

Understanding the Molecular Link Between Infection and Dementia Risk

Presented By: Keenan Walker, PhD
Multimodal Imaging of Neurodegenerative Disease (MIND) Unit



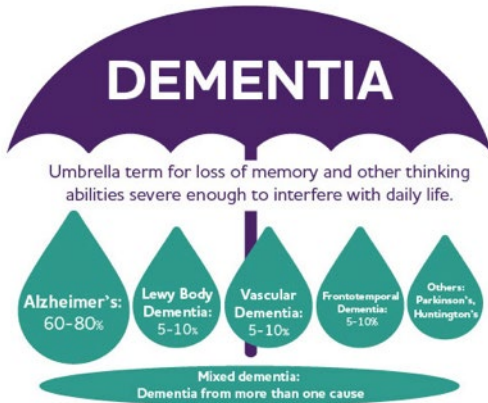
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ONE PROGRAM, MANY PEOPLE, INFINITE POSSIBILITIES

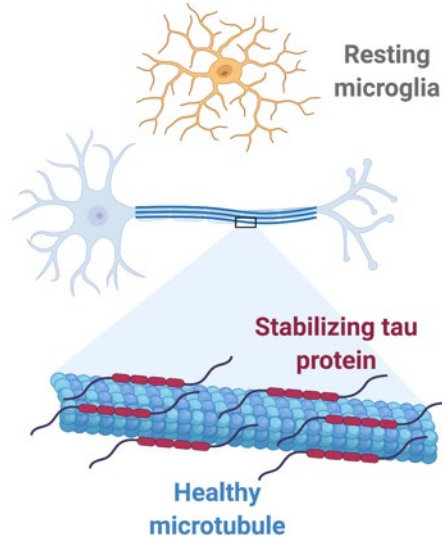
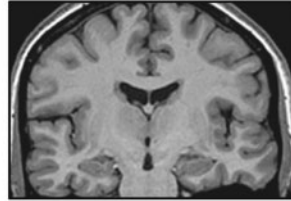


Alzheimer's Disease & Related Dementias

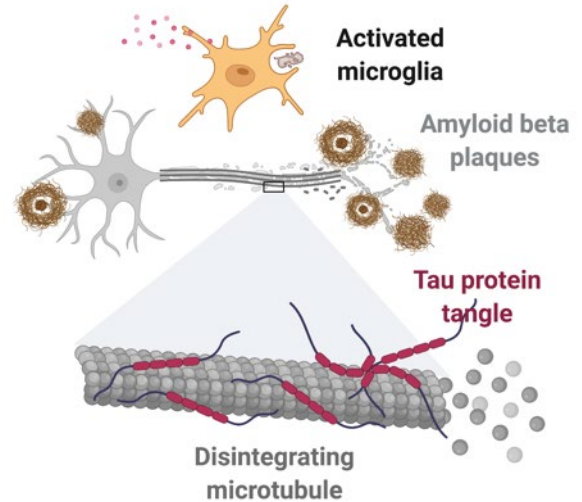
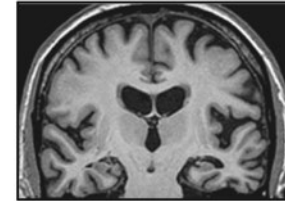
- 6.2 million Americans (11%) age 65 and older have Alzheimer's disease
- Most common form of dementia (60% to 80%)



