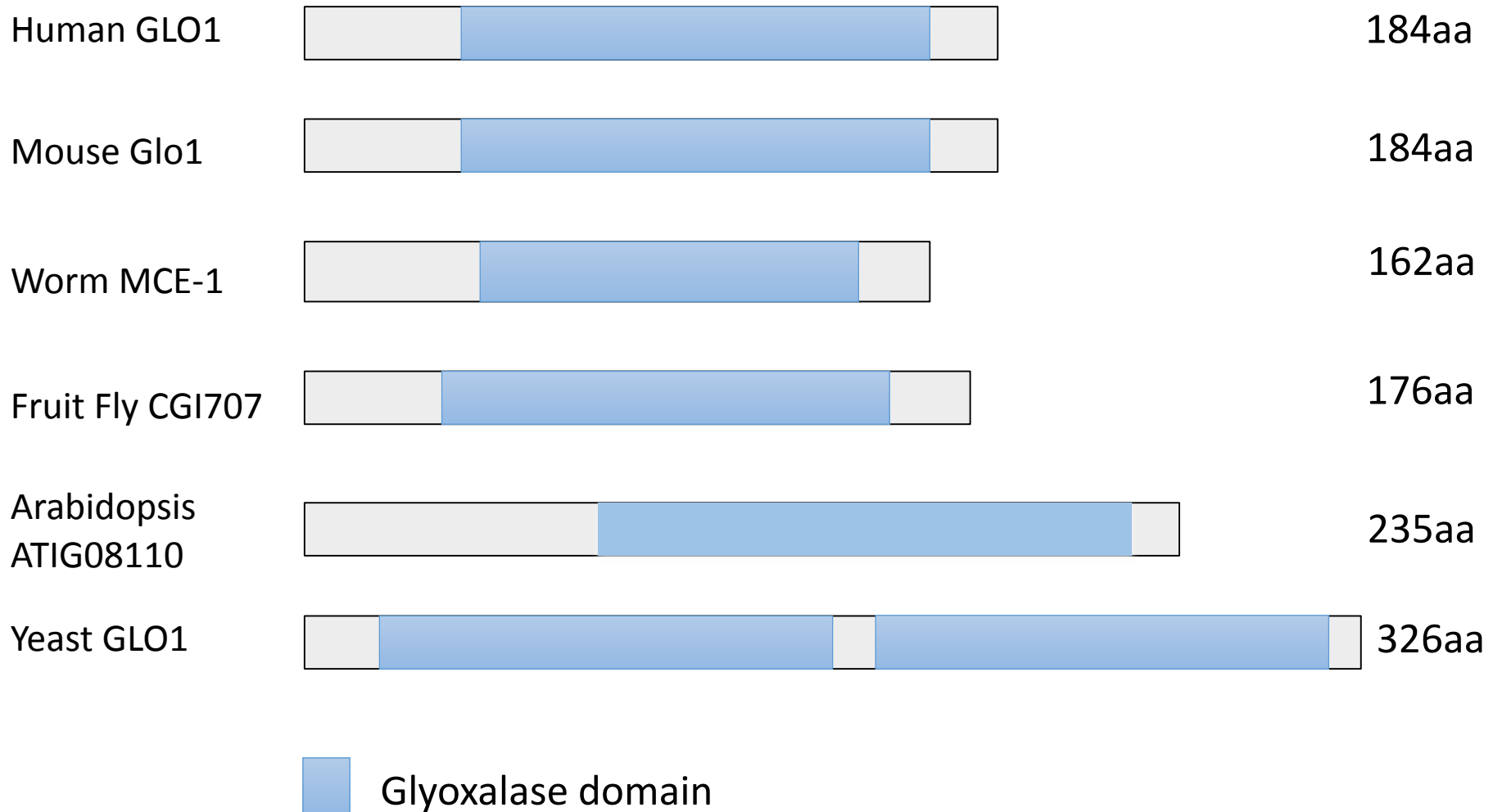
MG



Proteins that regulate Dopamine interact with GLO1

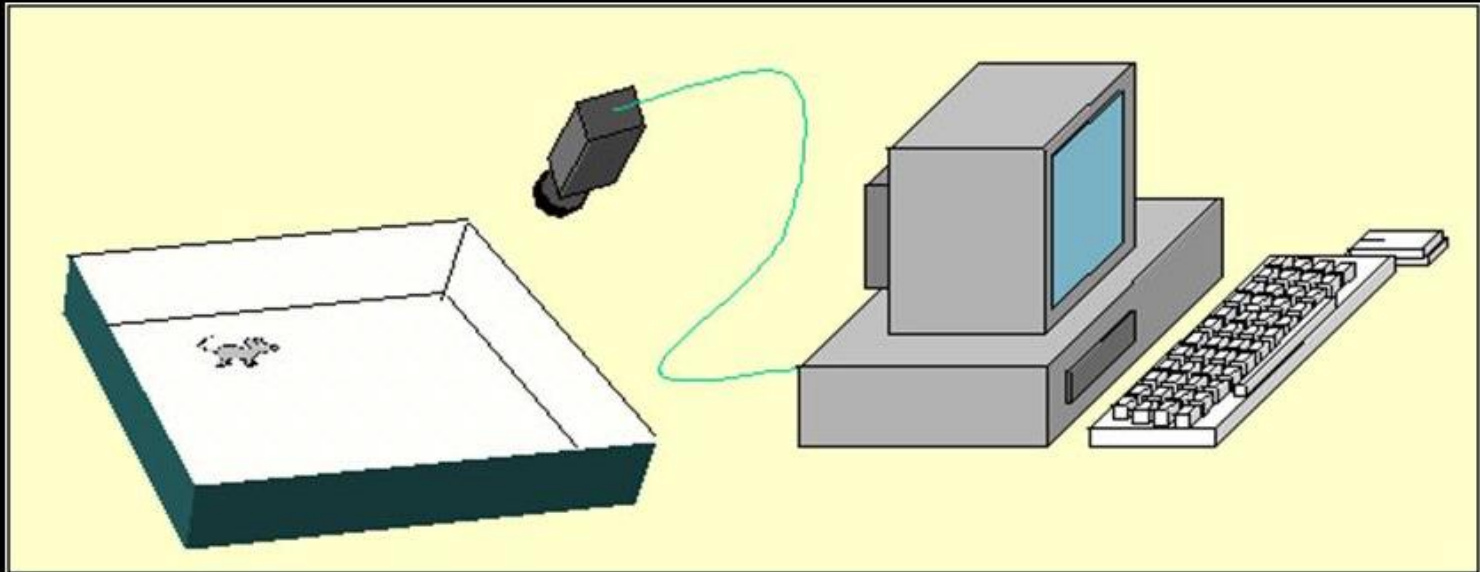


GLO1 is well conserved

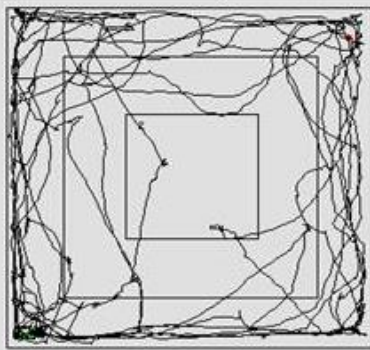


Mice exhibit anxious behavior when overexpressing GLO1 gene

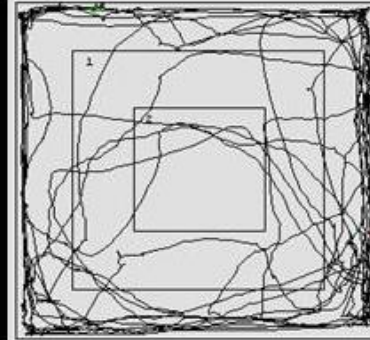
Open Field Test



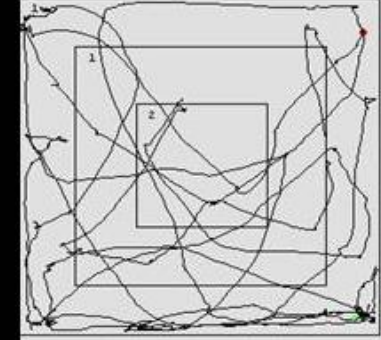
Animal No 35943	Group 310-N 069F
--------------------	---------------------



Animal No 35943	Group 310-N 069F
--------------------	---------------------



Animal No 35748	Group 322-C 029F
--------------------	---------------------



Elevated Plus Maze



MG is in manuka honey



Used as an antibacterial

Manuka honey may be a natural way to decrease anxiety!



