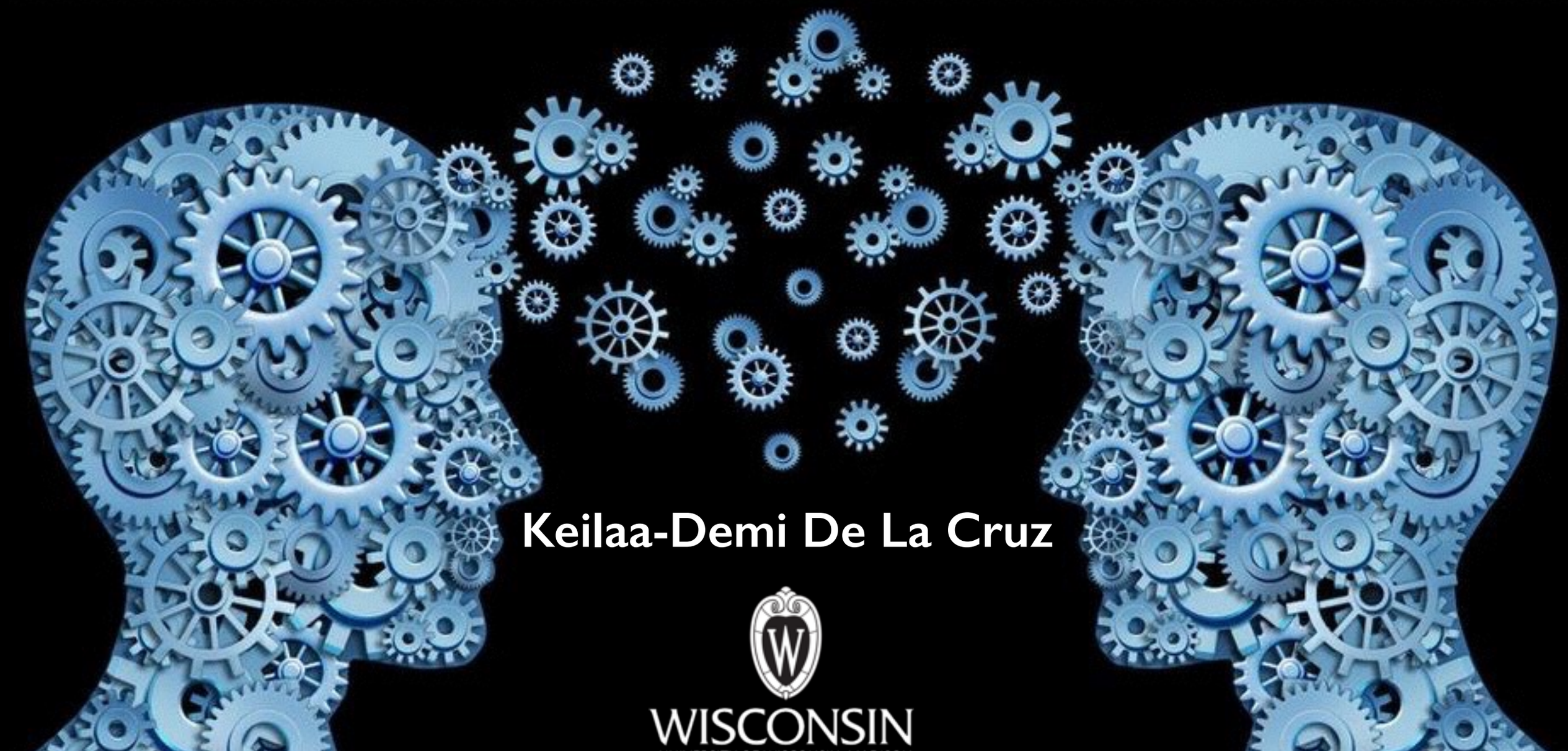
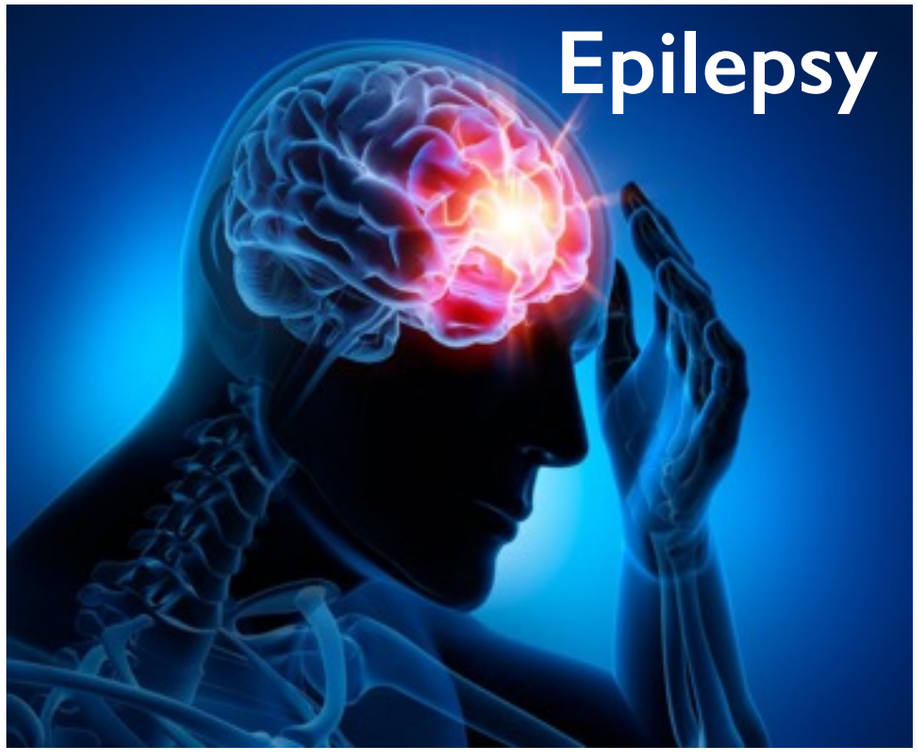
Pitt Hopkins Syndrome & TCF4 in Intellectual Disability



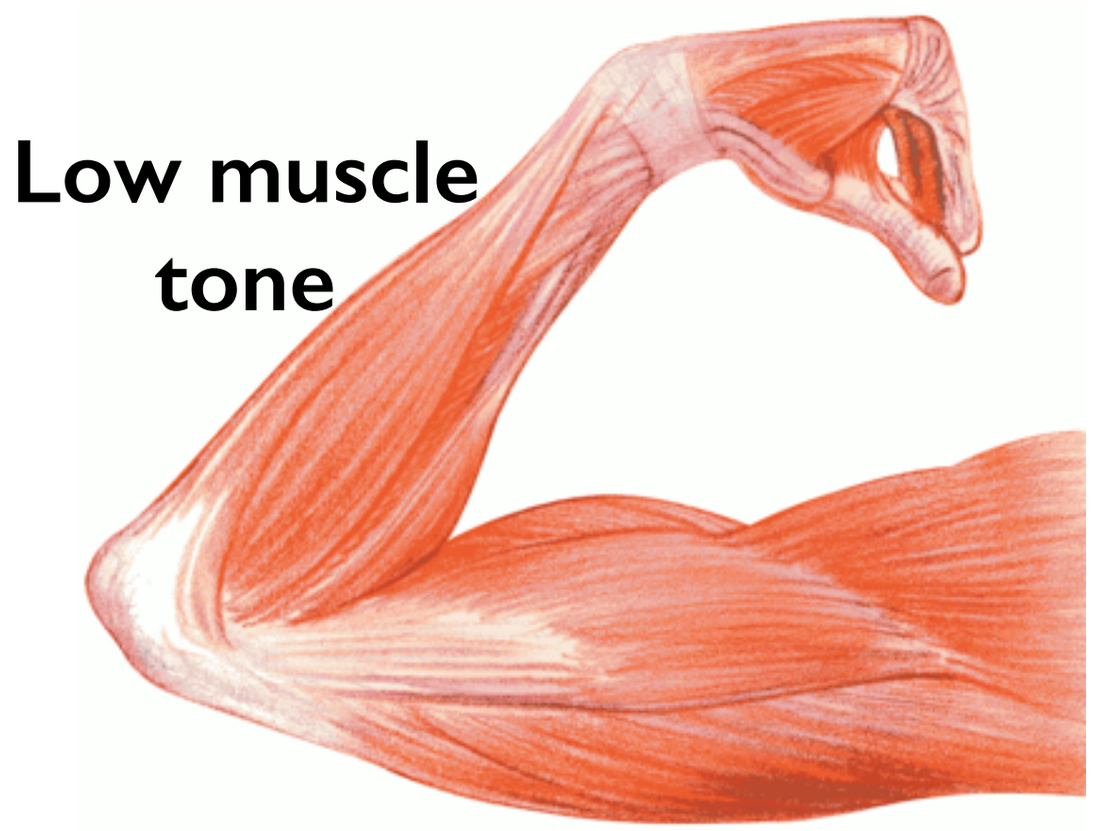
Keilaa-Demi De La Cruz

WISCONSIN
UNIVERSITY OF WISCONSIN-MADISON

What are the symptoms of Pitt Hopkins Syndrome?