Healthy brain



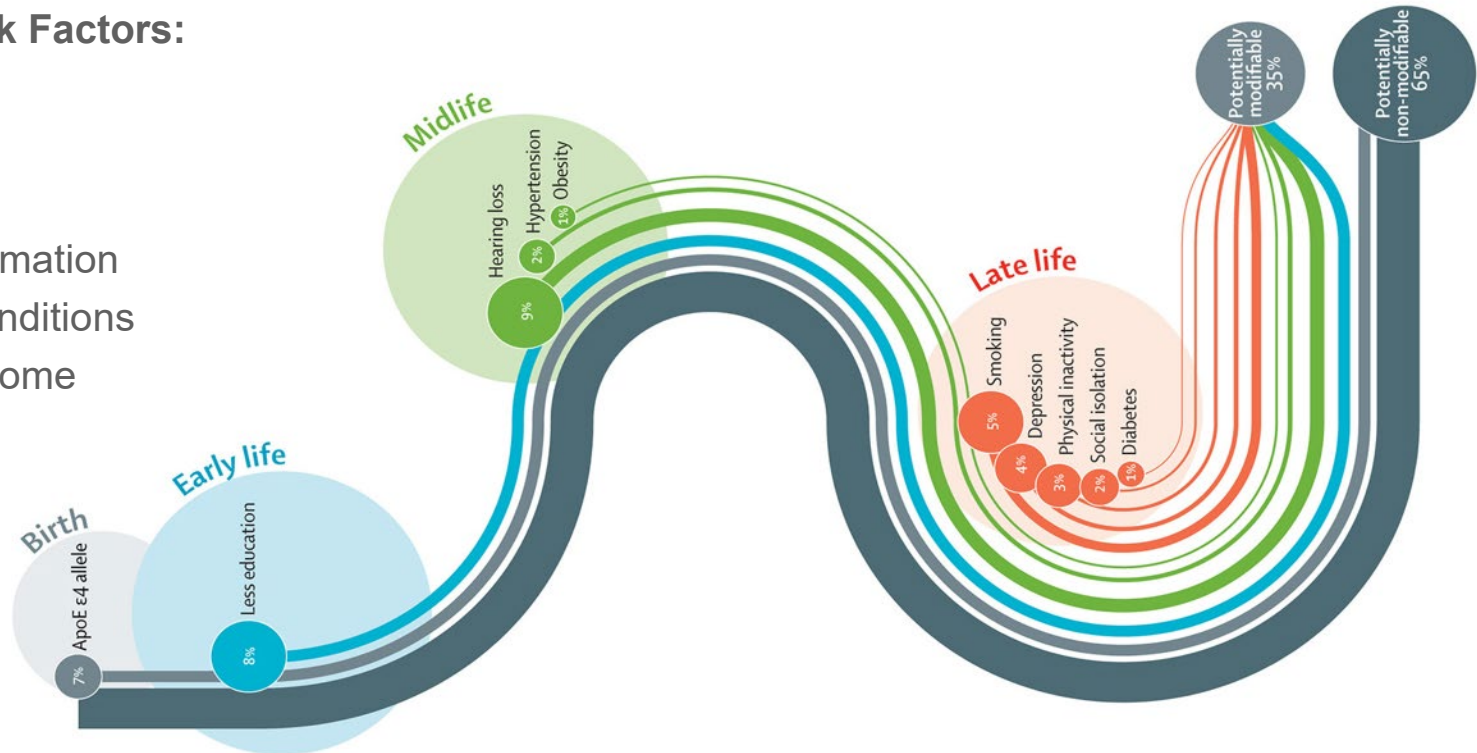
Alzheimer's brain



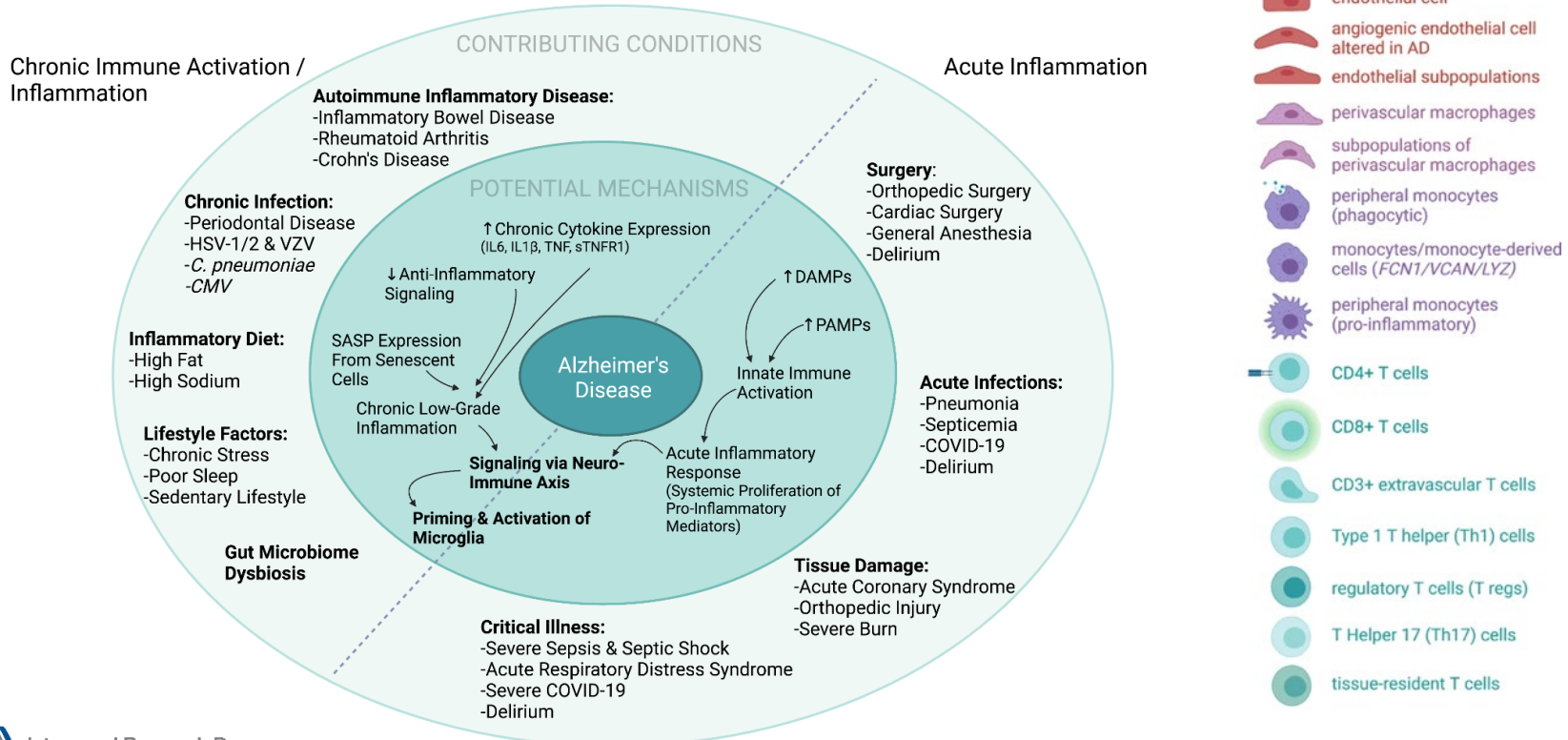
Systemic Health Conditions Influence Alzheimer's Disease and Dementia Risk.

AD/Dementia Risk Factors:

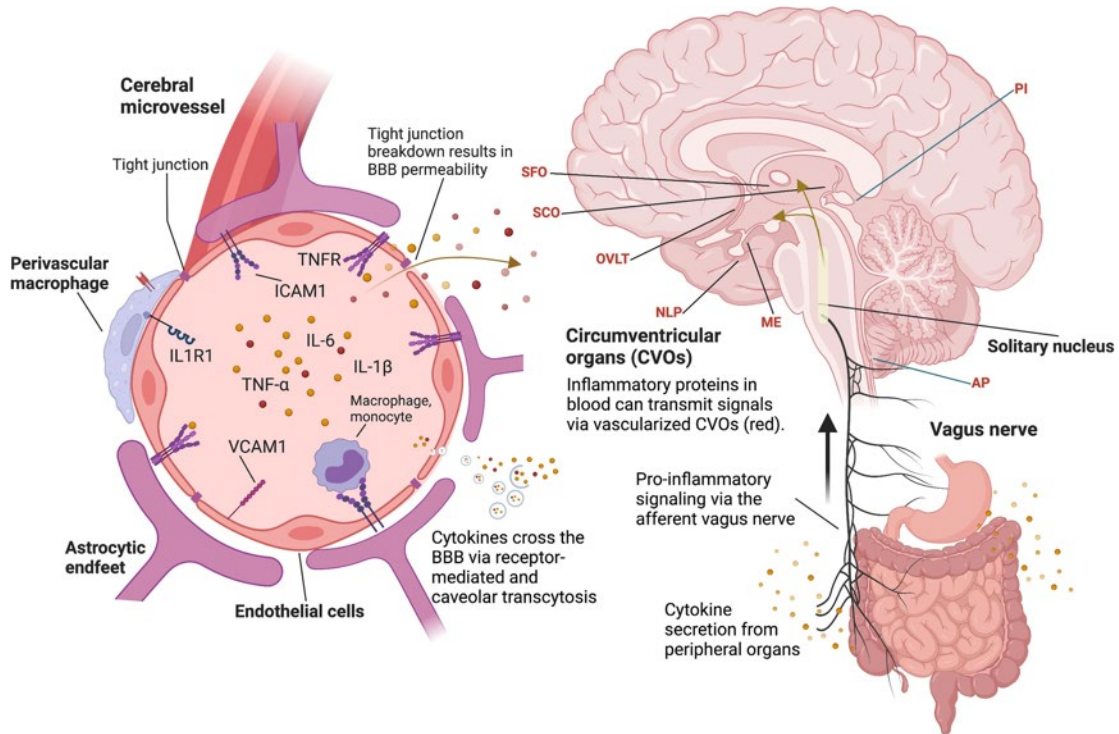
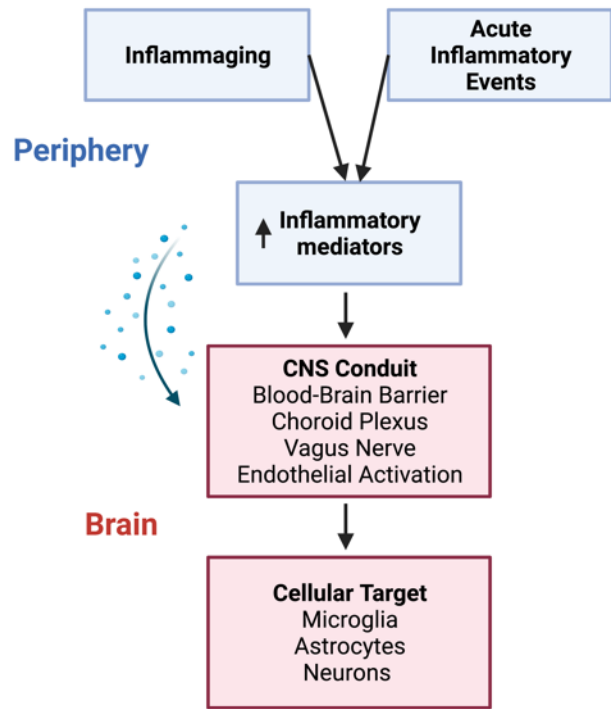
- Diabetes
- Hypertension
- Heart disease
- Systemic inflammation
- Autoimmune conditions
- Metabolic syndrome
- Obesity



Peripheral Immune Function in Alzheimer's Disease



Peripheral Immune Challenges Influence Neurobiology: Neuro-Immune Axis



Best Moves for Your \$1,400 Stimulus

APR 19 2021
Newsweek

**HOW
COVID
ATTACKS
THE
BRAIN**

Millions of survivors of the virus could be in for another health crisis, from chronic fatigue to psychotic breaks and Alzheimer's