Hypothesis 1:

MG in the diet will reduce anxiety while
GLO1 retains normal function

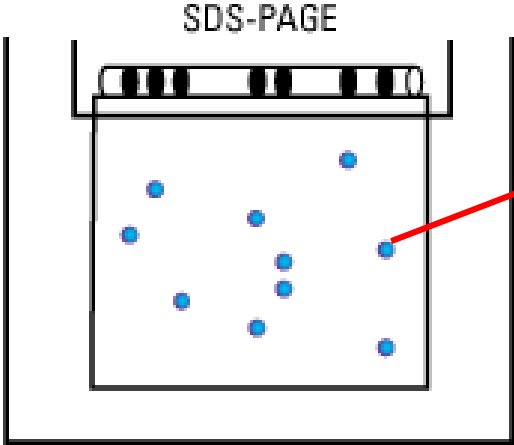
Mice on diets with and without manuka honey



2D gel comparison and MALDI-TOF MS of GLO1 - Expected Results



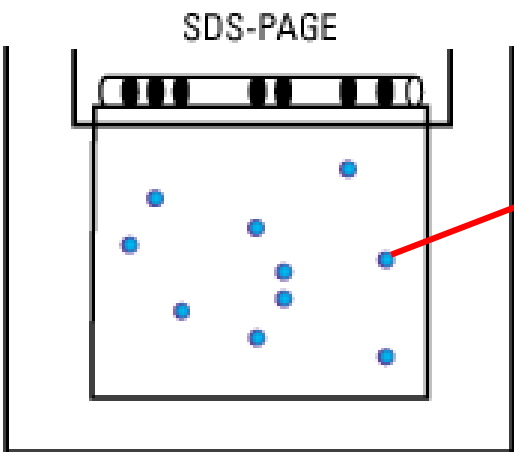
Control



GLO1



Honey diet



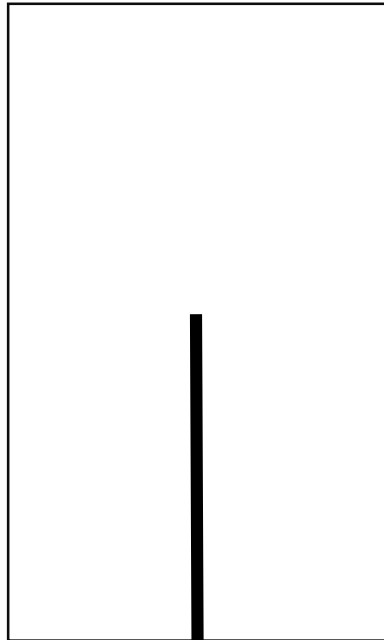
GLO1

