Reviewer’s report

Title: 118 SNPs of Folate-Related Genes and Risks of Selected Congenital Anomalies

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Reviewer: Andrew E. Czeizel

Reviewer’s report:

This paper presents an important and very work-consuming study with a bit disappointed results. All possible candidate gene polymorphisms in the origin of NDT and conotruncal cardiac defects were checked without the detection and/or confirmation strong association. Nevertheless this study is an important, though mainly negative step in the route of understanding better the etiology of two most important structural birth defects in the human being. I addition the detailed presentation of their laboratory analyses may help others to use their data for meta-analysis or to look for new directions.

I think the major problem is that this approach was not appropriate for the evaluation of maternal-fetus SNPs together. We know data regarding the role of hyperhomocystenemia in the origin a placental malfunction and the placenta has a double: fetal-embryonic and maternal origin. Thus we can imagine that the maternal factors are important in the gene-environmental interaction inducing finally these defects.

The international literature is very abundant in this topic, authors did their best to select more important previous publications, but I know some others as well. It would be better to cite the more relevant papers of the Hungarian group in this topic (Czeizel AE.: Reduction of urinary tract and cardiovascular defects by periconceptional multivitamin supplementation. Am J Med Genet 1996. 62: 179-183, Czeizel AE, Dobo M, Vargha P. Hungarian cohort-controlled trial of periconceptional multivitamin supplementation shows a reduction in certain congenital abnormalities. Birth Defects Res (Part A) 2004. 70: 853-861.)

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.