Clinical Significance

Provide risk assessment of CVDs development and guide appropriate folic acid supplementation for high-risk populations or anyone in need.

Suitable for patients with CVD, populations with family history of CVD, cheek-up crowd, etc.

Ordering Information

Product Name	Specification	Specimen	Target Gene Location
Universal Sequencing Detection Kit (SNP-U1)	20 T/Kit	2 mL of EDTA anticoagulated whole blood	MTHFR (c. 677 C>T), MTHFR (c. 1298 A>C), MTRR (c. 66 A>G)

Features

Reliable Detection

Powerful software analysis; Internal control can monitor the whole detection process and ensure the accuracy of the detection results reach to over 99%.

Easy Operation

Free of sample extraction; Pre-filled reagents; No requirements for specialized equipment or techniques.

High Efficiency

Results are available in an hour after loading samples; Reports are easy to read.

Integrated Solution

Tianlong integrated solution from devices to reagents can ensure great compatibility and minimized systematic errors.

Assay Workflow

1 Sample Collection

2 Sample Detection

3 Analysis and Report

*Detection directly after sample collection and report within 1 hour

Reference

1. Yuan S, Mason AM, Carter P, et al. Homocysteine, B vitamins, and cardiovascular disease: a Mendelian randomization study. BMC Med. 2021;19(1):97. doi:10.1186/s12916-021-01977-8

2. McNulty H, Pentieva K. Folate bioavailability. Proc Nutr Soc. 2004;63(4):529-536. doi:10.1079/PNS2004383

3. Ohrvik VE, Witthoft CM. Human folate bioavailability. Nutrients. 2011;3(4):475-490. doi:10.3390/nu3040475

4. Guieu R, Ruf J, Mottola G. Hyperhomocysteinemia and cardiovascular diseases. Ann Biol Clin (Paris). 2022;80(1):7-14. doi:10.1684/abc.2021.1694

5. Djuric D, Jakovljevic V, Zivkovic V, et al. Homocysteine and homocysteine-related compounds: an overview of the roles in the pathology of the cardiovascular and nervous systems. Can J Physiol Pharmacol. 2018;96(10):991-1003. doi:10.1139/cjpp-2018-0112

6. Patel KR, Sobczyńska-Malefora A. The adverse effects of an excessive folic acid intake. Eur J Clin Nutr. 2017;71(2):159-163. doi:10.1038/ejcn.2016.194

7. Raghubeer S, Matsha TE. Methylenetetrahydrofolate (MTHFR), the one-carbon cycle, and cardiovascular risks. Nutrients. 2021;13(12):4562. doi:10.3390/nu13124562

8. Yuan X, Wang T, Gao J, et al. Associations of homocysteine status and homocysteine metabolism enzyme polymorphisms with hypertension and dyslipidemia in a Chinese hypertensive population. Clin Exp Hypertens. 2020;42(1):52-60. doi:10.1080/10641963.2019.1571599

Version 1.0

Tianlong Science and Technology

Mail: inquiry@medtl.com
Phone: 86 029 82682132
Website:www.medtl.net
Address: No. 4266 Shanglin Road, Xi'an, China

Bring Technology to Life

TIAN LONG

Precision Medicine

Folic Acid Personalized Medication Solutions

Cardio-cerebrovascular Diseases

BACKGROUND

Folate (referring to the group of B9 vitamins) is a water-soluble vitamin that involves in the metabolism of homocysteine (Hcy), which has been implicated in the development of cardio-cerebrovascular diseases[1]. As a dietary micronutrient, folate cannot be synthesized by humans, but are widely distributed in a variety of green leafy vegetables and fruits. However, folate intakes from natural food have been increasingly recognized as a suboptimal resource for many individuals, owing to: 1) dietary folates are rather unstable whose vitamin activity can easily be damaged during food processing; 2) the bioavailability of the natural food folates is usually incomplete due to varied physiological conditions towards dietary folate interventions[2,3]. Therefore, exogenous folic acid supplementation is necessary for maintaining cardio-cerebrovascular health.

Hazards of Under-/Exceed- Intake of Folic Acid

Inadequate folic acid supply is associated with increased levels of Hcy in blood. As an independent risk factor for cardio-cerebrovascular diseases (CVDs), elevated plasma Hcy directly mediates endothelial cell injury, which is thought to induce vascular inflammation, plaque formation, blood flow disturbance and the progression of CVDs, such as hypertension, stroke and coronary heart disease (Figure 1)[4,5] .

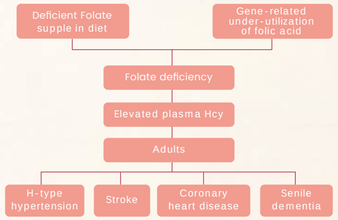

Figure 1: Hazards of insufficient folic acid intake

On the other hand, a growing body of evidence has raised an inverse correlation between folic acid and disease development, where persistent high levels of folic acid intakes are potentially linked to fold-increased risks of malignant tumors, including colorectal cancer, prostate cancer, invasive adenocarcinoma, etc.[6]

Consequently, modest folic acid consumption is essential for optimal human health, especially for people at high-risk of CVDs. Precise evaluation of appropriate folic acid supplementation for individuals with different requirements is thus extremely important.

MTHFR, MTRR Genes and Folate Metabolism

5,10-methylenetetrahydrofolate reductase (MTHFR) and methionine synthase reductase (MTRR) are key enzymes for folate metabolism (Figure 2). Strong evidence has shown that genetic polymorphisms in MTHFR (c. 677 C>T), MTHFR (c. 1298 A>C) and MTRR (c. 66 A>G) affect the gene activity, leading to reduced enzymatic activities and decreased efficiency of folate utilization.