Additional Points of Interest

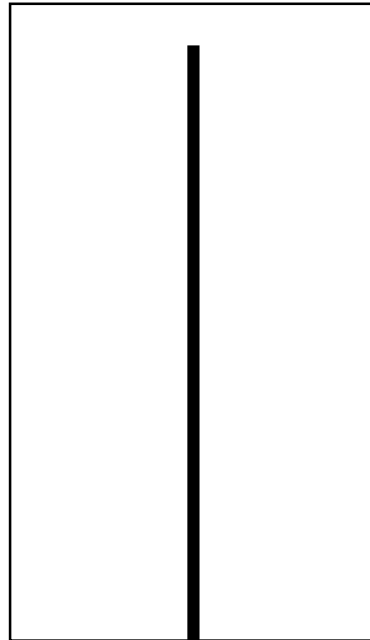


Additional Points of Interest

HPLC of MG



Control



Manuka
Honey Diet

Mouse Behavior



Further Studies – GLO1 in yeast

Human GLO1

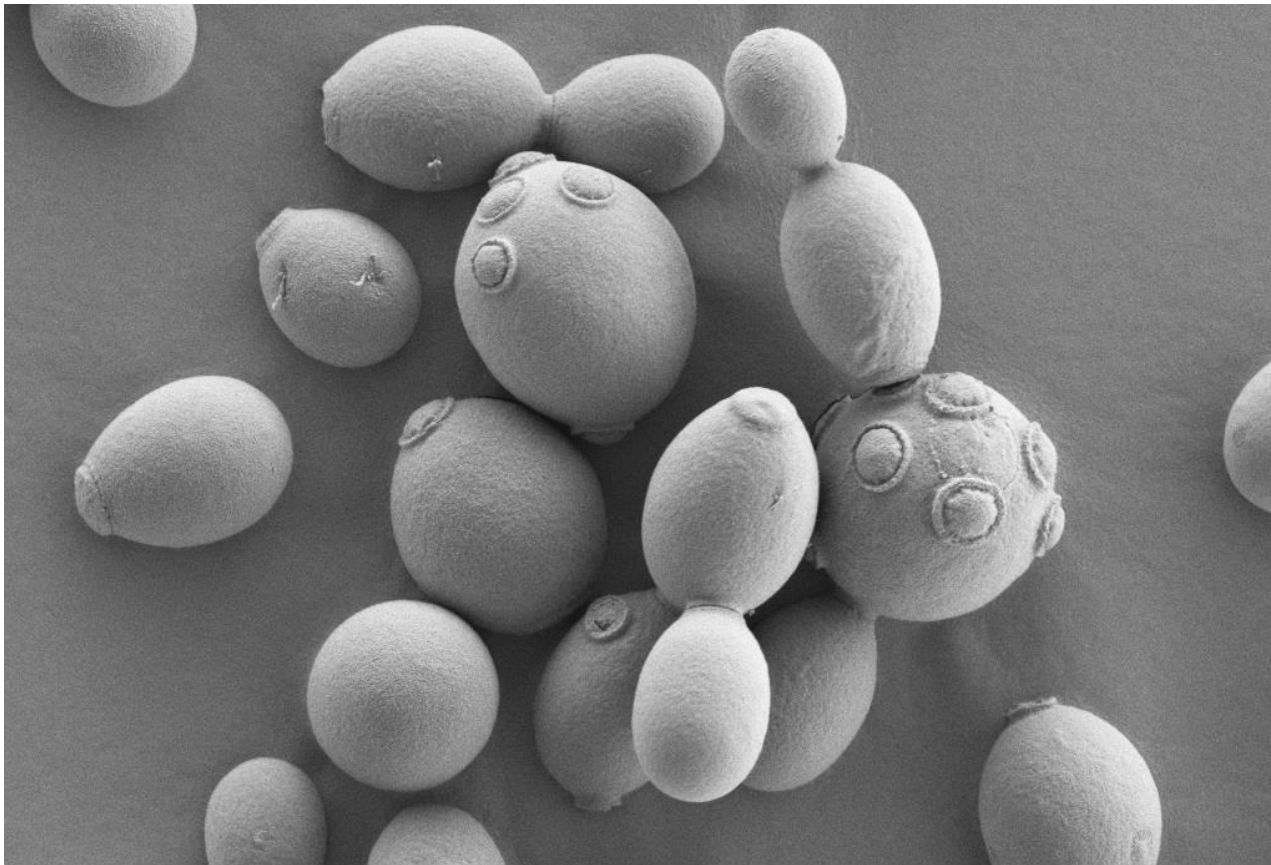


184aa

Yeast GLO1



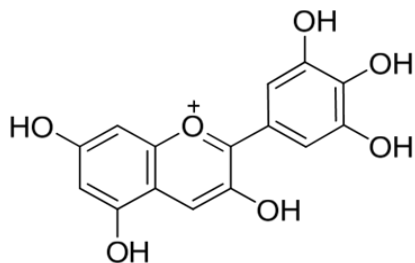
326aa



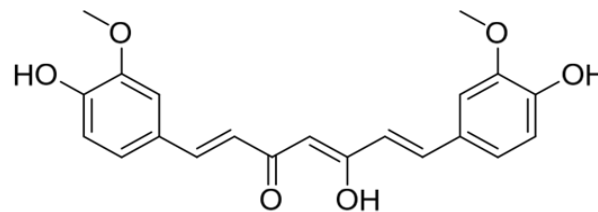
Hypothesis 2:

