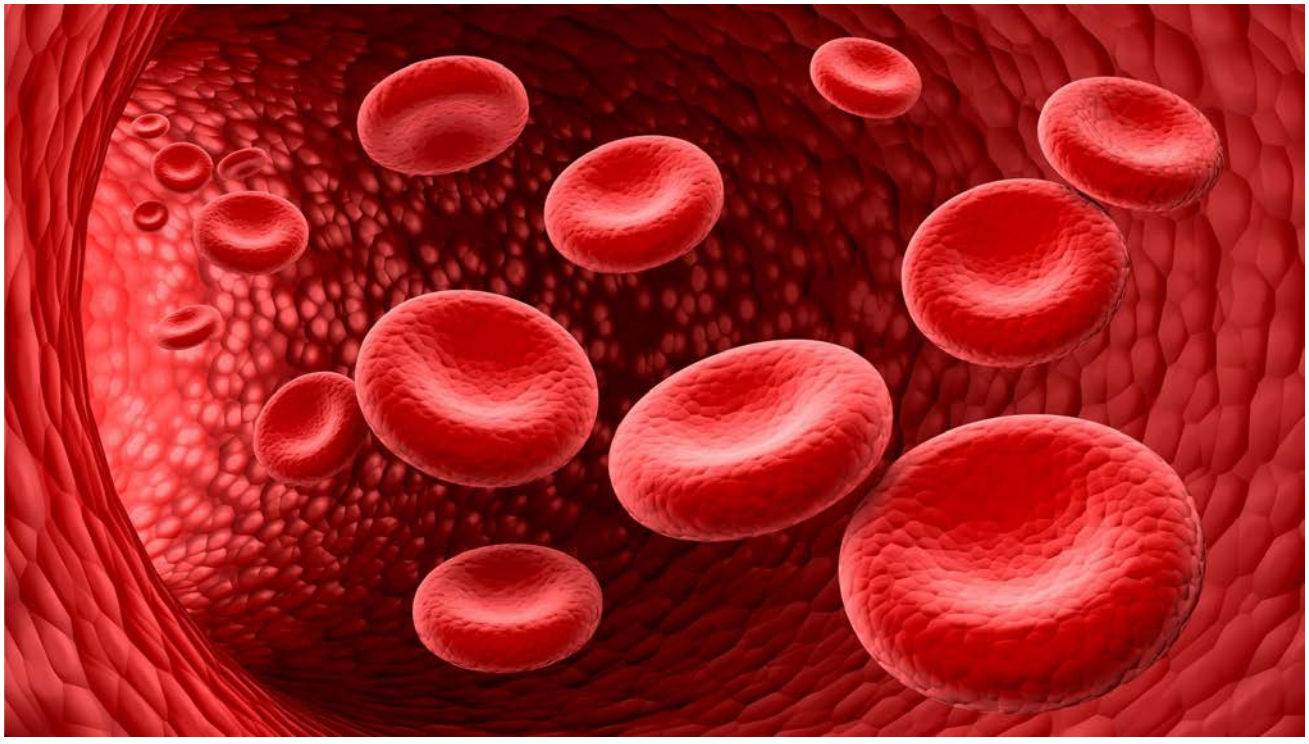
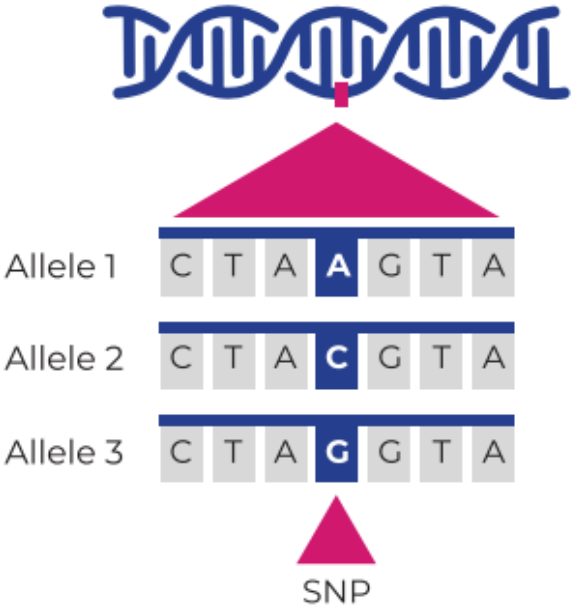
DNK s.r.o.
diagnostické centrum

