supervised admixture analyses using Whites with European ancestry and African Yorubian from the HAPMAP project and Native Americans from the Human Diversity Genome Project. Global admixture individual proportions were then used to compute the kinship for each pair of the individuals. We then employed a logistic mixed effect model adjusting for sex, age as fixed effects and the kinship as random effect (Model 1). We also explored an APOE-adjusted model (Model 2) and an interaction model (SNP*APOE – Model 3). Results: Global admixture analyses showed a 57% European, 34% African and 9% Native component. In addition to APOE, two loci reached genome-wide significance: in Model 1, a locus located on chromosome 2 lying within the MFS2D2 gene, and in Model 2 a locus on chromosome 6 lying in the HLA region (p-value=2.3*10^{-8}). Several LOAD-known genes were also enriched with significant variants, including ABCA7, MS4A cluster, SORL1. Conclusions: This is the largest GWAS on subjects of Caribbean Hispanic ancestry phenotyped for LOAD to our knowledge. Several known-loci are being confirmed by our analyses, and two potentially novel loci are being reported. We are currently performing additional analyses and models and functional experiments to further validate our findings.

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**CHR17Q21 H2 HAPLOTYPE STRATIFIED GWAS REVEALS DIFFERENTIAL ASSOCIATION FOR AD RISK VARIANTS**

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**Background:** MAPT encodes for tau, which forms neurofibrillary tangles, one of the neuropathological hallmarks of Alzheimer’s disease (AD). MAPT resides within a recombinational suppressive ~900 kb inversion on Chr17q21, resulting in an extended region of linkage disequilibrium and two major haplotypes, termed H1 and H2. The more common non-inverted H1 haplotype has been implicated as a risk factor for multiple neurodegenerative diseases, including AD. Using available genome-wide genotype data from the Alzheimer’s disease genetics consortium (ADGC) we tested the hypothesis that AD risk variants may exhibit chr17q21-haplotype-dependent association. We further extended this analysis genome-wide to determine if this approach may identify novel AD risk variants. **Methods:** Following quality control measures, approximately 3 million variants with a MAF ≥0.02 in all cohorts, and index variants identified by the IGAP consortium, were evaluated for association with AD. 21 ADGC cohorts were retained for analysis. The H2 tagging variant rs8070723 was used to stratify study participants into H2 carriers (H1H2+H2H2: 3,631 cases, 3,729 controls) and H2 non-carriers (H1H1: 5,958 cases, 5,523 controls). Variants were tested using multivariable logistic regression implemented in PLINK including the following covariates: age, sex, and PC1-3. Both joint (adjusting for cohort), and meta-analyses were performed. **Results:** Amongst the established IGAP index variants, five were significantly associated with AD (p<5E-02) in one of the haplotype-stratified datasets and not the other. Joint analysis for H2 non-carriers (H1H1) identified genome-wide significant variants on Chr19 and Chr2, at the established APOE and BIN1 loci respectively. Additional suggestive associations (p<1E-05) on Chr11 (MS4A4A), Chr4 (TBC1D9) and Chr8 (MMP16) were also observed. In the H2 carriers, no variants reached genome wide significance, but 4 at the BIN1, PICALM and MS4A4A loci had a p-value <1E-05. Three SNPs had a p-value <1E-05 in the H2 non-carriers but p >5E-02 in the H2 carriers. Both joint and meta-analyses yielded similar results. **Conclusions:** Chr17q21 (MAPT) haplotype-stratified analyses identified AD risk variants with context-dependent association. Additional analyses adjusting for APOE4, epistasis analysis, and gene expression correlations for candidate genes may provide additional insights into the molecular mechanisms underlying these observations.

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**THE ASSOCIATION BETWEEN C-REACTIVE PROTEIN AND POSTOPERATIVE DELIRIUM DIFFERS BY APOLOIPROTEIN E GENOTYPE**

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**Background:** Delirium and Alzheimer’s disease (AD) are common causes of late-life cognitive impairment with clear epidemiologic links; however, the pathophysiology underlying these links remains unclear. Apolipoprotein E (APOE) ε4, the strongest genetic risk marker for AD, has been widely studied as a potential risk marker for delirium, and recent work in older surgical patients free of dementia indicates that APOE ε4 does not confer significantly increased risk of delirium. However, APOE may influence risk of delirium indirectly by modifying the relationship of delirium with other risk factors such as inflammation. We tested whether APOE genotype modifies the established association between inflammatory marker C-reactive protein (CRP) and postoperative delirium. **Methods:** We examined patients without dementia age ≥70 undergoing major non-cardiac surgery in the SAGES: Successful Aging After Elective Surgery study. We collected blood, extracted DNA, and performed APOE genotyping using allele specific polymerase chain reaction assays, considering APOE ε4 vs. non-ε4 carriers. High plasma CRP, measured on postoperative day 2 (POD2) using ELISA, was defined utilizing the highest sample-based quartile (≥234.12 mg/L). Delirium status was determined with daily interviews rating the Confusion Assessment Method, augmented by a validated chart review. We used generalized linear models adjusted for age, sex, surgery type, and stratified by APOE ε4 carrier status, to determine whether APOE modifies the association between CRP and delirium. **Results:** Among the 557 patients (mean age 76.7 [standard deviation 5.2], 58% female, 81% orthopedic), 19% were APOE ε4 carriers. Postoperative delirium occurred in 24%. The relationship between CRP and delirium differed by APOE status. Among APOE ε4 carriers, we found a strong relationship between high POD2 CRP and delirium (relative risk [RR] (95% confidence interval [CI]): 3.0(1.4-6.7)). In contrast, among APOE ε4 non-carriers, high POD2 CRP was not significantly associated with postoperative delirium (RR[95% CI]: 1.2(0.8-1.7)). The p-value for the interaction between APOE and CRP on delirium risk was significant at p<.01. **Conclusions:** APOE ε4 carriers may be particularly vulnerable to the increased risk of delirium conferred by post-surgical inflammation (high POD2 CRP). If validated, this increased vulnerability may help to target future interventions for delirium prevention to the most susceptible group.