



Combined folate gene *MTHFD* and *TC* polymorphisms as maternal risk factors for Down syndrome in China

Y.P. Liao¹, D. Zhang¹, W. Zhou¹, F.M. Meng¹, M.S. Bao¹, P. Xiang²
and C.Q. Liu¹

¹Department of Cell Biology, Bengbu Medical College,
Bengbu, China

²The Central Laboratory, First Affiliated Hospital, Bengbu Medical College,
Bengbu, China

Corresponding author: C.Q. Liu
E-mail: ghoststories@sina.com

Genet. Mol. Res. 13 (1): 1764-1773 (2014)

Received November 27, 2012

Accepted August 10, 2013

Published March 17, 2014

DOI <http://dx.doi.org/10.4238/2014.March.17.4>

ABSTRACT. We examined whether polymorphisms in the methylenetetrahydrofolate dehydrogenase (*MTHFD*) and transcobalamin (*TC*) genes, which are involved in folate metabolism, affect maternal risk for Down syndrome. We investigated 76 Down syndrome mothers and 115 control mothers from Bengbu, China. Genomic DNA was isolated from the peripheral lymphocytes. Polymerase chain reaction and restriction fragment length polymorphism were used to examine the polymorphisms of *MTHFD* G1958A and *TC* C776G. The frequencies of the polymorphic alleles were 24.3 and 19.1% for *MTHFD* 1958A, 53.9 and 54.2% for *TC* 776G, in the case and control groups, respectively. No significant differences were found between two groups in relation to either the allele or the genotype frequency for both polymorphisms. However, when gene-gene interactions between these two polymorphisms together with previously studied C677T and A1298C polymorphisms in the methylenetetrahydrofolate reductase (*MTHFR*)

gene were analyzed, the combined *MTHFR* 677CT/TT and *MTHFD* 1958AA/GA genotype was found to be significantly associated with the risk of having a Down syndrome child [odds ratio (OR) = 3.11; 95% confidence interval (95%CI) = 1.07-9.02]. In addition, the combined *TC* 776CG and *MTHFR* 677TT genotype increased the risk of having a child with Down syndrome 3.64-fold (OR = 3.64; 95%CI = 1.28-10.31). In conclusion, neither *MTHFD* G1958A nor *TC* C776G polymorphisms are an independent risk factor for Down syndrome. However, the combined *MTHFD/MTHFR*, *TC/MTHFR* genotypes play a role in the risk of bearing a Down syndrome child in the Chinese population.

Key words: Down syndrome; Folate; *MTHFD*; *Transcobalamin gene*; Polymorphisms