

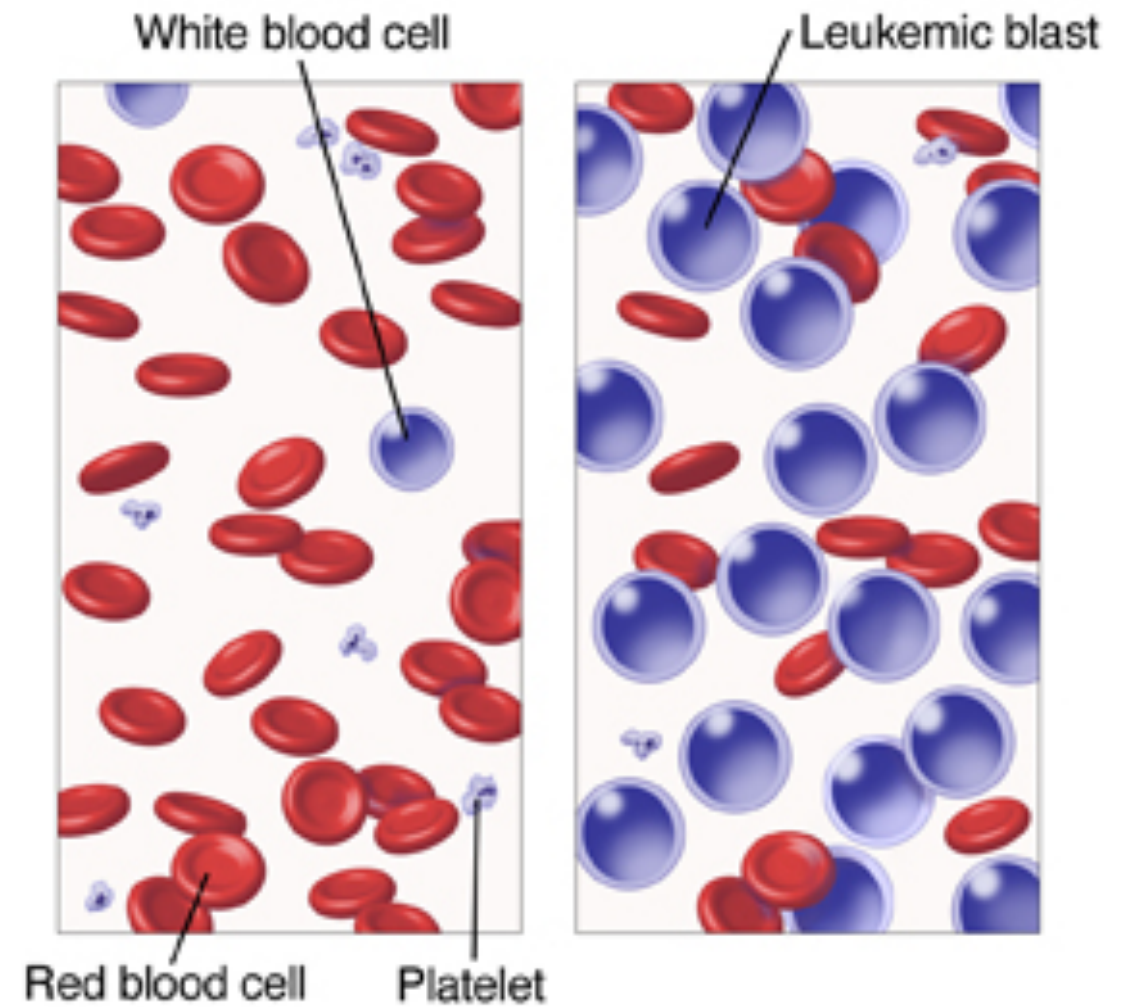


# Emberger Syndrome and GATA2

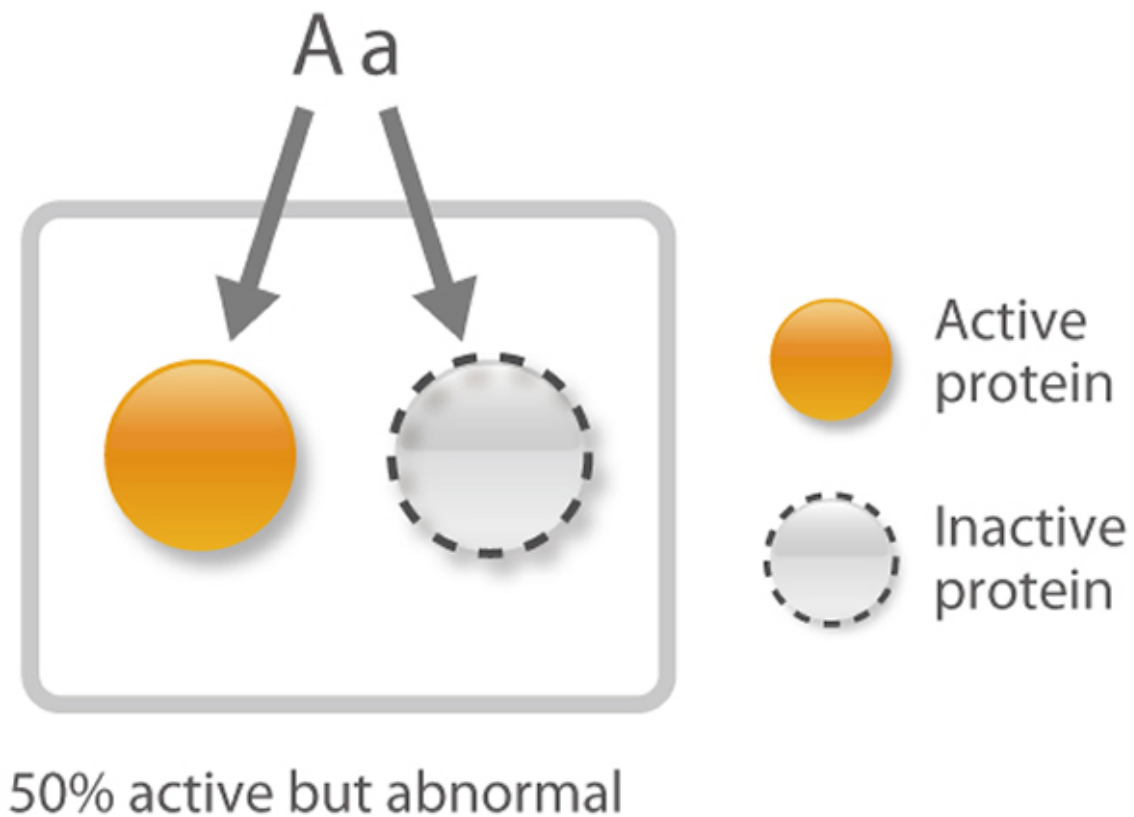
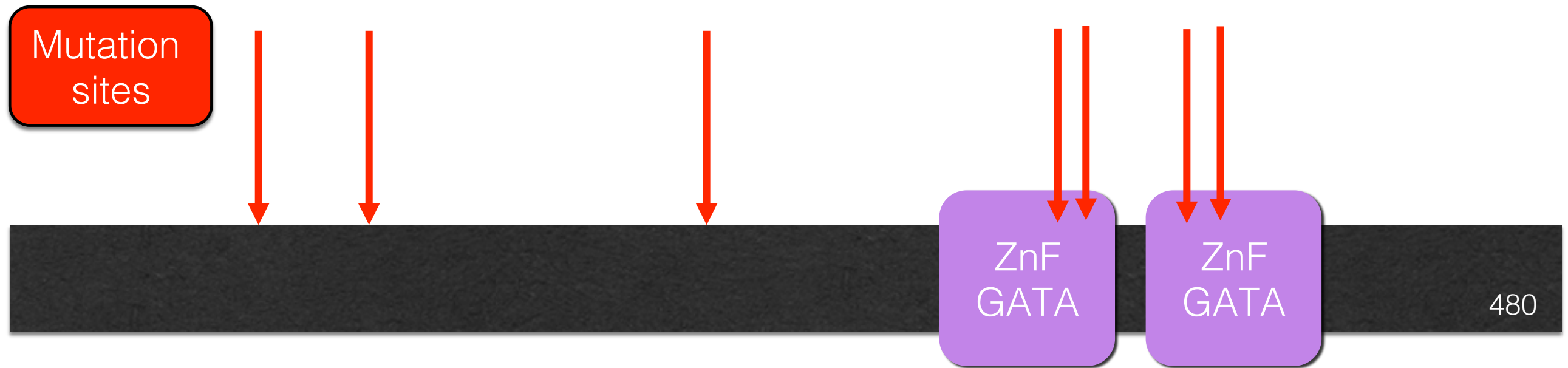
By: Nikita Tongas