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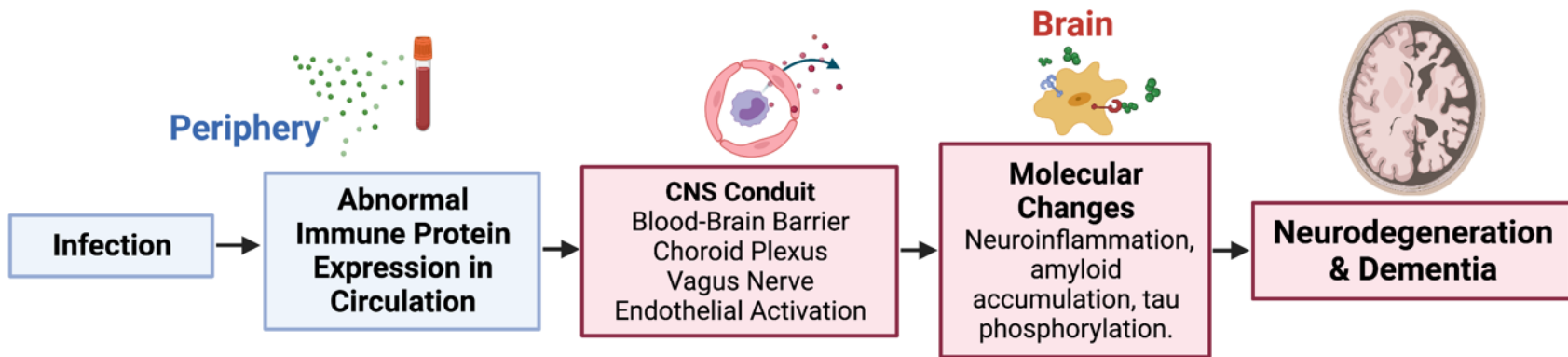
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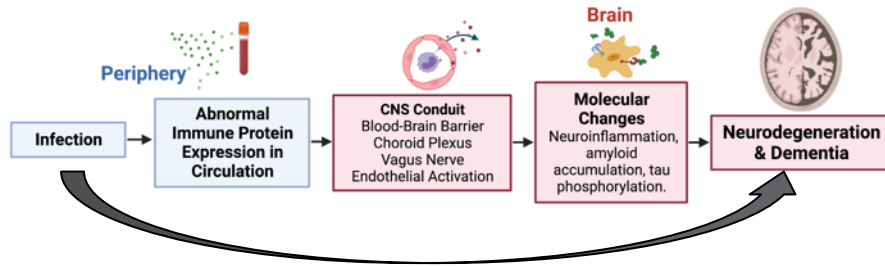
**HOW
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Millions of survivors of the virus could be in for another health crisis, from chronic fatigue to psychotic breaks and Alzheimer's

Proteomics identifies potential immunological drivers of postinfection brain atrophy and cognitive decline

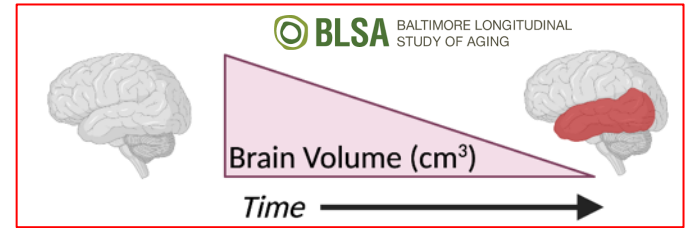


Examining the Link Between Infection, Peripheral Immunity, and Neurodegeneration



Infections Examined

- Gastrointestinal
- HHV
- Influenza
- Lower respiratory tract
- Miscellaneous bacterial
- Miscellaneous viral
- Pneumonia
- Skin /subcutaneous
- STDs
- Tuberculosis
- Urinary tract (UTI)
- Upper respiratory tract

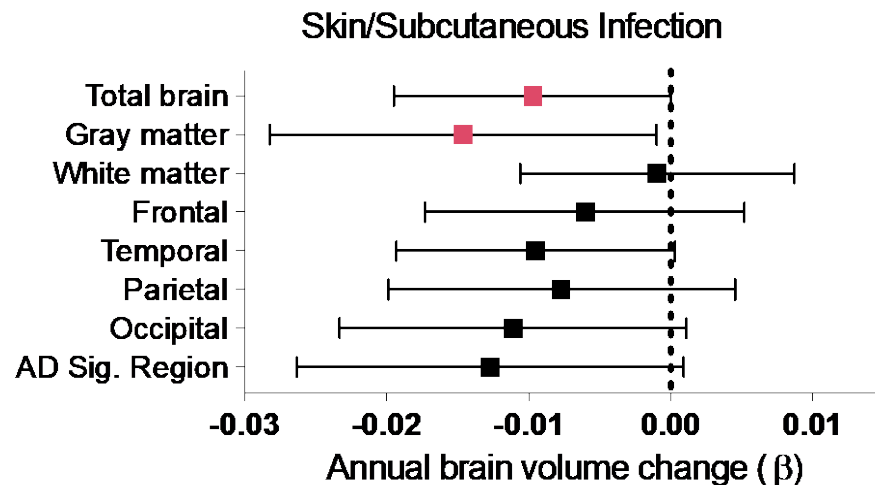
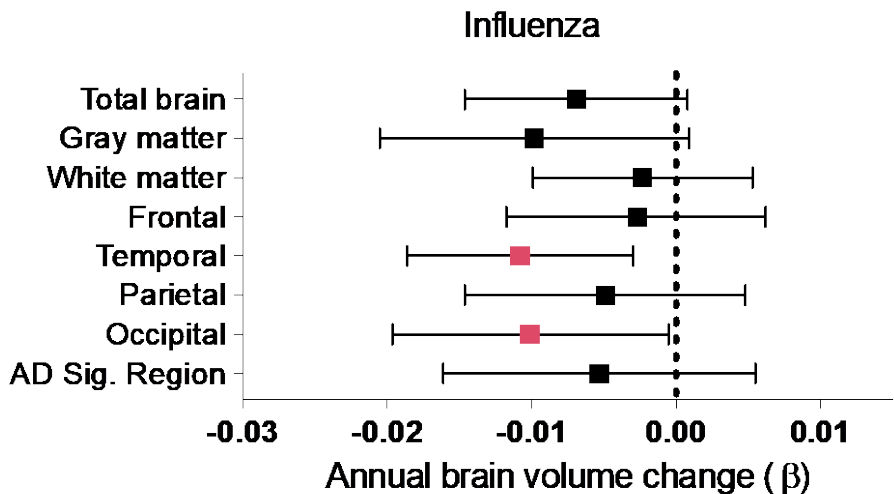


All-Cause, Alzheimer's & Vascular Dementia
UK Biobank ($n = 492, 230$)
Finland Multicohort ($n = 273, 132$)



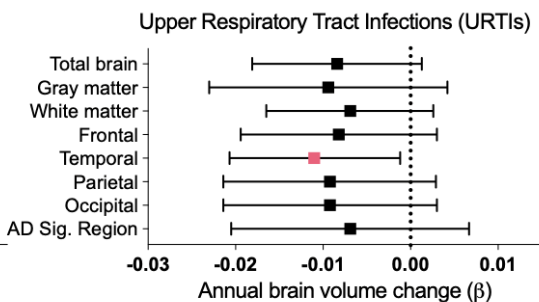
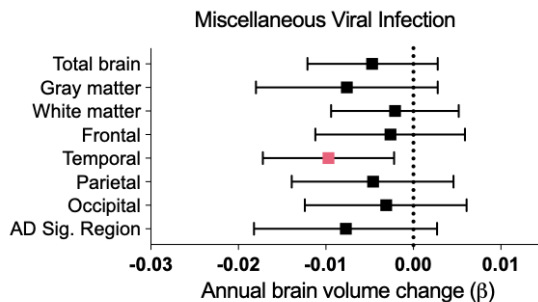
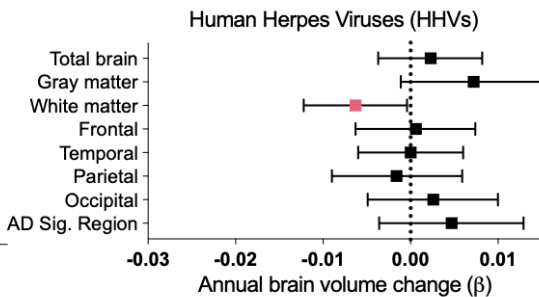
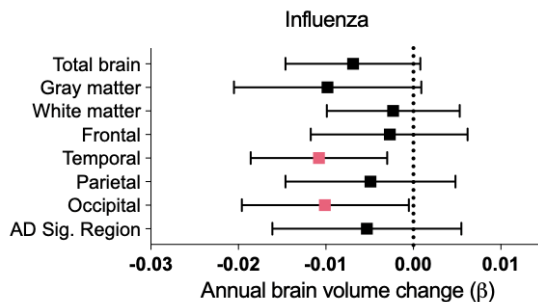
Acute and Chronic Infections are Associated with Brain Volume Loss

 **BLSA** BALTIMORE LONGITUDINAL STUDY OF AGING



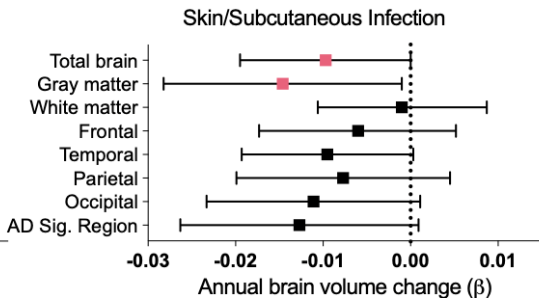
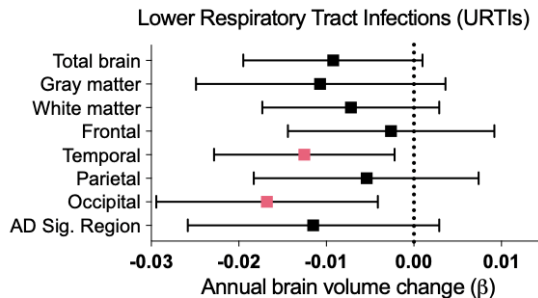
Results adjusted for intracranial volume, time, age, race, sex, education, comorbidity index, and the interaction between covariates and time.

