Dysregulation of the Metabolic-Inflammatory Axis in Multiple Sclerosis

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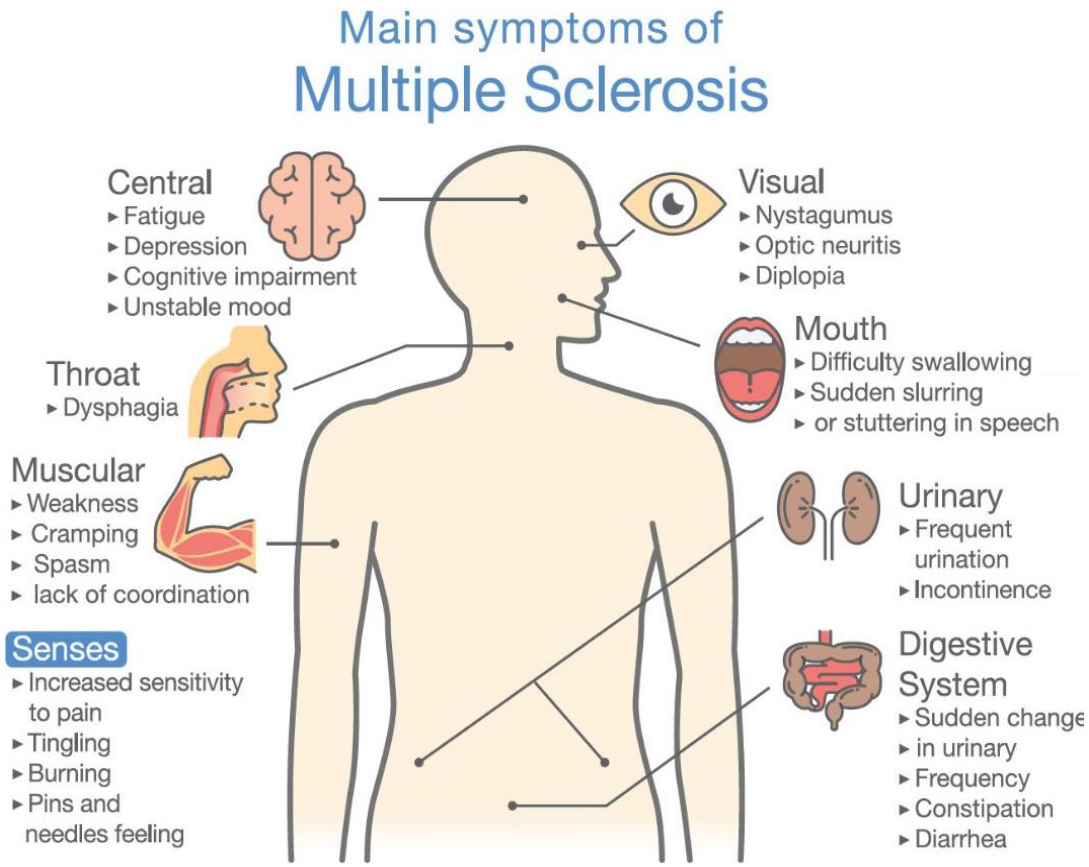
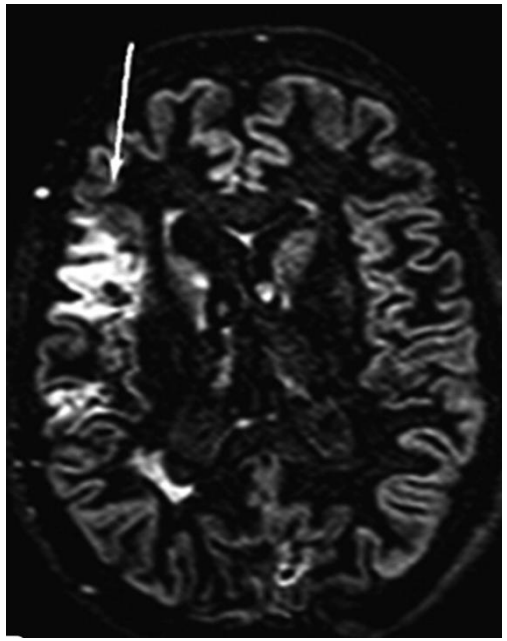
Multiple Sclerosis



