Clinical Significance

Indicate the risk of birth defects and guide appropriate folic acid supplementation

Suitable for couples preparing for pregnancy, pregnant women, or women with a history of poor pregnancy or childbirth

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

Accurate Result

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

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

High Efficiency

Results are available in an hour after loading samples; Easy to read reports.

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

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

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4. Ye F, Zhang S, Qi Q, et al. Association of MTHFR 677C>T polymorphism with pregnancy outcomes in IVF/ICSI-ET recipients with adequate synthetic folic acid supplementation. Biosci Trends. 2022;16(4):282-290. doi:10.5582/bst.2021.01306

5. Guo QN, Wang HD, Tie LZ, et al. Parental genetic variants, MTHFR 677C>T and MTRR 66A>G, associated differently with fetal congenital heart defect. BioMed Res Int. 2017;2017: 3043476. doi:10.1155/2017/3043476

6. Mierzejewska E. Methylene tetrahydrofolate reductase mutations as genetic risk factors for neural tube defects (NTF). Med Wieku Rozwoj. 1999;3(4):521-527.

7. Bulloch RE, Wall CR, McCowan LME, et al. The effect of interactions between folic acid supplementation and one carbon metabolism gene variants on small-for-gestational-age births in the screening for pregnancy endpoints (SCOPE) cohort study. Nutrients. 2020;12(6):1677. doi:10.3390/nu12061677

8. Wang W, Jiao XH, Wang XP, et al. MTR, MTRR, and MTHFR gene polymorphisms and susceptibility to nonsyndromic cleft lip with or without cleft palate. Genet Test Mol Biomark. 2016;20(6):297-303. doi:10.1089/gtmb.2015.0186

Version 1.0

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Bring Technology to Life

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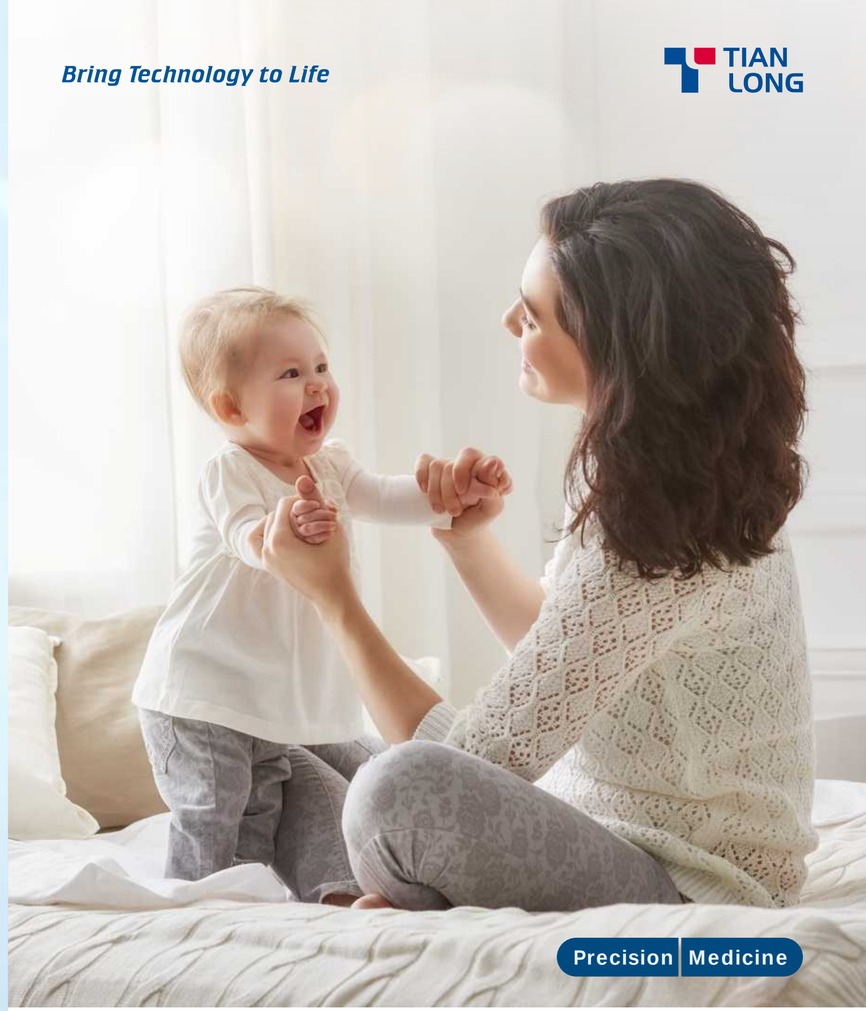

Folic Acid Personalized Medication Solutions

Maternal Health

BACKGROUND

Folate (referring to the group of B9 vitamins) is a water-soluble vitamin that plays a crucial role in the one-carbon metabolic pathway and is required for rapid cell proliferation and tissue growth of the uterus and the placenta, growth of the fetus and expansion of the maternal blood volume, etc.[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, especially for those preparing for or under pregnancy, 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 health outcomes in pregnancy, and prevention of birth and growth defects for infants and adolescents.