Laboratory diagnosis of hemostasis disorders

Diagnostic kits for the detection of SNP polymorphisms in genes associated with hemocoagulation and folate cycle



Single Nucleotide Polymorphisms (SNP)



Genetic polymorphism – presence of at least two sequence variants (alleles) in a population, with a minor allele frequency of at least 1 %.

SNP – polymorphic traits represented by a single nucleotide substitution at a specific point in the genome. They are not an unconditional cause of the development of the disease, but can cause a greater or lesser risk of its development under the influence of various factors: SNP of other genes, concomitant diseases, pregnancy, lifestyle, smoking. It has been shown that SNPs contribute to the development of multifactorial diseases such as coronary heart disease, arterial hypertension and others.

Multifactorial diseases

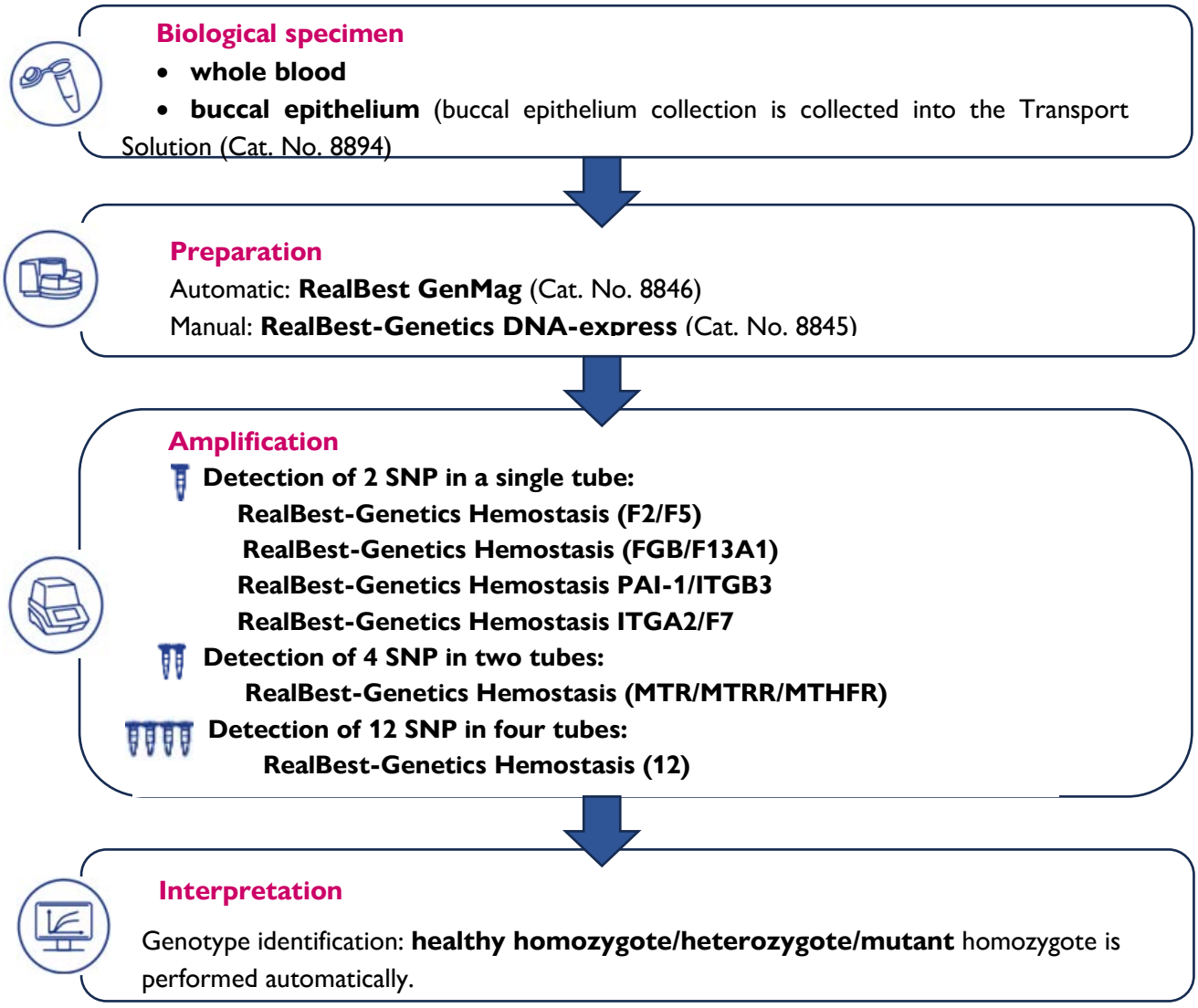
- determined by genetic and environmental factors
- most often they are polygenic, i.e. conditioned by SNP of several genes
- the detection of genetic risk factors indicates only a predisposition to a certain pathology, and not its presence
- environmental factors can be modified, and changing them can reduce the risk of developing the disease