Grey Matter MS Lesions
(Brain MRI)



(Filippi et al., American Journal of Neuroradiology 2010)

Chronic

Autoimmune

Progressive

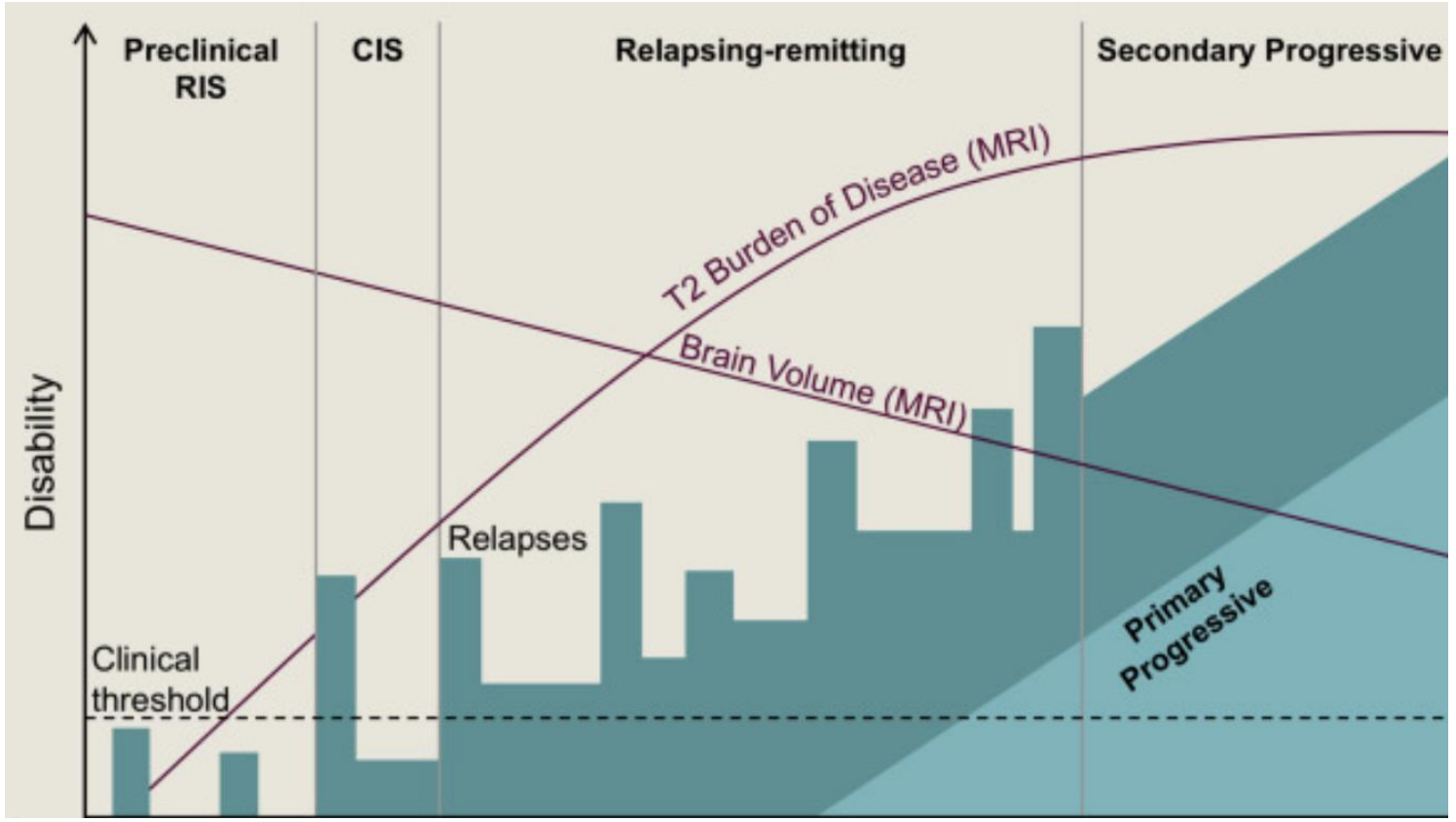
Neurodegenerative

Multiple Sclerosis

- Relapsing-Remitting MS
- Primary Progressive MS