Hazards of Under-/Exceed- Intake of Folic Acid

Insufficient Supplementation

Deficits in periconceptional folic acid supply has been accepted contributing to the increased risks of maternal complications and congenital malformations of newborns[1], as shown in Figure 1.

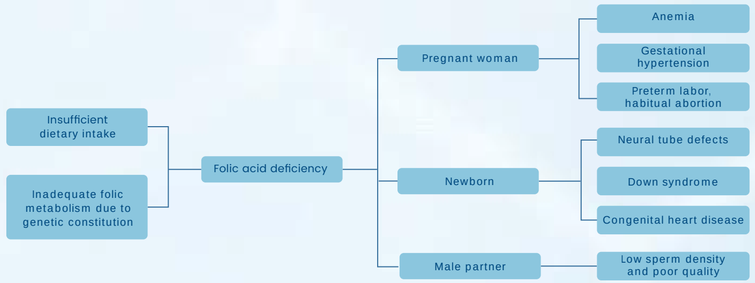

Figure 1: Hazards of folic acid deficiency

Excessive Supplementation

Excessive folic acid supplementation can also be harmful in human health, including:

- Interfere with zinc absorption which may limit fetal development;
- Gastrointestinal discomfort, such as vomiting, nausea and bloating;
- Neglect of vitamin B12 deficiency and induction of deficient B12-mediated abnormal development of fetal nervous system;
- Increased risk of breast cancer, colorectal cancer and prostate cancer.

MTHFR, MTRR Genes and Folate Metabolism

The 5,10-methylenetetrahydrofolate reductase (MTHFR) and methionine synthase reductase (MTRR) are the key enzymes in folate metabolism. 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.

As one of the wildly accepted major genetic factors for adverse pregnancy outcomes, proper supplementation of folic acid in pregnant women with C-to-T transition of the MTHFR 677 gene site is extremely important, since the MTHFR enzymatic activity of homozygous TT mutations reduced 70% and the heterozygous mutants reduced 35%, comparing to that of the wild-type genotype (CC)[4]. Risk assessment between the TT and wild-type genotypes towards examples of fetal viability are shown in Figure 2. This is also the case for MTHFR (c. 1298 A>C) where a 40% reduction of MTHFR activity has been observed for individuals with the CC variant and adequate maternal folic acid intake attenuates the occurrence of recurrent miscarriage, low birthweight, neural tube defects and etc.[5–7] Benefits of sufficient folic acid intake for pregnant women with polymorphisms of MTRR (c. 66 A>G) has also been documented for fetal defects, such as ventricular septal defect and cleft lip[5,8].

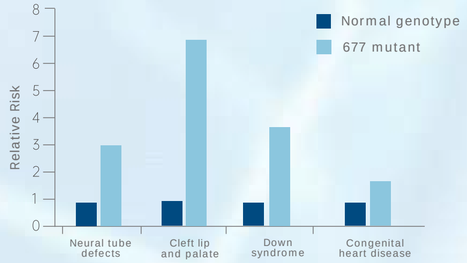

Figure 2: Comparison of the risk of birth defects between normal genotypes and 677 mutants

FOLIC ACID 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) with its exclusive pharmacogenomic reagents and the Fascan 48E multi-channel fluorescence quantitative analyzer. The results can provide genetic clues for risk assessment of birth defects 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	Folic Acid Supplementation During Pregnancy		
		3 Months Before Conception	Early Pregnancy (0 - 12 weeks)	Late Pregnancy (13-40 weeks)
No risk genotypes in MTHFR or MTRR	No risk	0.4 mg/d	0.4 mg/d	Dietary intake, no need for additional
No risk genotypes in MTHFR (c. 1298) or MTRR, but MTHFR (c. 677 CT)	Low risk	0.4 mg/d	0.4 mg/d	0.4 mg/d
Either MTHFR (c. 677/c. 1298) or MTRR has risk genotypes	Moderate risk	0.4 mg/d	0.8 mg/d	0.8 mg/d
Both of MTHFR (c. 677/c. 1298) and MTRR (c. 66) have risk genotypes	High risk	0.8 mg/d	0.8 mg/d	0.8 mg/d

Examples of Detection Results

Gene Locus	Genotype	Clinical Significance	Folic Acid Supplementation During Pregnancy		
			3 Months Before Conception	Early Pregnancy (0 - 12 weeks)	Late Pregnancy (13-40 weeks)
MTHFR (c. 677 C>T)	CT	Moderate risk in folate metabolism	0.4 mg/d	0.8 mg/d	0.4 mg/d
MTHFR (c. 1298 A>C)	AA				
MTRR (c. 66 A>G)	AG				