GSTP1 and TNF Gene variants and associations between air pollution and incident childhood asthma: the traffic, asthma and genetics (TAG) study.

Abstract:
Genetics may partially explain observed heterogeneity in associations between traffic-related air pollution and incident asthma. Our aim was to investigate the impact of gene variants associated with oxidative stress and inflammation on associations between air pollution and incident childhood asthma. Traffic-related air pollution, asthma, wheeze, gene variant, and potential confounder data were pooled across six birth cohorts. Parents reported physician-diagnosed asthma and wheeze from birth to 7-8 years of age (confirmed by pediatric allergist in two cohorts). Individual estimates of annual average air pollution [nitrogen dioxide (NO2), particulate matter≤2.5 μm (PM2.5), PM2.5 absorbance, ozone] were assigned to each child's birth address using land use regression, atmospheric modeling, and ambient monitoring data. Effect modification by variants in GSTP1 (rs1138272/Ala114Val and rs1695/Ile105Val) and TNF (rs1800629/G-308A) was investigated. Data on asthma, wheeze,
potential confounders, at least one SNP of interest, and NO2 were available for 5,115 children. GSTP1 rs1138272 and TNF rs1800629 SNPs were associated with asthma and wheeze, respectively. In relation to air pollution exposure, children with one or more GSTP1 rs1138272 minor allele were at increased risk of current asthma [odds ratio (OR) = 2.59; 95% CI: 1.43, 4.68 per 10 ?g/m3 NO2] and ever asthma (OR = 1.64; 95% CI: 1.06, 2.53) compared with homozygous major allele carriers (OR = 0.95; 95% CI: 0.68, 1.32 for current and OR = 1.20; 95% CI: 0.98, 1.48 for ever asthma; Bonferroni-corrected interaction p = 0.04 and 0.01, respectively). Similarly, for GSTP1 rs1695, associations between NO2 and current and ever asthma had ORs of 1.43 (95% CI: 1.03, 1.98) and 1.36 (95% CI: 1:08, 1.70), respectively, for minor allele carriers compared with ORs of 0.82 (95% CI: 0.52, 1.32) and 1.12 (95% CI: 0.84, 1.49) for homozygous major allele carriers (Bonferroni-corrected interaction p-values 0.48 and 0.09). There were no clear differences by TNF genotype. Children carrying GSTP1 rs1138272 or rs1695 minor alleles may constitute a susceptible population at increased risk of asthma associated with air pollution.