

Schizophrenia and TOP3B

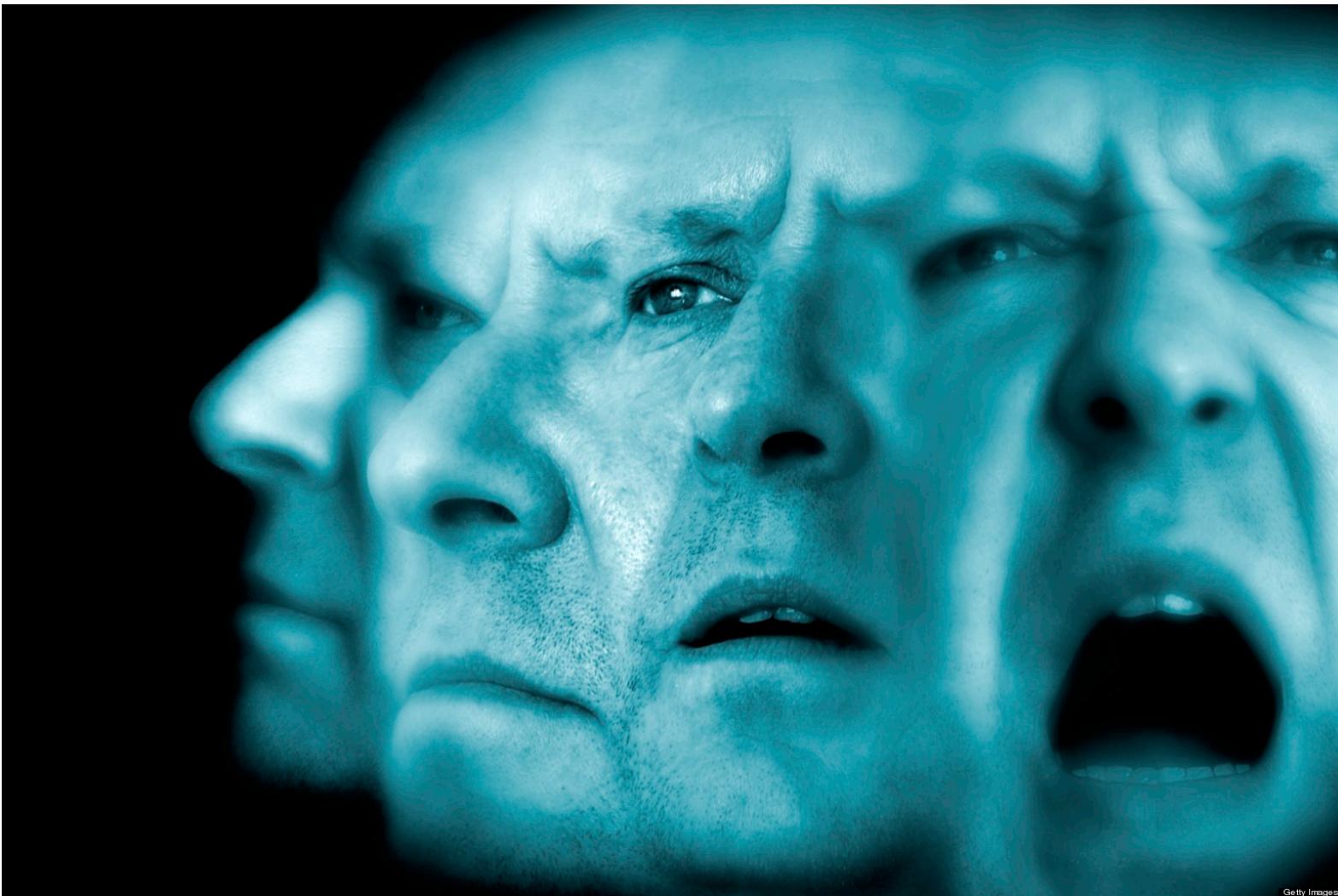
Kerry Zimdars

May 1, 2014

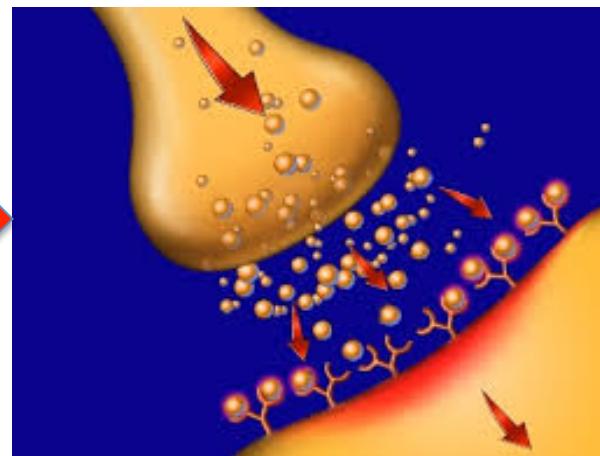
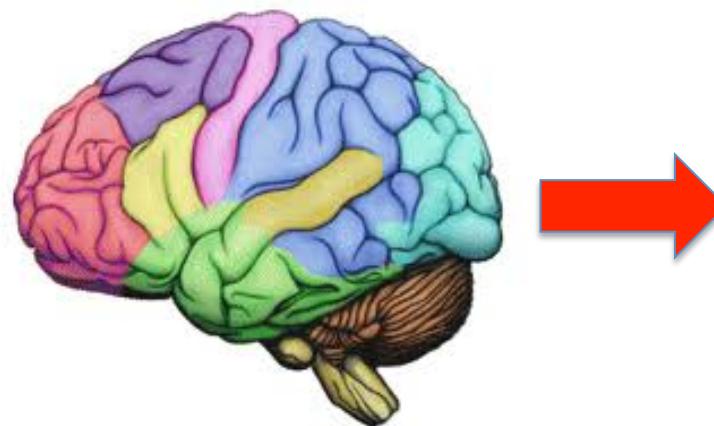
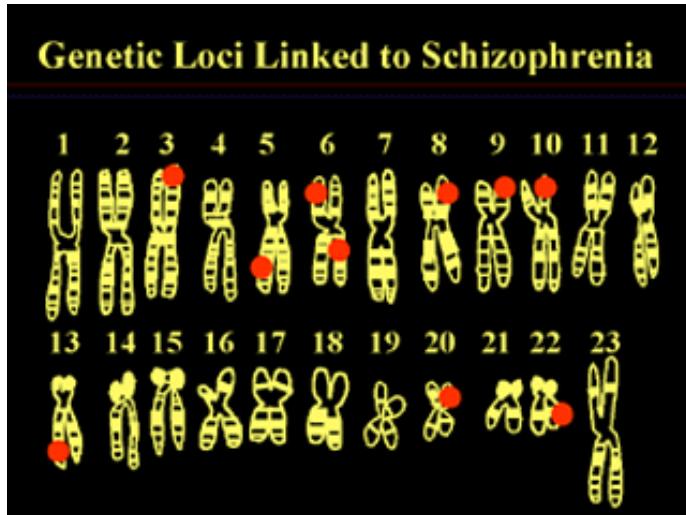
My Link to Schizophrenia



