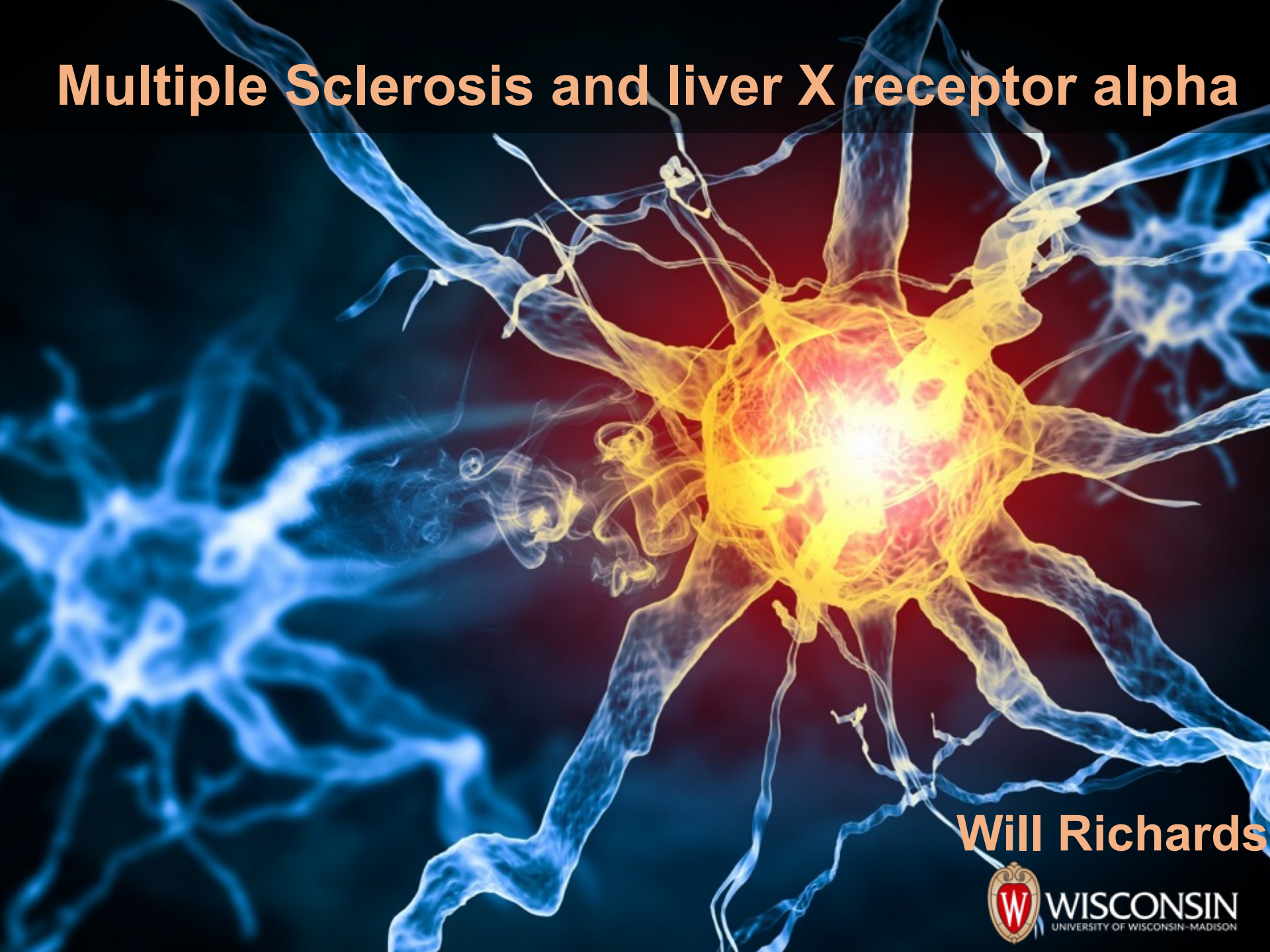


Multiple Sclerosis and liver X receptor alpha



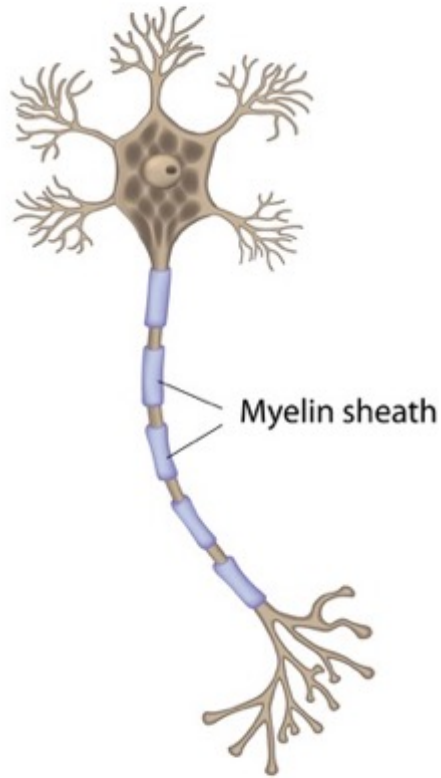
