

Blood-based biomarker profiles of genetic predisposition to Alzheimer’s disease: a population-based study



Qiuyu Wei¹; Lin Shi¹; Cuicui Liu^{1,2,3,4}; Min Zhu^{1,2,3,4}; Xun Yao Tian²; Heng Zhang^{1,2,3,4}; Na Tian^{1,2,3,4}; Keke Liu^{1,2,3,4}; Fernando Gonzalez-Ortiz⁵; Tingting Hou^{1,2,3,4*}; Yifeng Du^{1,2,3,4,6*}; Chengxuan Qiu^{1,6,7}

¹ Department of Neurology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong 250021, P.R. China.² Department of Neurology, Shandong Provincial Hospital, Shandong University, Jinan, Shandong 250021, P.R. China.³ Shandong Provincial Clinical Research Centre for Neurological Diseases, Jinan, Shandong 250021, P.R. China.⁴ Department of Neurology, Key Laboratory of Endocrine Glucose & Lipids Metabolism and Brain Aging, Ministry of Education, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong 250021, P.R. China.⁵ Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, the Sahlgrenska Academy at the University of Gothenburg, 43180 Mölndal, Sweden.⁶ Institute of Brain Science and Brain-Inspired Research, Shandong First Medical University & Shandong Academy of Medical Sciences, Jinan, Shandong 250117, P.R. China.⁷ Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institute-Stockholm University, 17165 Solna, Sweden.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS
We characterized blood-based biomarker(BBM) profiles of older adults with genetic predisposition to Alzheimer’s disease(AD), encompassing BBMs for AD, neurodegeneration, neuroinflammation, and systemic inflammation.	This population-based study included 3947 participants; of these, data on BBMs were available in 3837 participants for plasma phosphorylated tau(p-tau) variants and glial fibrillary acidic proteins(GFAP); 1415 for amyloid-β(Aβ), total tau, and neurofilament light chain(NfL); 1755 for brain-derived(BD)-tau; and 1815 for serum cytokines.	<i>APOE</i> -ε4 allele(vs. ε3/ε3) and higher polygenic risk score(PRS) were associated with elevated plasma p-tau217, decreased Aβ42/Aβ40, and increased GFAP and CLGI, whereas <i>APOE</i> -ε2 allele was linked to reduced p-tau217(all p<0.05). Neither <i>APOE</i> genotype nor PRS was associated with total tau and NfL(p>0.05). <i>APOE</i> -ε4 homozygosity was associated with increased BD-tau(p<0.05). These associations were stronger in participants aged≥75 years and females($p_{\text{interaction}} < 0.05$).	The BBM profiles of AD genetic predisposition are characterized by biomarkers for Alzheimer’s pathology, neuroinflammation, and systemic inflammation.