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Bring Technology to Life

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Statins Personalized Medication Solutions

BACKGROUND

Dyslipidemia refers to imbalanced plasma lipid profile, including either one or any combination of elevated total cholesterol (TC), elevated low-density lipoprotein cholesterol (LDL-c), elevated triglycerides (TG) or low high-density lipoprotein cholesterol (HDL-c)[1]. Dyslipidemia is a major established risk factor for the development of cardiovascular diseases, one of the leading causes of mortality and morbidity worldwide. According to GlobalData's estimates from 2022, the prevalence of dyslipidemia in adults in the Asia-Pacific region was over 965 million. In the West, the US contributed over 130 million cases of dyslipidemia, while the collective amount of which was extended more than 110 million in Germany, Spain, Italy, France and the UK[2].

Statins are the first-line cholesterol-lowering drugs being preferably and commonly prescribed for dyslipidemia treatment, cardiovascular risk reduction and prevention. However, side effects, especially severe adverse drug reactions associated with statin therapy, such as liver dysfunction, rhabdomyolysis, etc. may occur due to individual differences in drug responses, which are also a common problem in clinical practices[3].

Statins and Genetic Polymorphisms of SLCO1B1 & ApoE

The efficacy and side effects of statins are closely correlated with the polymorphisms of SLCO1B1 and ApoE genes, which encode one of the transporters SLCO1B1 (solute carrier organic anion transporter family member 1B1, also known as OATP1B1) and apolipoprotein E (ApoE), respectively[3].

SLCO1B1 is one of the major transport proteins facilitating the hepatic uptake of statins[4]. Genetic variation in SLCO1B1 can result in diminished hepatocellular uptake and increased plasma concentration of statins, which may thus lead to increased risks of systemic drug toxicity and adverse drug events[5]. The most common and well-characterized variants in the SLCO1B1 gene are the loss-of-function alleles of SLCO1B1*5 (c.388A + c.521C) and *15 (c.388G + c.521C). These two allelic variations are independent determining factors of rhabdomyolysis and carriers are documented to be associated with a tenfold increase in risks of myotoxicity[6].

ApoE is a key component of many lipoprotein particles, which plays an important role in the regulation of lipid transportation, accumulation and metabolism, as well as in the variability in responses towards statins therapy between individuals[7]. There are three common alleles of the ApoE gene, i.e. ε2 (c.388T + c.526T), ε3 (c.388T + c.526C) and ε4 (c.388C + c.526C), generating three isoforms of ApoE, where ApoE3 (ε3/ε3, ε2/ε4) is the wild-type, and ApoE2 (ε2/ε3, ε2/ε2) and ApoE4 (ε3/ε4, ε4/ε4) are considered as risk factors for increased atherogenic lipoprotein levels and increased LDL levels, respectively[8]. People carrying ApoE4 are generally less sensitive to statins therapy, while those with ApoE2 basically have satisfied outcomes of lipid-lowering therapies with multiple statins.

Detailed correlation among phenotype, genotype and corresponding risk assessments can be found in tables below.

STATINS PERSONALIZED MEDICATION SOLUTION

Considering the close correlation between the ApoE and SLCO1B1 genetic polymorphisms and therapeutic efficacy and adverse effects of drugs between individuals, Tianlong Personalized Medication Solution is designed to rapidly determine the genetic polymorphism of the most common variants in these two genes, including ApoE (c.388 T>C), ApoE (c.526 C>T), SLCO1B1 (c.388 A>G) and SLCO1B1 (c.521 T>C) in specimen with its exclusive pharmacogenomic reagents and the Fascan 48E multi-channel fluorescence quantitative analyzer. The results can provide genetic clues to guide rational drug selection or dosages and to reduce adverse drug reactions for statins in clinical practices.

Genotype Detection and Suggestions for Statin Therapy

Phenotype	ApoE Genotype	ApoE c.388 T>C	ApoE c.526 C>T	Risk Assessment	Medication Suggestions
ApoE2	ε2/ε3	TT	CT	High risk of macular degeneration and class III hyperlipidemia; relatively low risk of senile dementia, cerebral infarction, and coronary heart disease	Effective treatment with pravastatin, atorvastatin, rosuvastatin, fluvastatin and lovastatin. Poor drug effect with probucol and simvastatin
	ε2/ε2	TT	TT		
ApoE3	ε3/ε3	TT	CC	Normal genotype	Effective treatment with pravastatin, atorvastatin, rosuvastatin, fluvastatin, lovastatin, probucol and simvastatin
	ε2/ε4	TC	CT		
ApoE4	ε4/ε4	CC	CC	Relatively high risk of retinitis pigmentosa, senile dementia, cerebral infarction, myocardial infarction, and coronary heart disease	Effective treatment with probucol and simvastatin. Poor drug effect with pravastatin, atorvastatin, rosuvastatin, fluvastatin, lovastatin
	ε3/ε4	TC	CC		

SLCO1B1 Genotype	SLOCO1B1 c.388 A>G	SLOCO1B1 c.521 T>C	Risk Assessment	Dosing Recommendation
1*a/1*a	AA	TT	Normal risk of rhabdomyolysis or myonosus	Conventional or relatively large dosage of statins
1*a/1*b	AG	TT		
1*b/1*b	GG	TT		
1*a/*5	AA	TC	Moderate risk of rhabdomyolysis or myonosus	Moderate dosage of statins
1*a/*15 or *1b/*5	AG	TC		
1*b/*15	GG	TC		
*5/*5	AA	CC	High risk of rhabdomyolysis or myonosus	Relatively low dosage of statins
*5/*15	AG	CC		
*15/*15	GG	CC		

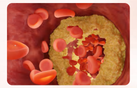
Examples of Detection Results

Gene	Gene Locus	Detection Results	Interpretation	Medication Suggestions
ApoE	c.526 C>T	ε3/ε3	Normal genotype	Effective treatment with pravastatin, atorvastatin, rosuvastatin, fluvastatin, lovastatin, probucol and simvastatin
	c.388 T>C			
SLCO1B1	c.388 A>G	*1a/*1b	Normal risk of rhabdomyolysis or myonosus	Conventional or relatively large dosage of statins
	c.521 T>C			

Ordering Information

Product Name	Specification	Specimen	Target Gene Location
LigSeq Reagent Kit (SNP-U4)	20 T/Kit	2 mL of EDTA anticoagulated whole blood	ApoE (c.388 T>C), ApoE (c.526 C>T), SLCO1B1 (c.388 A>G), SLCO1B1 (c.521 T>C)

Applicable Group



Atherosclerotic, hyperlipidemia or dyslipidemia patients with cardiovascular and cerebrovascular diseases

People with a family history of cardiovascular and cerebrovascular diseases

Routine physical examinees

Clinical Significance

Guide rational drug use of statins in clinical practices; Evaluate medication risks of adverse drug reactions and therapeutic effects

Forecast risks of coronary heart disease, senile dementia, retinitis pigmentosa, etc.

Features

Accurate Result

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

Easy Operation

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

High Efficiency

Results are available in approximately 70 min 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 in about 70 min.