Will Richards



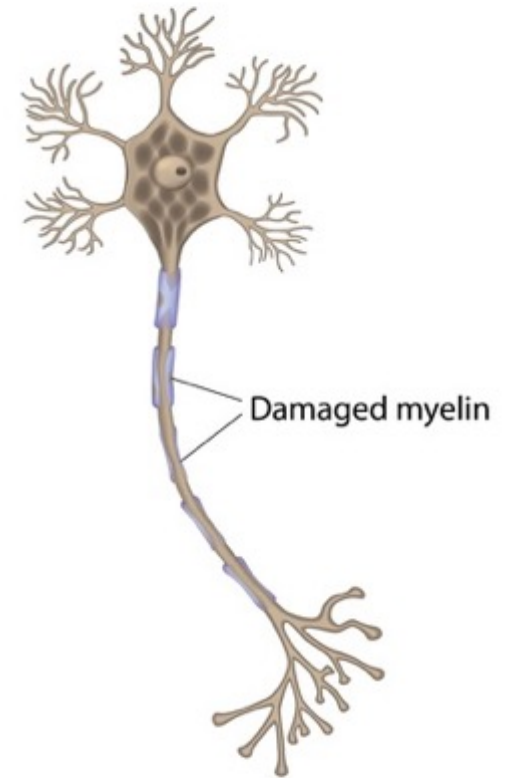
WISCONSIN
UNIVERSITY OF WISCONSIN-MADISON

Multiple Sclerosis (MS)