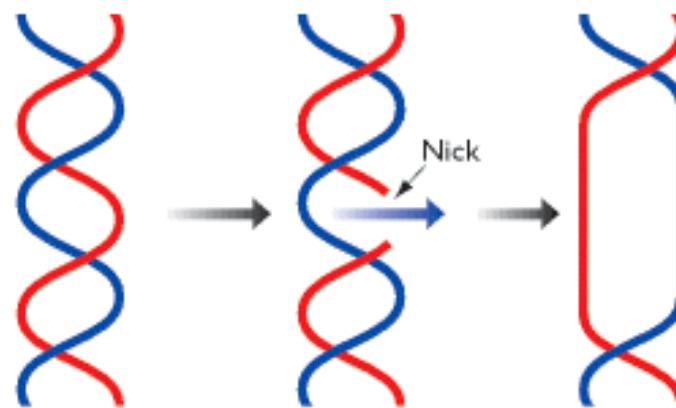
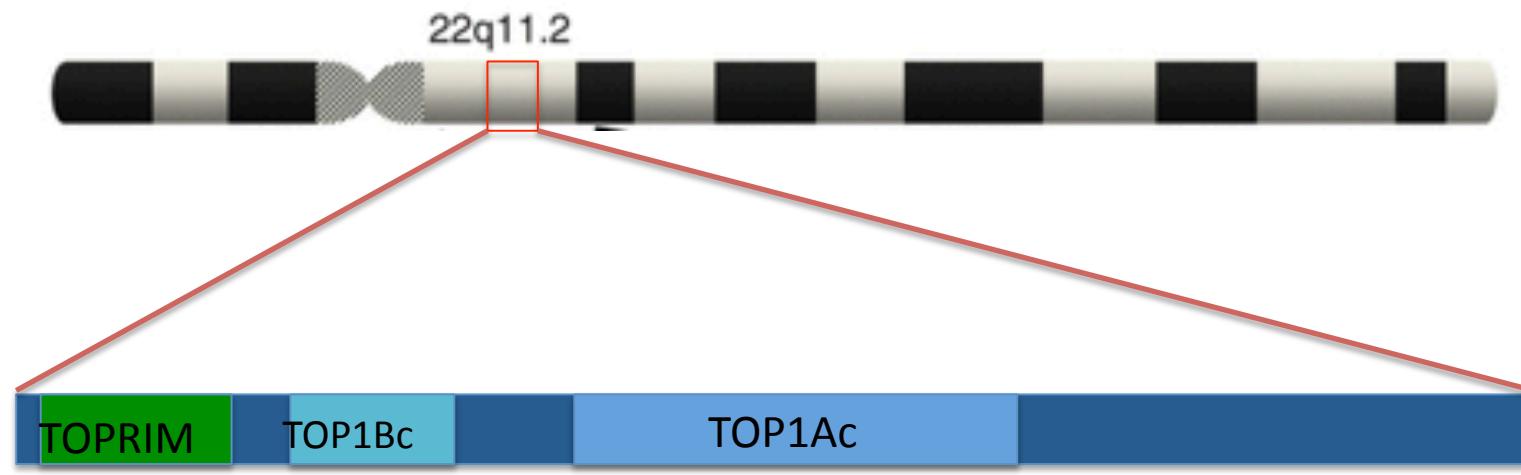
What is Schizophrenia?



What Causes Schizophrenia?



TOP3B: A Newly Identified Genetic Cause of Schizophrenia

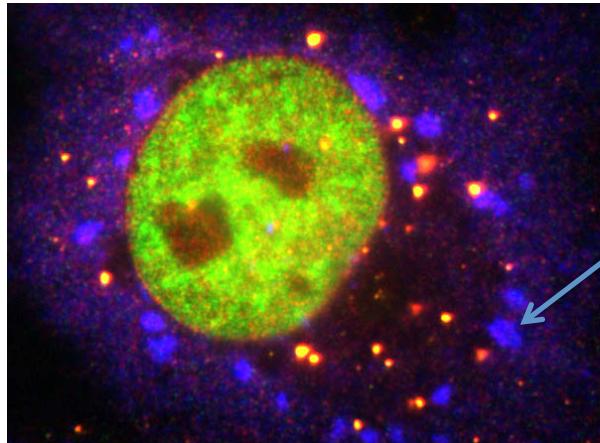
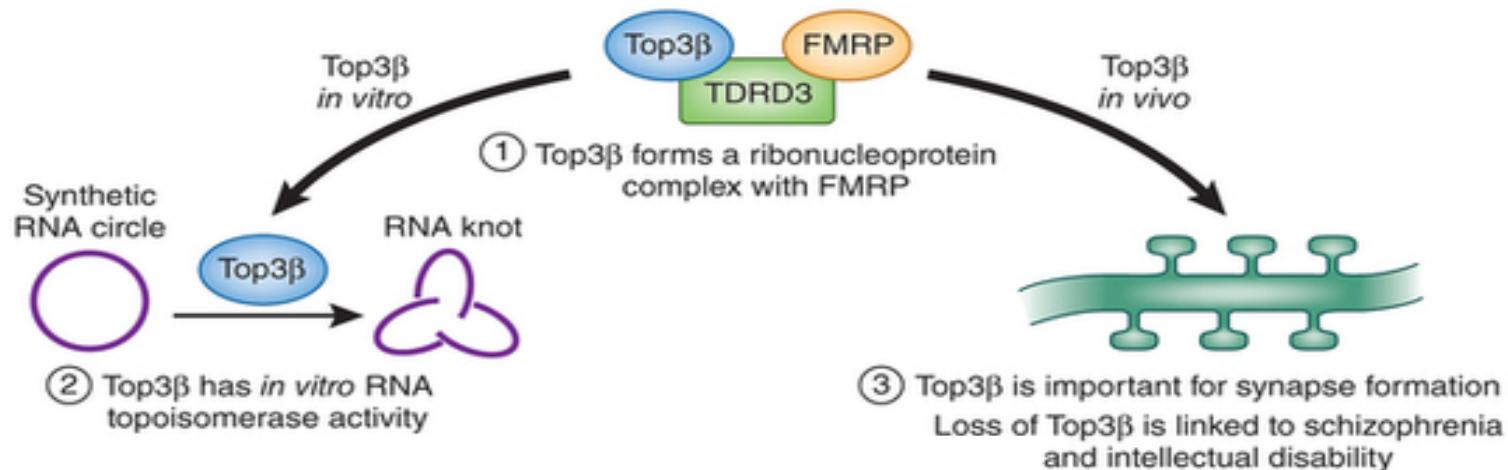


