Clinical Significance

Suitable for patients with common and H-type hypertension

Guiding rational medication to control blood pressure and lower the risk of cardio-cerebrovascular diseases.

Ordering Information

Product Name	Specification	Specimen	Target Gene Location
Universal Sequencing Detection Kit (SNP-U6)	20 T/Kit	2 mL of EDTA anticoagulated whole blood	CYP2D6*10, CYP2C9*3, ADRB1 (1165 G>C), AGTR1 (1166 A>C), ACE (I/D), NPPA (2238 T>C), CYP3A5*3

Features

Reliable Detection

Strong data analysis software; 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. Munakata M. Clinical significance of stress-related increase in blood pressure: current evidence in office and out-of-office settings. Hypertens Res. 2018;41(8):553-569. doi:10.1038/s41440-018-0053-1
- 2. Ozemek C, Laddu DR, Arena R, et al. The role of diet for prevention and management of hypertension. Curr Opin Cardiol. 2018;33(4):388-393. doi:10.1097/HCO.0000000000000532
- 3. Kaye AD, Jeha GM, Pham AD, et al. Folic acid supplementation in patients with elevated homocysteine levels. Adv Ther. 2020;37(10):4149-4164. doi:10.1007/s12325-020-01474-z
- 4. Raghubeer S, Matsha TE. Methylenetetrahydrofolate (MTHFR), the one-carbon cycle, and cardiovascular risks. Nutrients. 2021;13(12):4562. doi:10.3390/nu13124562
- 5. Rysz J, Franczyk B, Rysz-Górzyńska M, et al. Pharmacogenomics of hypertension treatment. Int J Mol Sci. 2020;21(13):4709. doi:10.3390/ijms21134709

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Hypertension Personalized Medication Solutions

BACKGROUND

Hypertension, a significant risk factor for cardiovascular diseases, is responsible for a great mass of cardiovascular-related mortalities and disabilities worldwide. The cause of hypertension is complex. Parameters, including inactive lifestyles, improper dietary patterns, chronic stress conditions and other psychological/psychosocial factors, are increasingly known contributing to the variability of blood pressure and the development and/or worsening of hypertension[1,2]. In addition to these common stimuli, accumulated homocysteine (Hcy) in blood has received growing attention over the years. An increasing number of evidence has suggested its synergistic correlation with the occurrence of a special type of hypertensive disorder, i.e., H-type hypertension.

H-type hypertension and folate metabolism

H-type hypertension is typically defined as hypertension with plasma levels of Hcy greater than 10 μmol/L (also known as hyperhomocysteinemia, HHcy). As a critical intermediate in methylation reactions, the maintenance of plasma Hcy within normal limits heavily depends on the efficacy of folate metabolism (Figure 1)[3]. However, due to improper dietary habits and/or genetic factors, folate intake or bioavailability in many individuals may not be sufficient.

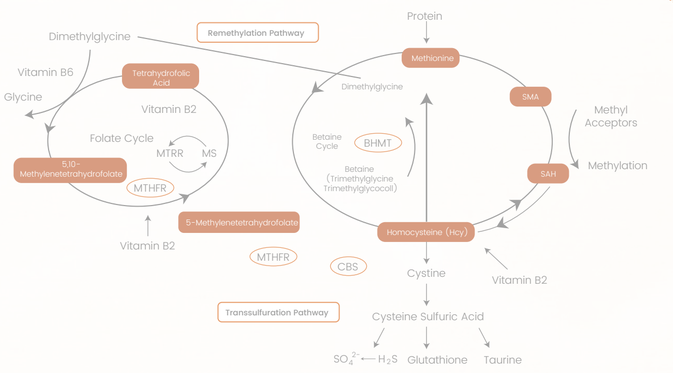

Figure 1: Metabolic pathways of Hcy/Folate

Mounting evidence has suggested a close correlation between the plasma Hcy level and genetic polymorphisms in 5,10-methylenetetrahydrofolate reductase (MTHFR) and methionine synthase reductase (MTRR), two of the key enzymes of the folate pathway. Comparing to the wildtype genotype, homozygous and/or heterozygous variants of the MTHFR gene reduce up to 60% of the biological activity of the corresponding enzymes, leading to decreased efficiency of folate utilization and increased risks of HHcy and adverse cardiovascular events, including H-type hypertension[4]. Similar results have also been detected for patients carrying MTRR mutants.

