

Epidemiology/Genetics Abstracts

Title: ASSOCIATION OF FOLATE METABOLIC PATHWAY GENES WITH HUMAN SPINA BIFIDA MENINGOMYELOCELE

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Background: Research studies over the last decade have indicated that maternal folate status is important as a risk factor for NTDs in humans. The genes involved in folate-homocysteine metabolism are potential candidate genes for human NTDs. This study has analyzed single nucleotide polymorphic (SNP) variants in these genes as potential risk factors for NTD susceptibility in our SBMM population.

Method: This SBMM population consists of 509 affected child/parent trios and 309 affected child/parent duos, mainly Caucasians of European descent and Hispanics of Mexican descent. The study involved a low density (< 1 SNP/Kb) SNP screen of 13 folate metabolic pathway genes and a high density (> 1 SNP/Kb) SNP screen of the folate carrier (SLC19A1) and receptor (FOLR1, FOLR2, FOLR3) genes. Family-based genetic association studies i.e. Reconstruction Combined Transmission Disequilibrium Test (RCTDT), and case-control methods were used.

Results: A positive association was found with SBMM in our population with a SNP (rs327592) located in intron 15 of the Methionine synthase reductase (MTRR) gene on chromosome 5 (RC-TDT p-value = 0.0154). The study also found a significant association for a SNP (rs2071010) in the first exon of the folate receptor 1 (FOLR1) gene on chromosome 11 (odds ratio; AG v GG = 0.459). These results indicate that the minor allele (A) in this intronic SNP may provide a protective effect.

Conclusion: The finding of the MTRR variant in this study is consistent with the MTRR 66A>G variant implicated as a maternal risk factor for spina bifida in previous studies. Furthermore, both mouse and human studies have suggested that variants in FOLR1 may be risk factors for SBMM. In conclusion, it will be important to genotype more SNPs on MTRR to follow up on this finding and to design functional studies for these and other significant variants that may be found.