TOP3B is Highly Conserved

Human	TOPRIM	TOP1Bc	TOP1Ac	862aa	
TOP3β					
Mouse	TOPRIM	TOP1Bc	TOP1Ac	862aa	96% ID
TOP3β					
Rat	TOPRIM	TOP1Bc	TOP1Ac	862aa	95% ID
TOP3β-1					
Chicken	TOPRIM	TOP1Bc	TOP1Ac	862aa	87% ID
TOP3β-1					
Worm	TOPRIM	TOP1Bc	TOP1Ac	862aa	55% ID
Y48C3A.14					
Zebrafish	TOPRIM	TOP1Bc	TOP1Ac	862aa	82% ID
TOP3β-1					
Chimp	TOPRIM	TOP1Bc	TOP1Ac	862aa	99% ID
TOP3β-1					
Panda	TOPRIM	TOP1Bc	TOP1Ac	862aa	96% ID
TOP3β-1					
Fly	TOPRIM	TOP1Bc	TOP1Ac	875aa	58% ID
TOP3β					
Plant	TOPRIM	TOP1Bc	TOP1Ac	865aa	53% ID
TOP IA					
Rice	TOPRIM	TOP1Bc	TOP1Ac	866aa	53% ID
Os09g0500600					

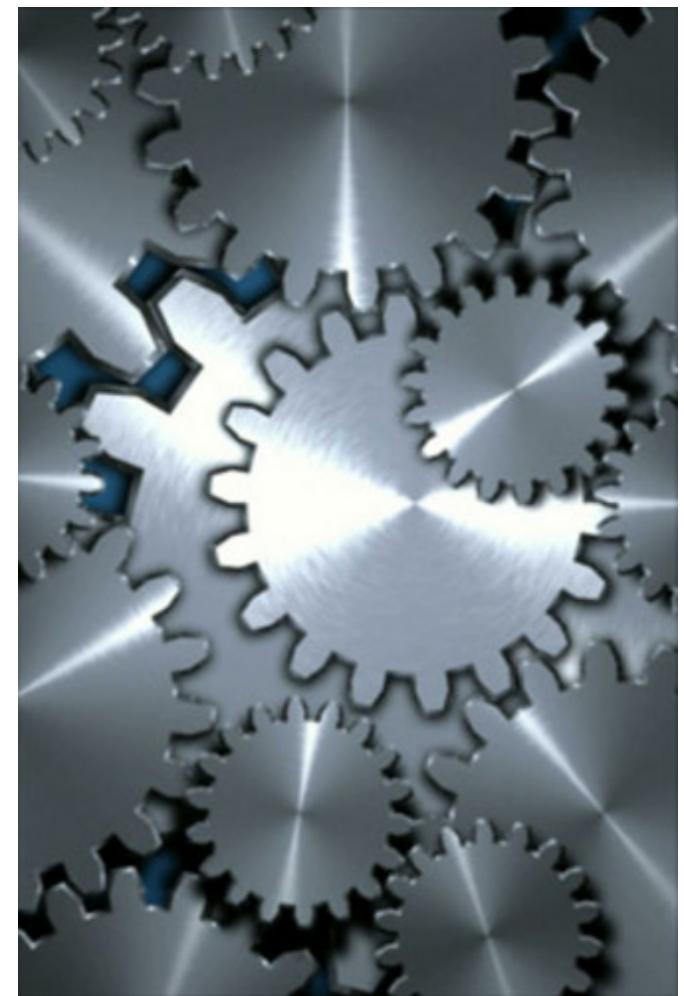


TOP3B has been Found to bind RNA and Other Proteins and Alter Brain Connections



What Remains Unknown?

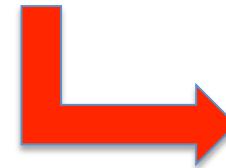
- The mechanism of how mutated TOP3B causes schizophrenia
- Hypothesis: wildtype TOP3 β directly interacts with proteins and RNAs in stress pathways, which are interrupted when TOP3B is mutated
- Primary Goal: To better understand how TOP3B mutation causes schizophrenia symptoms



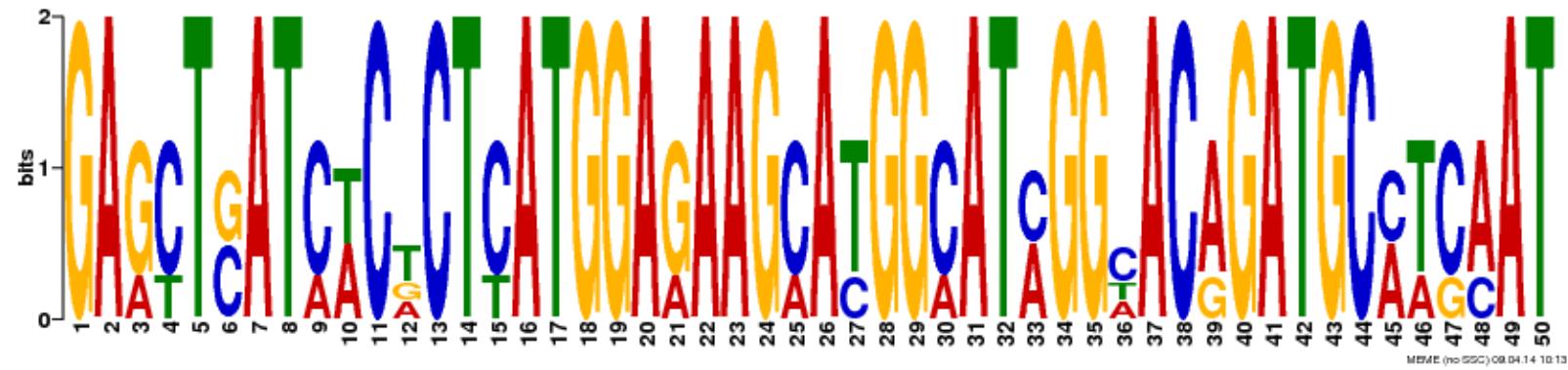
Specific Aim #1: To identify functional similarities of TOP3B gene sequences among organisms with complex and basic nervous systems.