Acute and Chronic Infections are Associated with Brain Volume Loss

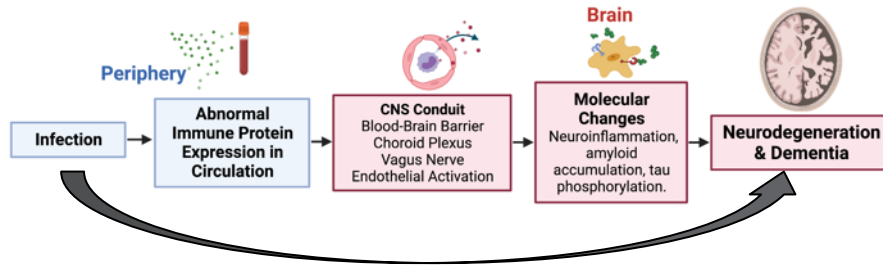


Results adjusted for intracranial volume, time, age, race, sex, education, comorbidity index, and the interaction between covariates and time..

Duggan,... Walker (2024). *Nature Aging*

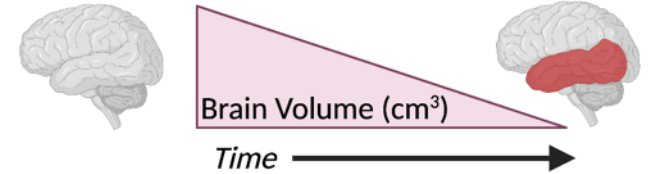
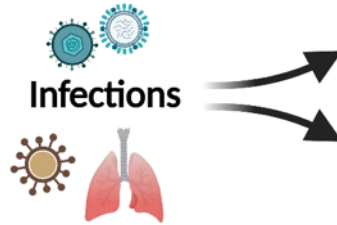


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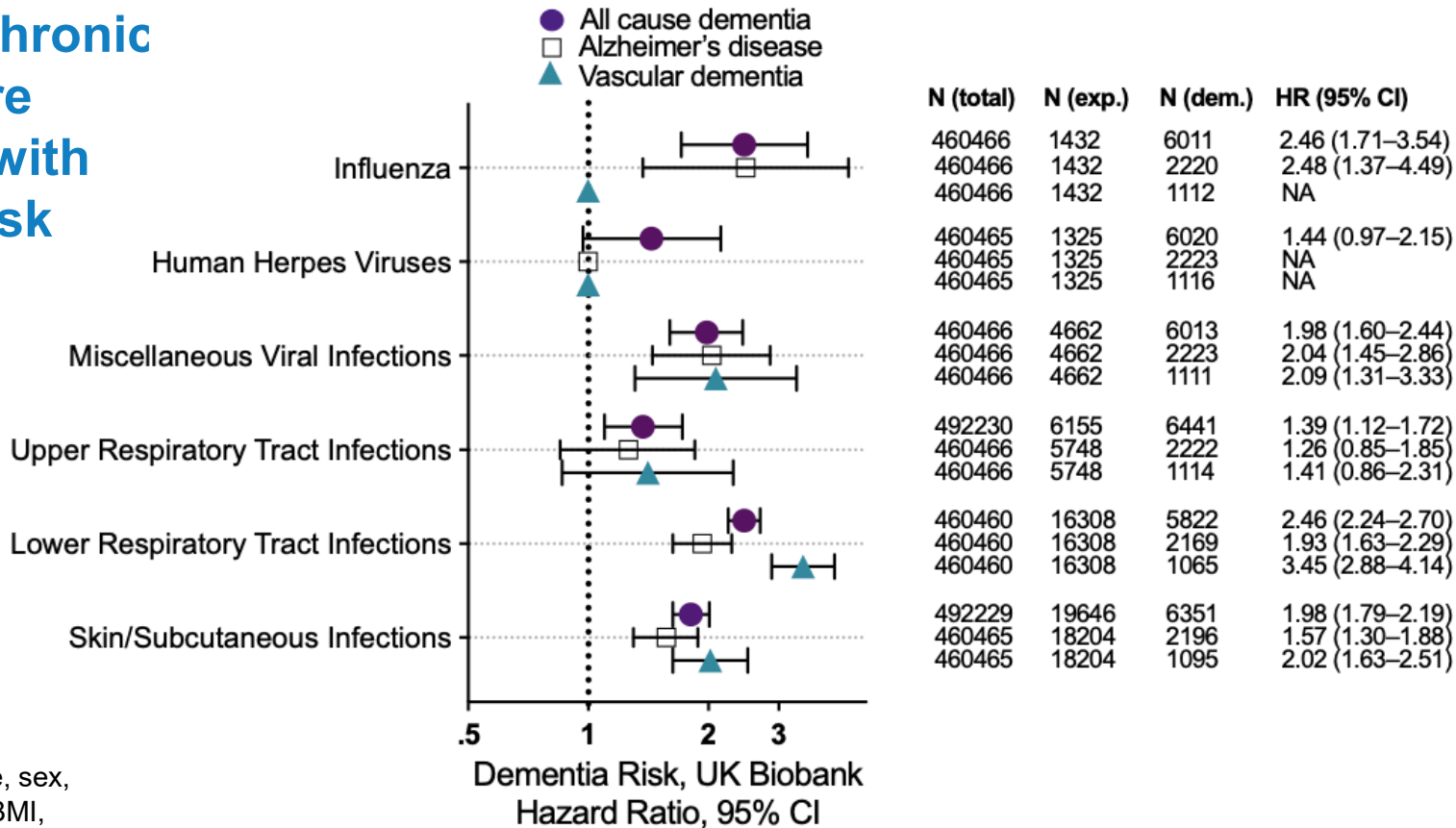


All-Cause, Alzheimer's & Vascular Dementia
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SomaScan[®] Inflammation and Immune Response Panel (942 Proteins)

