



FINE MAPPING OF REGIONS OF HOMOZYGOSITY AND THEIR ROLE IN ALZHEIMER'S DISEASE: INSIGHTS FROM THE PERUVIAN AND MEXICAN POPULATIONS (ID 2585 : Oral Presentation)

Presenter

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Lecture Time

17:20 - 17:35 (FRI, 04-04-2025)

Abstract

Aims

Objectives: we aimed to investigate the association between regions of homozygosity (ROH) and Alzheimer's Disease (AD). We explored local genetic ancestry and rare variant enrichment in the most prevalent consensus ROH regions to understand their potential role in AD pathogenesis.

Methods

Methods: We employed 351 Peruvians from the Genetic of Alzheimer's in Peruvian Population (GAPP) study (a recently established cohort of Peruvian mestizos and indigenous groups), and 823 Mexicans from the Mexican Health and Aging Study (MHAS). Using high quality imputed common variants, we identified the significant consensus ROH regions across samples and associations with AD. Genetic ancestry proportions were calculated within ROH regions, including union (i.e. max extension of each ROH across samples), consensus (i.e. strictly overlapping region shared across samples), and regions replicated between GAPP and MHAS.

Results

Results: A total of 59 ROHs in MHAS and 19 ROHs in GAPP were significantly associated with AD. 8 ROHs overlapped across MHAS and GAPP and were significantly associated with AD (best p-value= 0.01, 10-E05). Genetic ancestry analysis revealed increasing African proportions in overlapping consensus ROH regions in both cohorts (12.02 % within ROHs vs. 2.95 % in the overall genome).

Conclusions

Conclusions: This study highlights the importance of ROH in harboring potential clinically-relevant rare variants for AD risk in diverse populations and providing potential targets for further investigations and intervention. Our findings emphasize the significance of integrating genetic ancestry and ROH mapping in understanding AD etiopathogenesis, particularly in underrepresented populations.