# What is Embarger Syndrome (ES)?



# GATA2 association with ES





# What is the role of GATA2?

## *Gene Ontology*

Cellular  
Components

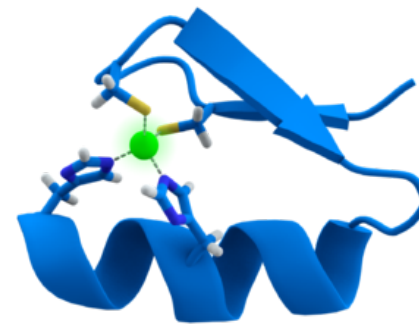
Molecular  
Functions

Biological  
Process

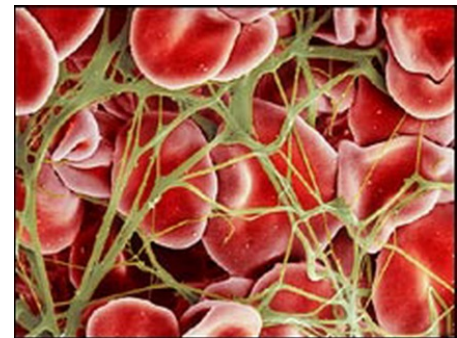


Nucleoplasm

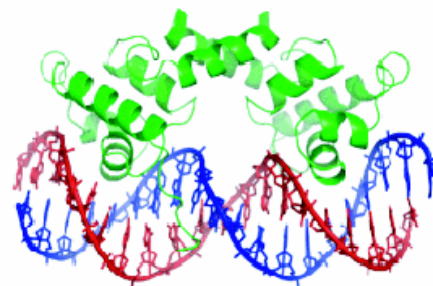
Zinc Ion  
Binding



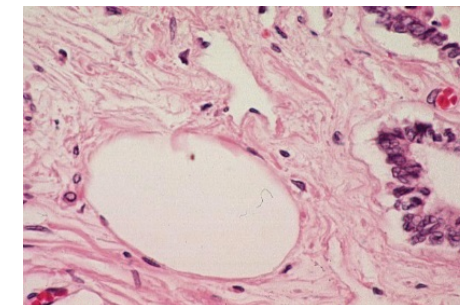
Hemostasis



Protein  
Complex

