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## Interleukin-1Beta (IL-1 $\beta$ ) genetic variation and plasma C-reactive protein levels in young adults: the CARDIA study

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**BACKGROUND:** Interleukin-1 (IL-1) is an inflammatory protein that modulates C-reactive protein (CRP) gene expression, but whether IL-1 $\beta$  genetic variation is associated with CRP levels in young adults is unknown. Because the effects of IL-1 are moderated by obesity, the associations of IL-1 $\beta$  genetic variation with CRP may be modified by body mass index (BMI). We examined these associations in CARDIA, a cohort study of coronary risk development in young adults, initially ages 18-30.

**METHODS:** Ten common (>5%) tag SNPs in the IL-1 $\beta$  gene, identified in a SNP discovery panel (<http://pga.gs.washington.edu>), were genotyped in 1788 African-Americans (AA) and 1918 European Americans (EA); and, haplotypes were estimated using *Phase* (v2.0). CRP levels were measured using immunonephelometry at two examinations (Years 7 and 15). Genetic associations with CRP and change in CRP were examined. GEE and GLM were used to examine the associations of IL-1 $\beta$  with CRP overall; and, we assessed effect modification by BMI. Analyses were stratified by race and adjusted for age, gender and center.

**RESULTS:** SNPs 302 and 12885 were associated with significantly lower CRP among AA and EA respectively. Variation in the IL-1beta gene also was associated with change in CRP: SNPs 7114, 8546 and 15235 were associated with significant increases and SNP 3298 with decreases in CRP among AA; and, SNPs 5277 and 8234 were associated with decreases in CRP among EA. Among AA (9 common haplotypes) and EA (5 common haplotypes) participants, there were no overall associations of common haplotypes with CRP. However, among AA participants with BMI  $\geq 30\text{kg/m}^2$ , a common haplotype comprised of minor alleles at SNPs 2143, 4006, 7114, 8546 and 15235 was associated with higher CRP at Years 7 and 15 and with greater increases in CRP from Year 7-15, compared to the most common haplotype.

**CONCLUSION:** Several common tag SNPs in the IL-1 $\beta$  gene were associated with CRP or change in CRP over time in both AA and EA. Obesity modified the association of a common haplotype (that included 3 SNPs individually associated with increases in CRP) with both level and change in CRP in AA. Further research is needed to confirm these novel associations in other populations.