- Secondary Progressive MS

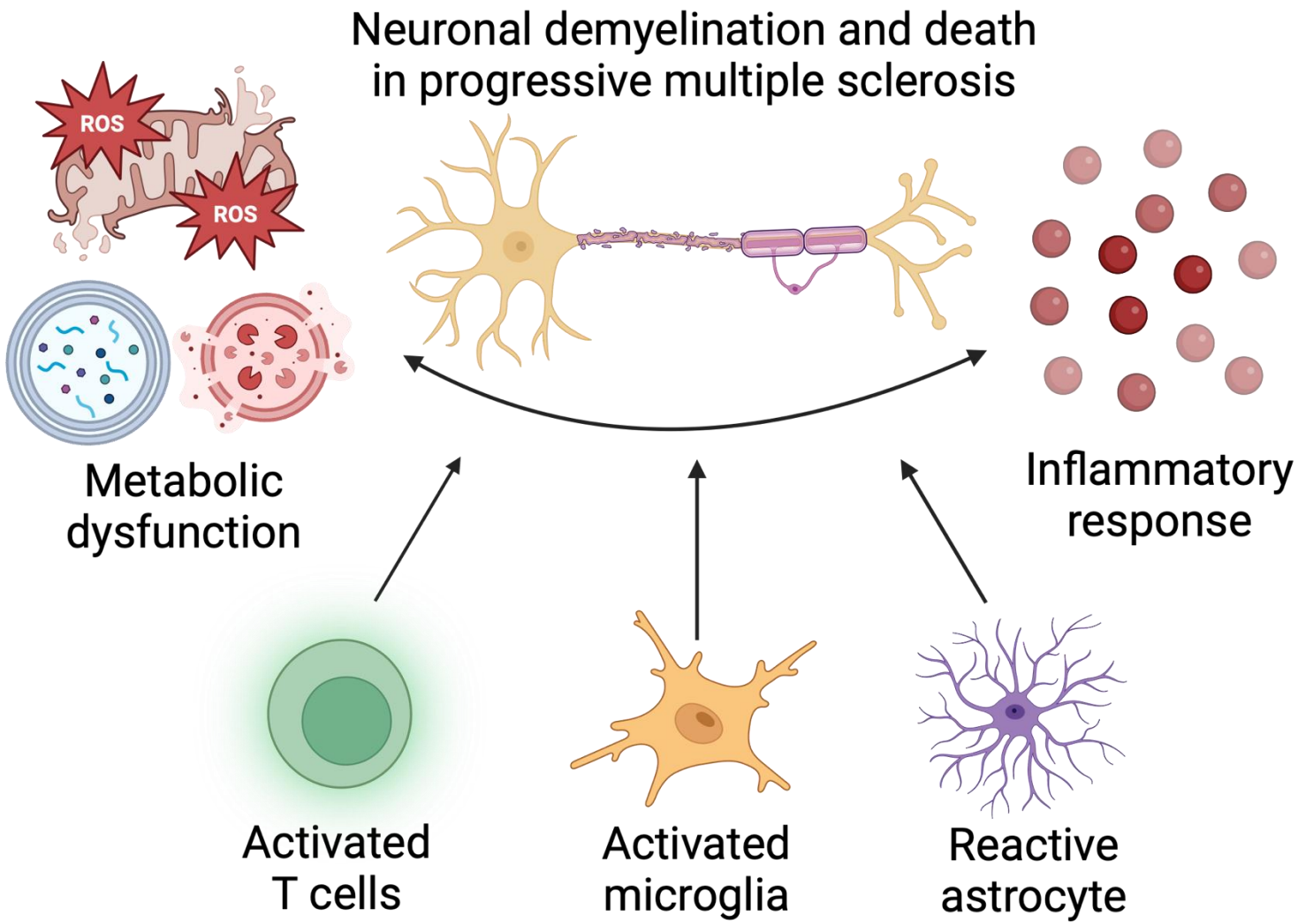
Progressive MS lacks effective treatment, leads to significant disability and a reduced quality of life

Better understanding of disease mechanism & development of new therapies against progressive MS