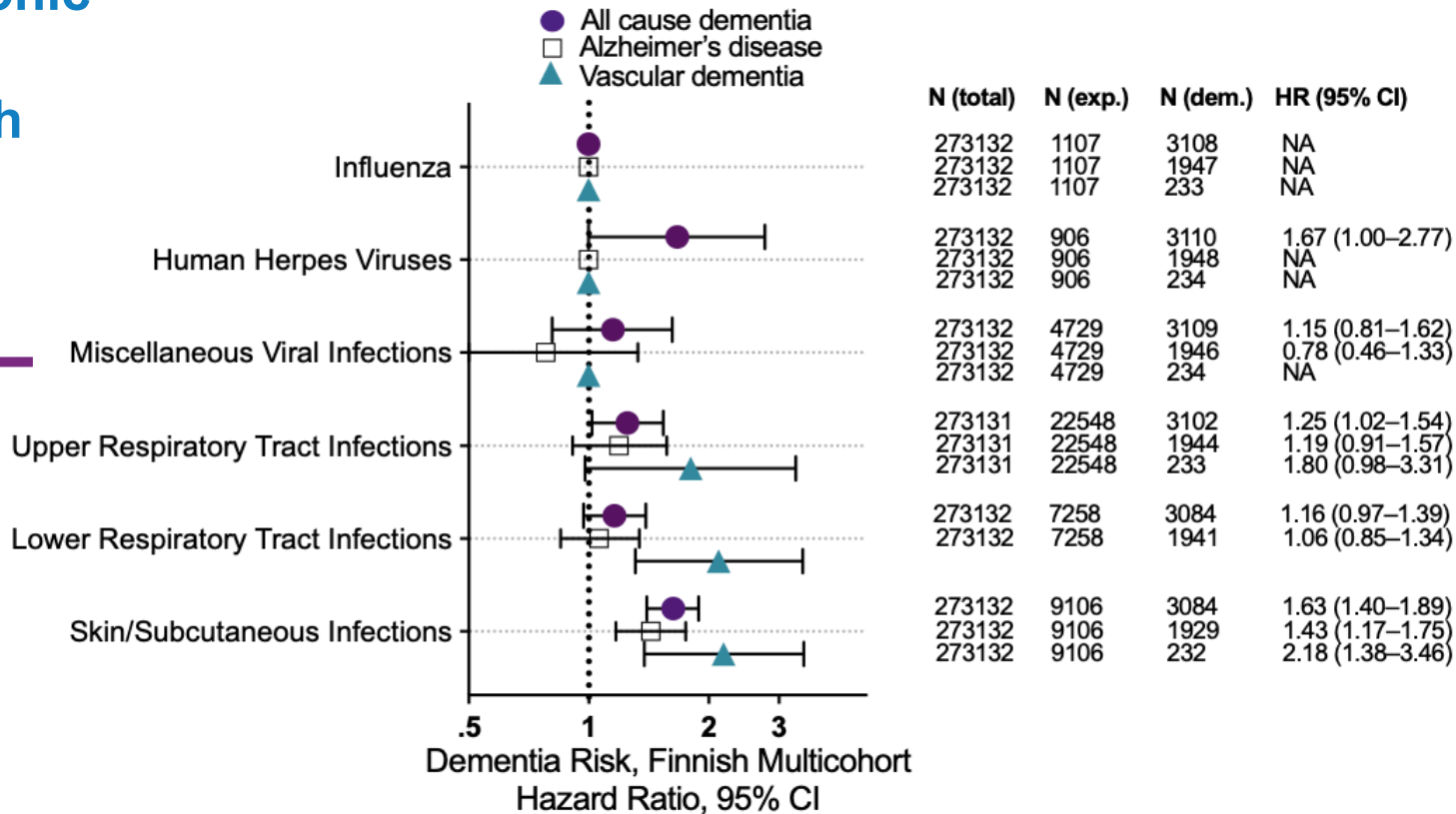
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UK Biobank



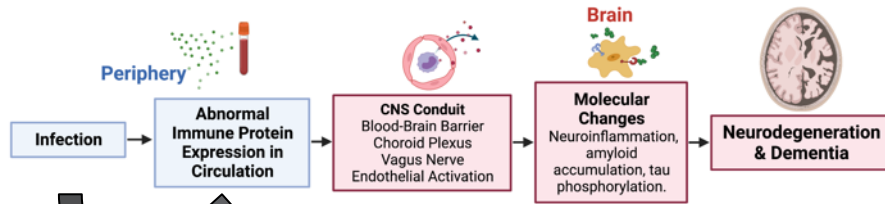
Models adjusted for age, sex, socioeconomic status, BMI, hypertension, and diabetes.

Acute and Chronic Infections are Associated with Dementia Risk Finnish Multicohort

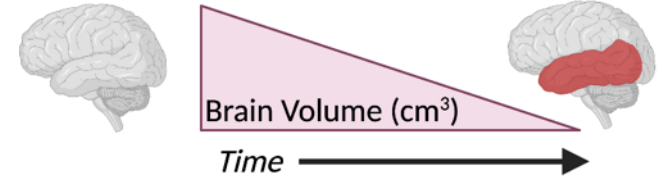


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Examining the Link Between Infection, Peripheral Immunity, and Neurodegeneration



Neurocognitive and Proteomic Characterization of Infections



Infections Examined

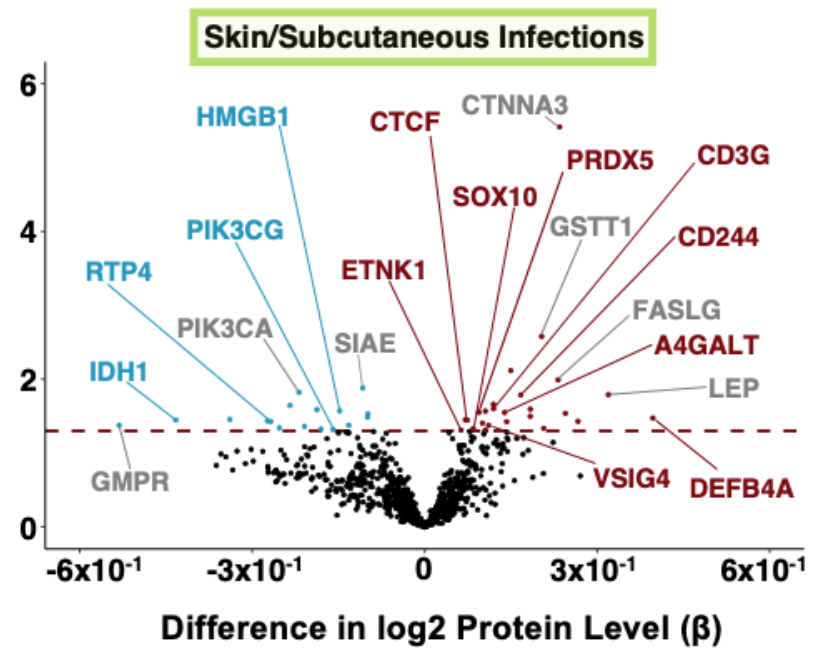
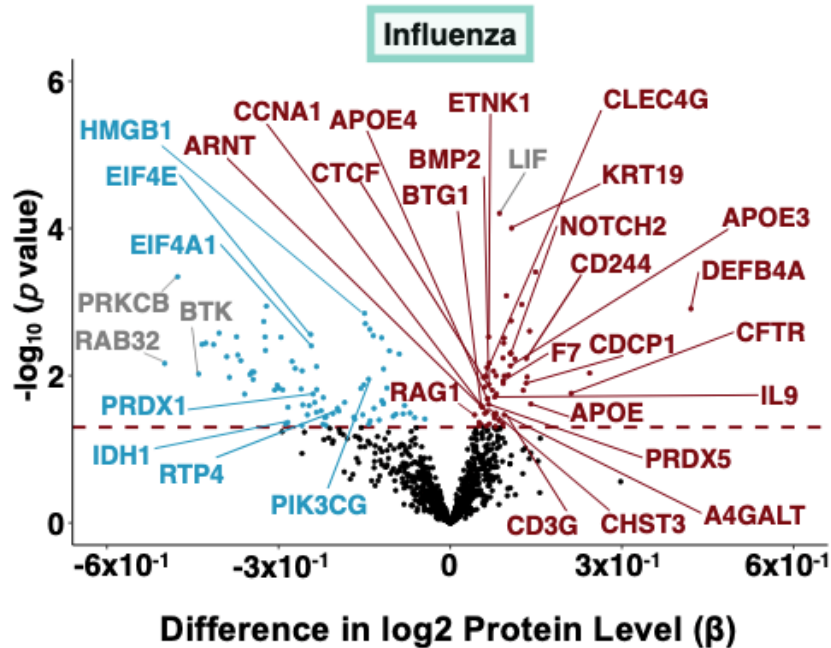
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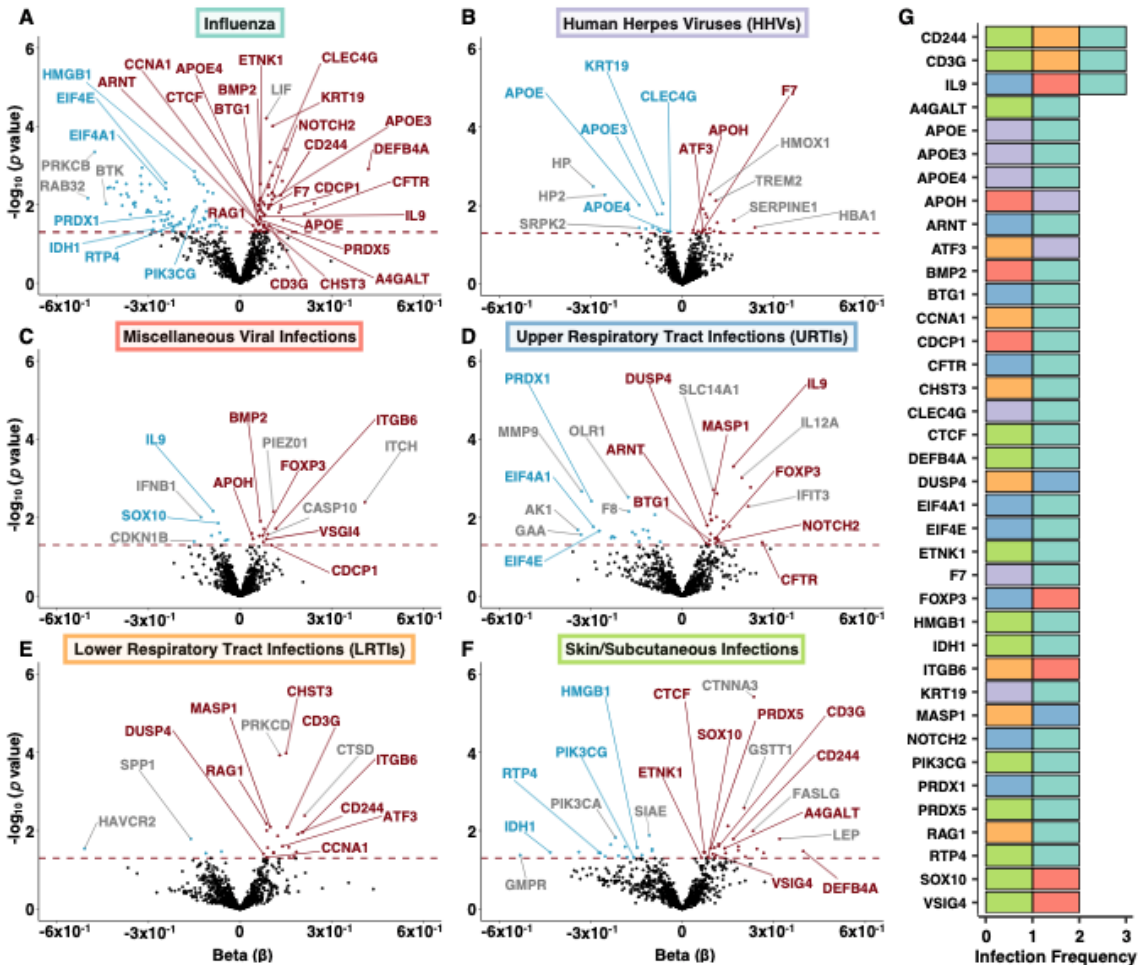
All-Cause, Alzheimer's & Vascular Dementia
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Infections Associated with Brain Atrophy Are Also Linked to Long-Term Proteomic Changes in Blood



