Social Determinants Of Health Are Associated With Plasma Proteomic Signatures Of Neurodegeneration In Latin America

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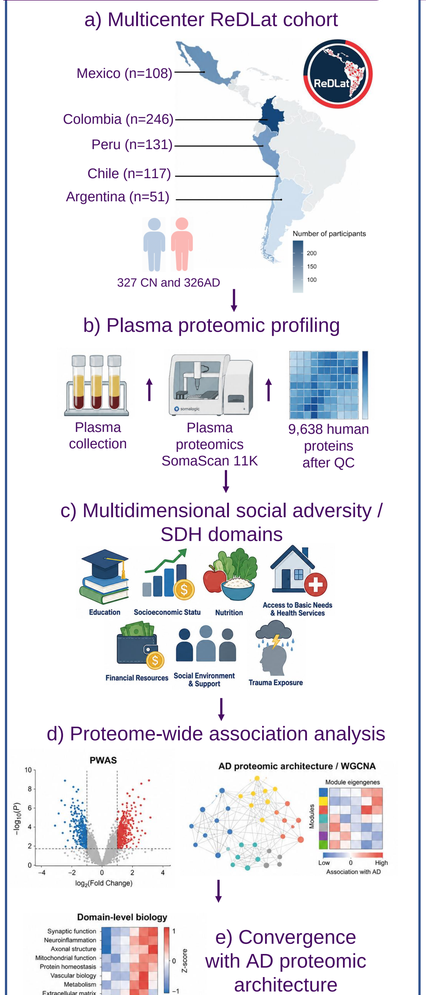
Matías Nicolás Pizarro, Ziyi Li, Ariel Caviedes, Joaquin Migeot, Federica Anastasi, Natalia Vilor-Tejedor, Paulina Orellana, Nickole Marin, Carolina Ochoa-Rosales, Felipe Cabral-Miranda, Hernando Santamaría-García, Paola Murgas, Andrea Slachevsky, David Aguillón, Diana L Matallana, José Alberto Avila-Funes, Leonel T. Takada, Juliana Acosta-Uribe, Maria Isabel Behrens, J. Nicholas Cochran, Martin Bruno, Nilton Custodio, Rosa Montesinos, Shireen Javandel, Stefanie D Pina-Escudero, Sid E. O'Bryant, Mike A. Nalls, Mark R. Cookson, Enzo Tagliazucchi, Jennifer S. Yokoyama, Agustin Ibañez, Yue Andy Qi, Claudia Duran-Aniotz, Multi-Partner Consortium to Expand Dementia Research in Latin America (ReDLat).

Multidimensional social adversity is associated with a biologically organized plasma proteomic signature that partially overlaps with Alzheimer's disease–related molecular architecture in Latin America.

INTRODUCTION

Dementia risk reflects cumulative biological, social, and environmental exposures across the life course. In Latin America, structural inequality, cardiometabolic burden, and barriers to timely diagnosis may shape neurodegenerative risk. Here, we tested whether multidimensional social adversity is associated with plasma proteomic variation and whether these signatures converge with Alzheimer's disease–related proteomic architecture.

METHODS



RESULTS

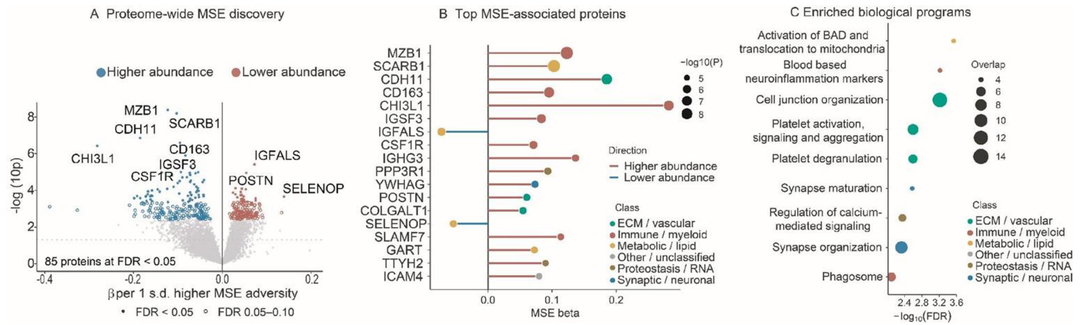


Figure 1. Plasma proteomic architecture of multidimensional social adversity. (A) Proteome-wide association between the standardized MSE adversity score and 9,638 plasma proteins. Points represent individual proteins; highlighted proteins indicate associations at FDR < 0.05 or suggestive associations at FDR 0.05–0.10, colored by direction of abundance change with higher MSE adversity. **(B)** Top MSE-associated proteins ranked by statistical evidence and effect size. Point size indicates −log10(P), line color indicates direction of association, and point color denotes biological class. **(C)** Curated enrichment of biological programs represented among MSE-associated proteins. Point size indicates protein overlap and color indicates biological class.