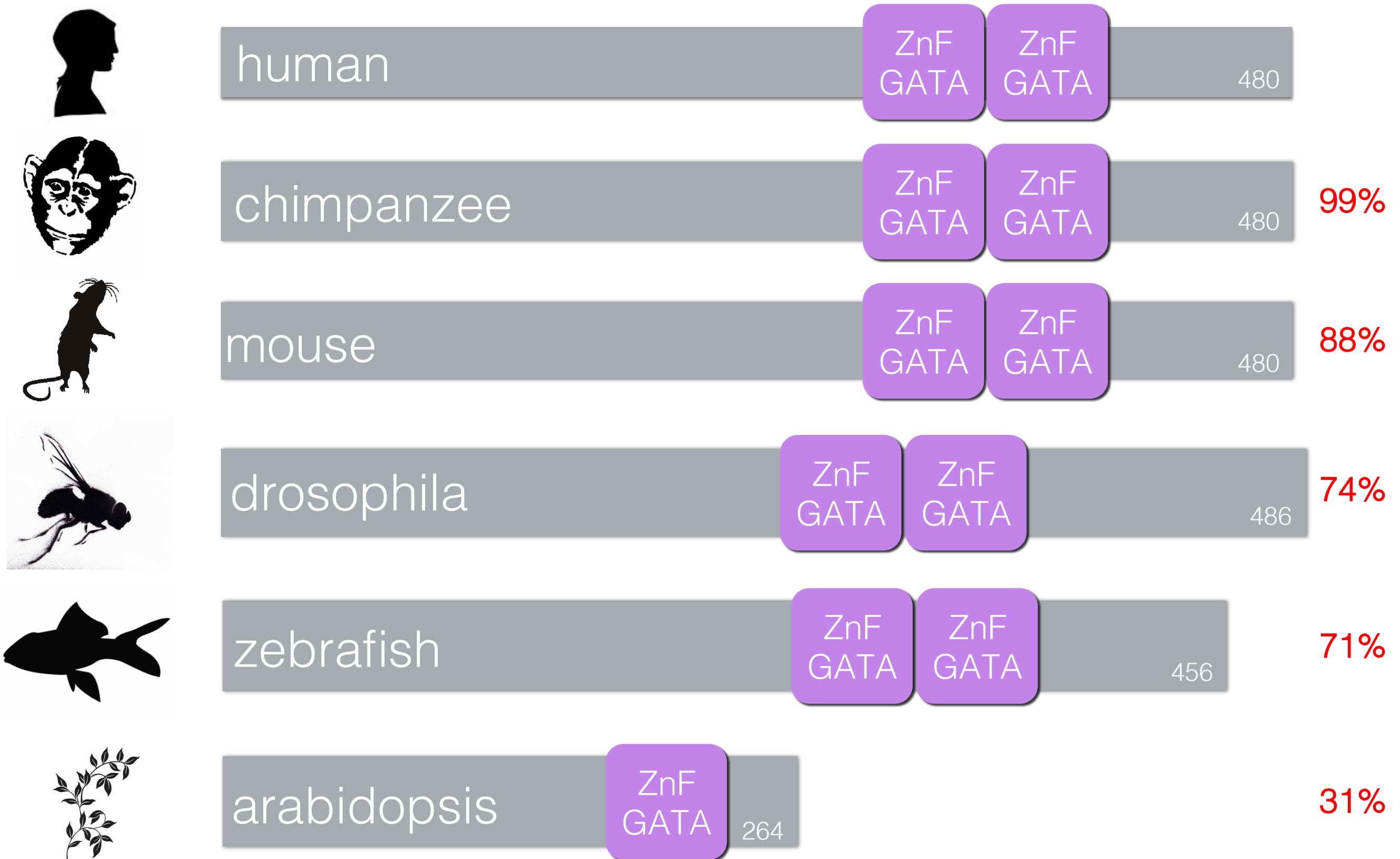


Transcription  
Factor Binding

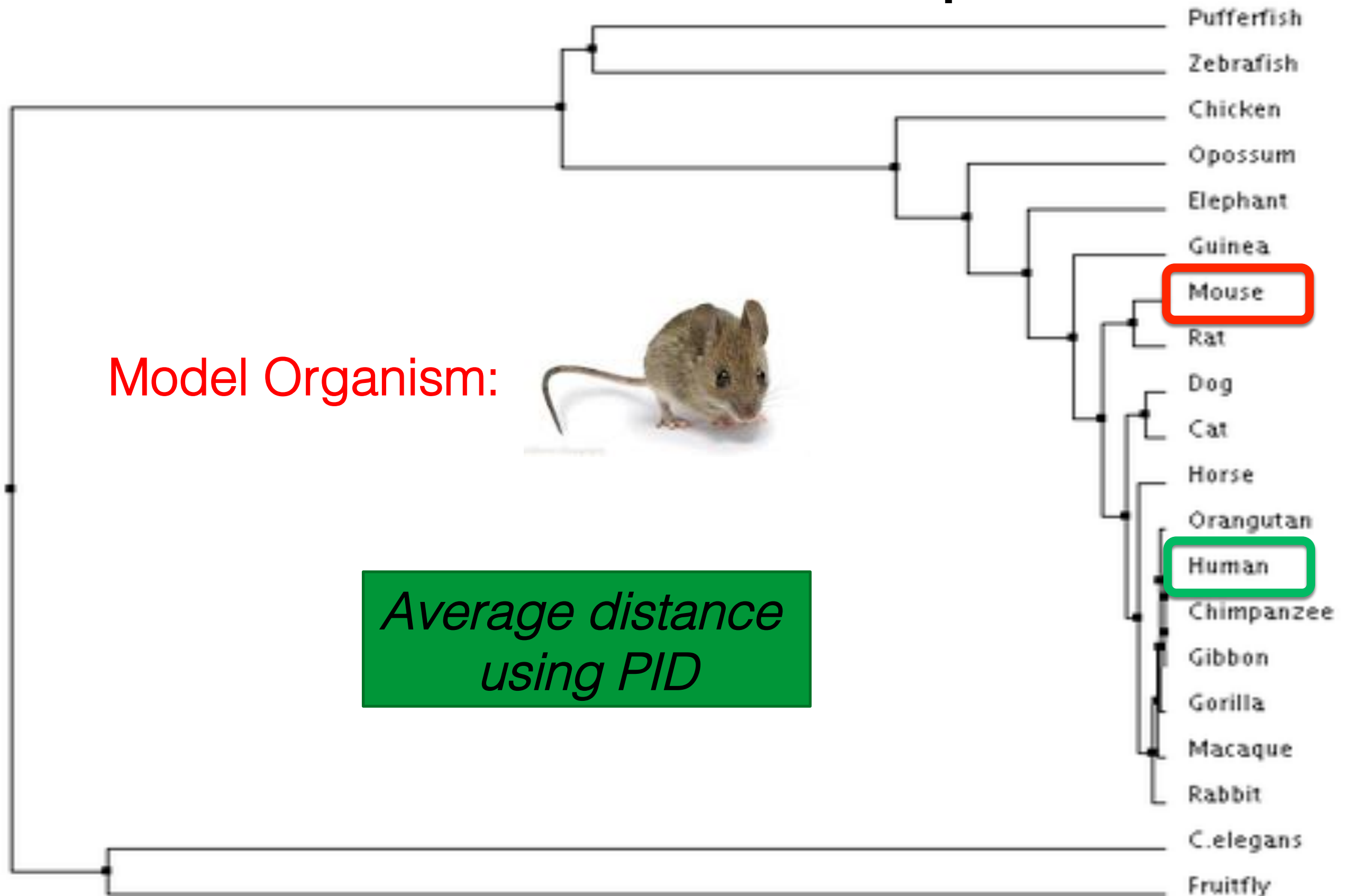


Regulation of  
body fluid  
levels

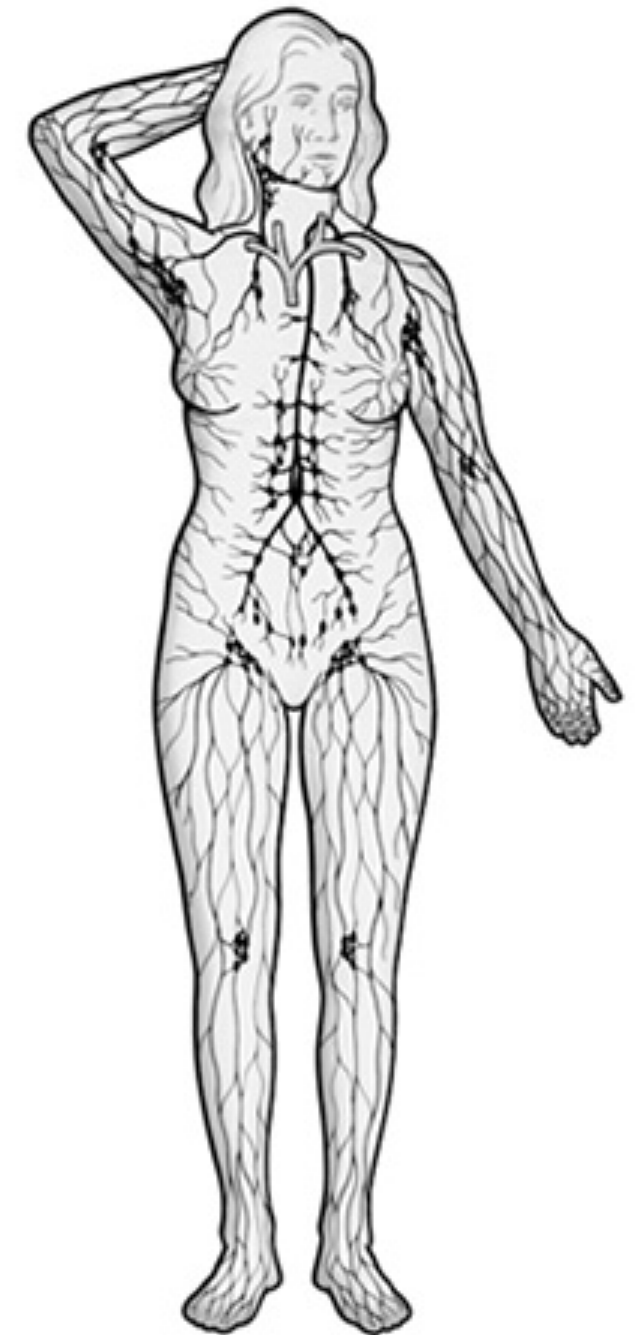
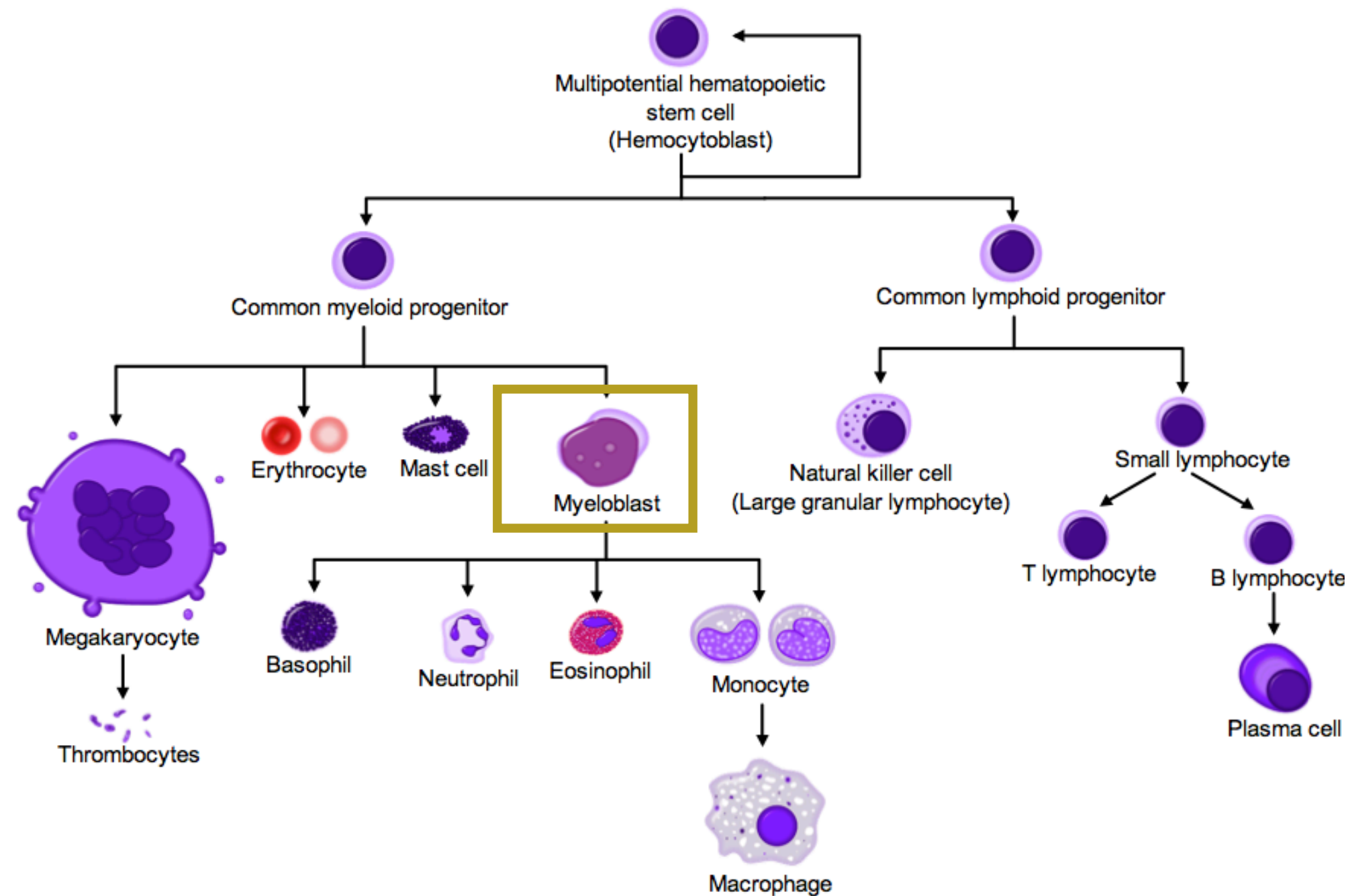
# How well conserved is GATA2?



# GATA2 across species



# What is the relationship between **GATA2** and **ES**?



**Goal:** To understand the pathology underlying **Emberger Syndrome** and **GATA2** haploinsufficiency

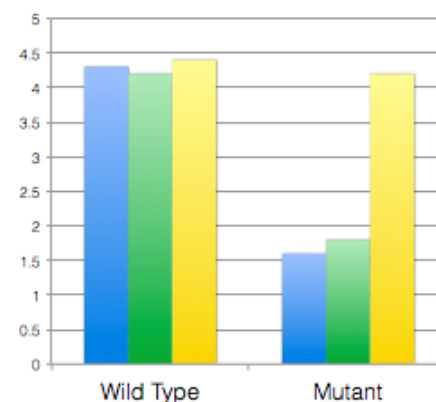
# Hypothesis: Mutations in *GATA2* regulate genes that affect the function of hematopoietic stem cells



Aim 1: Identify proteins that interact with *GATA2*

Aim 2: Identify interacting proteins that are differentially expressed in mutant mice

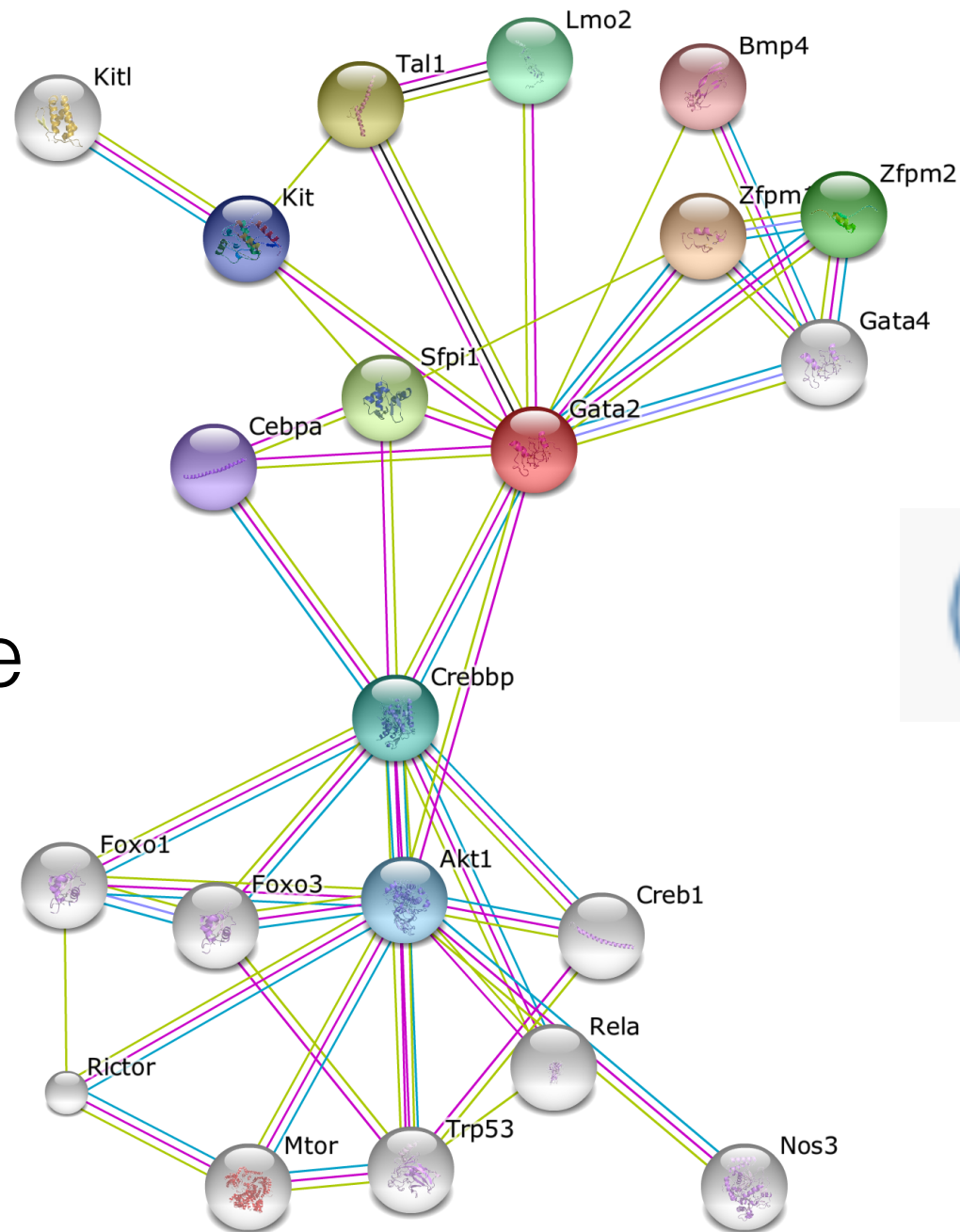
Aim 3: Determine if *GATA2* interacting proteins cause *ES* phenotypes



