Clinical Laboratory Improvement Amendment (CLIA)# - 5001072592

Iverson™ MTHFR Assay

OVERVIEW

Please contact us directly at support@iversongenetics.com for more information.

Iverson™ GENETIC DIAGNOSTICS, INC.

Empowering people to *improve* and *extend* their lives.

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MTHFR

MTHFR Pathophysiology

MTHFR (Methlyenetetrahydrofolate reductase) is a key enzyme in the metabolism of homocysteine. The most common MTHFR variant is C677T which causes the production of a thermolabile enzyme and decreased enzyme activity. A second MTHFR variant (A1298C) when associated with C677T causes further decreased MTHFR activity. Both conditions are related to low levels of plasma folate and elevated levels of homocysteine—a known risk factor for coronary artery disease, thrombosis and associated cardiovascular disorders including heart attacks and strokes.[1]

Incidence and Significance

The C677T variant is extremely common: 12-13% of the general population are homozygous for the variant.[2] In North America, the incidence of C677T variance was found to exist in the following levels: Caucasians (34%), Asians (30%), African-Americans (13%). The incidence of the A1298C variant was: Caucasians (30%), Asians (20%), and African-Americans (16%).[3] A separate study indicated that American Hispanics had a higher incidence of the two MTHFR mutations than those reported in Caucasians.[4]

In addition to the aforementioned consequences of elevated homocysteine, the C677T and A1298C variants are also associated with a variety of adverse pregnancy outcomes including recurrent miscarriages and neural tube defects.[5] Some mental health disorders (including schizophrenia depression and bipolar disorder) appear to be associated with C677T and A1298C.[6] C677T and A1298C have also been associated with insufficient DNA methylation, mutations and aberrant gene expression patterns.[7]

Clinical Utility

Identifying C677T and A1298C variants helps clinicians caring for patients (and families) by triggering increased homocysteine screening, informing genetic counseling, and in emphasizing the importance of developing diets and lifestyles that may decrease health risks before adverse events occur.

Who Should Get Tested?

Testing should be considered in patients and relatives of patients with elevated homocysteine levels. Other indications include: history of thrombosis, coronary artery disease, stroke, pregnancies with neural tube defects, recurrent pregnancy loss, and having other genetic thrombophilias (e.g. Factor V Leiden, or G20210A variants).

References

1. Kolling K, Ndrepepa G, Koch W, Braun S, Mehilli J, Schomig A, Kastrati A. Methylenetetrahydrofolate reductase gene C677T and A1298C polymorphisms, plasma homocysteine, folate, and vitamin B12 levels and the extent of coronary artery disease. *Am J Cardiol.* 2004;10:1201–1206.
2. Brattstrom L, Wilcken DE, Ohrvik J, Brudin L.Common methylenetetrahydrofolate reductase gene mutation leads to hyperhomocysteinemia but not to vascular disease: the result of ameta-analysis. *Circulation* 1998; 98:2520–6.
3. Langman, L.J.; Wong, B.Y.-L.; Boggis, C.; Rubin, L.A.; Cole, D.E.C.; (1998). The prevalence and linkage disequilibrium of three methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms varies in different ethnic groups.
4. Chowdary D, Streck D, Schwalb MN, Dermody JJ. High Incidence of Two Methylenetetrahydrofolate Reductase Mutations (C677T and A1298C) in Hispanics. *Genetic Testing.* 2003, 7(3): 255-257.
5. Marco, Patrizia De.; et al. Reduced folate carrier polymorphism (80A G) and neural tube defects. *Nature.* March 2003, Volume 11, Number 3, Pages 245-252
6. Gilbody S, Lewis S, Lightfoot T. Methylenetetrahydrofolate reductase (MTHFR) genetic polymorphisms and psychiatric disorders: a HuGE review. *Am J Epidemiol.* 2007 Jan 1;165(1):1-13. Epub 2006 Oct 30.
7. Newman, P. E. (1999) Can reduced folic acid and vitamin B12 levels cause deficient DNA methylation producing mutations which initiate atherosclerosis?. *Med. Hypotheses* 53:421-424.[Medline]

Sample Requirements and Shipping Instructions

Please contact us directly at **support@iversongenetics.com** or **206.732.1478** for assistance or additional questions.

I. Specimen Requirements

Peripheral blood drawn in an EDTA (purple-top) tube.

- Ship minimum 200 micro liters, preferable 5cc of whole blood in a lavender-top (EDTA) tube.
- Shipped at room temperature (18˚ – 26˚C). DO NOT FREEZE WHOLE BLOOD
- Stored for 72 hours refrigerated (20˚ – 80˚C), stable for up to 3 days, refrigerated for repeat testing only

II. Domestic Shipping Instructions

1. **Materials and Equipment**
   - Iverson specimen kit containing patient specimen.
   - FEDEX clinical pack, Large – a plastic overwrap used to ship the specimen to Iverson
   - FEDEX USA Airbill pre-printed with Iverson Genetic Diagnostics Inc. shipping info
   - FEDEX adhesive outer sleeve for the FEDEX airbill.
2. **Place the Iverson Assay specimen kit into the FEDEX clinical Pak.**
3. **Check the box on the Clinical Pak indicating that the packaging is in compliance with the IATA 650 packaging regulations.**
4. **Complete the FEDEX Airbill noting the following areas:**
   A. *Sec 6. Special Handling:* Under the question, "Does this shipment contain dangerous goods?" Check "No."
   B. *Release Signature:* Do not sign here
5. **Place the package in the designated FEDEX pickup location at your site.**
6. **If your site does not have standard FEDEX pickup please call (800) GO FEDEX to arrange pickup.**