Normal

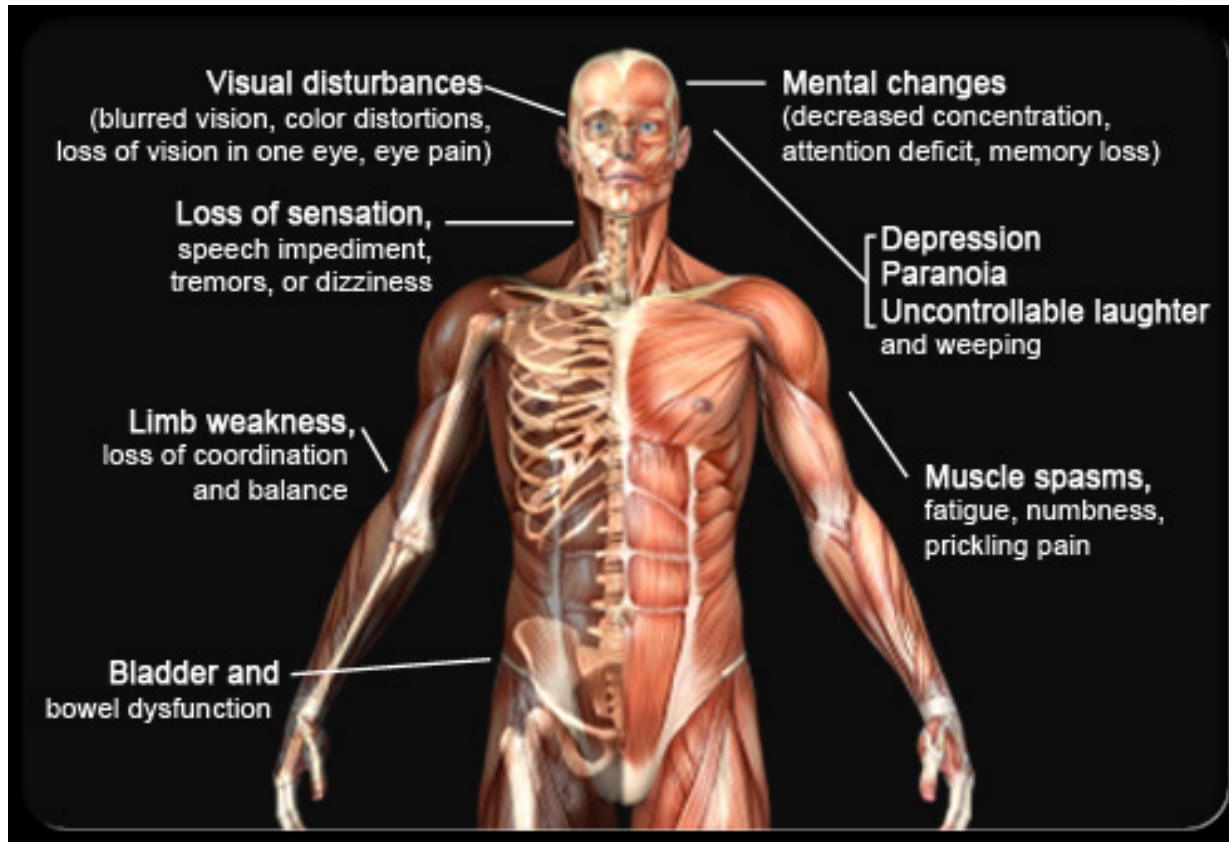


Multiple Sclerosis



An autoimmune disorder that attacks myelin sheaths

Symptoms of MS



MS associated gene



Biological Process

- Lipid Homeostasis
- Inflammation
- Innate Immunity