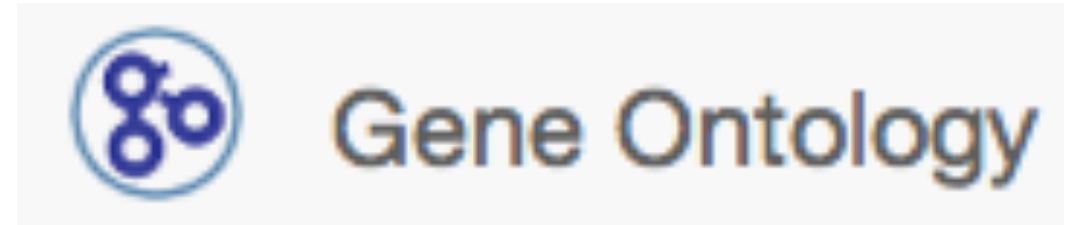


# Aim 1: Identify proteins that interact with **Gata2** that regulate hematopoietic function

## Approach:

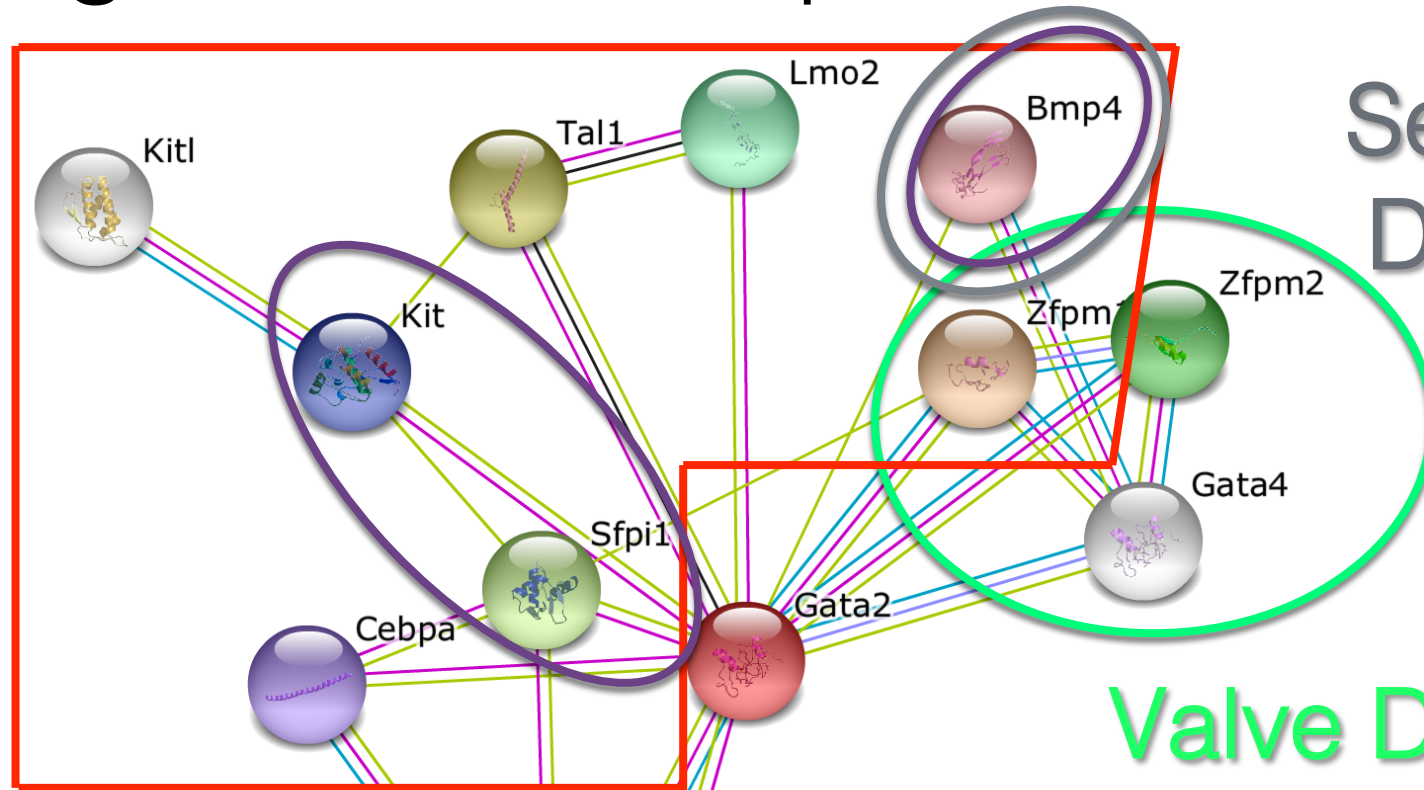


STRING  
database



# Aim 1: Identify proteins that interact with **Gata2** that regulate