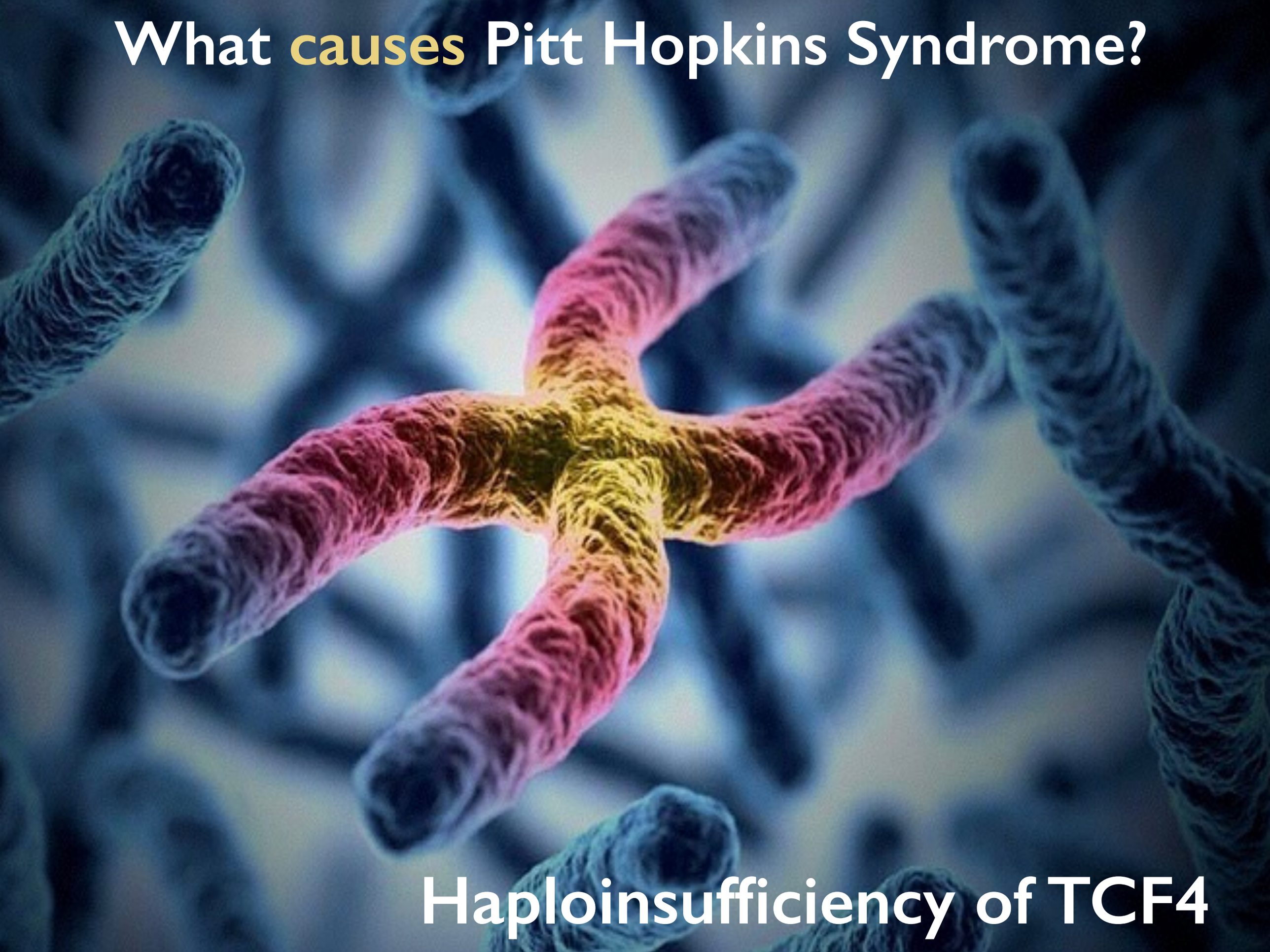


Lack of speech



Low muscle tone

What causes Pitt Hopkins Syndrome?

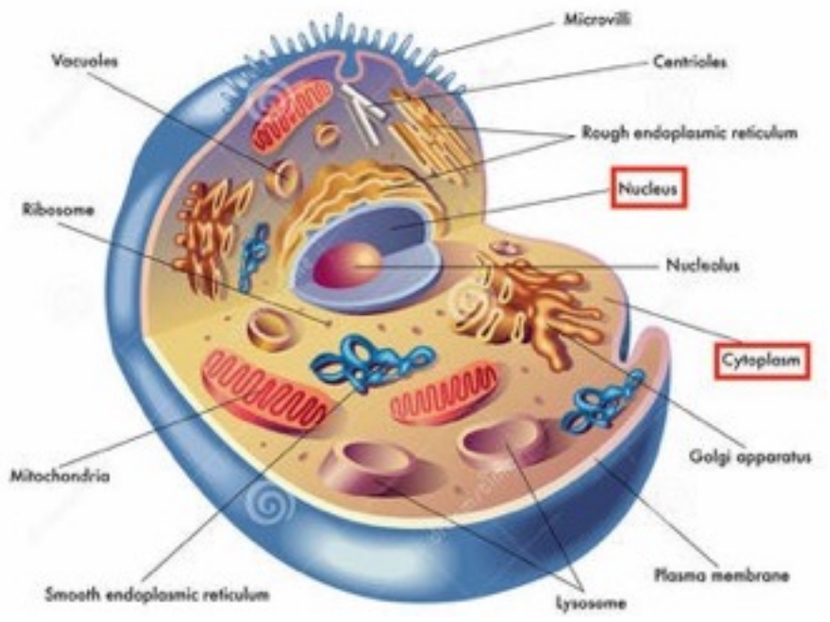


Haploinsufficiency of TCF4

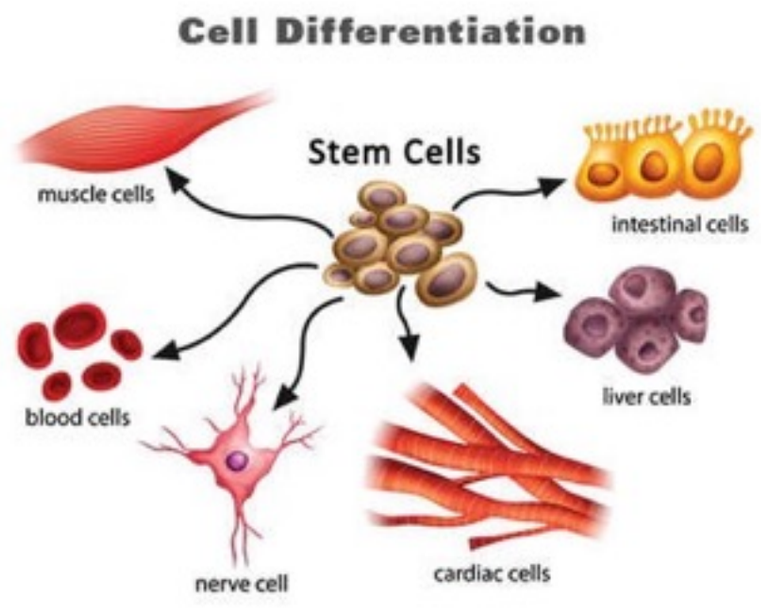
Where and how does TCF4 work?

Where and how does TCF4 work?