Results adjusted for age, race, sex, education, eGFR and comorbidity index.



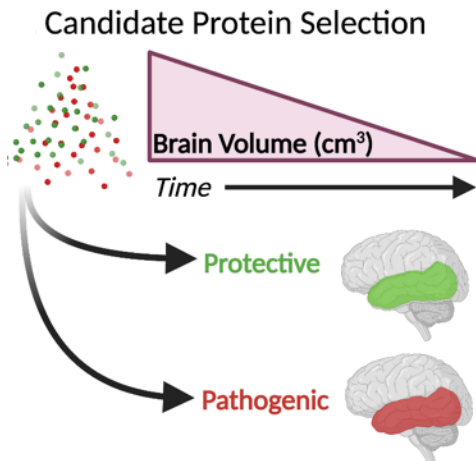
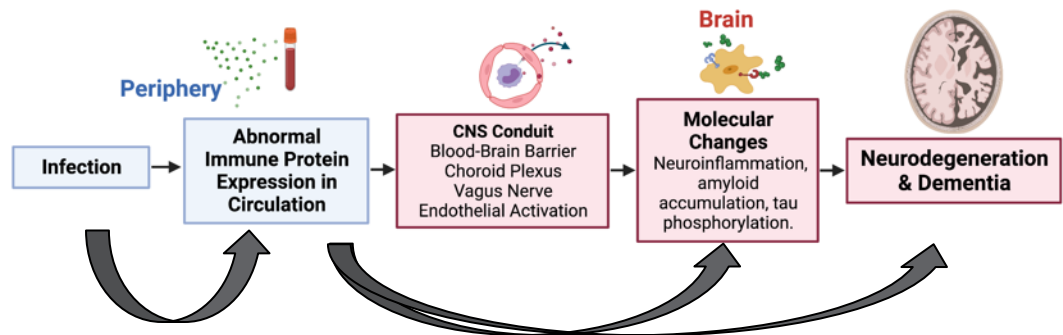
Infections Associated with Brain Atrophy Are Also Linked to Long-Term Proteomic Changes in Blood

Many proteins associated with multiple infections.

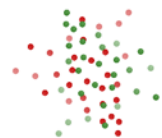
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Examining the Link Between Infection, Peripheral Immunity, and Neurodegeneration



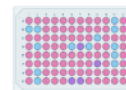
Candidate Proteins



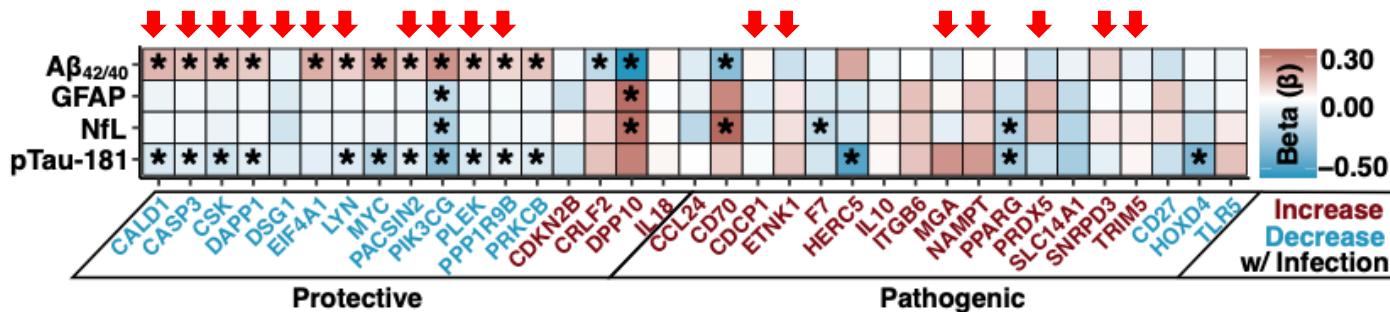
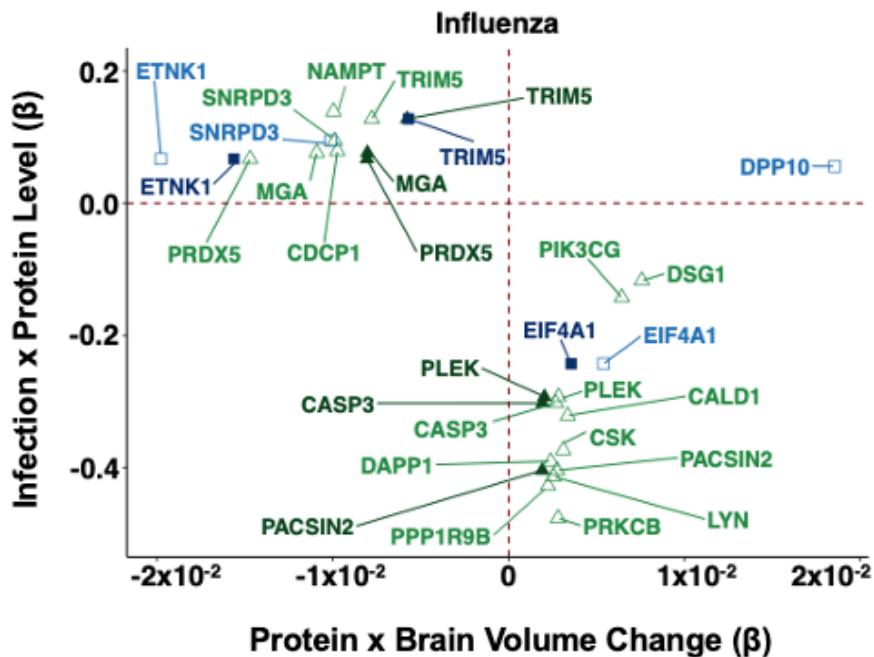
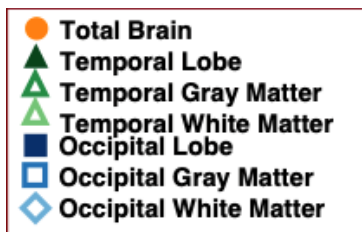
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Plasma ADRD Biomarkers