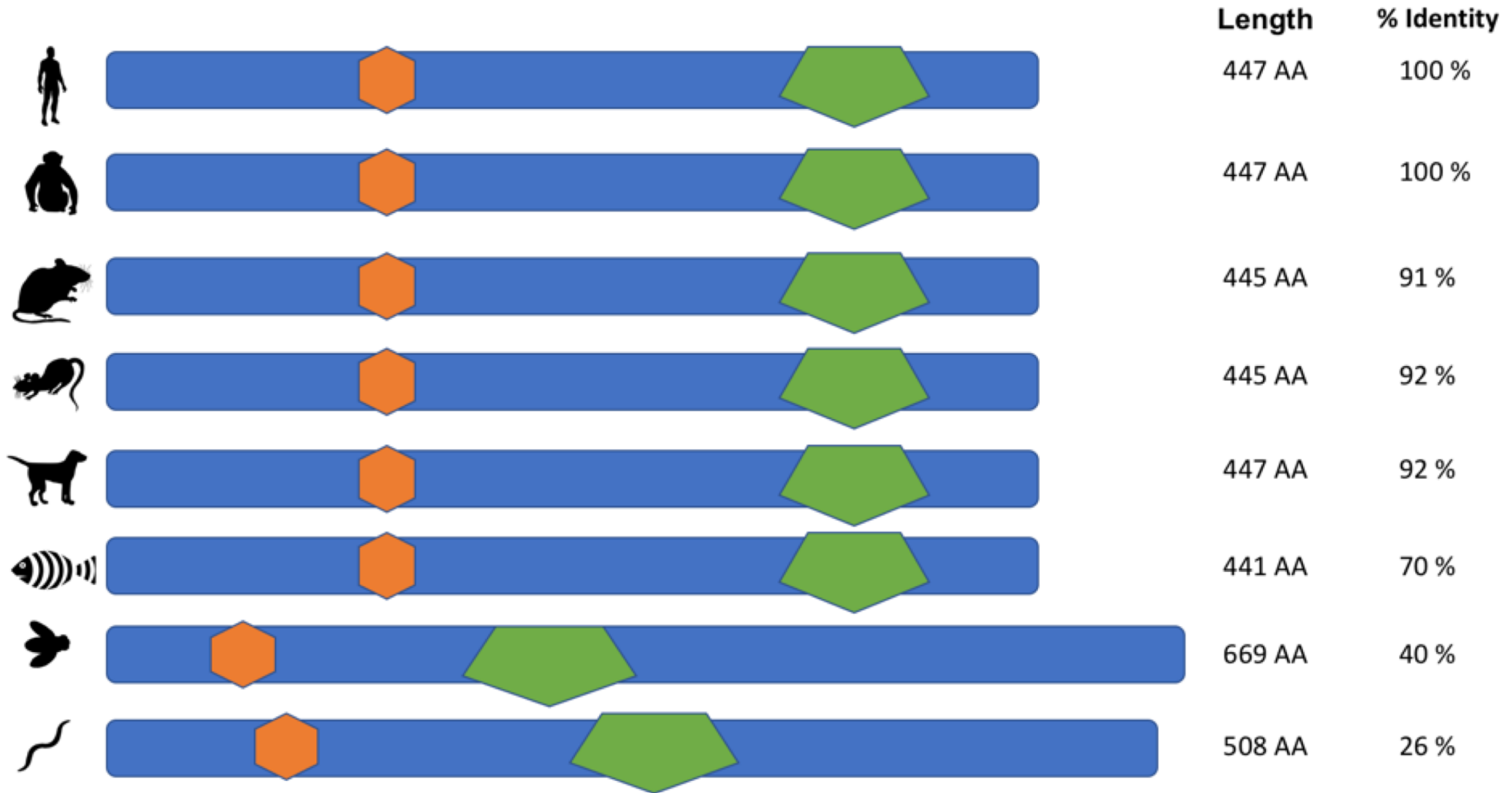
Molecular Function

- DNA Binding
- Protein Binding
- Hormone Receptor

Cellular Component

- Nucleus

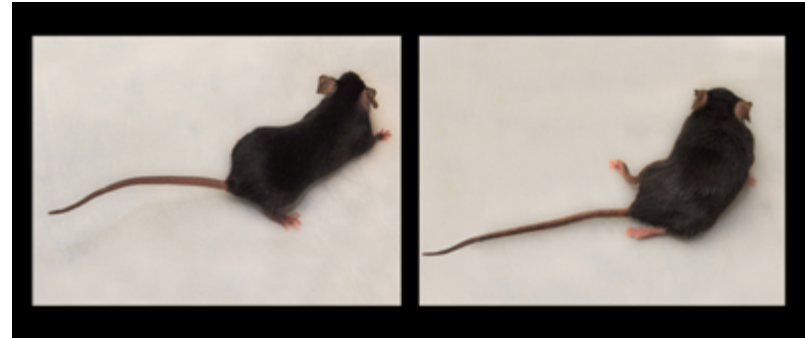
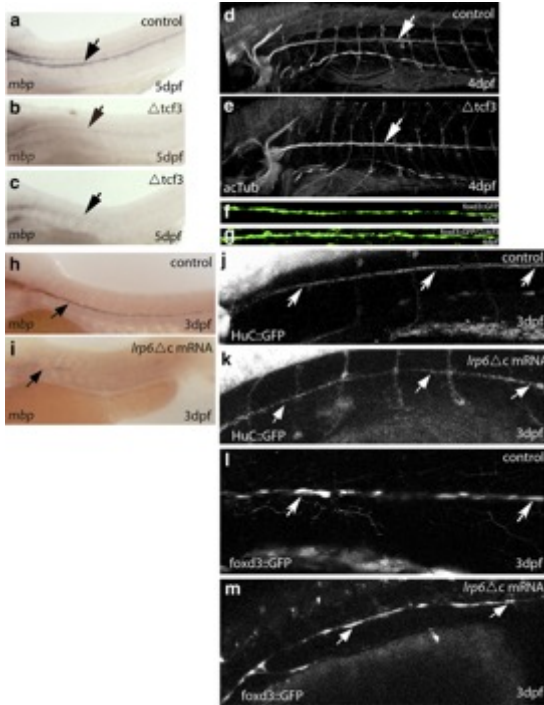
LXRA throughout time