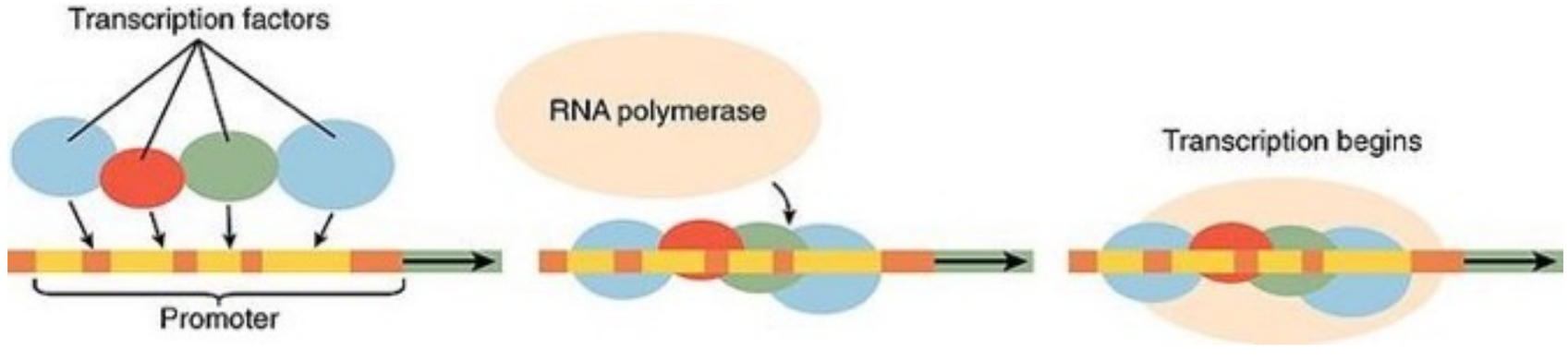
Cellular Component



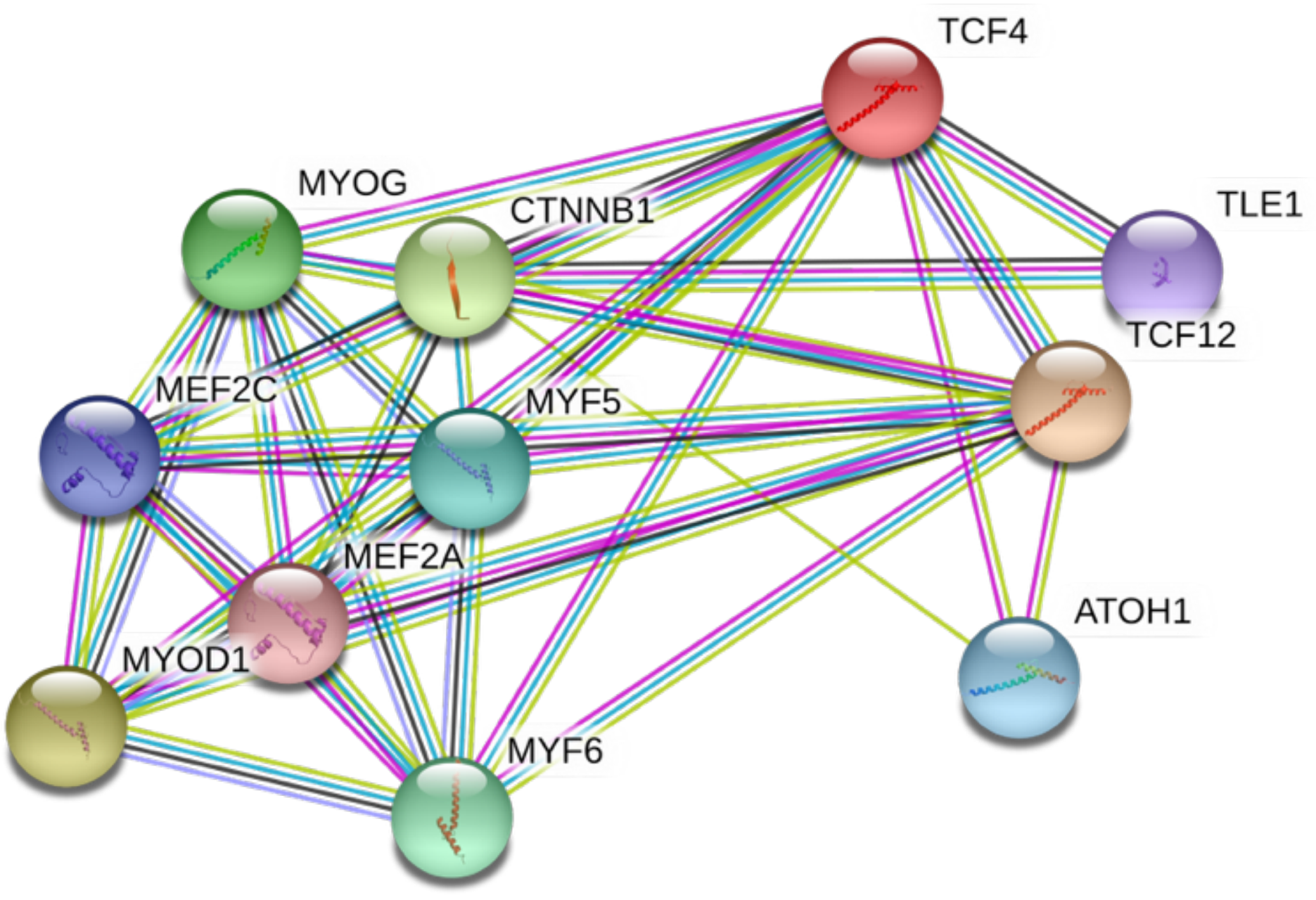
Biological Process



Molecular Function



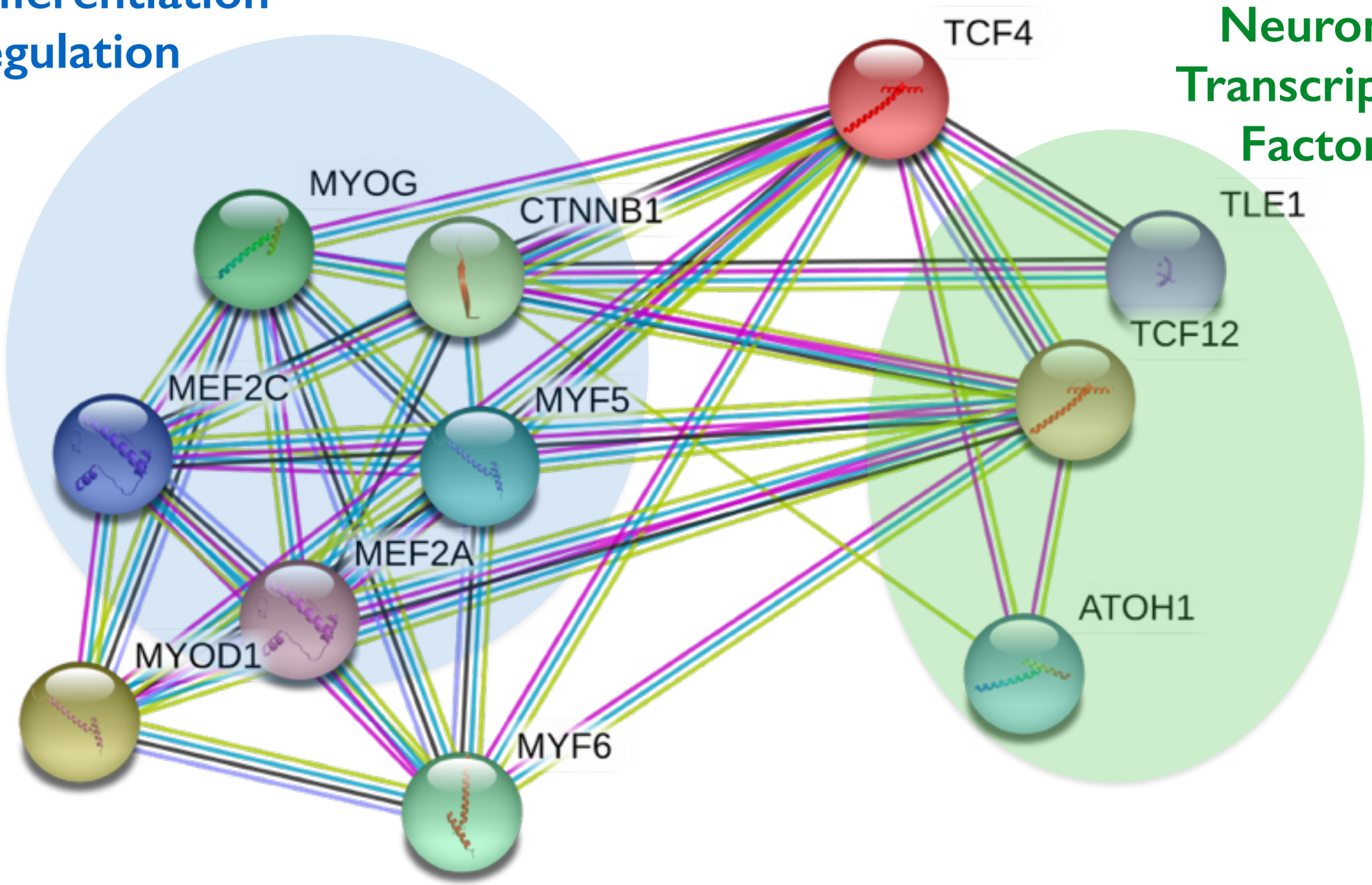
What proteins interact with TCF4?