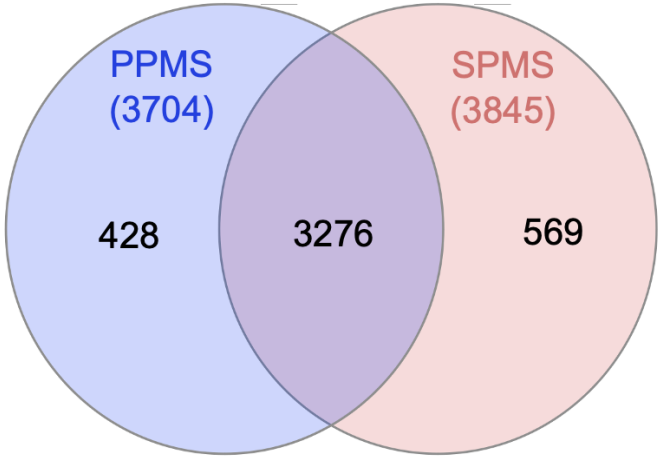


(Adapted from Allan et al., *Neuron* 2018)

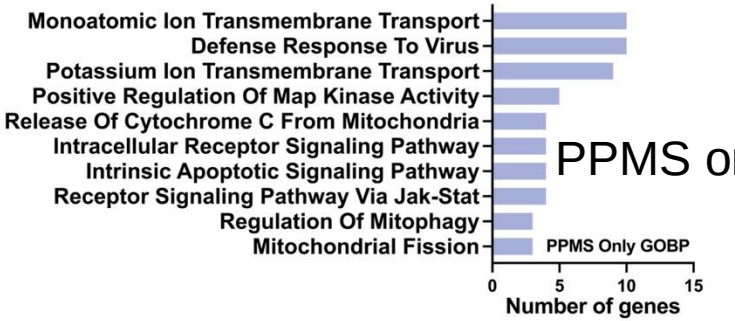
Metabolic-Inflammatory Axis in Progressive MS



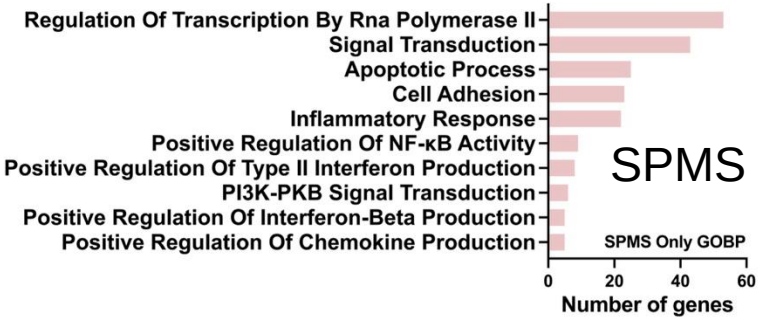
Progressive MS: Divergent Pathways & Convergent Damage



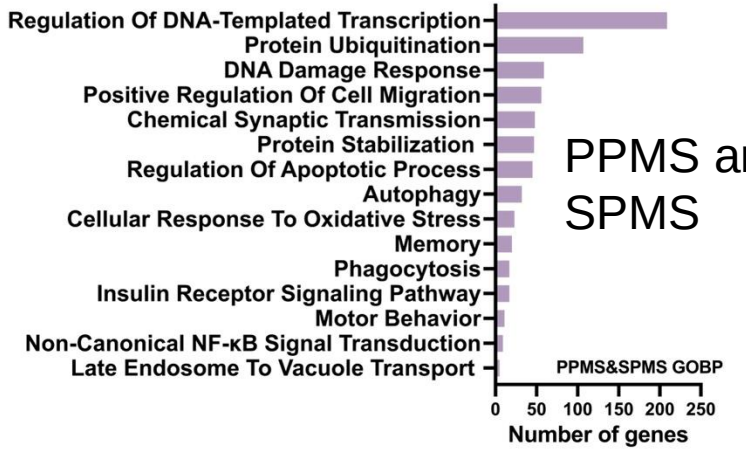
Shared and unique DEGs between comparisons of
PPMS lesions vs healthy controls
SPMS lesions vs. healthy controls
(Grey matter tissues)