Zinc finger domain

Ligand binding domain

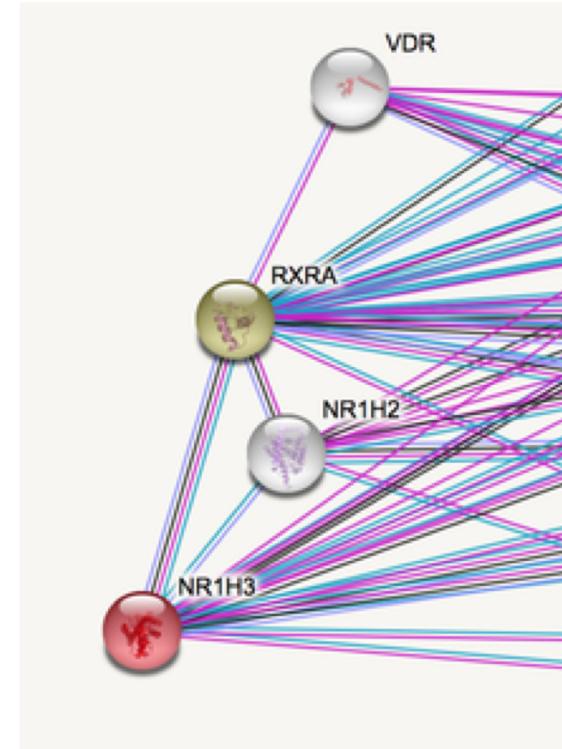
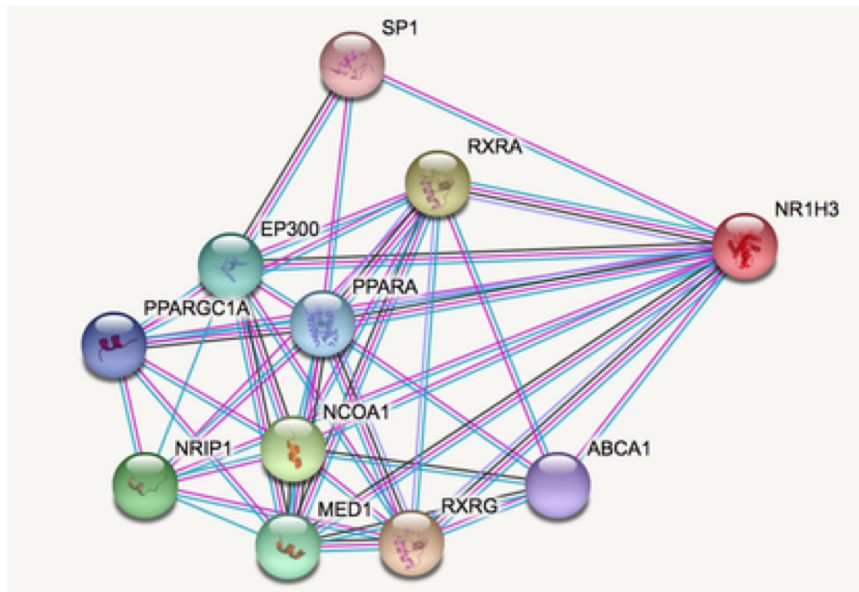
Why zebrafish and mice?



- Genetic similarity
- Transparent
- Quick development
- High throughput
- Can study myelination

- Genetic similarity
- Disease model for demyelination (EAE)
- Can study myelination

What proteins does LXRA interact with?

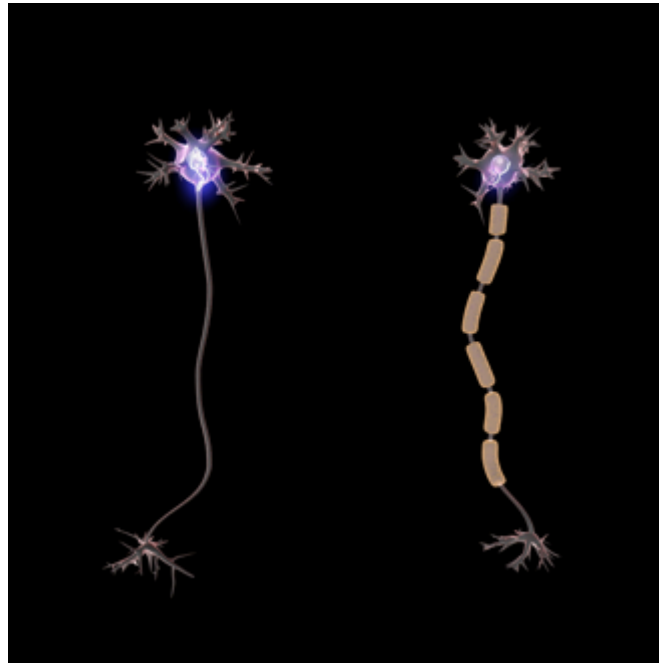


Interacts with RXR to mediate retinoid response

What is the overall goal?