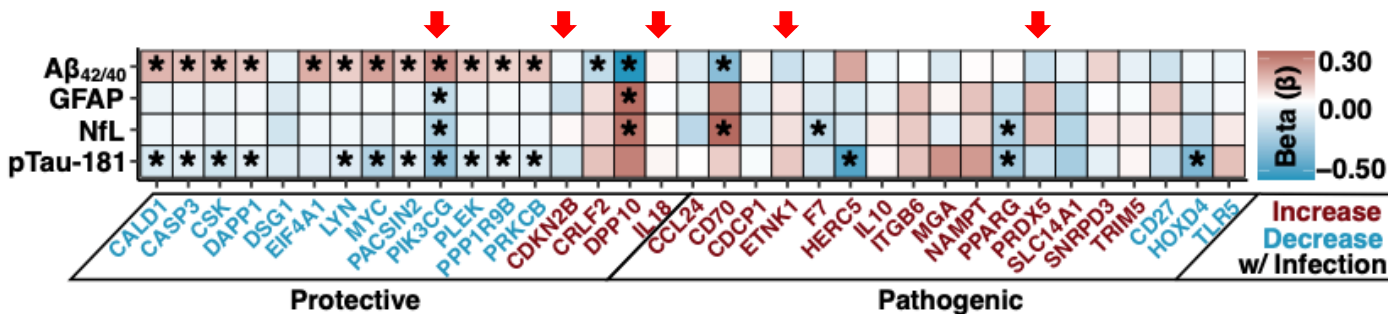
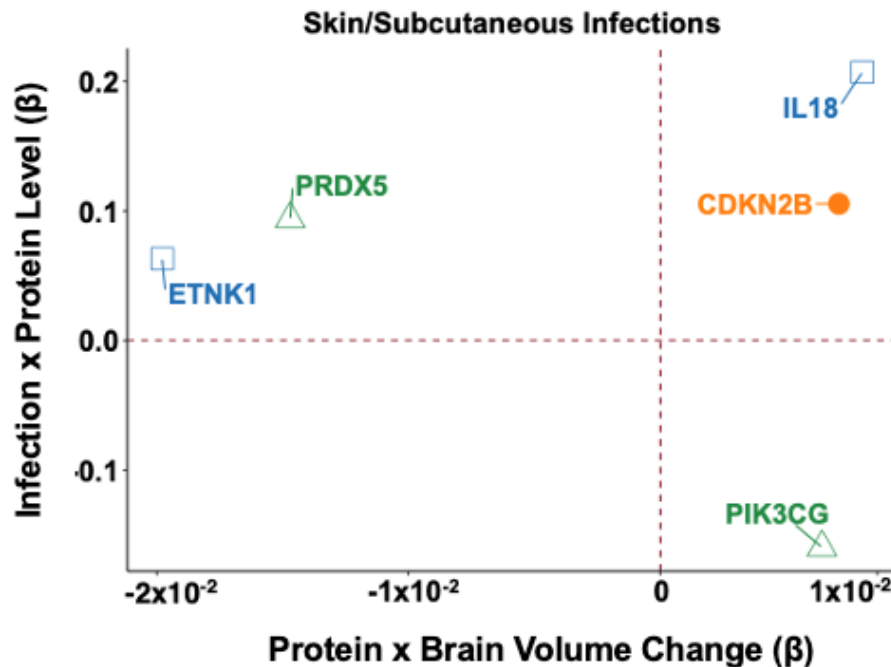
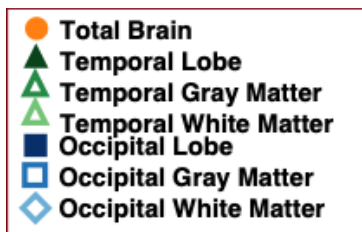
A β
GFAP
NfL
pTau-181



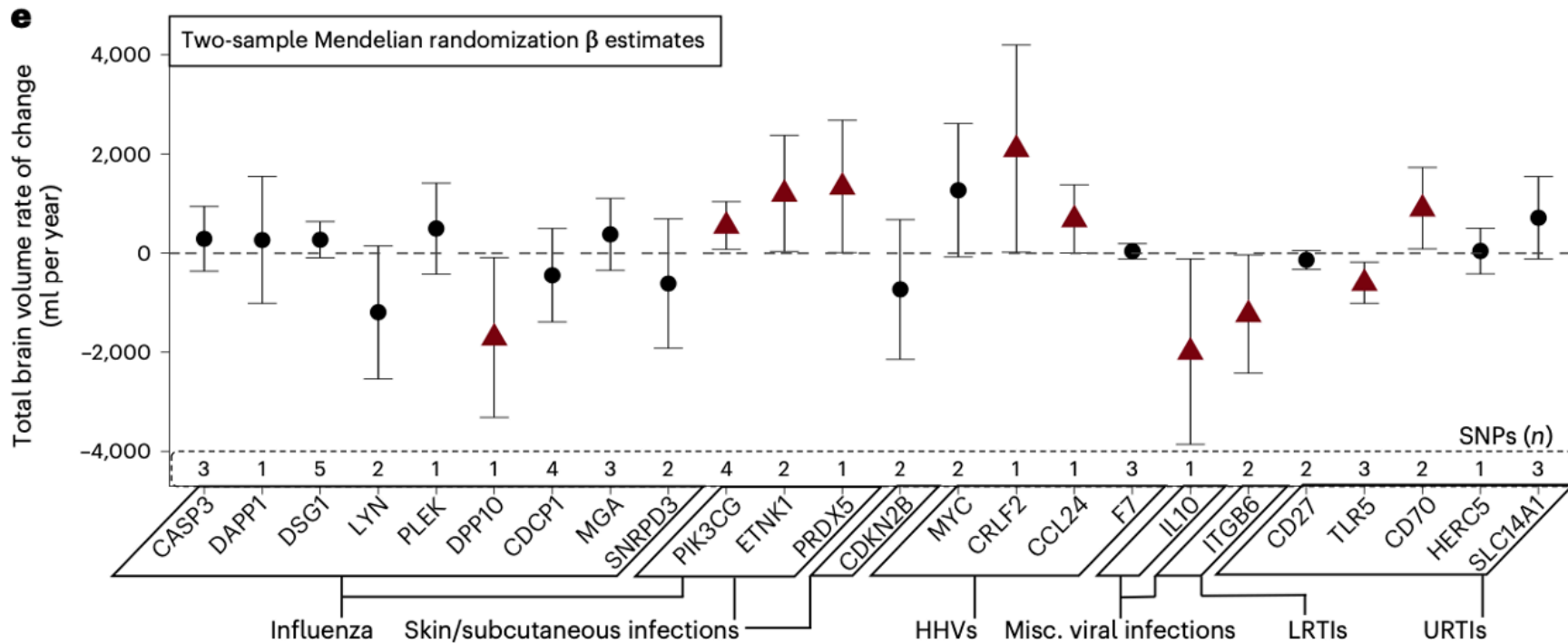
Proteins Associated with Influenza Linked to Brain Volume Change