The MEME Suite
Motif-based sequence analysis tools



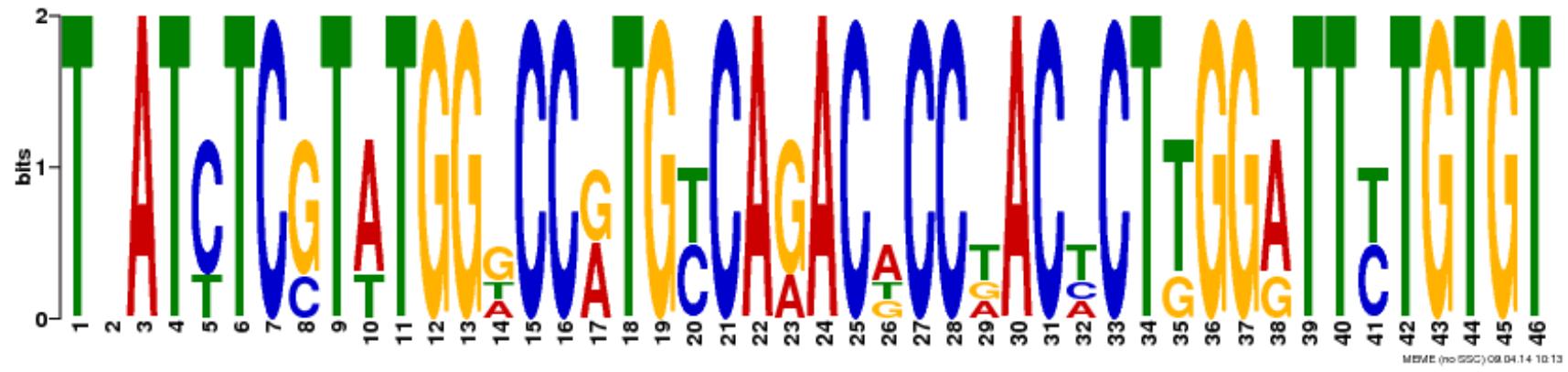
Specific Aim #1: Motif #1



BP: G-protein coupled receptor protein signaling pathway
Regulation of cytokine production
Immune Response
Inflammatory response