One of the most studied genetic risk factors for developing multifactorial diseases are SNP genes associated with hemocoagulation and folate cycle.

Indications for molecular-genetic testing for the presence of SNPs

- family history: family members with thrombotic and/or thromboembolytic complications, especially under 50 years of age,
- complicated obstetric history: difficulties during pregnancy, thrombotic difficulties after pregnancy and childbirth, two or more interruptions in fetal development in the early stages, birth of children with malformations, etc.,
- planned preparation for pregnancy or extracorporeal fertilization (especially in women who have a history of thrombosis or a family history of thromboembolic complications
- planned hormonal contraceptives or hormone replacement therapy,
- planned massive surgical interventions, long-term immobilization.

RealBest® Technology: Solution for differential diagnosis of SNP in genes of hemocoagulation system and folate cycle.



Basic characteristics of SNP in genes of hemocoagulation system and folate cycle

Gene/SNP	Mutation effect	Aggravating factors
MTHFR (methylenetetrahydrofolate reductase), **C677T**	10x higher risk of developing hyperhomocysteinemia for homozygotes (T/T). Risk associated with the development of thrombosis and atherosclerosis, pregnancy difficulties and fetal malformations	*F5*: G1691A; *F2*: G20210A; Deficiency of vitamins B6, B12, folic acid, defects of other genes of the folate cycle; smoking
MTHFR **A1298C**	Decrease in enzyme activity, the risk of developing hyperhomocysteinemia	
MTR (methionin synthase), **A2756G**	Decrease in methionine concentration and accumulation of homocysteine in the bloodstream: increased risk of cardiovascular disease, pregnancy problems	*MTRR*: A66G; *F5*: G1691A; *F2*: G20210A; deficiency of B6, B12, folic acid; smoking
MTRR *(*methionine synthase reductase*),* ***A66G***	Decrease in enzyme activity, increased risk of developing hyperhomocysteinemia. The risk of developing thrombotic complaints, fetal malformations	*MTR*: A2756G; *F5*: G1691A; *F2*: G20210A; deficiency of B6, B12, folic acid; smoking
F2 *(coagulation factor II , prothrombin),* ***G20210A***	Increased level of prothrombin in plasma: increased risk of developing venous thrombosis, pregnancy difficulties	*F5*: G1691A; smoking
F5 *(coagulation factor V, proaccelerin),* ***G1691A - Leiden mutation***	Increased risk of thrombosis and embolism: heterozygotes (G/A) have a 7x higher risk, homozygotes (A/A) have a 20x higher risk. Risk of developing birth and gynecological problems	Hormonal contraceptives, protein C and S deficiency hyperhomocysteinemia; *F2*: G20210A; smoking
F7 *(coagulation factor VII, proconvertin),* ***G10976A***	Reduction of factor VII concentration in plasma, 2x reduction in the risk of developing thrombosis and myocardial infarction even in coronary atherosclerosis	Absence of *F5*: G1691A; *F2*: G20210A; Presence of *F13*: G103T
F13 *(fibrin-stabilizing factor XIII),* ***G103T***	Formation of thinner fibrin clots: reduced risk of developing cardiovascular diseases (thrombosis, myocardial infarction)	Absence of *F5*: G1691A; *F2*: G20210A; *FGB*: G(-455)A; Presence of *F7:* G10976A
PAI-1 *(plasminogen activator inhibitor-1),* ***5G(-675)4G***	Decrease in fibrinolytic activity of blood: increased risk of thrombosis, as well as the development of obstetric and gynecological problems	*ITGB3:* T1565C; *F5*: G1691A; *F2*: G20210A; ACE: del287
ITGA2 *(integrin alpha-2),* ***C807T*** *(c.C759T)*	Increased platelet adhesion: homozygotes (T/T) have been shown to be at increased risk of developing thrombotic complications	*F5*: G1691A; *F2*: G20210A
ITGB3 *(integrin beta-3),* ***T1565C*** *(c.T176C)*	Platelet hyperaggregation: increased risk of developing thrombosis and embolism. Increased risk of rupture of atherosclerotic plaques. In carriers of the T allele, the effectiveness of using aspirin is reduced.	*F5*: G1691A; *F2*: G20210A
FGB *(coagulation factor I, fibrinogen),* ***G(-455)A***	Increase in plasma fibrinogen concentration: increased risk of developing ischemic and cardiovascular diseases, difficulties during pregnancy and the postpartum period	*FGB*: G(-455)A; smoking