What proteins interact with TCF4?

Cell Differentiation
Regulation

Neuronal
Transcription
Factors



What do we already know?

Nerve Cells

+

Haploinsufficiency

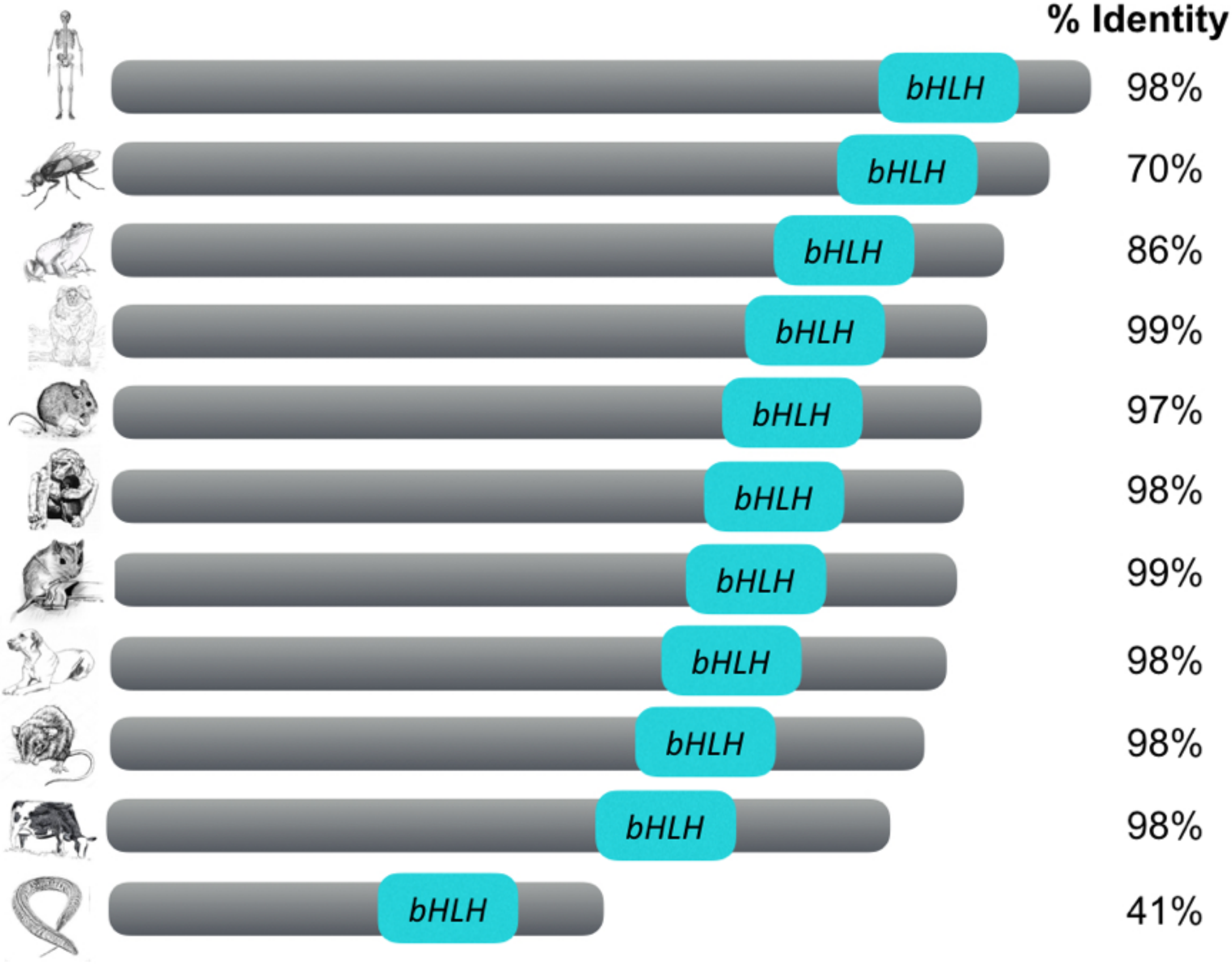
Gap In Knowledge

+

Muscle Tissue Cells

Haploinsufficiency

Is TCF4 conserved across species?



Why use mice to study TCF4?

$

What is the primary goal?

To determine if TCF4 is required for the differentiation of muscle tissue cells during embryonic development

Aim 1

Identify TCF4 mutations that affect cell differentiation processes in muscle tissue

Aim 2

Identify new genes important for muscle tissue development in TCF4 mutants

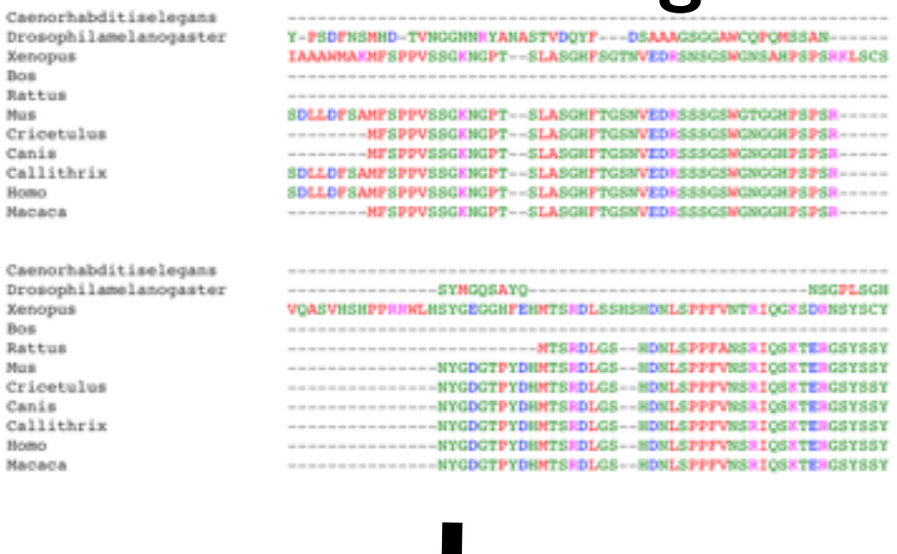
Aim 3

Identify new TCF4 interacting proteins involved in muscle tissue development

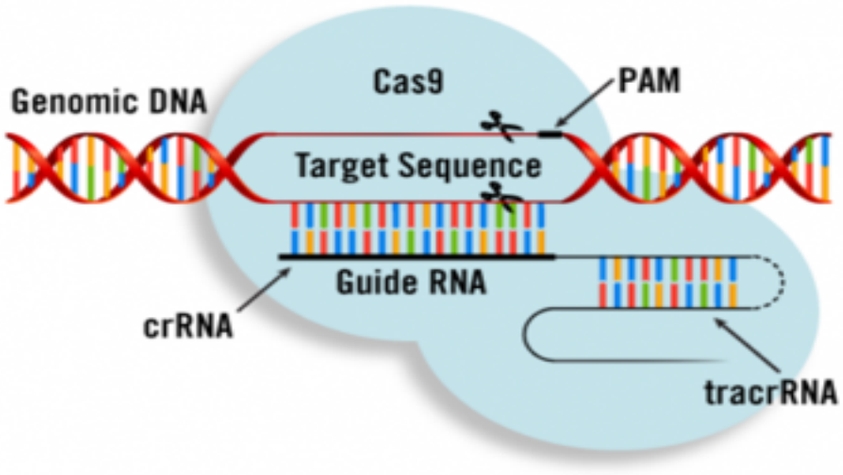
Hypothesis: Deletion of the TCF4 will inhibit the process of cell differentiation in cells found in muscle tissue