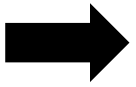
?



To understand the role LXRA has in myelination of nerves.

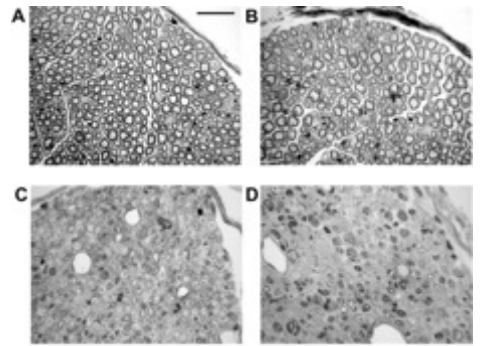
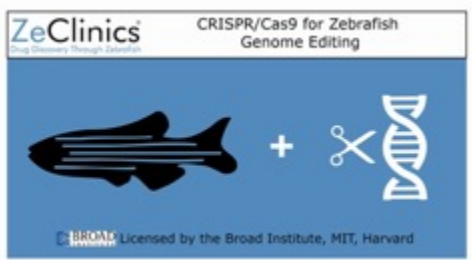
Aim 1: Identify important conserved amino acids for myelination

Clustal Omega



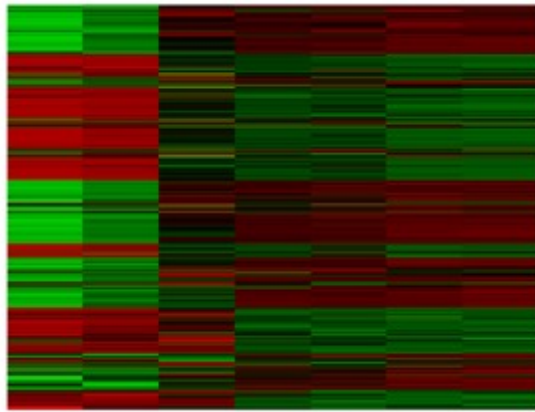
Species/Abbrv
1. Homo_sapiens
2. Mus_musculus
3. Rattus_norvegicus
4. Pan_troglodytes
5. Danio_rerio
6. Drosophila_melanog
7. Caenorhabditis_eleg
8. Canis_lupus_familiar

Species/Abbrv
1. Homo_sapiens
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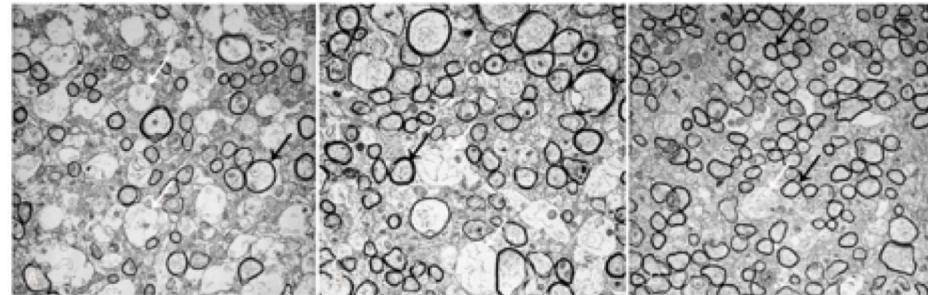


Hypothesis: Mutation of amino acids in the ligand binding domain show a reduction of myelination

Aim 2: Characterize differentially expressed genes in the CNS in LXRA deficient mice