SURPRISE: Sensory perception of smell

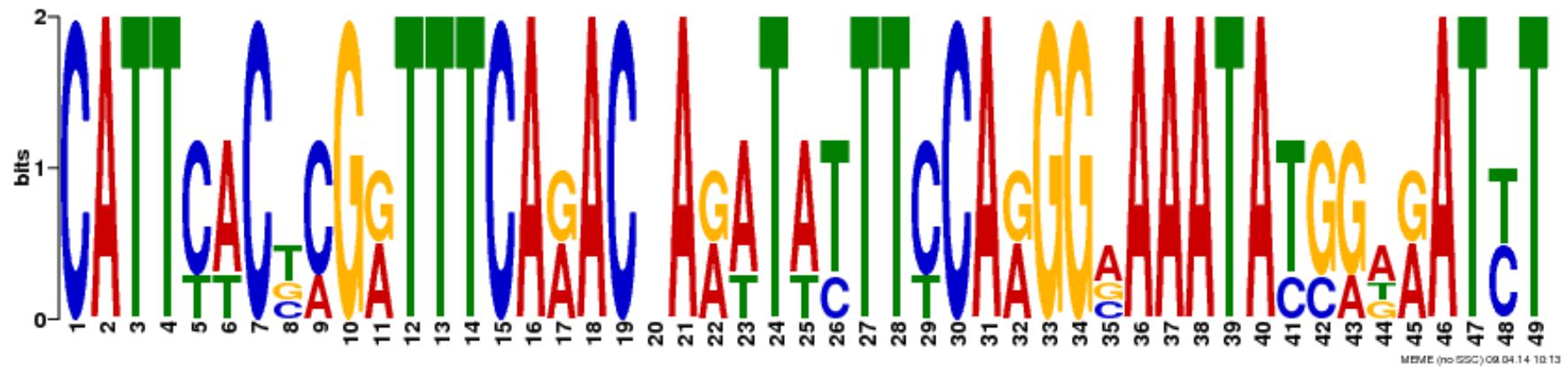
Specific Aim #1: Motif #2



BP: Positive regulation of interleukin-2 biosynthetic process

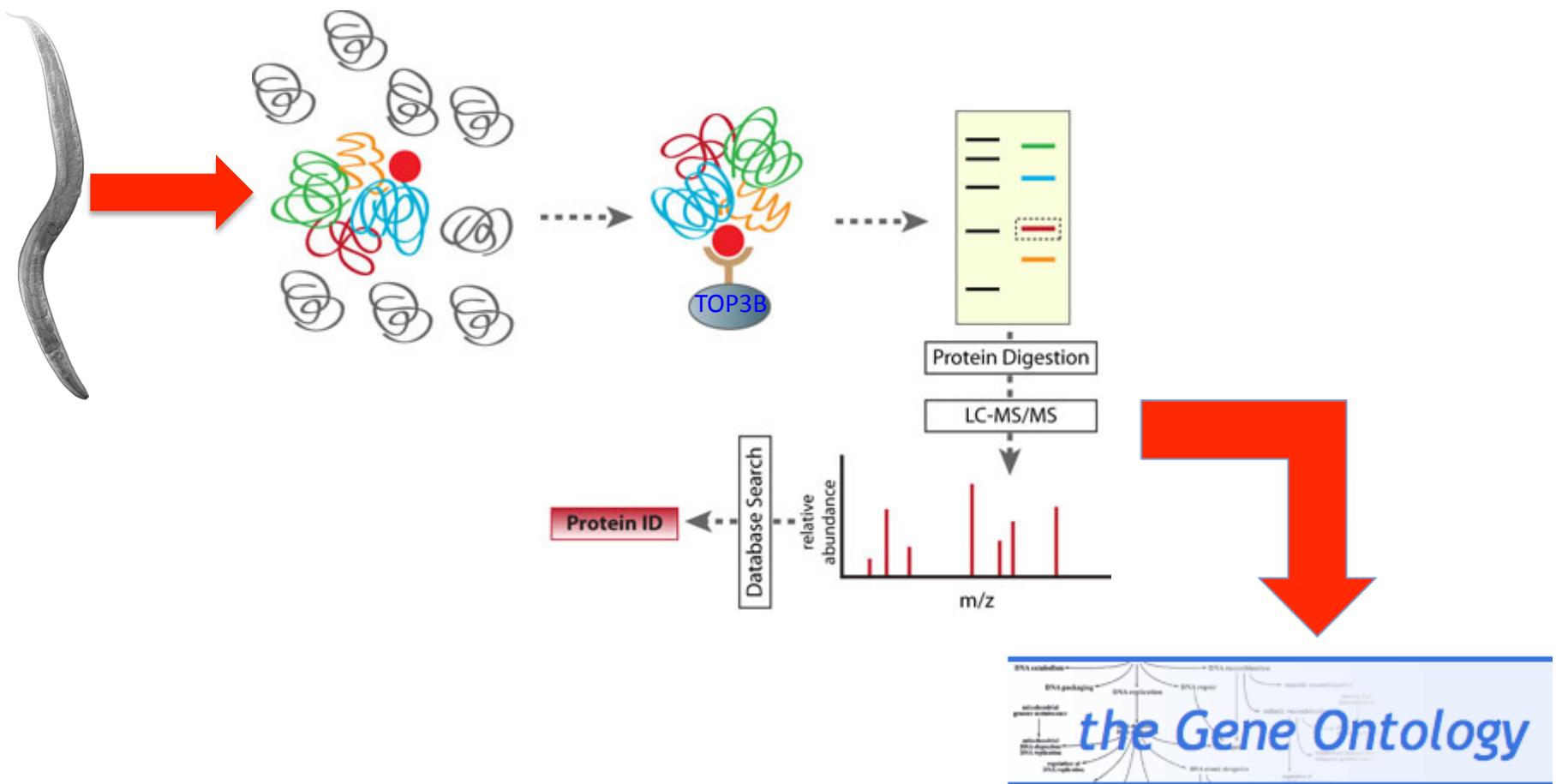
SURPRISE: Bacterium response

Specific Aim #1: Motif #3

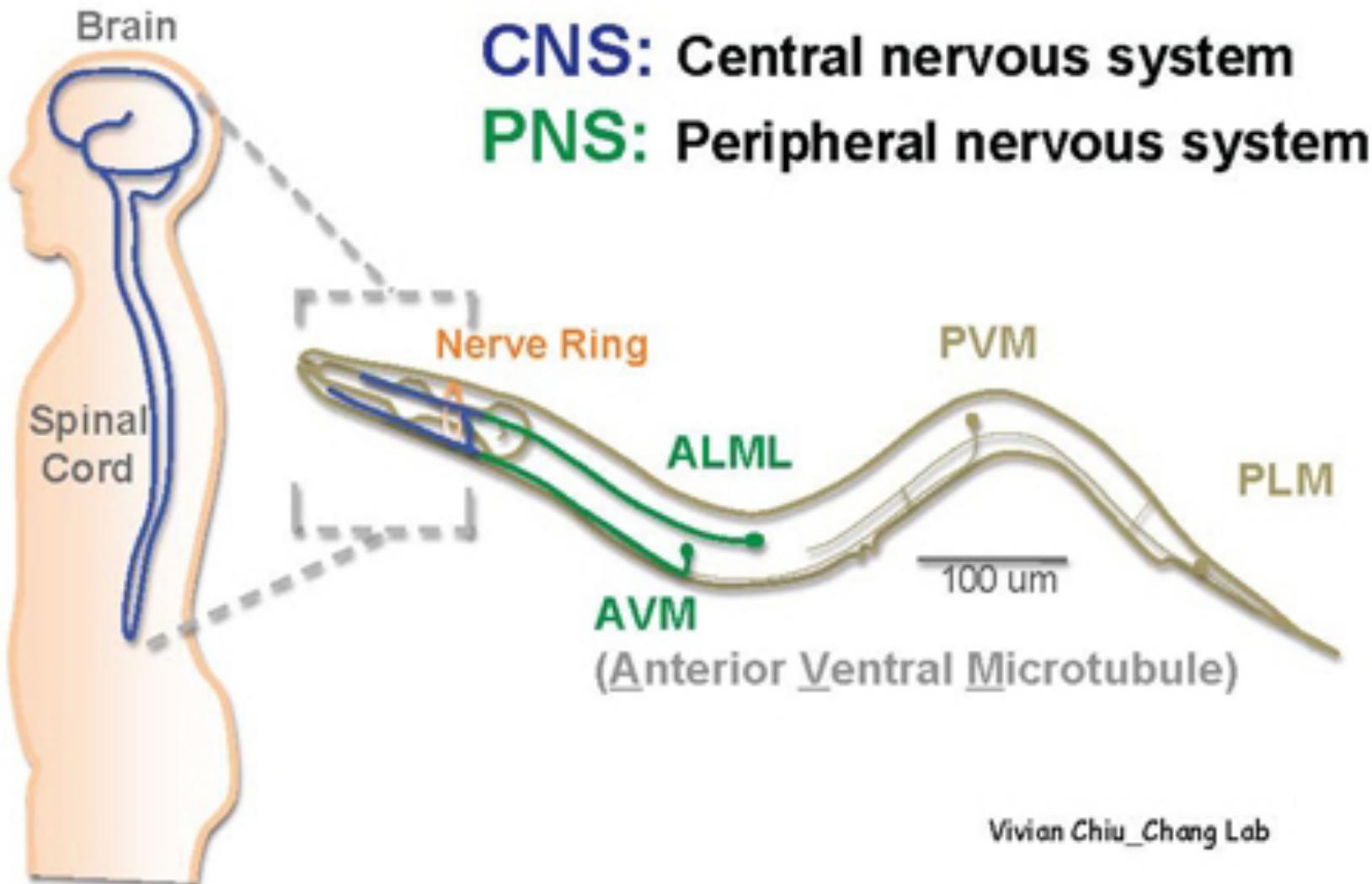


BP: G-protein coupled receptor protein signaling pathway
Sensory perception of smell