Aim 1: Identify TCF4 mutations that affect cell differentiation processes in muscle tissue

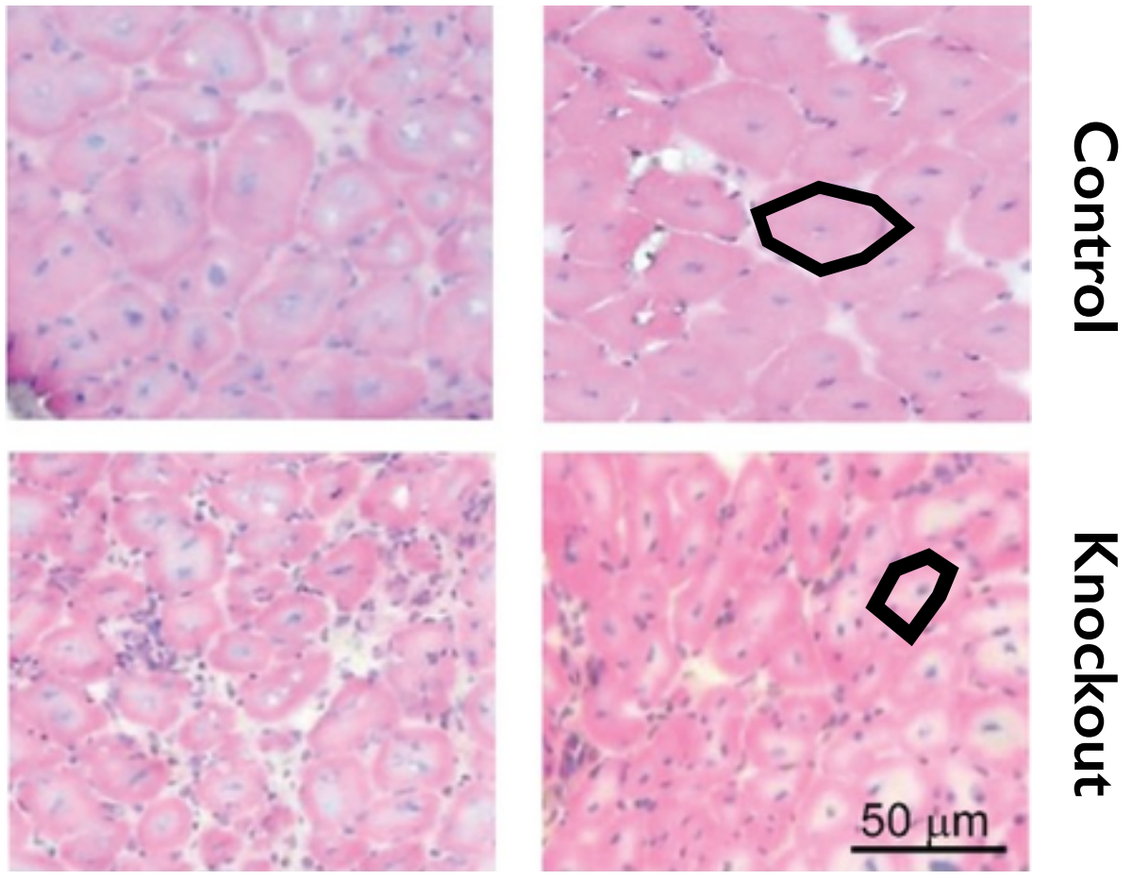
Clustal Omega



CRISPR/Cas9



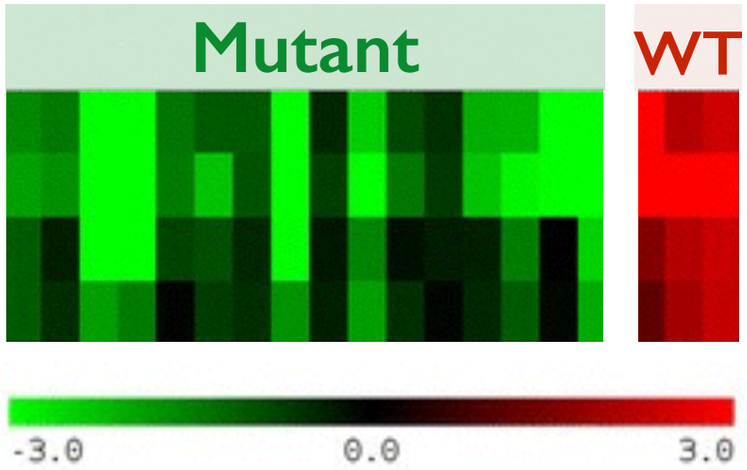
Cryosection & Immunohistochemistry in Muscle Tissue



Hypothesis: Lower muscle tone will be observed in TCF4 knockout mutant mice

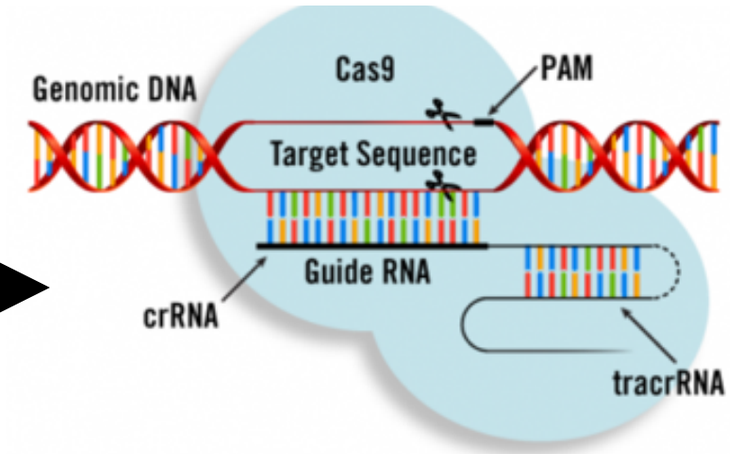
Aim 2: Identify new genes important for muscle tissue development in TCF4 mutants