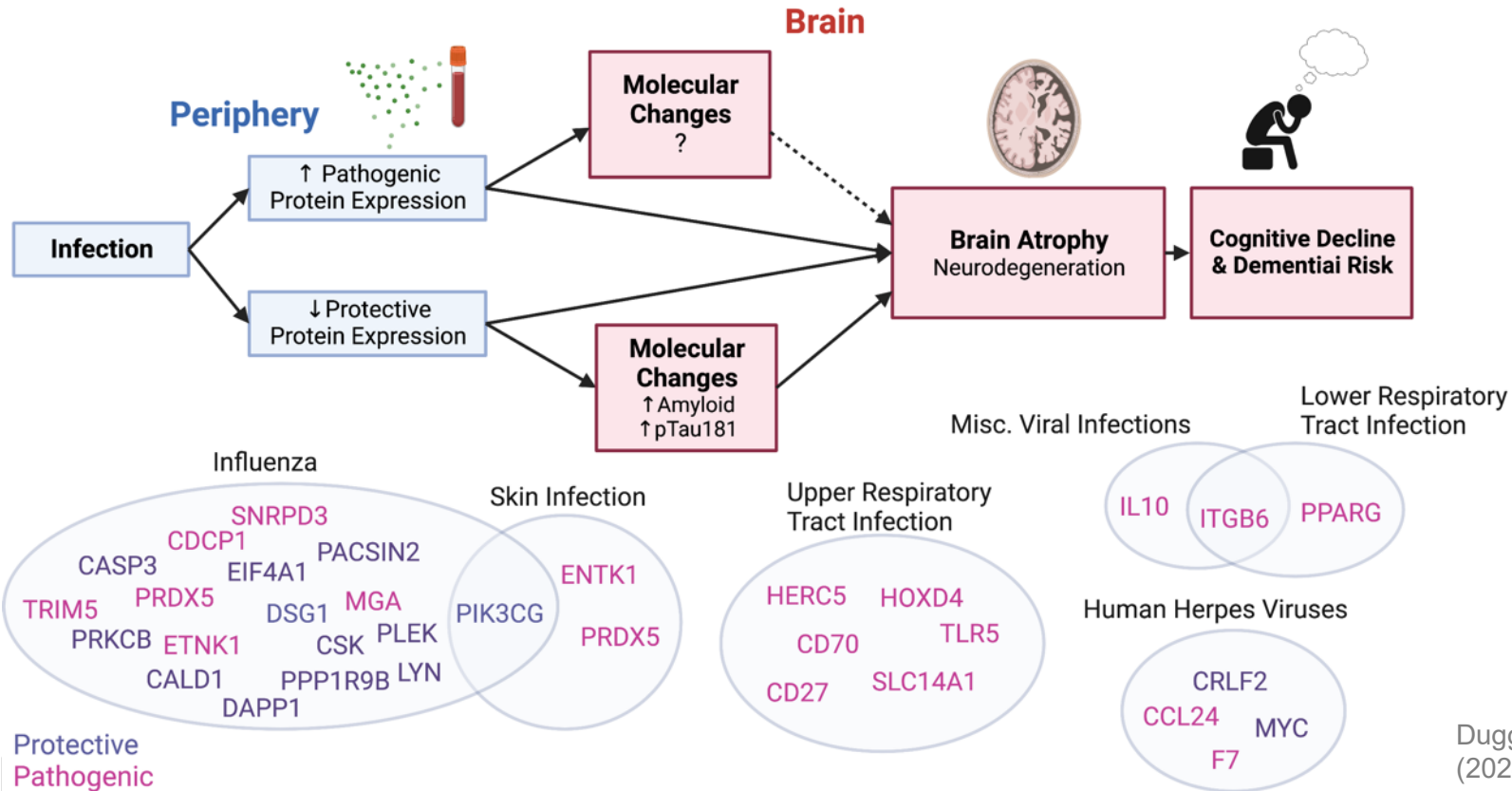
Proteins Associated with Skin Infection Linked to Brain Volume Change



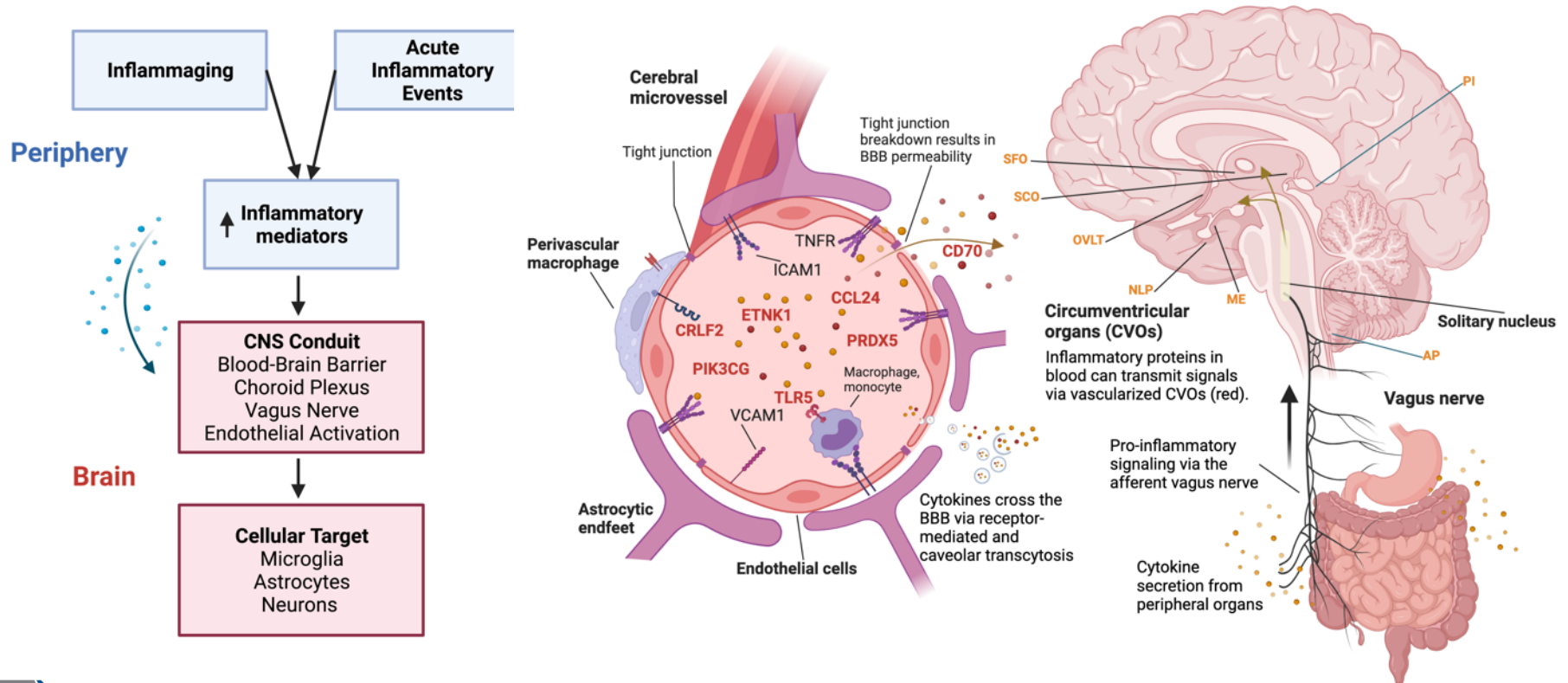
Mendelian Randomization Supports Causal Associations Between Proteins and Brain Atrophy



Candidate Protein Summary



Infection-Related Immune Protein Changes May Drive Neurodegeneration



Acknowledgements



Intramural Research Program
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MIND Lab Members & NIA

Michael Duggan

- Heather Dark
- Zhongsheng Peng
- Jenifer Cordon
- Cassie Joynes
- Cass Blew
- Shannon Drouin
- Susan Resnick
- Luigi Ferrucci
- Yang An
- Murat Bilgel
- Mustapha Bouhrara
- Julián Candia
- Teresa Tian
- Tosh Tanaka
- Abhay Moghekar

ARIC Collaborators

- Josef Coresh
- Rebecca Gottesman
- Gabriela Gomez
- Jingsha Chen
- Pascal Schlosser
- Priya Palta
- Yifei Lu
- Thomas Mosley
- Adrienne Tin
- Myriam Fornage
- Yunju Yang
- Morgan Grams
- Linda Zhou
- Adrienne Tin
- Ron C. Hoogeveen
- Kevin Sullivan
- Peter Ganz
- Eric Boerwinkle
- Christie Ballantyne

SomaLogic

- Clare Patterson
- Hannah Beigel
- Missy Simpson
- Yolanda Hagar
- Joe Gogain
- Stephen Williams



Funding

- National Institute on Aging (NIA) Intramural Research Program
- Distinguished Scholar's Program (NIH)
- The Atherosclerosis Risk in Communities study has been funded in whole or in part with Federal funds from NIH



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Thank you for listening.

Questions?