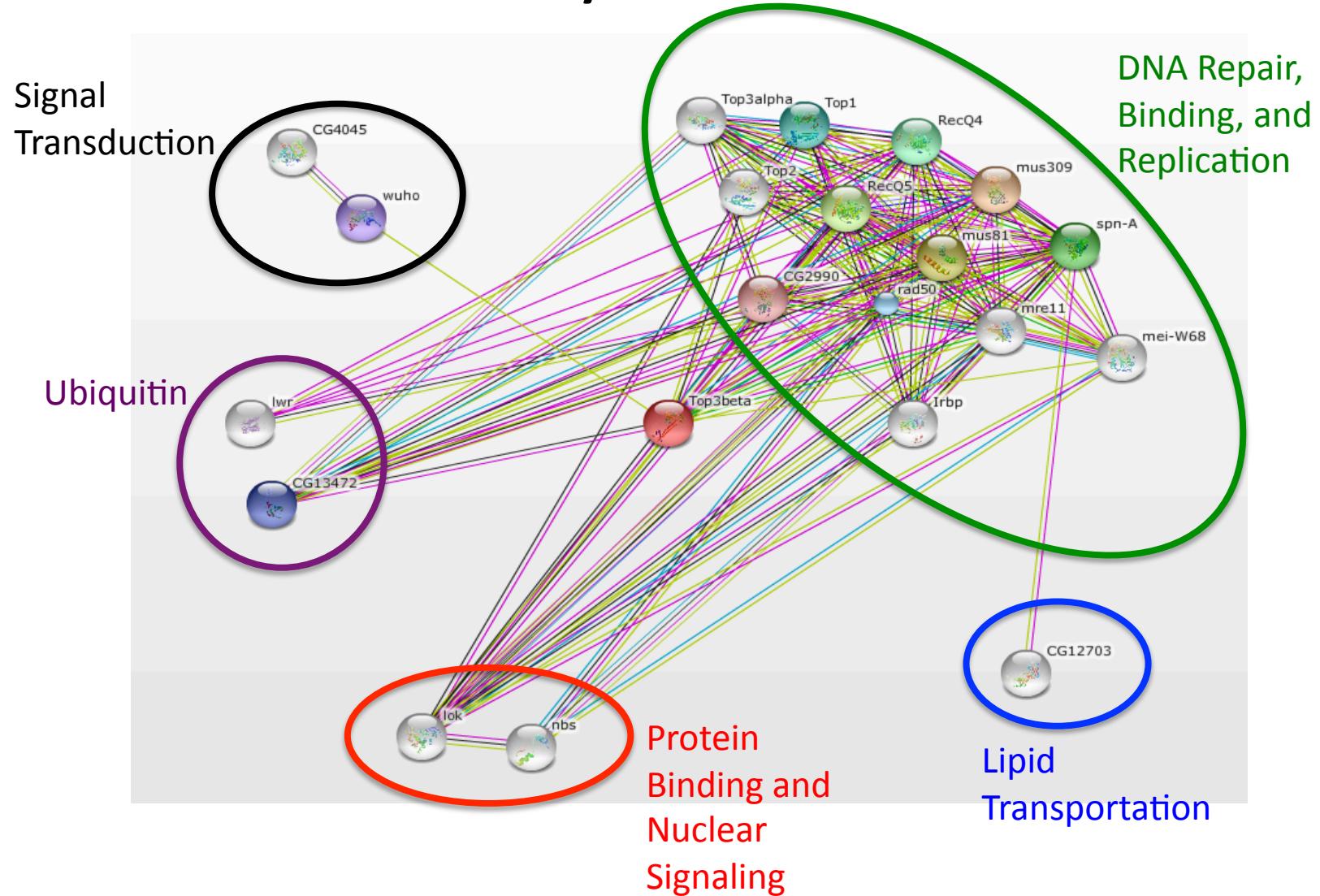
Specific Aim #2: To identify novel protein interactions of TOP3 β .



Why C. elegans?