RNA-seq

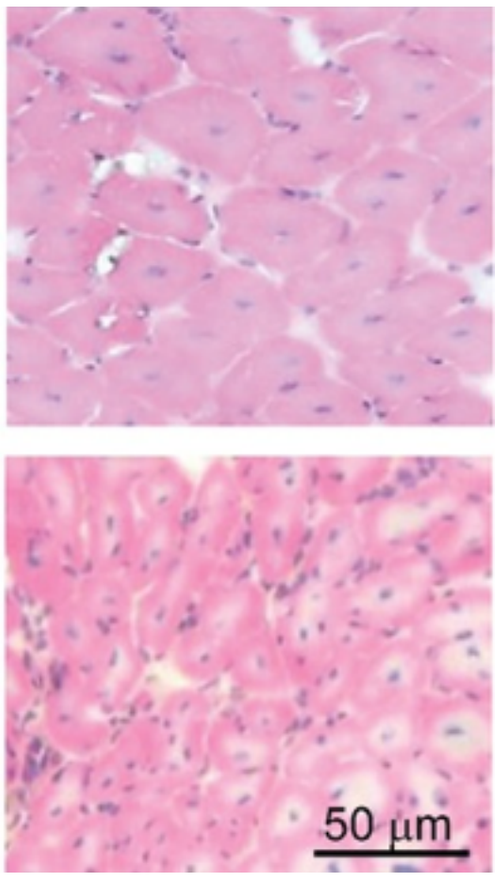


GENEONTOLOGY
Unifying Biology

CRISPR/Cas9



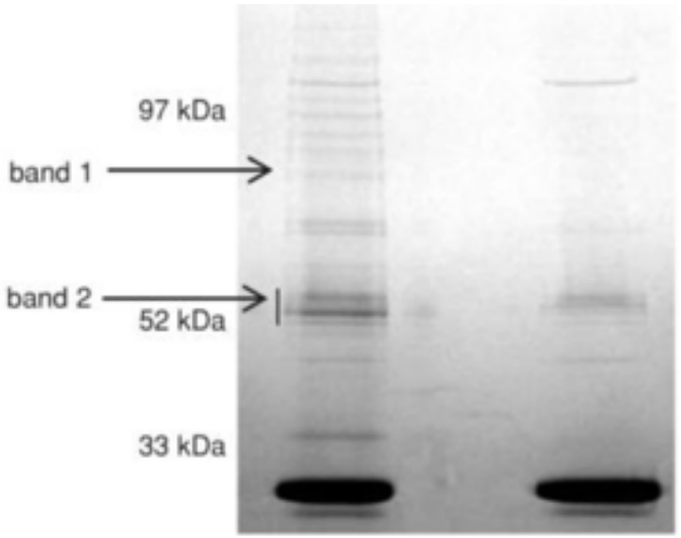
Cryosection Muscle Tissue



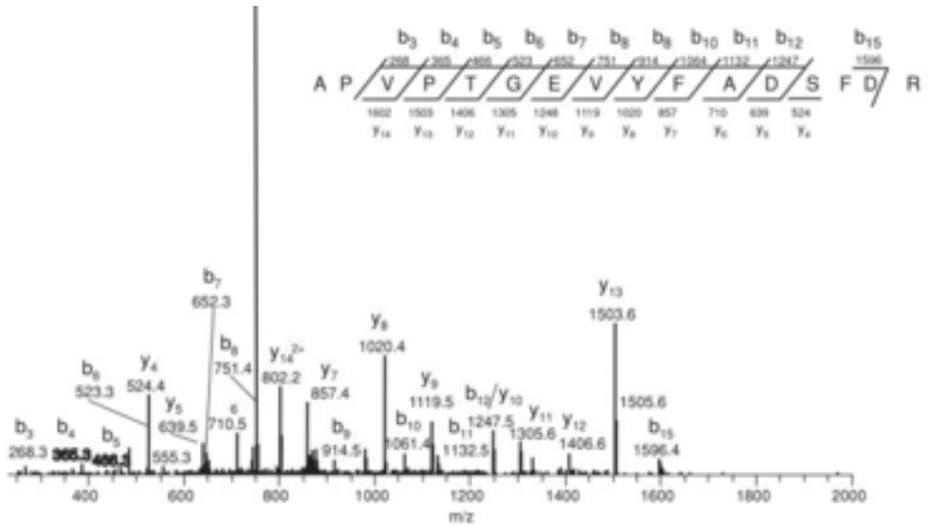
Hypothesis: Knockout will result in identifying genes associated with muscle cell differentiation and muscle function

Aim 3: Identify new TCF4 interacting proteins involved in muscle tissue development

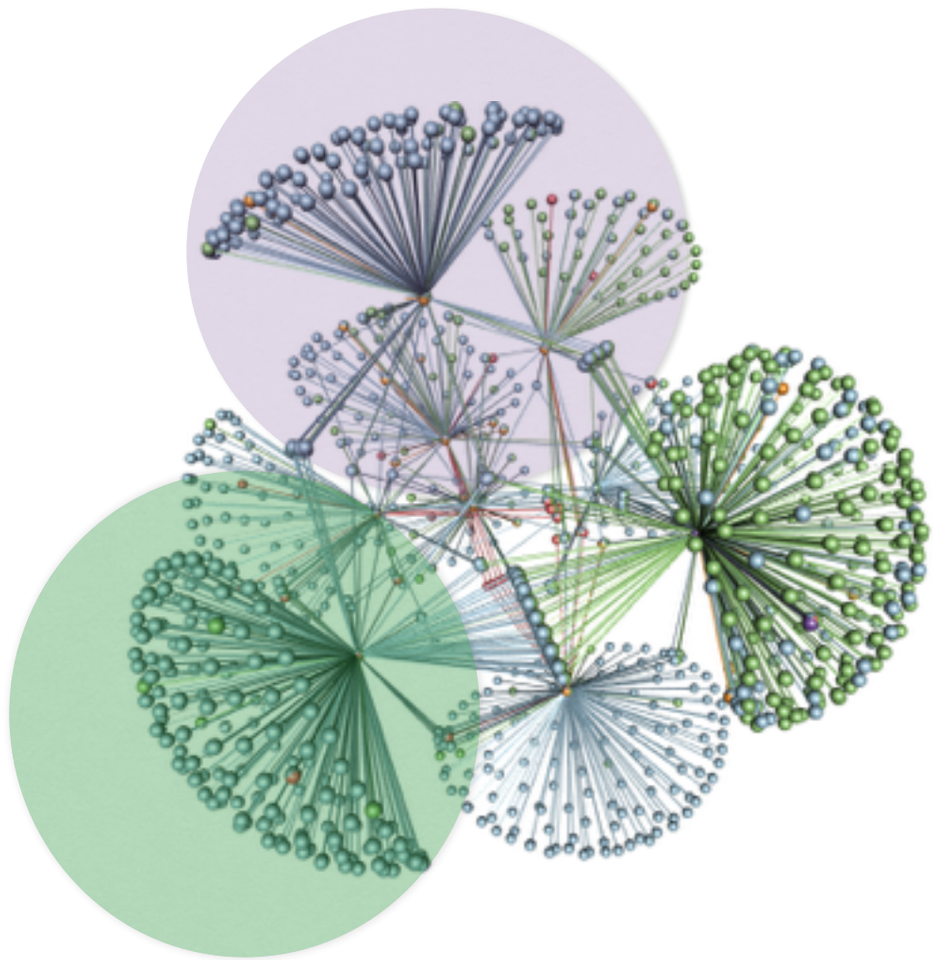
Tandem Affinity Purification



Mass Spectroscopy



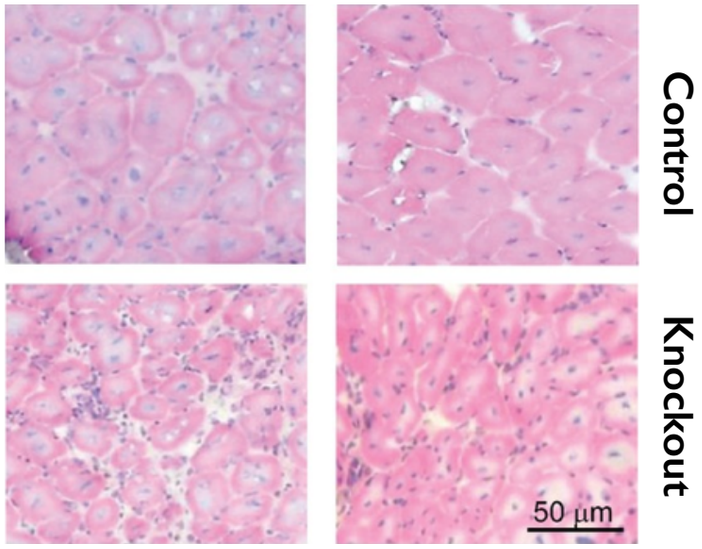
Muscle Cell Differentiation

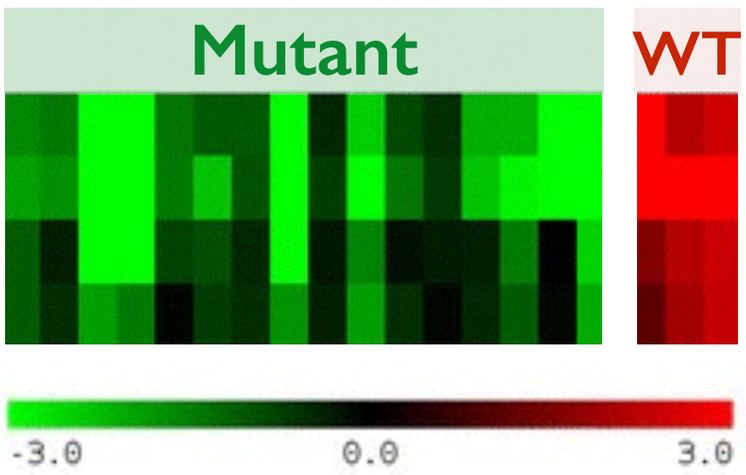


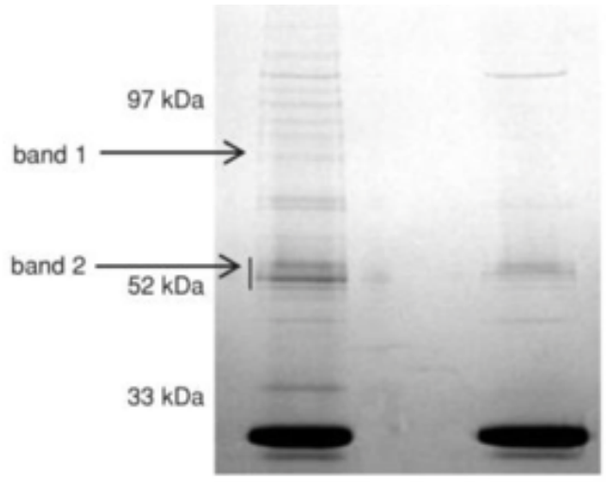
Muscle Tissue Development

Hypothesis: TCF4 will be identified as an important transcription factor for muscle cell differentiation & muscle tissue development

