

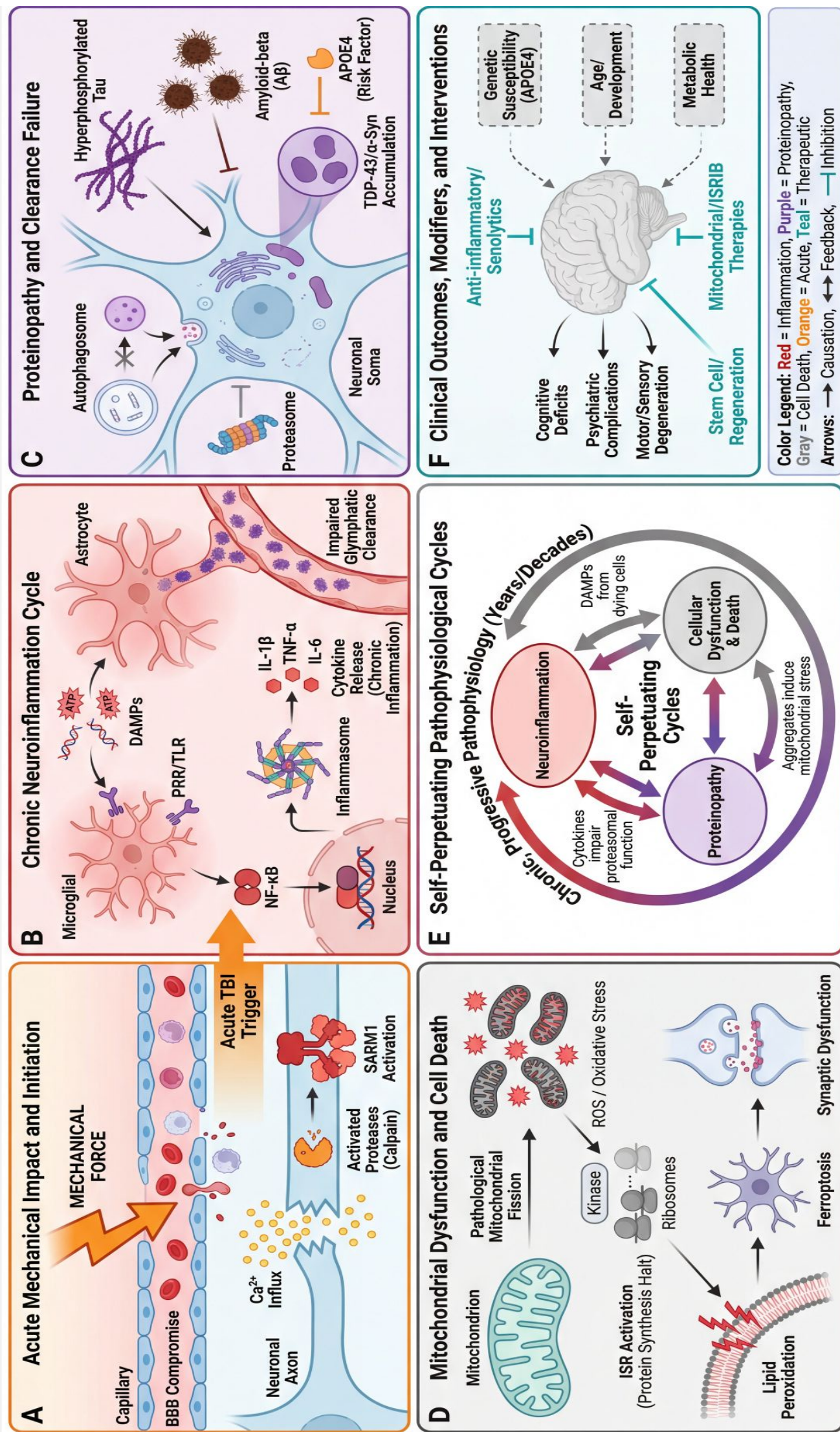
Mapping Causal Pathways From Traumatic Brain Injury To Dementia A Systematic Synthesis With Computational Inference

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Ahmed Shaheen^{1,5}, Fabio Dennstädt^{2, 3}, Nour Shaheen¹, Irina Filchenko⁴

1.Alexandria Faculty of Medicine, Egypt, 2.Department of Radiation Oncology, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland, 3.Department of Digital Medicine, University of Bern, Bern, Switzerland, 4.Department of Neurology, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland, 5. Montreal Faculty of Medicine, CA.

BioClaritas, a fully automated agentic AI framework, synthesized 823 clinical and preclinical abstracts into a traceable six-phase causal network linking TBI to neurodegeneration, surfacing SARM1, cGAS-STING1, and cis-tau/PIN1 pathways beyond prior literature.

INTRODUCTION	METHODS	RESULTS	Figure	Conclusion
Traumatic brain injury (TBI) affects 20.8 million people annually and increases the risk of later-life neurodegeneration, including Alzheimer's disease, early-onset dementia, CTE, and Parkinson's disease (~1.92-fold higher dementia risk). However, the multiscale mechanisms linking TBI to neurodegeneration remain poorly characterized, and traditional systematic reviews cannot integrate the breadth of clinical and preclinical evidence required for causal modeling. We developed BioClaritas, a scalable agentic AI framework that uses large language models to extract, integrate, and formalize disease mechanisms into a reproducible, traceable causal network, and applied it to model TBI-to-dementia progression.	A systematic PubMed search (January 2014–May 2025) identified 1,347 articles. Automated abstract screening with GPT-4.1-mini, followed by human adjudication, yielded 425 clinical and 398 preclinical abstracts with mechanistic outcomes. GPT-4.1-mini extracted structured subject-relation-object triples from each abstract. Triples were embedded using four biomedical sentence-transformer models; SapBERT was selected based on Noise Ratio and Silhouette Coefficient performance. A PCA ($\leq 80\%$ variance) then UMAP (15 dimensions) pipeline preceded HDBSCAN clustering. Clusters were synthesized into structured evidence summaries by an LLM and integrated into a traceable disease network, available through an interactive HTML DAG visualization.	HDBSCAN identified 67 clinical and 59 preclinical pathway clusters, integrated into a mechanistic framework spanning six pathological phases: (I) primary mechanical injury, (II) vascular and blood-brain barrier compromise, (III) neuroinflammatory cascades, (IV) metabolic crisis and mitochondrial dysfunction, (V) proteinopathy, and (VI) cell death with accelerated brain aging. Beyond established mechanisms, the network identified SARM1-mediated axonal degeneration, cGAS-STING1 interferon amplification, and cis-tau/PIN1 seeding, glymphatic-sleep disruption, and gut-brain axis dysbiosis. Compared with the expert-curated review by Katramadou et al. (2026), BioClaritas showed strong topological concordance while independently identifying additional cross-disciplinary feedback mechanisms.		BioClaritas demonstrates a fully automated, traceable agentic AI pipeline for large-scale disease modeling. By integrating 823 clinical and preclinical abstracts, it reconstructed a six-phase TBI-to-neurodegeneration cascade while identifying mechanisms beyond conventional reviews. Its scalable architecture provides a foundation for future quantitative disease simulation and therapeutic target prioritization. CONTACT  Email: ahmed.shaheen.1@umontreal.ca Tele: 0201010991021 