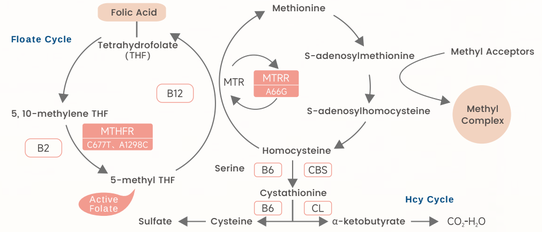

Figure 2: Homocysteine and folate metabolism

Of the three mutations, nucleic substitutions at position 677 and/or 1298 of MTHFR are frequently detected in individuals with elevated Hcy levels. Comparing to the wild-type phenotype, up to 60% of decreased MTHFR enzymatic activities have been detected in homozygous and/or heterozygous variants[7]. The correlation between increased risks of CVD-associated diseases and the MTHFR 677TT genotype is exemplified in Figure 3.

Moreover, the transition of adenine (A) to guanine (G) in the MTRR 66 gene site is also involved in enhanced expression of Hcy. People carrying MTRR 66AG/GG mutants are likely under a higher risk of hypertriglyceridemia and CVDs[8].

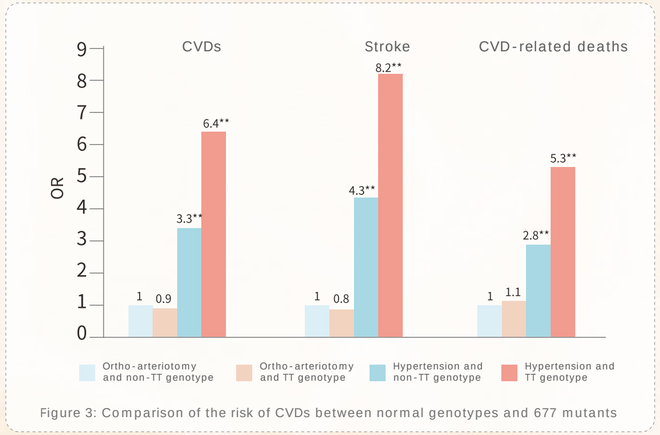

Figure 3: Comparison of the risk of CVDs between normal genotypes and 677 mutants

FOLATE PERSONALIZED MEDICATION SOLUTIONS

Tianlong Folic Acid Personalized Medication Solution is designed to rapidly determine the presence of MTHFR/MTRR polymorphisms including MTHFR (c. 677 C>T), MTHFR (c. 1298 A>C) and MTRR (c. 66 A>G) in specimen with its exclusive pharmacogenomic reagents and the Fascan 48E multi-channel fluorescence quantitative analyzer. The results can provide genetic clues for risk assessment of CVDs development and guide appropriate folic acid supplementation.

Gene Locus	Genotype and Risk assessment
MTHFR (c. 677 C>T)	CC (normal); CT (normal); TT (risk)
MTHFR (c. 1298 A>C)	AA (normal); AC (normal); CC (risk)
MTRR (c. 66 A>G)	AA (normal); AG (risk); CG (risk)

Risk Assessment and Protocols for Folic Acid Supplementation

Result	Risk Assessment	Suggested Doses	Recommended Dose upon Hcy Levels		Recommendations for Monitoring Hcy Levles
No risk genotypes in MTHFR or MTRR	No risk	0.8 mg/d	Hcy ≥ 10 μmol/L	0.8 mg/d	Appropriate monitoring
			Hcy = 6.3-10 μmol/L	0-0.4 mg/d	
			Hcy ≤ 6.3μmol/L	No need for additional supplementation	
No risk genotypes in MTHFR (c. 1298) or MTRR, but MTHFR (c. 677 CT)	Low risk	0.8 mg/d	Hcy ≥ 10 μmol/L	0.8 mg/d	Appropriate monitoring
			Hcy = 6.3-10 μmol/L	0-0.4 mg/d	
			Hcy ≤ 6.3μmol/L	No need for additional supplementation	
Either MTHFR (c. 677/c. 1298) or MTRR has risk genotypes	Moderate risk	1.0 mg/d	Hcy ≥ 10 μmol/L	1.0 mg/d	Periodic monitoring
			Hcy = 6.3-10 μmol/L	0.4 mg/d	
			Hcy ≤ 6.3μmol/L	No need for additional supplementation	
Both of MTHFR (c. 677/c. 1298) and MTRR (c. 66) have risk genotypes	High risk	1.2 mg/d	Hcy ≥ 10 μmol/L	1.2 mg/d	Strong recommendation of close monitoring
			Hcy = 6.3-10 μmol/L	0.8 mg/d	
			Hcy ≤ 6.3μmol/L	0.4 mg/d	

Examples of Detection Results

Gene Locus	Genotype	Clinical Significance	Suggested Doses	Recommended Dose upon Hcy Levels		Recommendations for Monitoring Hcy Levels
MTHFR (c. 677 C>T)	CT	Moderate risk in folate metabolism	1.0 mg/d	Hcy ≥ 10 μmol/L	1.0 mg/d	Periodic monitoring
MTHFR (c. 1298 A>C)	AC			Hcy = 6.3-10 μmol/L	0.4 mg/d	
MTRR (c. 66 A>G)	AG			Hcy ≤ 6.3μmol/L	No need for additional supplementation	