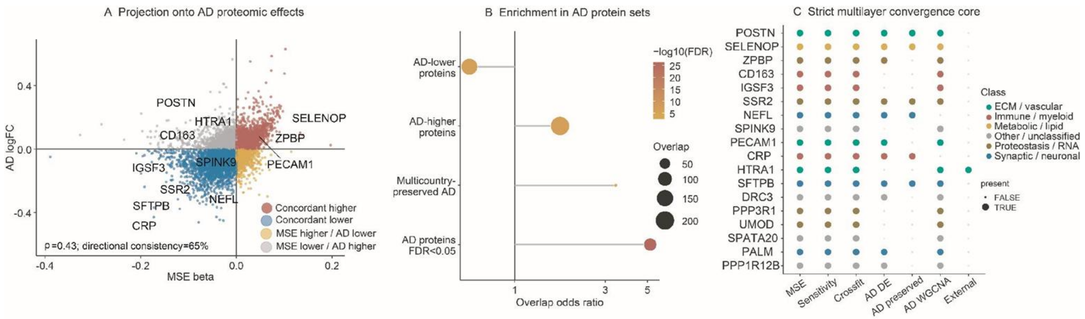


Figure 2. MSE-associated proteomic effects converge with Alzheimer's disease proteomic architecture. (A) MSE-associated protein effects projected onto AD differential abundance effects, highlighting directional concordance and discordance between both proteomic signatures. **(B)** Enrichment of MSE-associated proteins across AD-related protein sets. Point size indicates overlap and color indicates −log10(FDR). **(C)** Strict multilayer convergence core identifying prioritized proteins supported across MSE discovery, robustness, cross-fitted selection, AD differential abundance, AD preservation, AD WGCNA architecture, and external evidence.

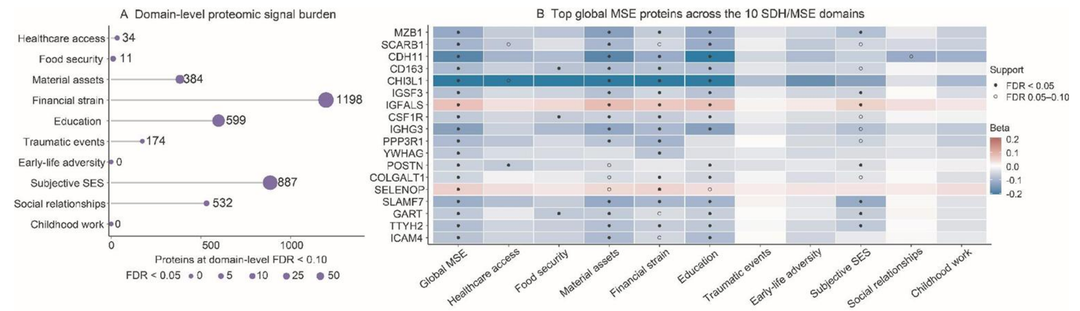


Figure 4. Domain-level dissection of the multidimensional social adversity proteomic signature.(A) Domain-level proteomic signal burden across the 10 SDH/MSE domains, showing proteins associated at FDR < 0.10 and FDR < 0.05. **(B)** Domain-specific beta estimates for top global MSE-associated proteins, illustrating partially shared and domain-specific proteomic patterns across social adversity domains.

CONCLUSION

Multidimensional social adversity was associated with a biologically organized plasma proteomic signature in Latin America. Beyond the global architecture, we nominate **CD163, CHI3L1, SELENOP, and POSTN** as candidate proteins linking social adversity to immune activation, neuroinflammation, oxidative stress, and extracellular matrix remodeling, providing a plausible molecular bridge between structural disadvantage and neurodegeneration related biology.

REFERENCES

Selected references and DOI links available via QR code

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