Considering the importance of MTHFR and MTRR in folate metabolism and the development of H-type hypertension, folic acid supplementation under scientific guidance is essential, especially for H-type hypertension patients (Table 1 & 2).

Table 1 Genetic polymorphisms and corresponding risk assessment

Gene Locus	Genotype and Risk Assessmen
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)

Table 2 Risk assessment and recommendation for folic acid supplementation

Result	Risk Assessment	Suggested Doses	Recommended Dose upon Hcy Levels		Recommendations for Monitoring Hcy Levels
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/MTRR and the MTHFR c.677 C>T locus is heterozygous (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	
MTHFR or MTRR contains 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 and MTRR contain risk genotypes	High risk	1.2mg/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	

HYPERTENSION PERSONALIZED MEDICATION SOLUTIONS

Although hypertension may induce severe health outcomes, it is controllable under appropriate therapeutic strategies. According to different nosogenesis and genetic nature of hypertension, applications of anti-hypertensive medication might be varied across individuals. At present, five key classes of anti-hypertensive drugs are frequently used during practice, including diuretics, calcium antagonists, angiotensin-converting enzyme inhibitors, angiotensin receptor inhibitors and β-adrenergic receptor blockers. These drugs target different genes and their genetic polymorphisms across individuals may modulate different drug responses towards anti-hypertension treatment via interfering with core genes in the pathomechanisms of hypertension development, drug-metabolizing processes and/or drug transportation[5].

With the help of specific ligases and fluorescence capture probes, Tianlong personalized hypertension medication solution intends to assist hypertension treatment via utilizing its pharmocogenomic reagents and the Fascan 48E multichannel fluorescence quantitative analyzer to capture information of 7 hypertension pharmacogenetic-related genetic loci (CYP2D6*10, CYP2C9*3, ADRB1 (1165 G>C), AGTR1 (1166 A>C), ACE (I/D), NPPA (2238 T>C), CYP3A5*3). The correlation between genetic variants and drug-metabolizing capacities is exemplified in Table 3. For patients with H-type hypertension, additional assessment of folate bioavailability and appropriate supplement regimen according to the Tianlong SNP-U1 kit are also recommended.

Table 3 Association of anti-hypertensive drugs-related gene loci with phenotypes

Classification	Medication	Gene Locus	Genotype	Phenotype
β-adrenergic receptor blocker	Metoprolol Carvedilol Alprenolol Labetalol	ADRB1 (c.1165 G>C)	GG	Normal sensitivity
			GC	Relatively high sensitivity
			CC	High sensitivity
		CYP2D6 (c.100 C>T)	CC	Normal metabolic capacity
			CT	Relatively weak metabolic capacity
			TT	Weak metabolic capacity
Angiotensin II receptor inhibitor	Losartan Irbesartan Candesartan Valsartan	AGTR1 (c.1166 A>C)	AA	Normal sensitivity
			AC	Relatively high sensitivity
			CC	High sensitivity
		CYP2C9 (c.1075 A>C)	AA	Normal losartan activation ability; Normal ARB metabolic capacity
			AC	Relatively weak losartan activation ability; Relatively weak ARB metabolic capacity
			CC	Weak losartan activation ability; Weak ARB metabolic capacity
Angiotensin-converting enzyme inhibitors	Benazepril Fosinopril Enalapril Perindopril Ramipril	ACE (I/D)	II	Normal enzymatic activity
			ID	Relatively high enzymatic activity
			DD	High enzymatic activity
Calcium antagonists	Nifedipine Felodipine Lacidipine Amlodipine Cilnidipine	NPPA (T2238C)	TT	Normal enzymatic activity
			TC	Relatively low enzymatic activity
			CC	Low enzymatic activity
		CYP3A (A6986G)	AA	Normal metabolic capacity
			AG	Relatively weak metabolic capacity
			GG	Weak metabolic capacity
Diuretic	Chlorothiazide Hydrochlorothiazide Bendroflumethiazide Chlorthalidone	NPPA (T2238C)	TT	Normal sensitivity
			TC	Relatively high sensitivity
			CC	High sensitivity

Note: examples are listed for better understanding the detection results which do not limit the scope of drug use.