Nordic Laboratories

PATIENT:	**Sample Report**			TEST REF:	**###-##-#####**
TEST NUMBER:	##########	COLLECTED:	dd/mm/yyyy	PRACTITIONER:	**Nordic Laboratories**
PATIENT NUMBER:	##########	RECEIVED:	dd/mm/yyyy	ADDRESS:	
GENDER:	Female	TESTED:	dd/mm/yyyy		
AGE:	75				
DATE OF BIRTH:	dd-mm-yyyy				

TEST NAME: LIPIDgen (12 SNPs)

This is the result of your Lipidgen analysis. The polymorphisms tested by us do not represent a fatality, but illustrate your individual genetic predisposition. The enzymes encoded by you are expressed differently as to their activity depending on your polymorphisms. They may have a positive or negative influence on your state of health. The expression of most of the genes tested can be influenced by environmental factors, lifestyle and nutrition. This makes individual therapy approaches possible.

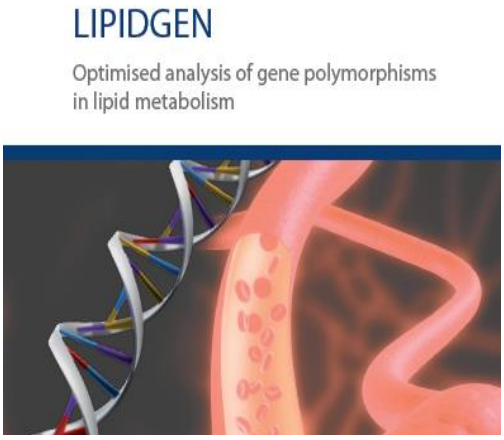

Table of contents

1. Introduction

Blood lipids, in particular cholesterol, play an important role in the development of vascular diseases. If too much cholesterol is present in the blood, damage to the arterial walls may be caused in the long term. This is how arteriosclerosis may develop and the risk of cardiac infarction increases. In simple terms, there are two different forms in which the water-insoluble cholesterol (blood lipid) is transported in the body. The blood lipids have to be coupled to proteins.

A distinction is made between

1. HDL (high density lipoproteins) and
2. LDL (low density lipoproteins).

The HDL level in the blood indicates how much cholesterol from the periphery returns to the liver and thus did not get stuck in the vessels. This is why this value should be as high as possible. Therefore, this parameter is also called "good" cholesterol. A high LDL level, however, indicates that cholesterol is circulating in the body and can settle on the vascular walls. This is why LDL is also called "bad" cholesterol. This level should be as low as possible. There are also some sub-classes of LDL that differ with respect to size. The small LDL fractions are particularly dangerous - also because they are easily oxidisable.

The gene variants tested in the following provide information about how these processes can be controlled individually by you and which measures are reasonable in order to ensure an ideal lipid metabolism for the variants present and to minimise the risk of cardiovascular diseases.

Previous findings:

Total cholesterol:	6.83 mmol/l
HDL cholesterol:	1.16 mmol/l
LDL cholesterol:	4.81 mmol/l
Triglyceride:	1.51 mmol/l

Presence of small atherosclerotic LDL particles of the classes 3

TEST NAME: LIPIDgen (12 SNPs)

2. Tabular presentation of results

Gene	Tested polymorphism	Patient's genotype		Influenced by sport, nutrition, life-style	phenotype Influence on lipid metabolism
APOE	**C112A; A158C**	**E4/E4**	**vt/vt**	✔	**Relative increase of total, LDL- and sdLDL cholesterol**
APOA1	**G75A**	**G/A**	**wt/vt**	✔	**Slightly lowered HDL**
APOCIII	**C3228G**	**C/G**	**wt/vt**	✔	**Increased triglycerides, Increased relative risk of CAD, tendency to sdLDL**
APOB100	Codon 3500		wt/wt	✘	No negative influence
APOA5	T1131C	T/T	wt/wt	✔	No negative influence
CETP	I405V	I/I	wt/wt	✔	**Only marginally delayed degradation of HDL**
CETP	**Taq G279A**	**G/A**	**wt/vt**	✔	
FABP2	A54T	A/A	wt/wt	✔	No negative influence
ABCA1	R219K	R/R	wt/wt	✔	No negative influence
LPL	D9N	D/D	wt/wt	✔	No negative influence
LPL	N291S	N/N	wt/wt	✔	No negative influence
LPL	S474X	S/S	wt/wt	✔	No negative influence
LDLR	AvaI		wt/wt	✔	No negative influence
LDLR	HincII		wt/wt	✔	
PPAR-g	**Pro12Ala**	**Pro/Ala**	**wt/vt**	✔	**No negative influence**