PPMS only → metabolic dysfunction



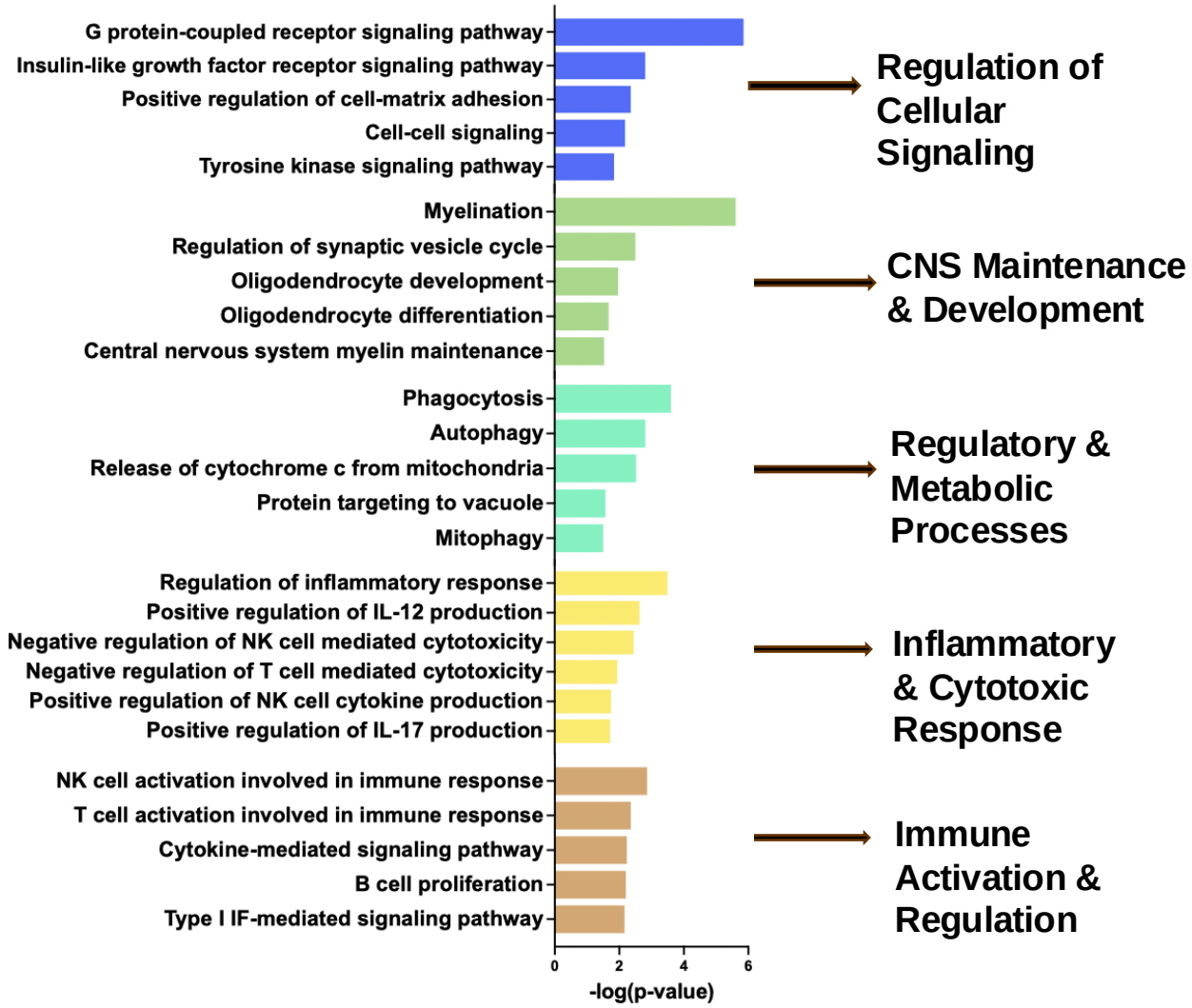
SPMS only → inflammation mediated

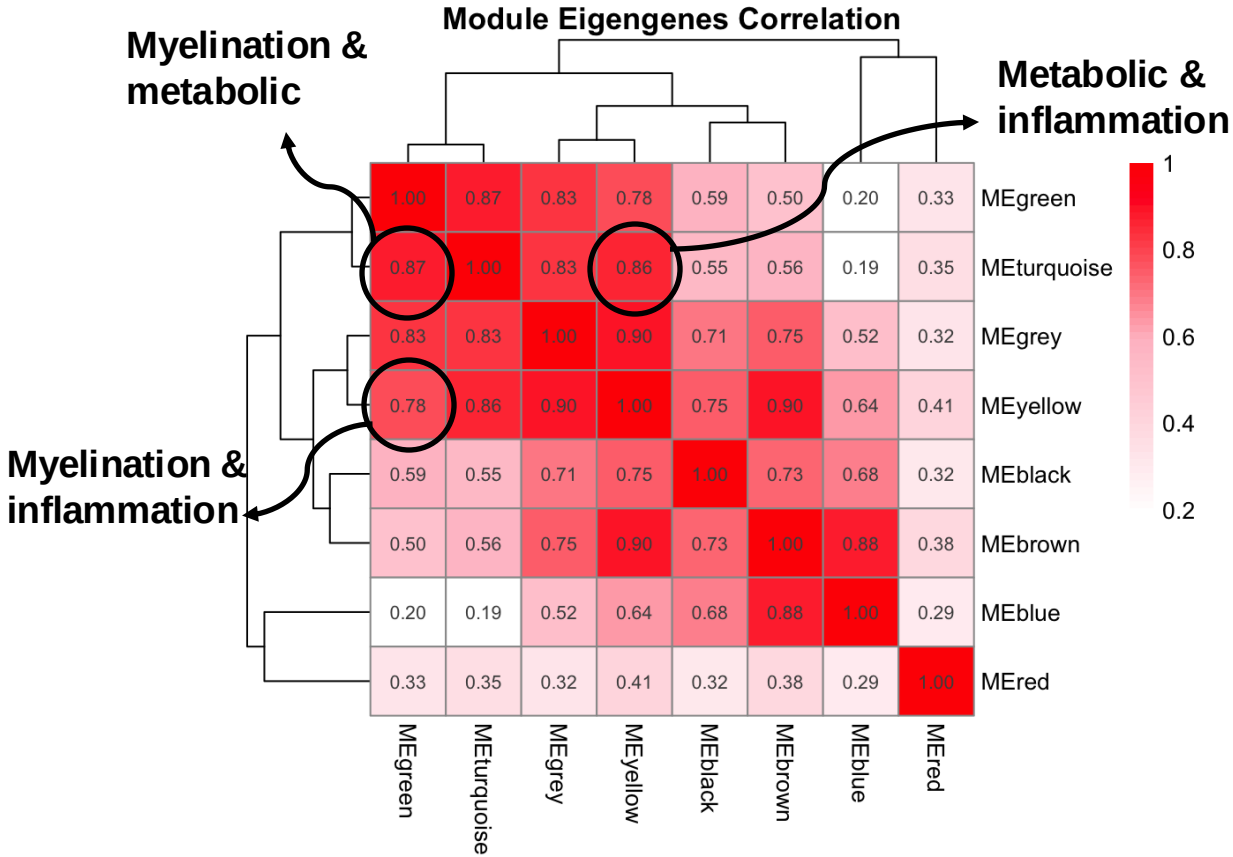