hematopoietic function

**Hematopoiesis**

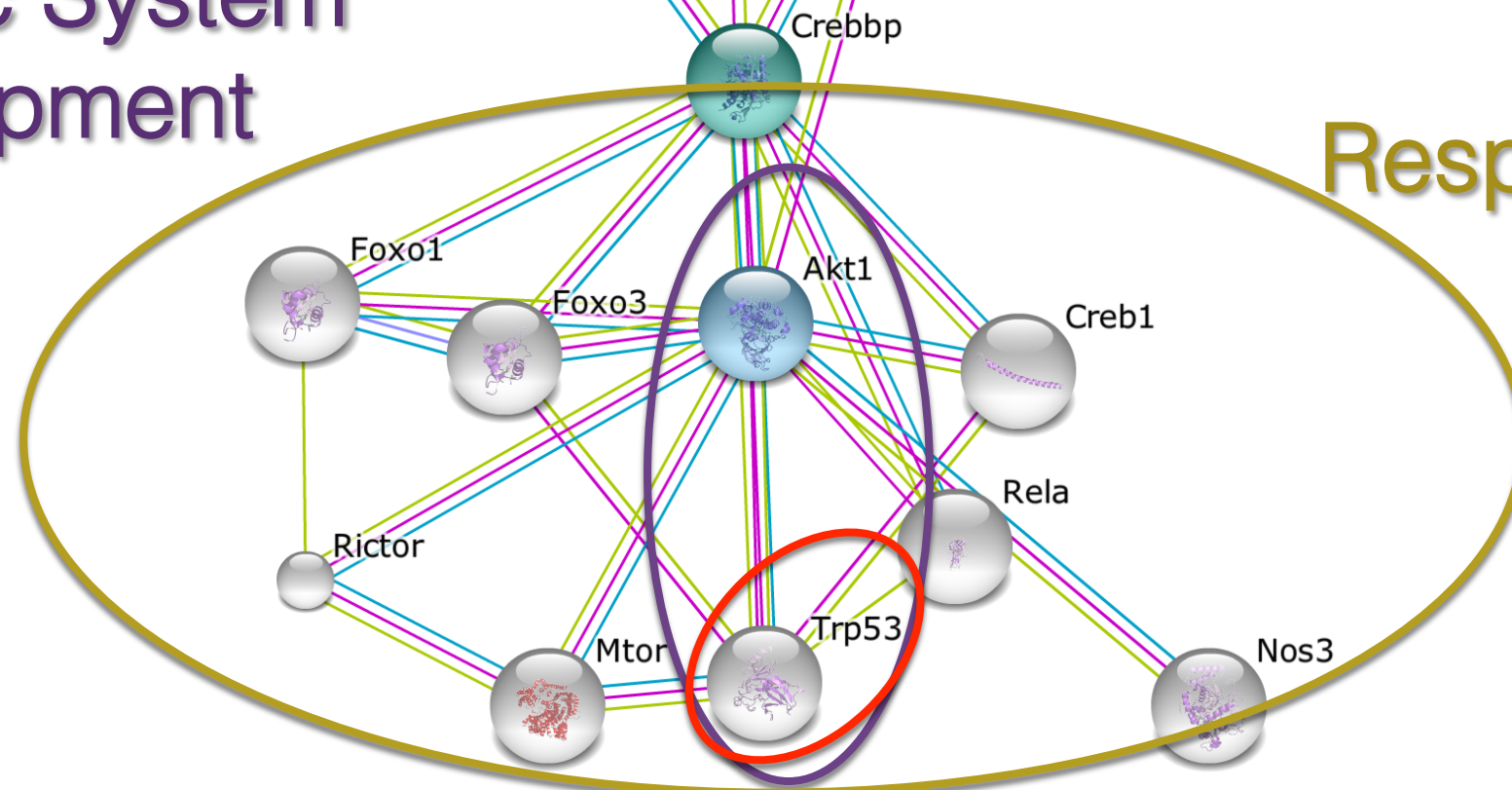


**Sensorineural Development**

**Valve Development**

**Lymphatic System Development**

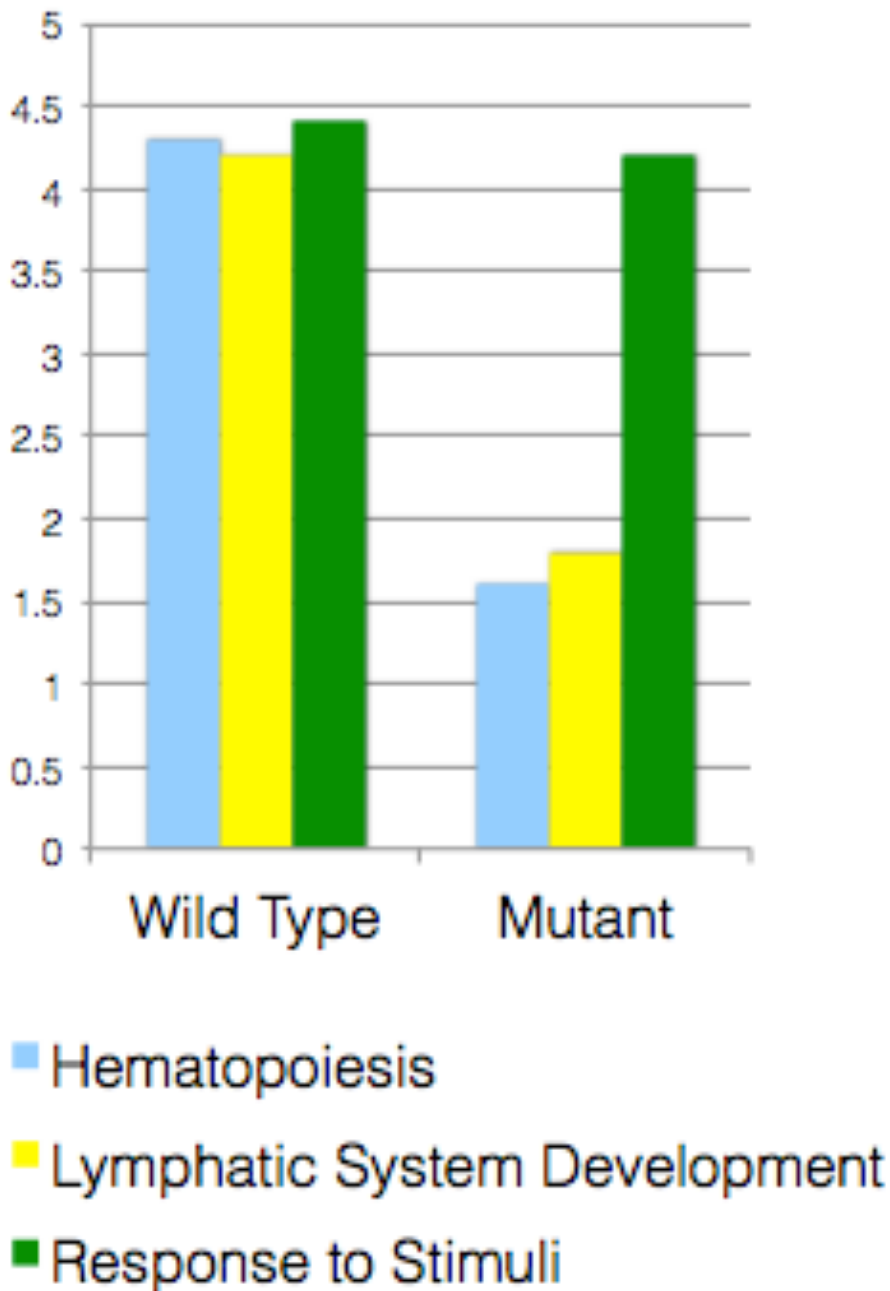
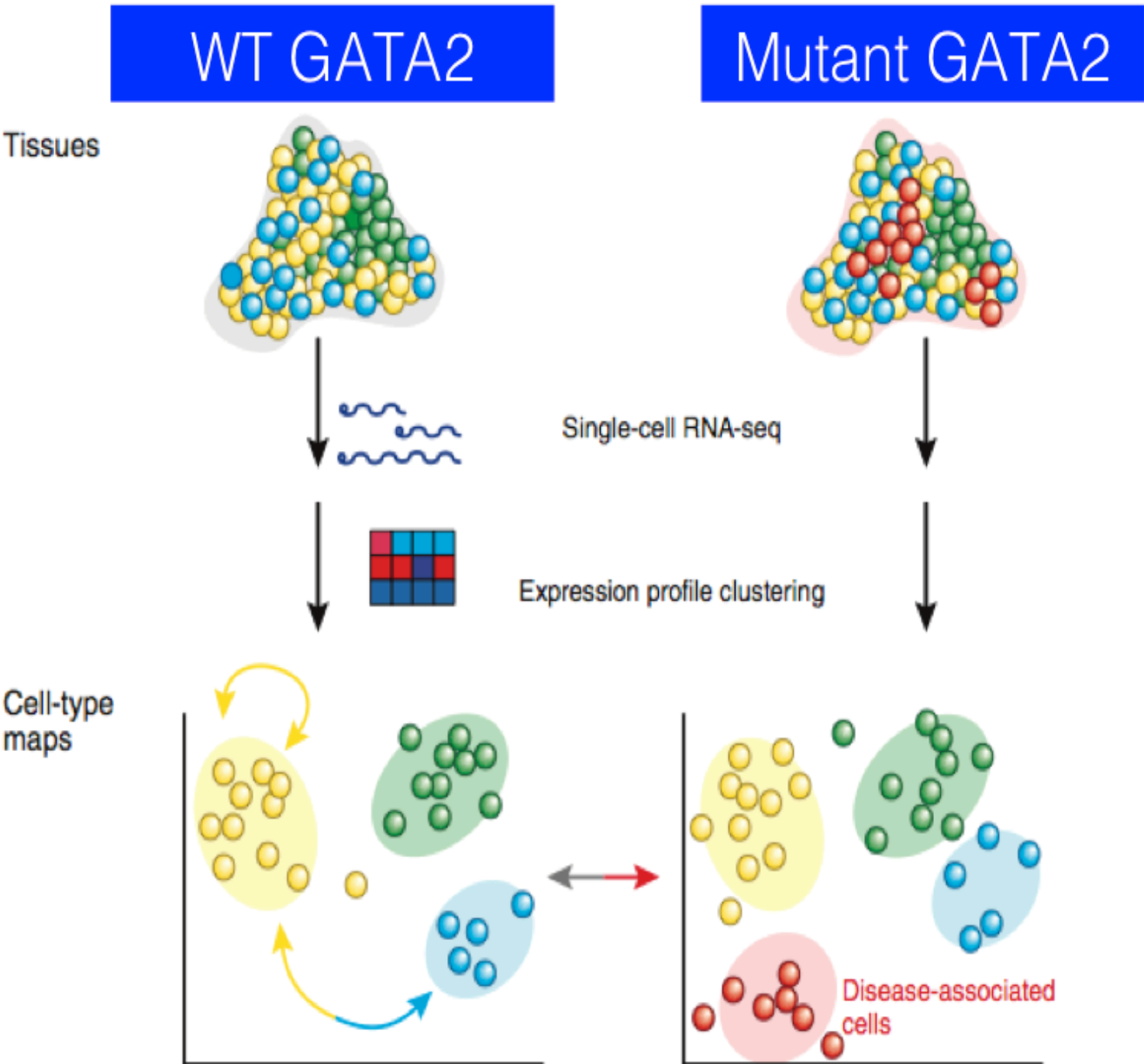
**Response to Stimuli**