Specific Aim #2: Current Known Pathways in Humans



Specific Aim #2: Potential Additional Pathways



Signal
Transduction

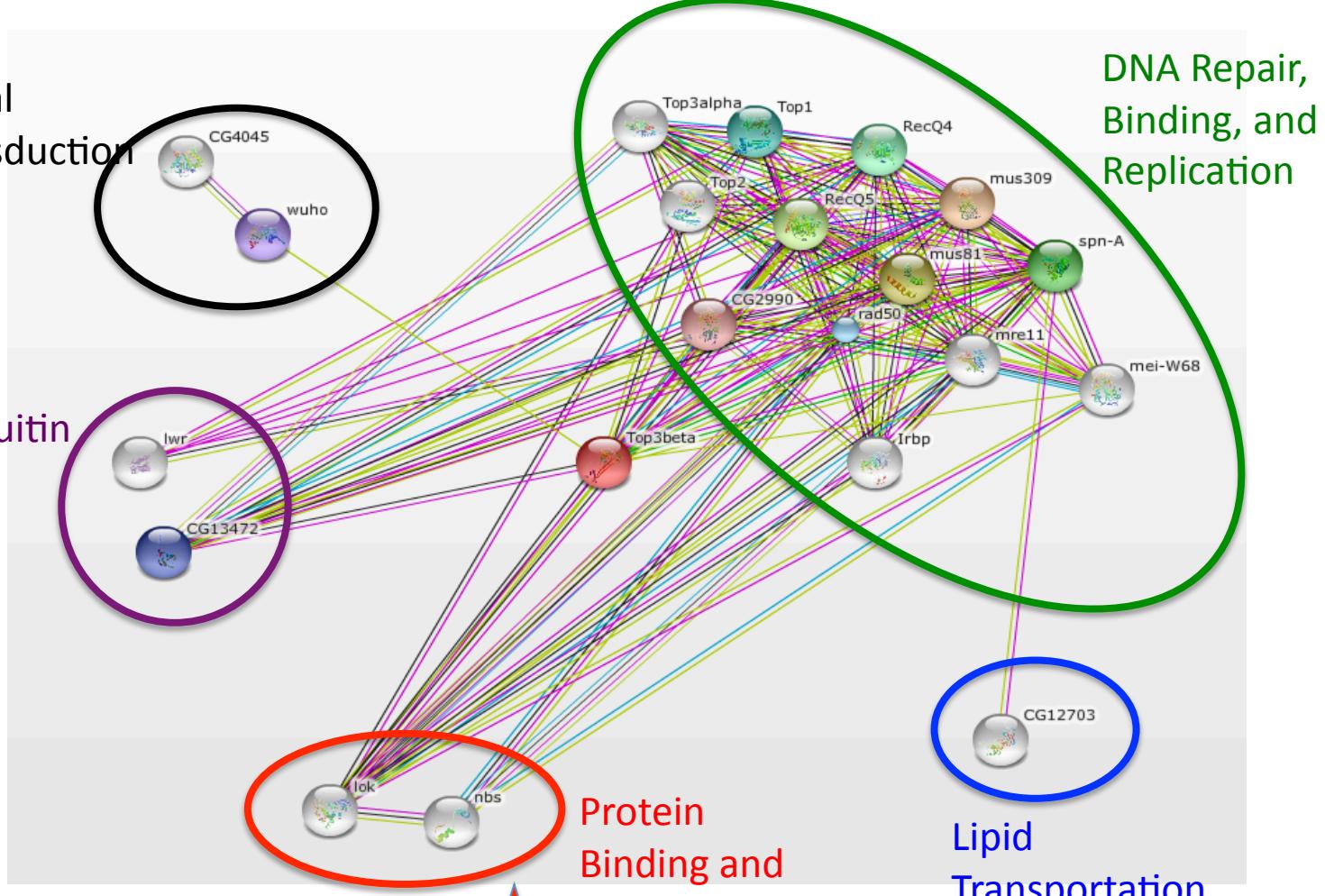


Ubiquitin



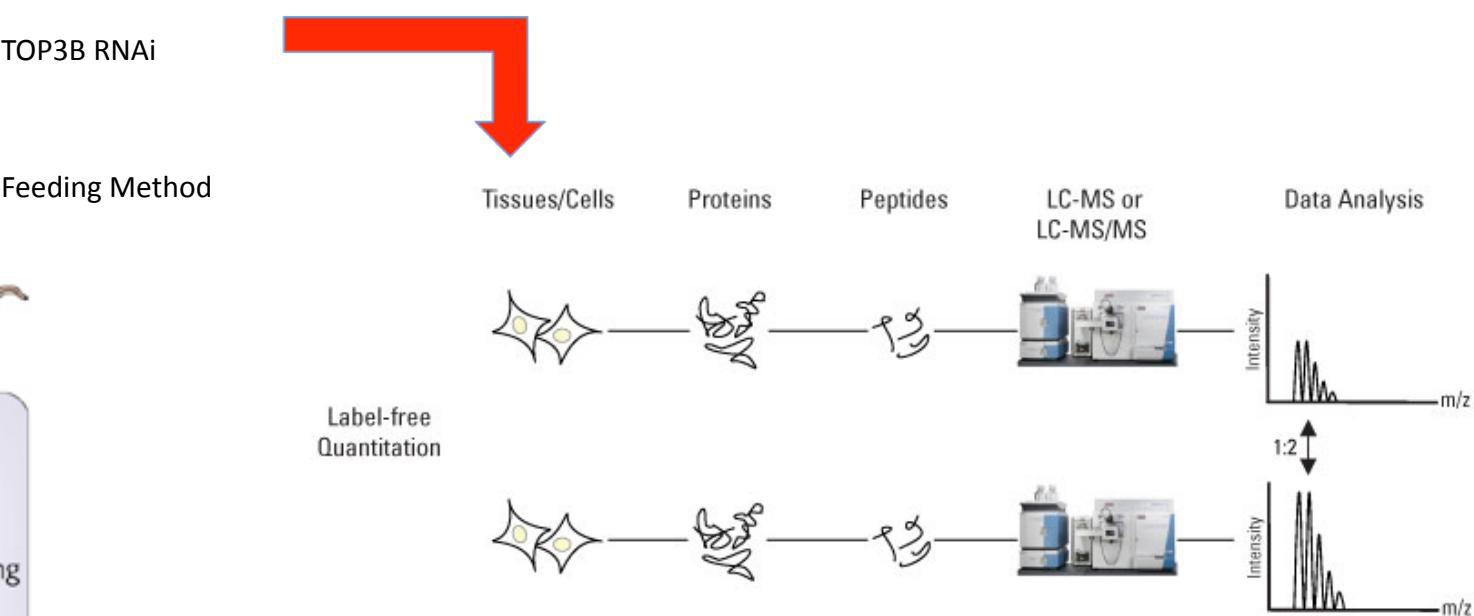
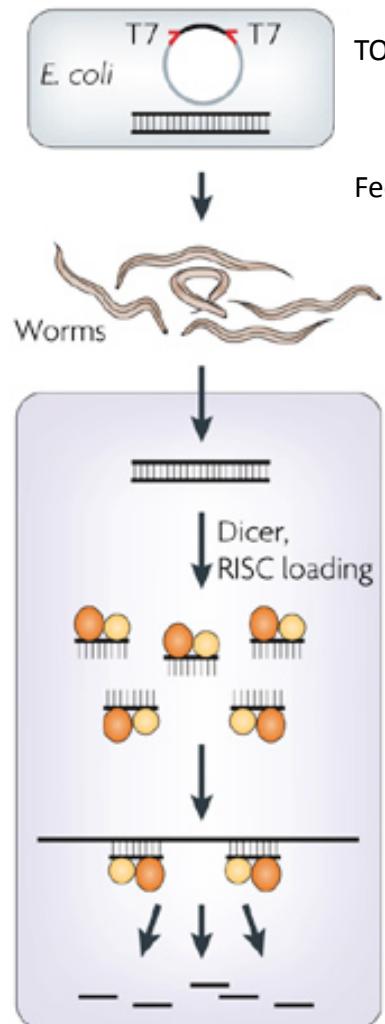
Protein
Binding and
Nuclear
Signaling

STRING 9.1



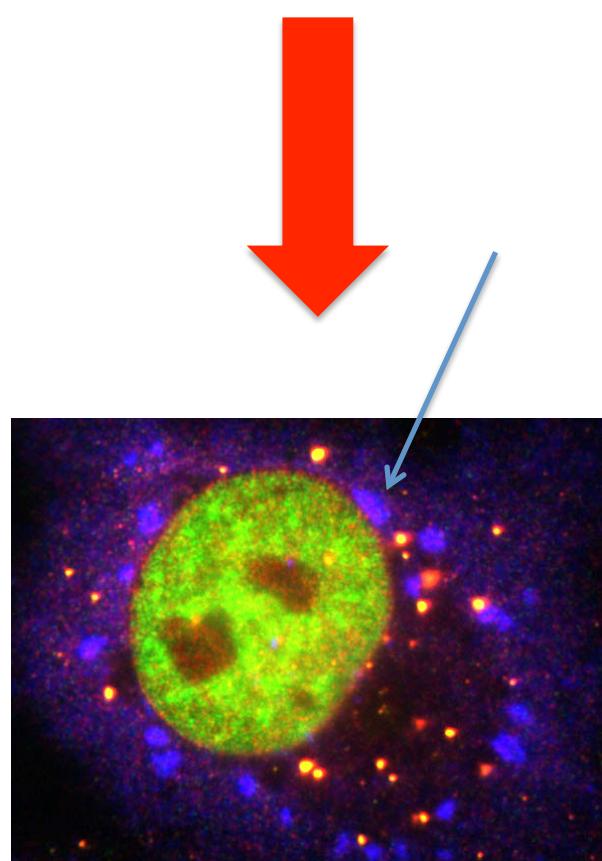
Specific Aim #3: To determine if TOP3 β mutation affects pathways of interacting proteins and if a schizophrenia-like phenotype results.

