Proteomic Investigation of Tetrahydrobiopterin-Related Pathways in Multiple Sclerosis

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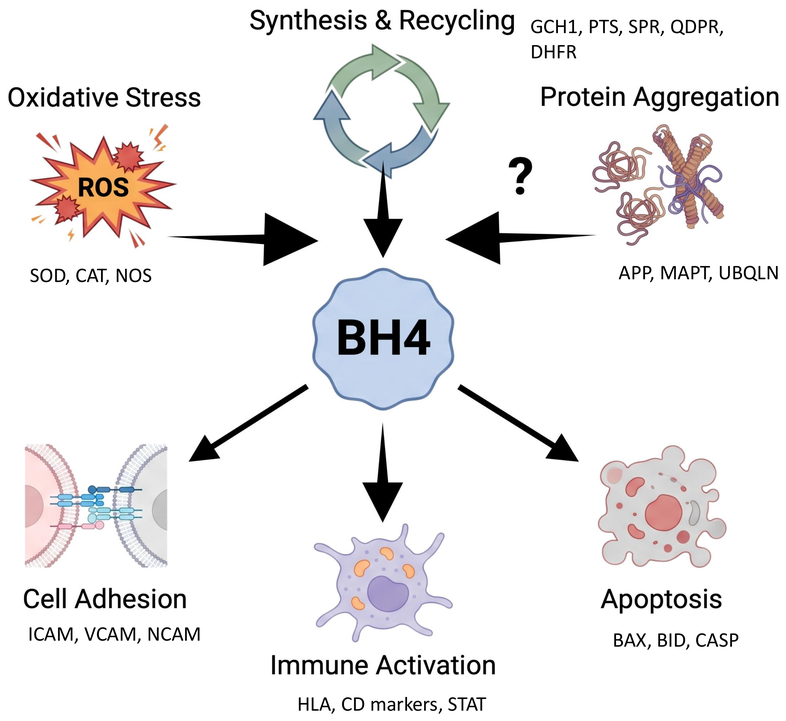
Introduction

Tetrahydrobiopterin (BH4) is an essential cofactor for multiple important physiological mechanisms. Dysregulation of BH4 pathways has been implicated in neuroinflammation and may contribute to the pathophysiology of neurological diseases, including multiple sclerosis (MS). Beyond our group, limited research has explored BH4-related upstream and downstream pathways in MS. Proteins of interest included those involved in BH4 synthesis & recycling, as well as downstream pathways like oxidative stress, protein aggregation, cell adhesion, immune activation, and apoptosis. Publicly available proteomics datasets offer an opportunity to investigate these pathways across human MS samples.

Objective

Reanalyze public human MS proteomics data to examine BH4-related protein expression and downstream pathways, identify reproducible proteomic patterns, and better characterize how BH4 metabolism may relate to MS pathophysiology.

