

Peripheral Immune Signatures Predict Incident Dementia and Cognitive Decline: A Population-Based Cohort Study

Comprehensive immunophenotyping in a large longitudinal cohort reveals an immune risk score that predicts dementia and relates to neurodegeneration.

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1. BACKGROUND



Immunity and inflammation are key contributors to dementia pathogenesis.



Peripheral and central immunity interact bidirectionally and influence disease progression.



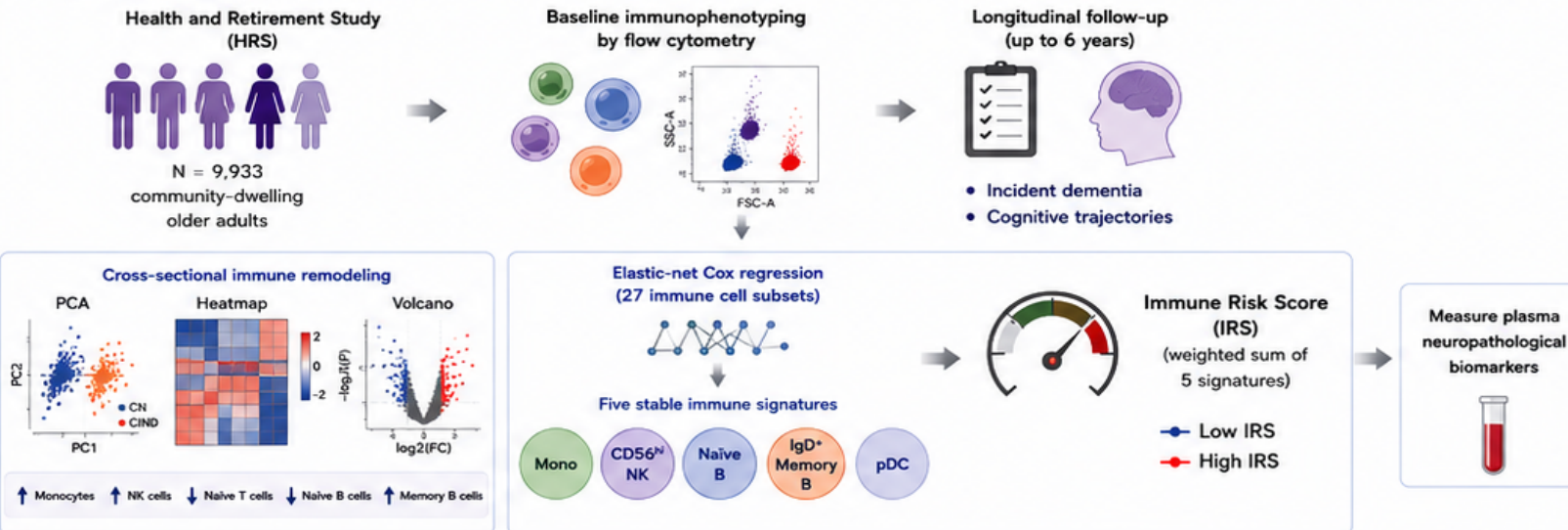
Peripheral immune alterations are reported in dementia, but evidence is mainly cross-sectional and limited to few markers.



OBJECTIVE

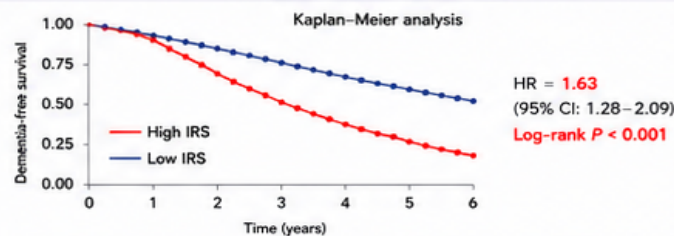
To determine whether comprehensive peripheral immune profiles predict dementia risk and cognitive decline, and to explore their relationship with plasma neuropathological biomarkers in a large longitudinal cohort.

2. STUDY DESIGN

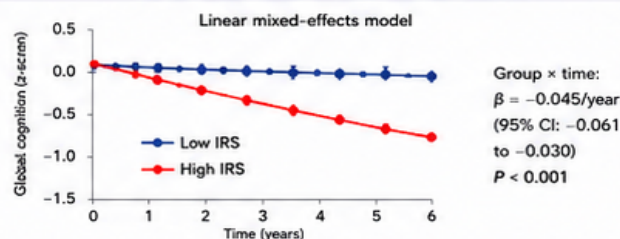


3. KEY FINDINGS

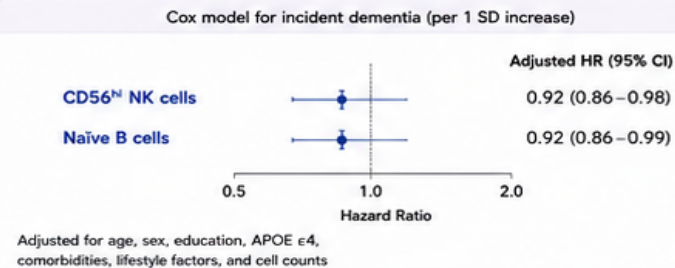
High IRS predicts incident dementia



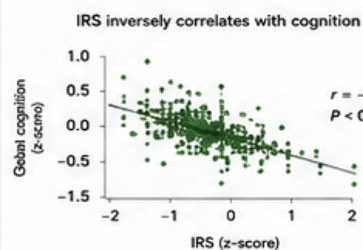
High IRS is associated with faster cognitive decline



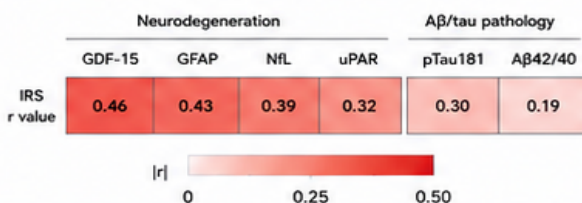
Independent protective immune subsets



4. IRS ASSOCIATES WITH BIOMARKERS

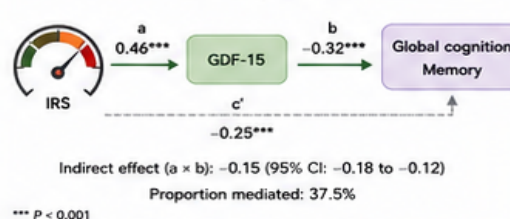


Stronger associations with neurodegeneration than with A β /tau pathology



5. MEDIATION ANALYSIS

IRS is associated with cognition partially mediated by GDF-15



6. IMPLICATIONS

- Risk stratification**: Identify individuals at high risk for dementia and faster decline
- Target identification**: Highlight immune pathways for therapeutic intervention
- Precision immunotherapy**: Guide development and selection of immune-modulating therapies
- Accessible biomarkers**: Blood-based immune signatures for scalable clinical application