Diagnostic kits for the detection of SNP polymorphisms in genes associated with hemocoagulation and folate cycle

Cat. №	Kit name	Number of tests	Gene: Polymorphisms
			Extraction kits for the isolation of nucleic acids
8845	**RealBest-Genetics DNA-express**	50	-
8846	**RealBest GenMag**	96 (2x48)	-
			SNP detection kits
3802 CE	**RealBest-Genetics Hemostasis (F2/F5)**	48	*F2*: 20210G/A; *F5*: 1691G/A
3803 CE	**RealBest-Genetics Hemostasis (MTR/MTRR/MTHFR)**	48	*MTR*: 2756A/G; *MTRR*: 66A/G; *MTHFR:* 677C/T; *MTHFR:* 1298A/C
3831 CE	**RealBest-Genetics Hemostasis (FGB/F13A1)**	48	*FGB*: (-455)G/A; *F13A1*: c.103G/T
3832 CE	**RealBest-Genetics Hemostasis ITGA2/F7**	48	*ITGA2:* 807C/T; *F7:* 10976G/A
3833 CE	**RealBest-Genetics Hemostasis PAI-1/ITGB3**	48	*PAI-1:* -6755G/4G**;** *ITGB3:* 1565T/C
3801	**RealBest-Genetics Hemostasis (12)**	48	*F2*: 20210G/A; *F5*: 1691G/A; *F7:* 10976G/A; *F13A1*: c.103G/T**;** *FGB*: (-455)G/A; *ITGA2:* 807C/T; *ITGB3:* 1565T/C**;** *PAI-1:* -6755G/4G *MTR*: 2756A/G; *MTRR*: 66A/G; *MTHFR:* 677C/T; *MTHFR:* 1298A/C

Features and advantages of the diagnostic kit

- **Ready Master Mix for PCR**: Simplification of analysis procedures and high stability of test quality
- **Universal protocol:** Multiple different tests in one run
- **Multiplexes:** determination of two SNPs in one tube
- **Specimens**: whole blood or buccal epithelium
- **Compatible devices:** CFX96 (Bio-Rad, USA), Gentier 96E/R (Xi'an TianLong, Science and Technology Co., Ltd., China)
- **High stability of the kit:** storage at a temperature of 2–8 ° C; transport up to 26 °C not more than 10 days

Diagnostické centrum DNK, s.r.o.
Brestová 14, 821 02 Bratislava
+421 911 299 324, +421 911 211 404
dnk@pharma.sk, diagnostika@pharma.sk
www.pcr.sk