PPMS and SPMS → shared vulnerabilities

- autophagy
- oxidative stress
- synaptic transmission

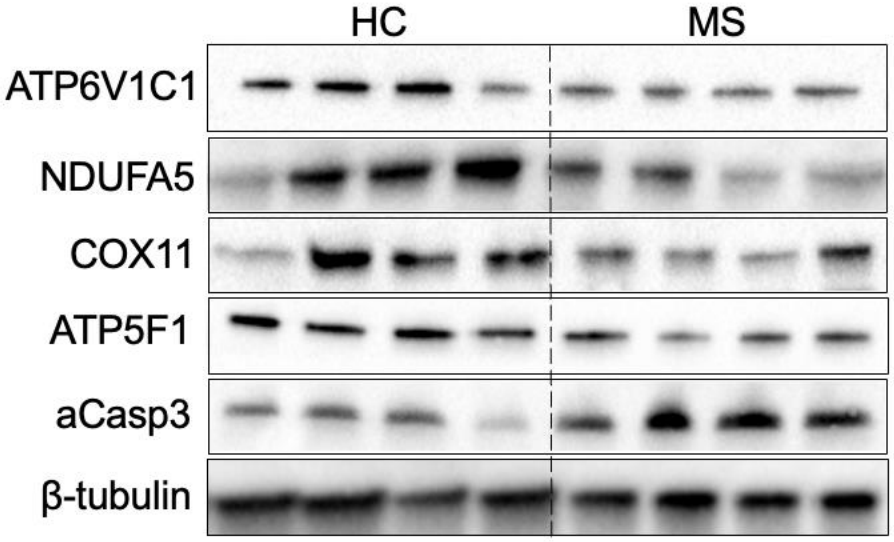
Weighted Gene Co-expression Network Analysis (WGCNA)