# Aim 2: Identify **GATA2** interacting proteins that are differentially expressed in mutant mice

Approach: RNA Sequencing

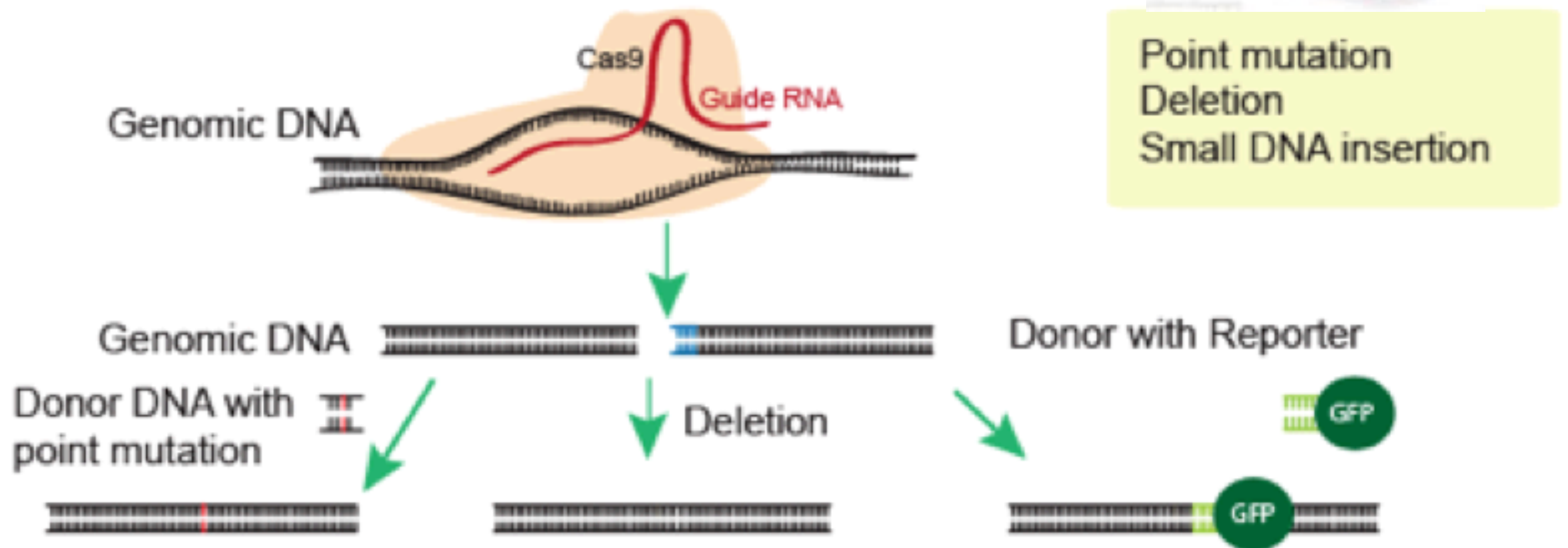
Predicted Results:





# Aim 3: Determine if differentially expressed interacting proteins cause **ES** phenotypes

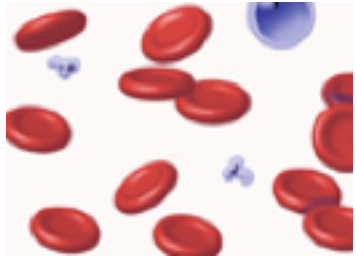
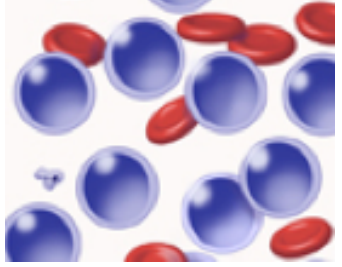