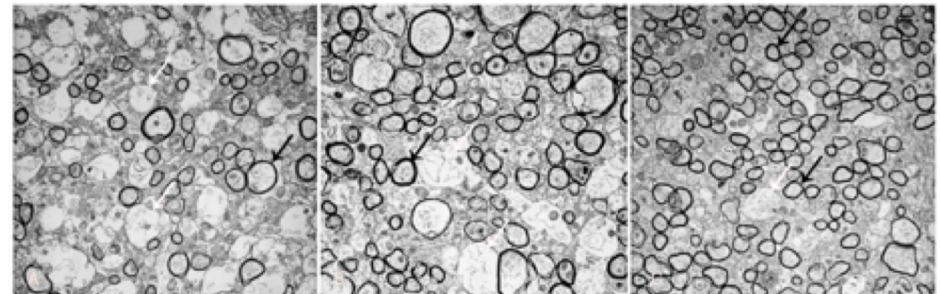
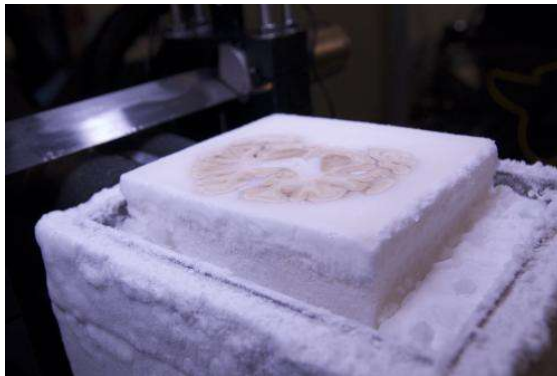
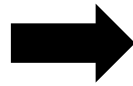
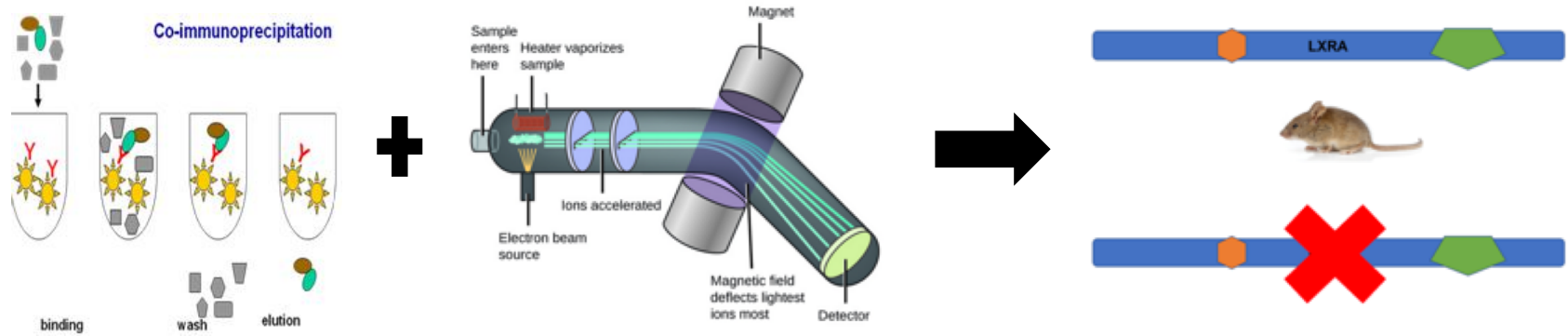


GENEONTOLOGY
Unifying Biology



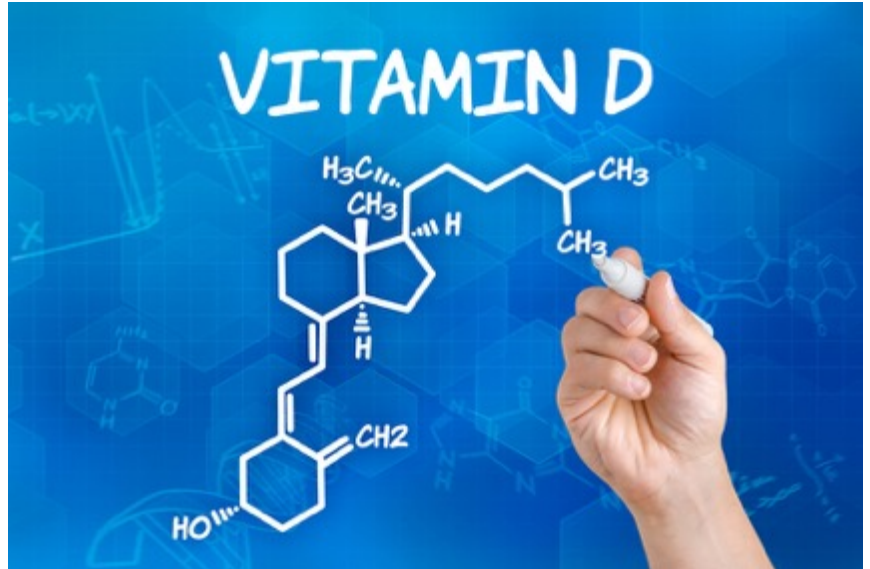
Hypothesis: Genes involved in lipid homeostasis will be downregulated

