Rs2237717 (by Tyler Cole)

The rs2237717 SNP (major: C, minor: T) is located in intron 11 within the *MET* proto-oncogene. The *MET* gene is primarily linked to tumor metastasis (PMID: 18175071). However, *MET* has also been shown to have roles in general neurodevelopment (PMID: 12397180) and in the development of autism specifically (PMID: 19360663). The Rs2237717 SNP has been linked to schizophrenia, ability to recognize facial emotion, and chronic rhinosinusitis.

Association with schizophrenia and cognitive ability

Since it has been shown that schizophrenic patients have a lower incidence of cancer despite more exposure to risk factors, and that relatives without schizophrenia appear to also have a protective effect, it has been hypothesized that alterations in cancer genes (like *MET*, containing rs2237717) may be involved in the pathogenesis of schizophrenia (PMID: 18331573). In a study by Burdick et al (PMID: 20080979) which investigated SNPs within the *MET* gene as they related to schizophrenia, it was found that rs2237717 resided in an enriched haplotype of one of the four haplotype blocks they investigated in the *MET* gene. This haplotype in 'Block 3' of the study was the most commonly underrepresented in the schizophrenia case group (p = 2.5e-4, OR = 0.40, 95% CI = 0.24—0.65). Rs2237717 was one of three SNPs in the haplotype block to survive correction with permutation (p = 0.002), with 37.9% of the cases and 49.6% of the controls showing the ancestral allele (C). The ancestral allele is thus considered a protective allele against schizophrenia. This test was replicated, including with a dominant model and the results remained significant (p = 0.001) with similar SNP associations. These data represent the first report of an association between *MET* and schizophrenia and the second of an association of *MET* with susceptibility to neuropsychiatric illness (autism). They also reported the *MET* haplotype inversely correlated with schizophrenia (containing rs2237717) had a significant impact on neurocognition, such that carriers in the comparison group performed significantly better than non-carriers on a test of general cognitive ability.

Association with facial emotional perception

Another study by Lin et al (PMID: 22558359) showed the rs2237717 SNP is associated with facial emotional perception. The CT genotype enhanced facial emotional perception as compared to those with the TT genotype, and showed no difference in those with the CC genotype (ANOVA p = 0.016 and GLM p = 0.018, controlled for age, gender, and education). There was also an interaction of rs2237717 with rs1130233 in the *AKT* gene in the same signaling pathway, in which the C carrier/G carrier group showed better facial emotional perception than those with the TT/AA genotype (ANOVA p = 0.035 and GLM p = 0.015), controlled for neurocognitive functions. According to the authors, this is the first study to suggest that genetic factors can affect performance of facial emotion perception.

Association with chronic rhinosinusitis

The *MET* gene has been implicated in nasal polyp development (PMID: 19532090), and Castano et al (PMID: 20416453) showed that rs2237717 is associated with chronic rhinosinusitis in patients with nasal polyps (genotypic P nominal = 0.09, empirical P = 0.04, OR = 1.4, CI = 1.0-1.9). This suggests that polymorphisms in the MET gene, including rs2237717, may play a role in the susceptibility to develop CRS. Study findings apply to patients with severe CRS unresponsive to surgery.