Conclusion





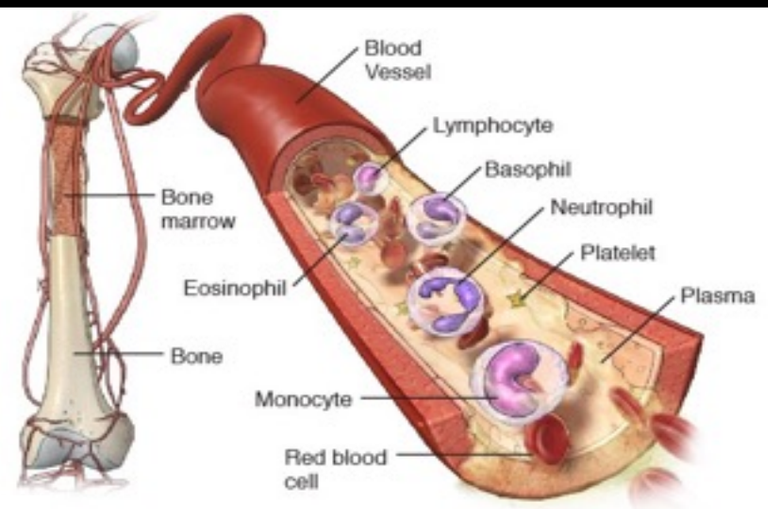


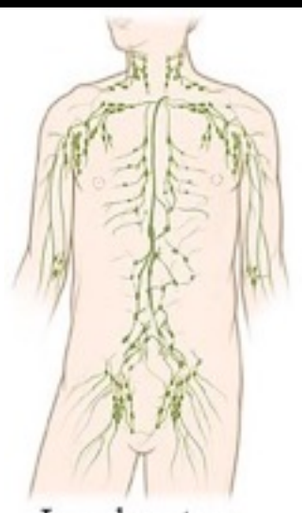
Lower muscle tone will be observed in mutant mice

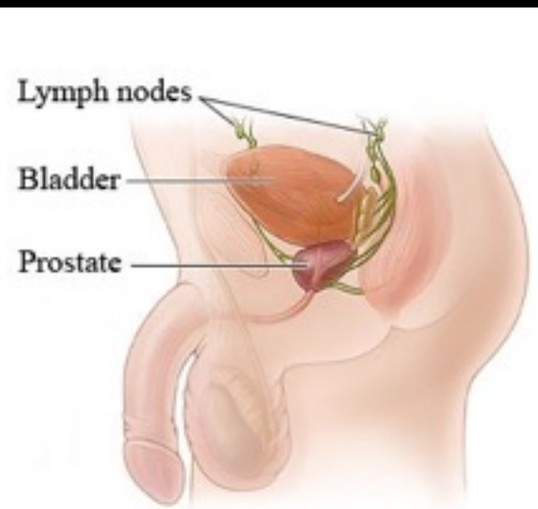
RNA-Seq will reveal lower expression of cell differentiation-related genes in mutant mice

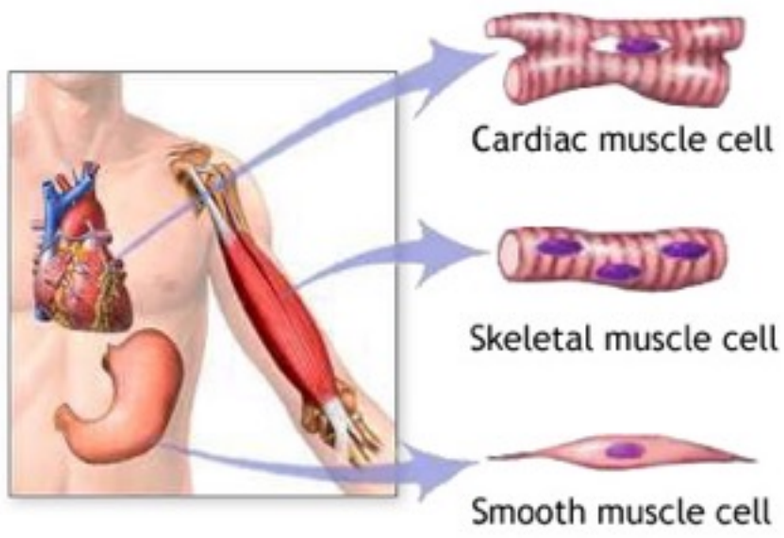
TAP & MS will identify new proteins important for cell differentiation in muscle tissue

