Methylenetetrahydrofolate reductase (MTHFR) is an enzyme critical in both folate and homocysteine metabolism. It is a FAD-dependent enzyme that catalyzes the irreversible conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate which in turn serves as a methyl donor in the remethylation of homocysteine (Hcy) to methionine. The enzyme therefore resides at an important metabolic branch point directing the folate pool towards Hcy remethylation and DNA methylation at the expense of DNA and RNA biosynthesis.

A missense mutation at bp677 predisposes to mild or moderate hyperhomocysteinemia. In addition, cardiovascular disease, neural tube defects, pregnancy complications, neuropsychiatric disease, renal failure and colorectal neoplasias have been reported to be associated with the 677C→T mutation.

Investigations of MTHFR deficiencies recapitulate the transition in medical genetics from isolation of genes involved in single gene disorders to identification of variants involved in complex multifactorial diseases.

Contents

1. Molecular Biology of Methylenetetrahydrofolate Reductase (MTHFR) and Overview of Mutations/Polymorphisms
   Daniel Leclerc, Sahar Sibani and Rima Rozen

2. Assays for Methylenetetrahydrofolate Reductase Polymorphisms
   Arve Ulvik and Per Magne Ueland

3. Biochemical Characterization of Human Methylenetetrahydrofolate Reductase and Its Common Variants
   Kazuhiro Yamada and Rowena G. Matthews

4. Severe Methylenetetrahydrofolate Reductase Deficiency
   Mary Ann Thomas and David S. Rosenblatt

5. Mild MTHFR Deficiency and Folate Status
   Paul F. Jacques and Silvina Furlong Choumenkovitch

6. Riboflavin and Methylenetetrahydrofolate Reductase
   Steinar Hustad, Jørn Schneede and Per Magne Ueland

7. The Molecular Dynamics of Abnormal Folate Metabolism and DNA Methylation Implications for Disease Susceptibility and Progression
   S. Jill James

8. Methylenetetrahydrofolate Reductase 677C→T Polymorphism and Risk of Arterial Occlusive Disease
   Mariska Klerk and Petra Verhoef

9. Methylenetetrahydrofolate Reductase and Venous Thrombosis
   Miranda B.A.J. Keijzer and Martin den Heijer

10. Neural Tube Defects, Other Congenital Malformations and Single Nucleotide Polymorphisms in the 5,10 Methylenetetrahydrofolate Reductase (MTHFR) Gene: A Meta-Analysis
    Stein Emil Vollset and Lorenzo D. Botto

11. Pregnancy Complications
    Willianne L.D.M. Nelen and Henk J. Blom

12. Neuropsychiatric Disease and Methylenetetrahydrofolate Reductase
    Björn Regland

13. Methylenetetrahydrofolate Reductase Polymorphisms and Renal Failure
    Manuela Föddinger and Gere Sunder-Plassmann

14. MTHFR Polymorphisms and Colorectal Neoplasia
    Jimmy W. Crott and Joel B. Mason

15. Methylenetetrahydrofolate Reductase Polymorphisms: Pharmacogenetic Effects
    Bernd Christian Schwahn and Rima Rozen