Figure 1. BH4 Metabolism and MS-relevant Downstream Pathways



Methods

Figure 2. PRISMA Diagram for Dataset Screening

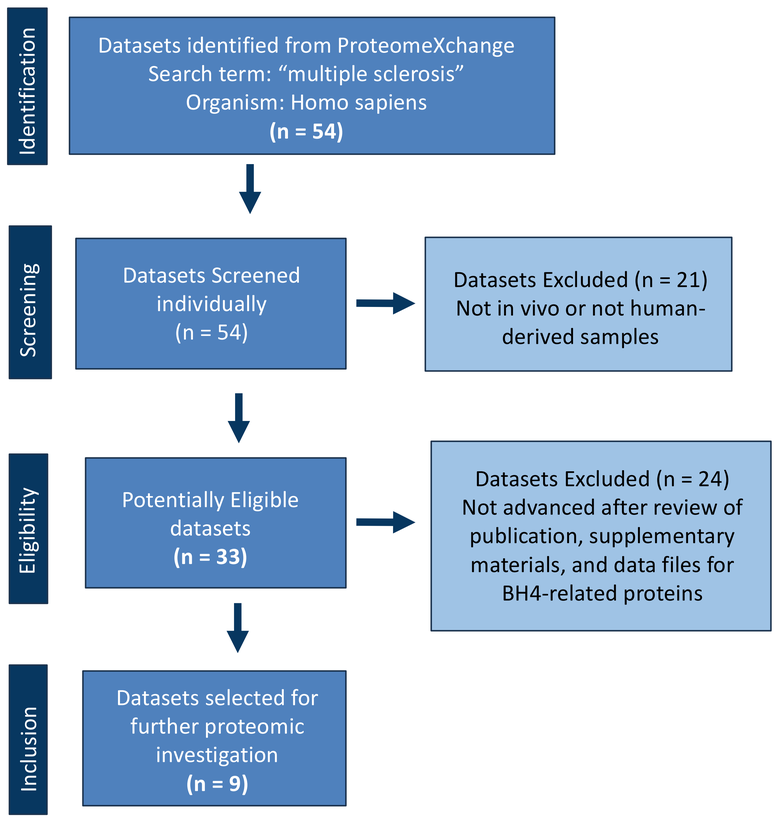
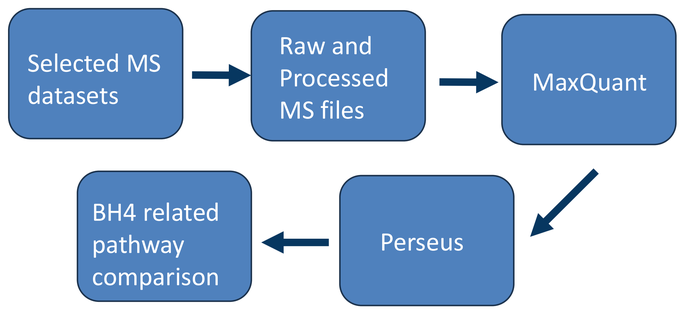


Figure 3. Planned Proteomic Reanalysis Workflow



Results

Table 1. Characteristics of Selected MS Proteomic Datasets

Dataset	Biospecimen / Source	Study Groups	Representative Proteins Noted in Screening
PXD004572	Cerebrospinal fluid	Multiple sclerosis vs neurological controls	QDPR, CAT, SOD1, ICAM1, HLA-DRA, MAPT
PXD004540	Cerebrospinal fluid	Relapsing-remitting multiple sclerosis vs other neurological disease controls	SPR, PTS, CAT, FAS, ICAM1, APP
PXD011785	Peripheral blood CD4+ and CD8+ T cells	Multiple sclerosis vs healthy controls	QDPR, SOD1, GPX4, CASP3, CD3D, APP
PXD026529	Progressive multiple sclerosis gray matter	Progressive multiple sclerosis; comparator not reported	SPR, QDPR, PCBD1, SOD1, BAX, ICAM1
PXD038555	Serum extracellular vesicles and exosomes	Relapsing-remitting multiple sclerosis vs Parkinson disease and dementia	NOS2, GPX3, CAT, ICAM1, C3, APOE
PXD047800	Postmortem brain tissue	Multiple sclerosis vs neurologically normal autopsy tissue	SPR, QDPR, PCBD1, SOD1, ICAM1, MAPT
PXD008344	Postmortem gray and white matter	Multiple sclerosis vs control brain tissue	SPR, QDPR, DHFR, GPX1, CASP3, MAPT
PXD048002	Plasma extracellular vesicles	Relapsing-remitting multiple sclerosis treatment responders vs nonresponders	QDPR, GPX1, SOD2, CD44, C1QB, TARDBP
PXD066920	Decellularized gray-matter brain tissue	Multiple sclerosis gray matter vs control gray matter	QDPR, SOD2, GPX4, CYCS, C3, MAPT

Representative proteins shown; not an exhaustive list. Protein detection during screening does not indicate differential expression.

Conclusion

The 9 datasets cover several sample sources and initial screening noted BH4 recycling and salvage enzymes such as QDPR and SPR in most of them. Reanalysis with a standardized workflow will test whether BH4-related proteomic patterns are reproducible across MS datasets, which lays the groundwork for evaluating BH4 metabolism as a mechanistic and biomarker axis.

References & Acknowledgements

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