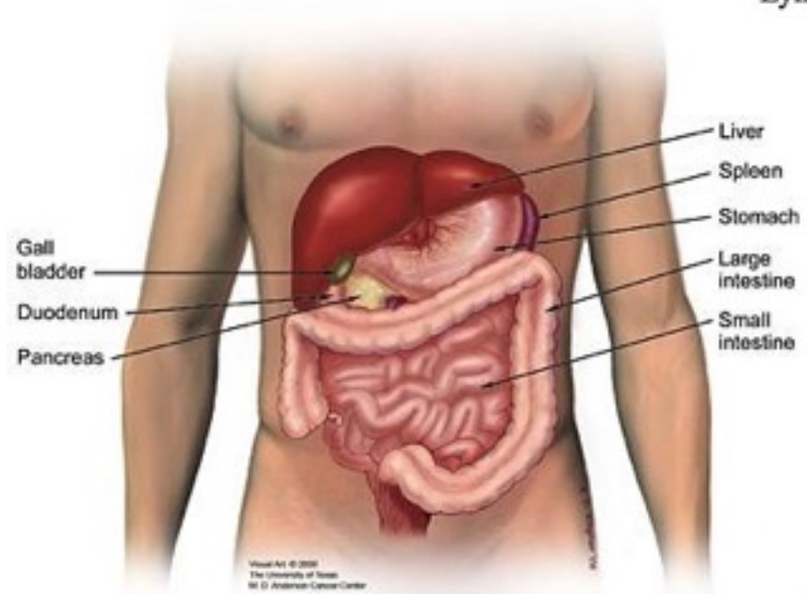
Future Directions

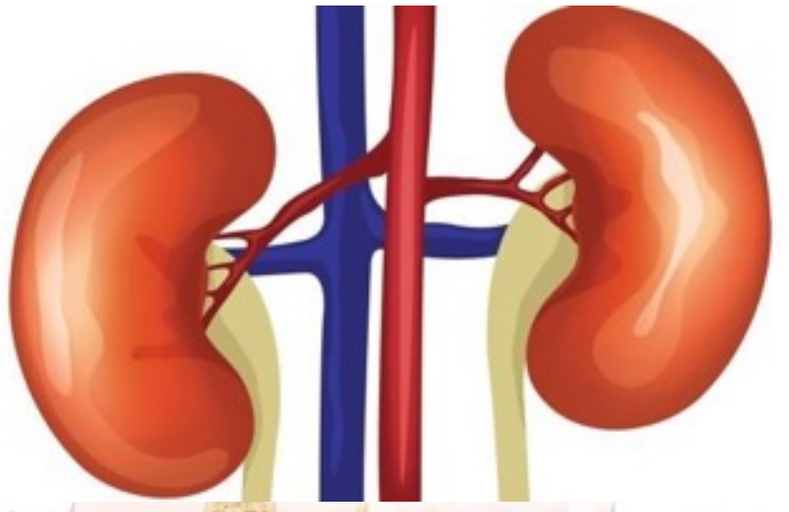


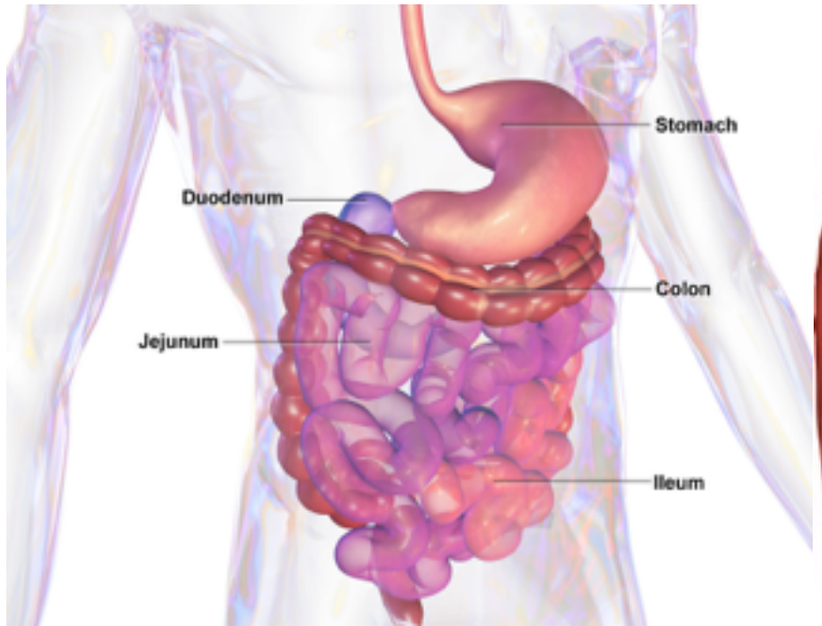

Lymph system

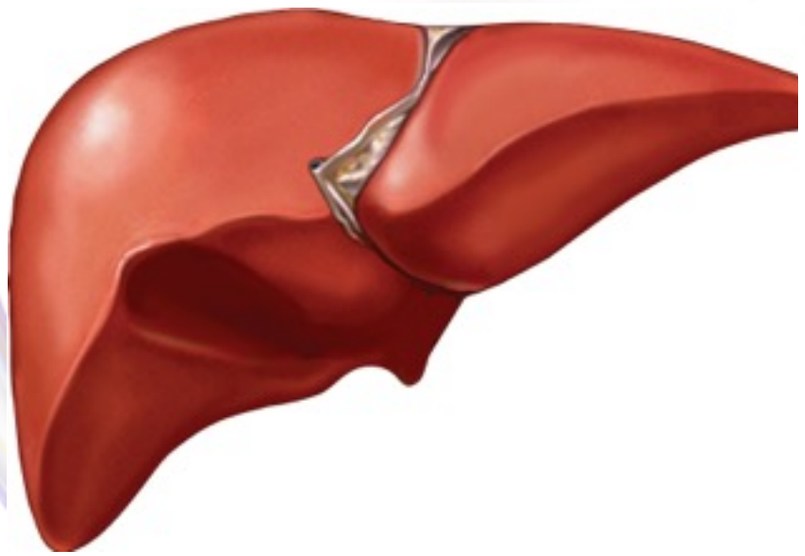


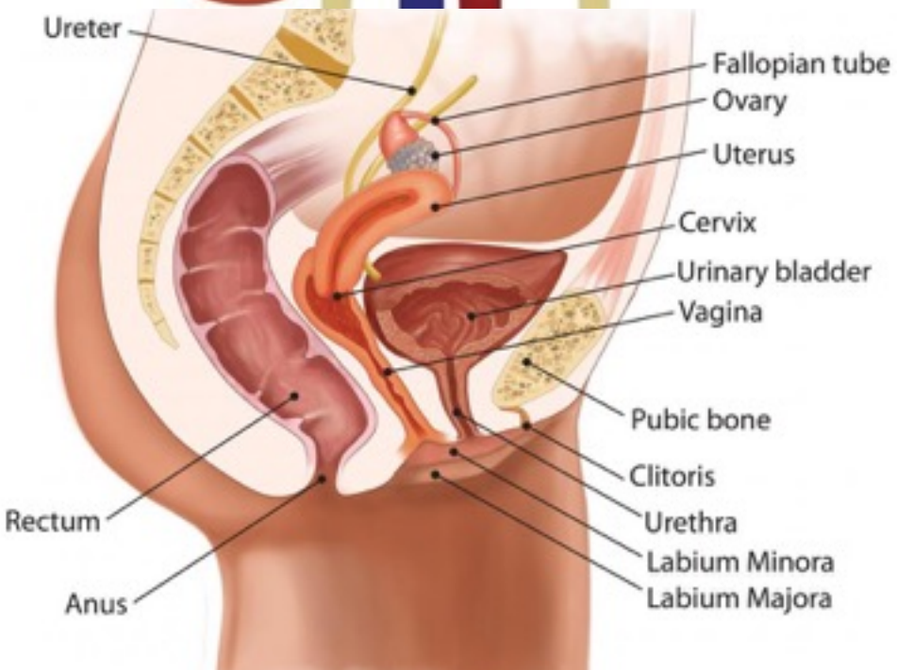












References

1. http://www.executivechronicles.com/time-to-recognize-intellectual-property-rights/
2. https://philmaffetone.com/can-bad-genes-beat-good-lifestyle/
3. https://biologywise.com/cell-differentiation
4. https://anatomybody-charts.us/labeled-diagram-of-the-human-cell/labeled-picture-of-human-cell/
5. http://pediaa.com/how-do-transcription-factors-bind-to-dna/
6. https://medicalxpress.com/news/2014-07-proteins-scientists-drug-discovery-tool.html
7. https://lijiading01.appspot.com/art_5122901699198976.html
8. https://www.epilepsyqueensland.com.au/about-epilepsy-1
9. http://www.upstart.net.au/speech-pathology-giv-australians-a-voice/
10. http://pluspng.com/png-82614.html
11. https://www.drrobertjones.com/questions-you-should-ask-your-hair-transplant-surgeon/
12. http://www.drcoplan.com/wp-content/uploads/2013/06/dreamstime_xs_13773435.jpg
13. https://www.dreamstime.com/royalty-free-stock-photos-house-mouse-standing-mus-musculus-rear-feet-image31422158
14. https://www.webmd.com/women/ss/slideshow-thyroid-symptoms-and-solutions
15. https://www.homenaturalcures.com/bone-marrow-home-remedy/
16. https://www.webmd.com/men/lymph-nodes-in-the-male-retroperitoneum-and-pelvis
17. https://medlineplus.gov/ency/imagepages/19841.htm
18. https://www.pancan.org/facing-pancreatic-cancer/about-pancreatic-cancer/what-is-the-pancreas/
19. https://en.wikipedia.org/wiki/Gastrointestinal_tract#/media/File:Blausen_0432_GastroIntestinalSystem.png
20. http://www.thehealthsite.com/diseases-conditions/revealed-14-hidden-symptoms-of-kidney-disease/
21. http://www.wisegeek.org/what-is-an-enlarged-bladder.htm#
22. https://www.bioscience.co.uk/products/crisprcas9-genome-engineering
23. https://www.researchgate.net/figure/Tri-lineage-differentiation-potential-of-tissue-cells-Cells-from-bone-marrow-BM-A-C_fig4_259200292
24. https://www.researchgate.net/figure/Results-of-three-step-validation-of-RNAseq-differential-gene-expression-analysis-Each_fig5_282072768
25. https://s3.amazonaws.com/go-public/image/go-logo.large.png
26. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4752115/
27. https://upload.wikimedia.org/wikipedia/commons/5/53/Multiplex_Human_HIV-1_protein-protein_interaction_network_%28edge-colored_visualization%29.png
28. https://newgateclocks.com/italian-numone148k-extra-large-roman-numeral-wall-clock-oversized-black
29. Peippo, M., & Ignatius, J. (2012, April). Pitt-Hopkins Syndrome. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3366706/>
30. What is Pitt Hopkins syndrome? (2017, October 18). <https://pitthopkins.org/what-is-pitt-hopkins-syndrome/>
31. Pitt-Hopkins syndrome - Genetics Home Reference. (n.d.). <https://ghr.nlm.nih.gov/condition/pitt-hopkins-syndrome>
32. Micro Genomics. (2018). CGH-Array/Molecular Karyotype. < http://www.microgenomics.it/tecnologie/cariotipo-molecolare-array-cgh/?lang=en>
33. Rosenfeld JA, Leppig K, Ballif BC, Thiese H, Erdie-Lalena C, et al. Genotype-phenotype analysis of *TCF4* mutations causing Pitt-Hopkins syndrome shows increased seizure activity with missense mutations. Genet Med. 2009;11:797–805

ANY QUESTIONS?