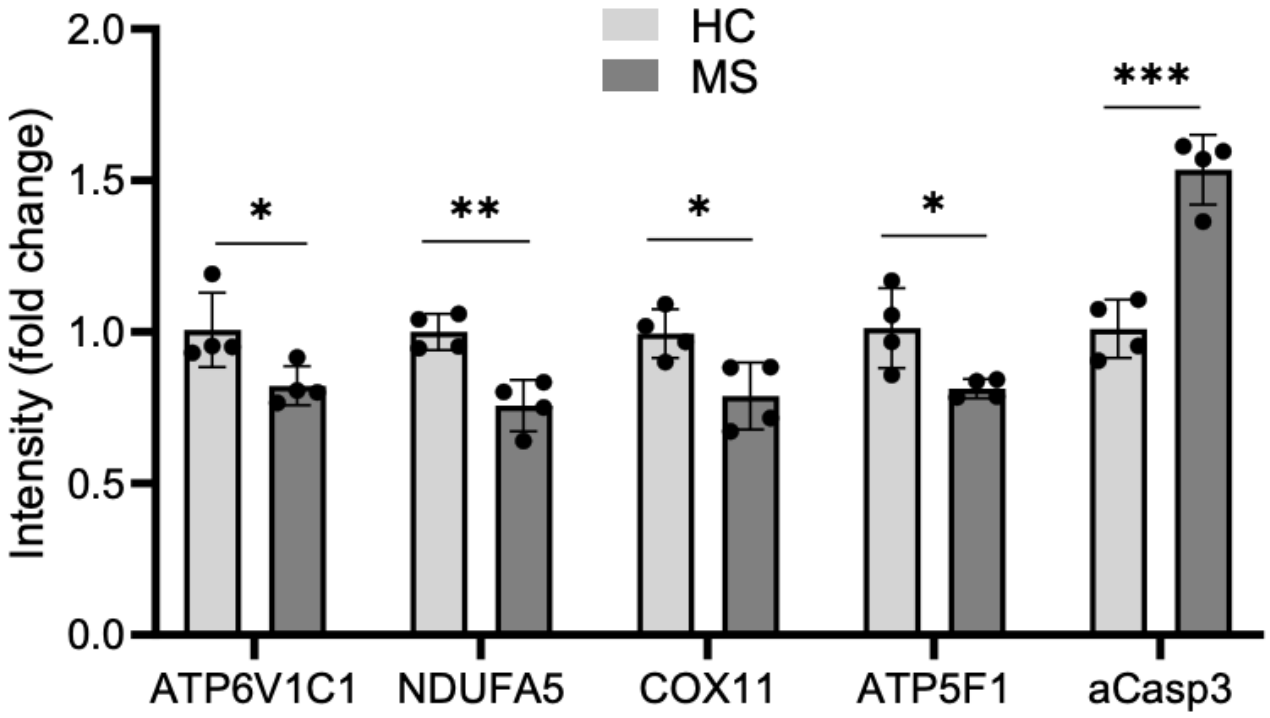


Validation in Human Postmortem MS Brain Tissues

Genes of Interest	SPMS Fold Change (log_2)	PPMS Fold Change (log_2)
ATP6V1C1	-1.722	-2.310
NDUFA5	-2.086	-2.168
COX11	-2.467	-2.505
ATP5F1	-1.972	-2.466

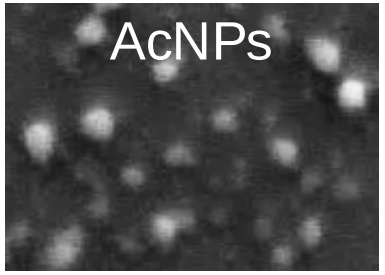


Grey matter lesion tissues of progressive MS and healthy controls



Pharmacological Modulation in SH-SY5Y Neuronal Cells

Lysosome-targeting acidic nanoparticles



(Zeng et al., *Nat Commun*, 2023)
(Lo et al., *ACS Nano*, 2024)
(US Patent No. 10925975)