MECHANISM OF FOLATE METABOLISM: METHYLENETETRAHYDROFOLATE REDUCTASE *(MTHFR)* GENE POLYMORPHISMS IN MALAYSIAN MOTHERS WITH DOWN SYNDROME CHILDREN

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All technical staffs
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4. Enhanced Research Title and Objectives

(if any)

Original Title as Proposed:

Mechanism of folate metabolism*:* Methylenetetrahydrofolate reductase *(MTHFR)* gene polymorphisms in Malaysian mothers with Down syndrome children

Improved/Enhanced Title:
Mechanism of folate metabolism*:* Status of Iron, Folic Acid and Vitamin B in Down syndrome Individuals

Original Objectives as Proposed:

To investigate:

i. the relationship of abnormal folate intake with the risk factor for maternal meiotic nondisjunction and Down syndrome
ii. the mechanism involves in folate metabolic pathway in mothers of children with Down syndrome

Improved/Enhanced Objectives:

To determine:

i. the nutritional status of iron, folic acid and vitamin B and also hematological parameters in DS individuals in comparison to controls
ii. the effect of folate supplementation

5. Report

5.1 Proposed Executive Summary

Trisomy 21 (Down syndrome, DS) is a common chromosomal abnormality occuring in about 1 in 700 live births. Studies to date have found the relationship between folate metabolism and chromosomal nondisjunction. Folate metabolic pathways involve many genes and one of that is methylenetetrahydrofolate reductase (*MTHFR*) and its polymorphism might be a risk factor for having a child with Down syndrome. The association of two important *MTHFR* gene single nucleotide polymorphisms 677C→T and 1298A→C with Down syndrome will be studied. If this is the case, an inadequate folate intake together with certain polymorphisms of some genes can increase the possibility to conceive a child with Down syndrome. Therefore, people with Down syndrome may be more likely to carry these forms of these genes from their parents and experience associated problems in folate metabolism. The participants are mothers of a child with Down syndrome and age-matched mothers for the case control study. Nutritional status with special emphasis on folate intake will be studied using a nutritional questionnaire and plasma homocysteine and methionine will be measured. The genotyping will be done by Polymerase Chain Reaction (PCR) followed by restriction fragment length polymorphism (RFLP) and gel electrophoresis. This study is important to understand the relationship of *MTHFR* gene polymorphisms and folate metabolism with maternal risk for Down syndrome and involving both in heterozygous and homozygous conditions. The discovery from this research will contribute for future studies on the folate pathway and occurrence of Down syndrome.