C. elegans

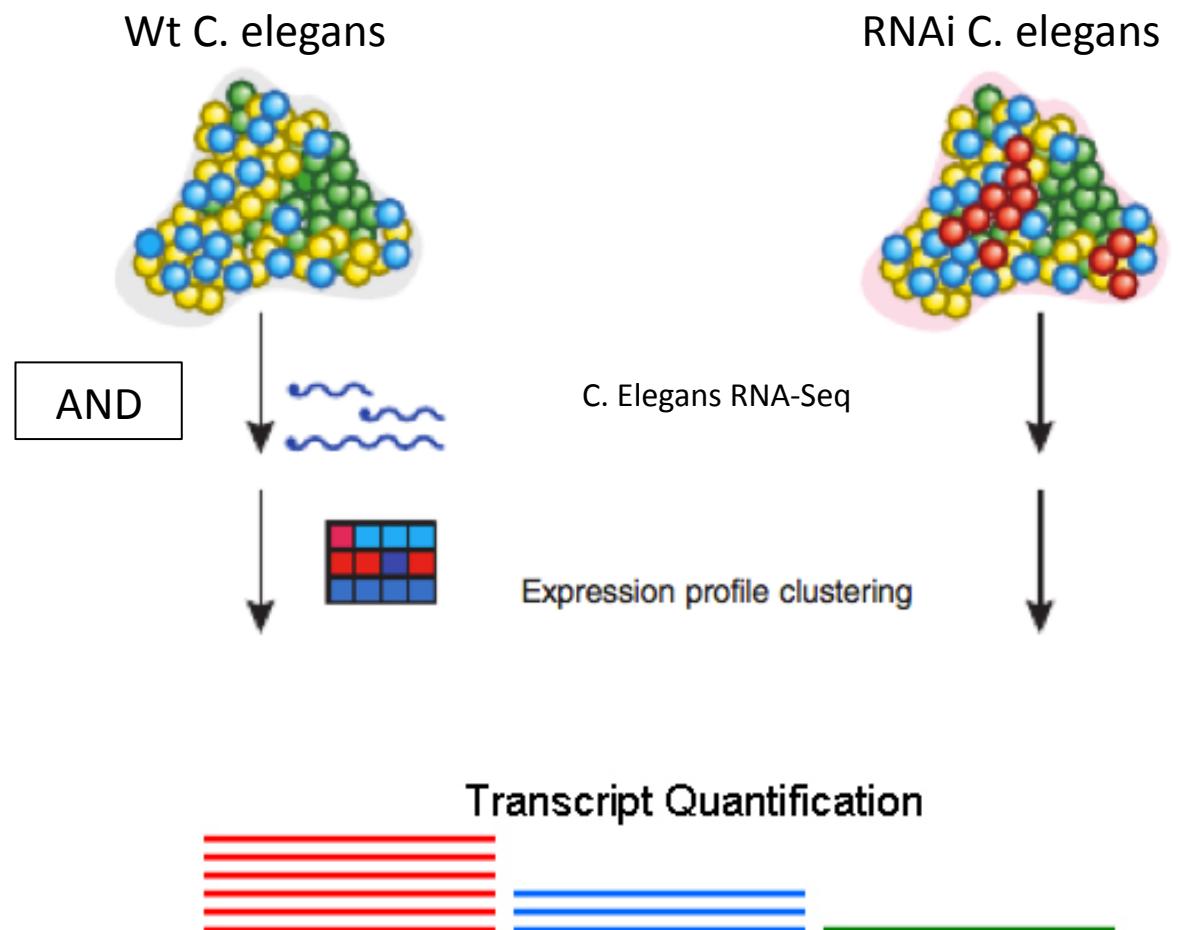


Specific Aim #3: Measuring Stress Granules Changes

RCK1 Staining



RNA-Seq



Specific Aim #3: Current TOP3B RNAi Findings to Expand on



Increased inflammatory response:
stomach inflammation
pancreas inflammation
Glomerulonephritis
dermatitis



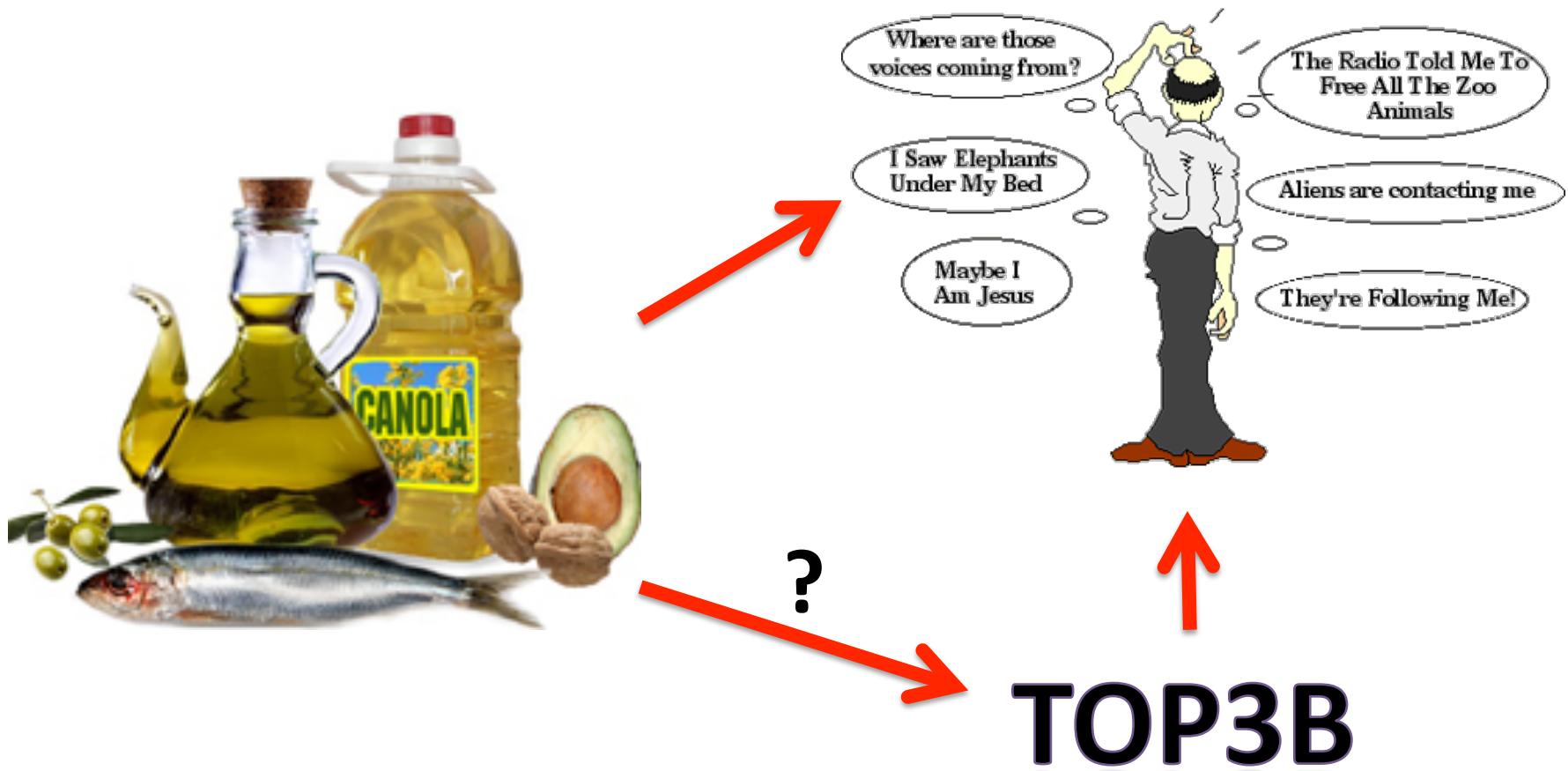
Neuroanatomy defective:
Phenotype that is a defect in nervous system

Why Is This Research Important?

TOP3B



Future Research: Studying the Effects of PUFA on TOP3B



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**THANK YOU FOR
LISTENING**



ANY QUESTIONS?

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