Aim 3: Determine protein interactions that differ between WT and LXRA mutant mice



Hypothesis: LXRA interacts with genes involved in lipid homeostasis in WT but not mutant

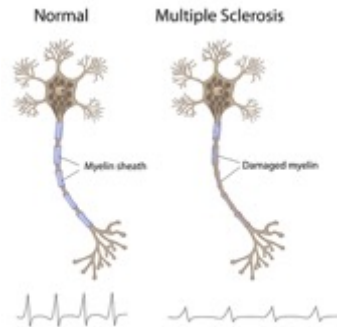
Future Directions



Determine the role of LXRA in Vitamin D deficiency in MS patients

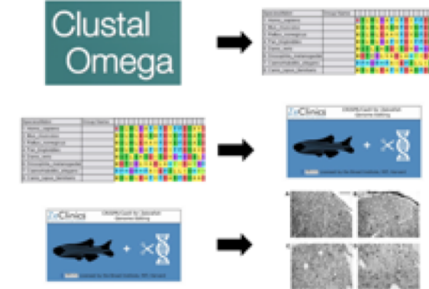
Determine if LXRA targeting is a possible drug therapy

Multiple Sclerosis and LXRA



Demyelination

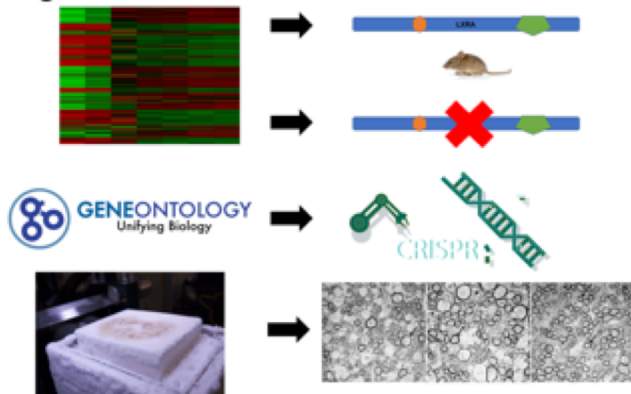
Aim 1: Identify important conserved amino acids for myelination



Hypothesis: Mutation of amino acids in the ligand binding domain show a reduction of myelination

Aim 1

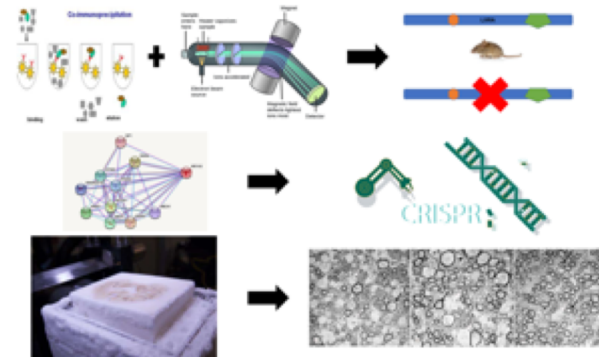
Aim 2: Characterize differentially expressed genes in the CNS in LXRA deficient mice



Hypothesis: Genes involved in lipid homeostasis will be downregulated

Aim 2

Aim 3: Determine protein interactions that differ between WT and LXRA mutant mice



Hypothesis: LXRA interacts with genes involved in lipid homeostasis in WT but not mutant

Aim 3

References

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