Approach: CRISPR/Cas9 Knockout



**ES** Phenotypes: Lymphedema & high myeloblast count

# Aim 3: Determine if differentially expressed interacting proteins cause ES phenotypes

## Predicted Results:

<i>Function of gene</i>	<i>Wild Type</i>	<i>Wild Type Knockout</i>
Hematopoiesis	 <p>Normal myeloblast count</p>	 <p>Abnormal myeloblast count</p>
Lymphatic System Development	 <p>No Lymphedema</p>	 <p>Lymphedema</p>

# Future Directions

## Target-based



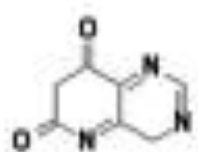
*Overexpression of  
a protein of interest*

↓ Add compounds



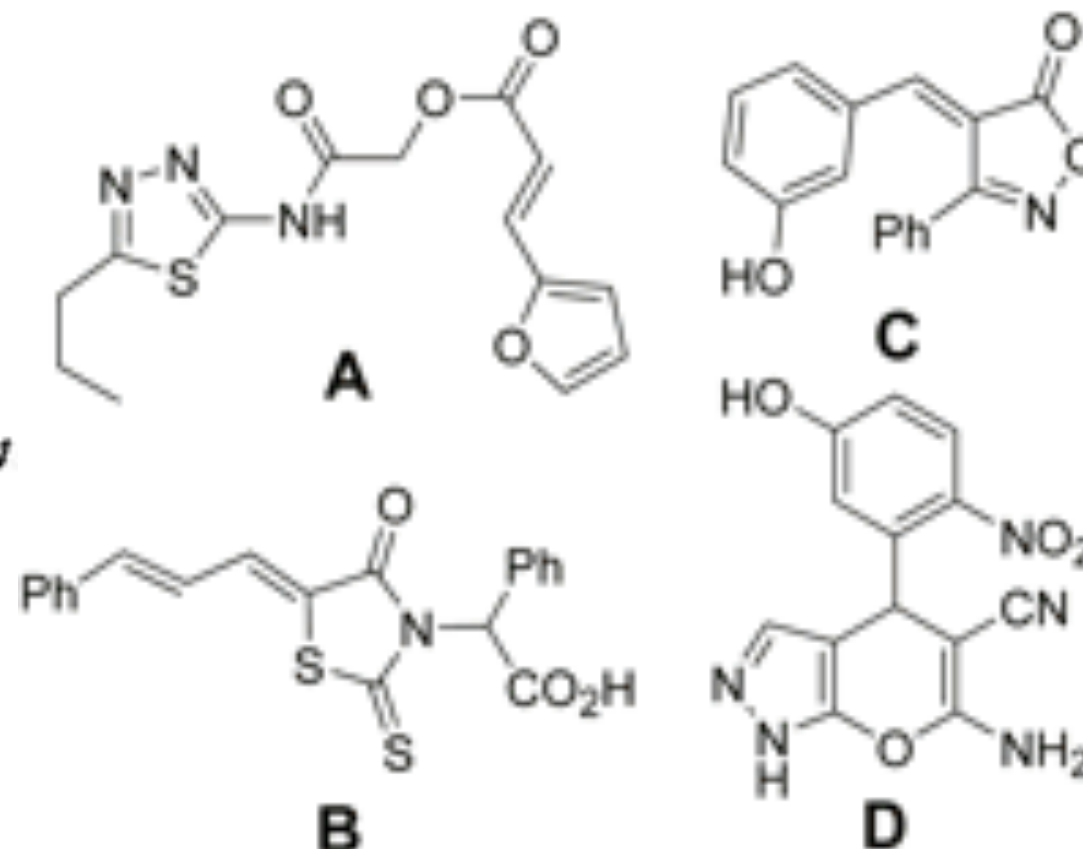
*Screen for compounds that  
bind/modulate protein function*

↓ Add compounds to  
cells/organisms



*Assay for  
phenotypic outcome*

## Chemical Genetics





# References

## Images

<http://www.lymphedemablog.com>

<http://www.fairview.org/healthlibrary/Article/40351>

[http://en.wikipedia.org/wiki/Dominance\\_\(genetics\)](http://en.wikipedia.org/wiki/Dominance_(genetics))

<http://tenrandomfacts.com/category/health-and-human/page/4/>

[http://upload.wikimedia.org/wikipedia/commons/archive/2/2b/20120908142012!Diagram\\_cell\\_nucleus\\_no\\_text.svg](http://upload.wikimedia.org/wikipedia/commons/archive/2/2b/20120908142012!Diagram_cell_nucleus_no_text.svg)

[http://en.wikipedia.org/wiki/Zinc\\_finger](http://en.wikipedia.org/wiki/Zinc_finger)

<https://encrypted-tbn3.gstatic.com/images?q=tbn:ANd9GcR873GcdzhI2A2MBRy0o2OB629VlibVIG76Z6Vdxm37rnKils34>

<http://www.thp.uni-koeln.de/~berg/figs/bindingsite3.gif>

<http://genericpharmaindustry.com/blood-clotting-microgel-particles-could-lead-to-treatments-for-uncontrolled-bleeding/>

<http://www.pathguy.com/histo/030.htm>

[http://csls-text3.c.u-tokyo.ac.jp/active/03\\_06.html](http://csls-text3.c.u-tokyo.ac.jp/active/03_06.html)

<http://www.aetiology.co.nz/the-lymph-system/>

<http://string-db.org/>

<http://t0.gstatic.com/images?q=tbn:ANd9GcQlvr6VX0uoyMldUB4nIN9f9XQEkdC9BQZR69liAYswlqaOOSK11XeURM1R>

<http://geneontology.org/>

<http://www.nature.com/nmeth/journal/v11/n1/pdf/nmeth.2764.pdf>

[http://www.clipartguide.com/\\_pages/0511-1108-1012-0275.html](http://www.clipartguide.com/_pages/0511-1108-1012-0275.html)

## Articles

Babushok, DV. and Bessler, M. (2015). Genetic predisposition syndromes: When should they be considered in the work-up of MDS  
*Elsevier: Best Practice and Research Clinical Haematology*. Vol. 28: 55-68.

Dickinson, RE. et al. (2014). The evolution of cellular deficiency in *GATA2* mutation. *Blood*. Vol. 123.6: 863-874.

Mansour, S. et al. (2010). Emberger Syndrome – Primary Lymphedema With Myelodysplasia: Report of Seven New Cases. *American Journal of Medical Genetics*. Part A: 2287–2296.

Collin, M. et al. (2015). Haematopoietic and immune defects associated with *GATA2* mutation. *British Journal of Haematology*.

Ostergaard, P. et al. (2011). Mutations in *GATA2* cause primary lymphedema associated with a predisposition to acute myeloid leukemia (Emberger syndrome). *Nature Genetics*. Vol. 43.10: 929–931.

# Questions?