Slightly decreasing GLO1 can decrease anxiety without MG becoming toxic

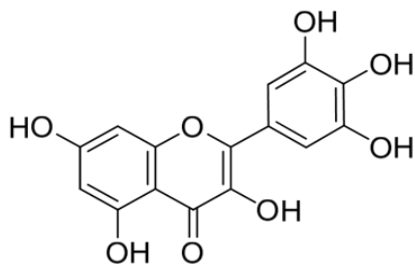
GL01 small molecule inhibitors



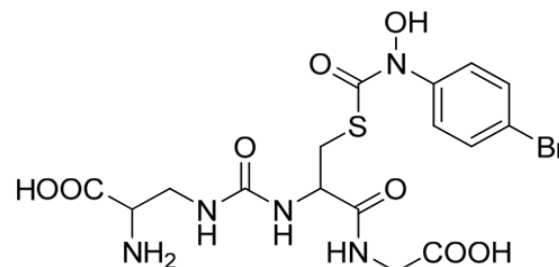
Delphinidin



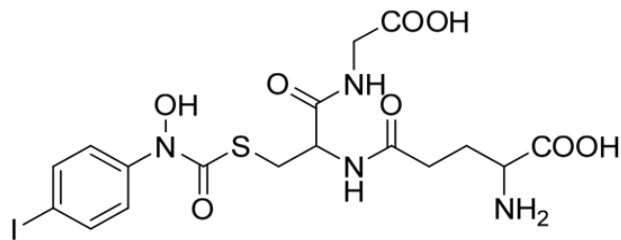
Curcumin



Myricetin



2-amino-3-(3-(3-((4-bromophenyl)(hydroxy)carbamoylthio)-1-(carboxymethylamino)-1-oxopropan-2-yl)ureido)propanoic acid



2-amino-5-(1-(carboxymethylamino)-3-(hydroxy(4-iodophenyl)carbamoylthio)-1-oxopropan-2-ylamino)-5-oxopentanoic acid

Microarray – GLO1 decreases with inhibitors

Dose of Inhibitor				
	None	Low	Medium	High
Control	Red	Red	Red	Red
Drug 1	Red	Orange	Yellow	Light Yellow
Drug 2	Red	Orange	Light Yellow	Very Light Yellow
Drug 3	Red	Orange	Yellow	Light Yellow

Decreasing GLO1 

Future Directions

- Regulation of GLO1 expression
- Phenotypes in other model organisms
- MAOA and MAOB



Questions?



References

- Al-Balas Q, Hassan M, Al-Oudat B, Alzoubi H, Mhaidat N, Almaaytah A. Generation of the First Structure-Based Pharmacophore Model Containing a Selective “Zinc Binding Group” Feature to Identify Potential Glyoxalase-1 Inhibitors. *Molecules*. 2012; 17(12):13740-13758.
- "Anxiety Disorders." *National Institute of Mental Health*. Retrieved February 5, 2013 from <http://www.nimh.nih.gov/health/topics/anxiety-disorders/index.shtml>
- Distler M. G., Plant L. D., Sokoloff G., Hawk A. J., Aneas I., Wuenschell G. E., et al. (2012). Glyoxalase 1 increases anxiety by reducing GABAA receptor agonist methylglyoxal. *J. Clin. Invest.* 122, 2306–2315. doi: 10.1172/JCI61319
- Distler, M. G., and A. A. Palmer. "Role of Glyoxalase 1 (Glo1) and Methylglyoxal (MG) in Behavior: Recent Advances and Mechanistic Insights." *PubMed* (2012): n. pag. *NCBI*. Web. 7 Feb. 2013. doi: 10.3389
- Altschul S.F., Gish W., Miller W., Myers E.W. and Lipman D.J. (1990) Basic local alignment search tool. *J. Mol. Biol.* 215: 403-410.
- Sigrist CJA, de Castro E, Cerutti L, Cuče BA, Hulo N, Bridge A, Bougueleret L, Xenarios I. *New and continuing developments at PROSITE*. *Nucleic Acids Res.* 2012; doi: 10.1093/nar/gks1067
PubMed: [23161676](#) [\[Full text\]](#) [\[PDF version\]](#)
- "Glyoxalase System." Clinical Sciences Research Institute. Warwick. Retrieved February 28, 2013 from http://www2.warwick.ac.uk/fac/med/research/csri/proteindamage/researchinterest/glyoxalase_i_inhibitors
- "Percent Identity of Genomic DNA Sequences, of Introns and Exons, and of Amino Acid Sequences." N.p., n.d. Web. 21 Feb. 2013.
- STRING (Search Tool for the Retrieval of Interacting Genes/Proteins). N.p., n.d. Web. 23 Apr. 2013.