wt/wt: wild type — wt/vt: heterozygous variant — vt/vt: homozygous variant

✘ not influenceable — ✔ influencable

3. Interpretation of the individual genes

APOE

Two polymorphisms for apolipoprotein E are present that both play a central role in lipid metabolism and can be influenced by nutrition and lifestyle. This concerns the polymorphisms in the codon 112 and 158. Their expressions always have to be evaluated with respect to each other resulting in six possible constellations. Each individual constellation leads to different risks and requires different recommendations as to behavior and nutrition in order to counteract these risks.

The constellation E4/E4 (2% of the population) contributes to an highly increased risk of dyslipidemia and related arteriosclerosis, as carrier of the E4-allele will have increased Triglycerides, LDL, increased sdLDL, oxidative stress and chronic inflammation and oxidized LDL. HDL level is often decreased. Individuals should not smoke or drink alcohol and should reduce the intake of olive oil and other mono-unsaturated fatty acids, as all of these conditions increase the risk of sdLDL formation. Nutrition should be low fat and reduced carbohydrates and should contain high amounts of anti-oxidants. An increased intake of carbohydrates would decrease the amount of protective HDL cholesterol. Supplementation with omega-3-fatty acids is recommended.

APOA1

The tested polymorphism is situated at location 75G/A. This polymorphism has an impact on HDL-levels. As HDL has protective properties, all actions should be taken to reach high HDL levels. This polymorphism is extremely important for females. Especially the intake of polyunsaturated fatty acids (PUFA) has an opposite impact on HDL-level, according to the variant polymorphism.

The genotype G/A is present in approx. 26% of the middle European population. As carrier of the A allele you are tending to higher HDL levels, consumption of polyunsaturated fatty acids is beneficial for the protective HDL level.

APOB100

Apolipoprotein B-100 is a key component of LDL cholesterol, and plays an important role in the binding of LDL to the LDL receptors. A genetic variant of ApoB at position 3500 carries a glutamine (Q) instead of an arginine (R). Another, but very rare ApoB variant carries a tryptophan (W) instead of an arginine (R). Carriers of variant ApoB-100 have an increased risk for hypercholesterolemia. The clinical implications are the same as for the family Hypercholesterolemia (LDL receptor defect). Untreated carriers of a variant ApoB-100 have an increased risk for arteriosclerosis. Under current knowledge this risk can be reduced by cholesterol-lowering therapy.

Your wild type form is not associated with impaired LDL-levels

TEST NAME: LIPIDgen (12 SNPs)

APO CIII

APOCIII plays a crucial role in lipid metabolism. It slows down the breakdown of triacylglycerol, which results in higher blood level of triglycerides. The polymorphism 3175G is associated with a 4 times higher risk for hypertriglyceridemia as well as increased risk for the development of atherosclerosis, CAD, and formation of small dense LDL.

Your heterozygous genotype is associated with higher triglyceride.levels and by this with an increased risk for the formation of small dense LDL particles. Carriers of the G allele should reduce the consumption of fats.

APOA5

Variants of this polymorphism may cause increased plasma cholesterol and triglyceride levels (triglycerides are natural fats). This polymorphism has a particularly great effect when the supply with omega-6 fatty acids exceeds 6% of the total energy supply. The cardiovascular risk is increased additionally by the fact that more aggressive small LDL particles are formed under these circumstances. Women and men are affected equally. Higher consumption of alcohol may cause increased LDL levels.

Your wild type constellation does not cause an increased risk of high triglyceride levels in the blood. This constellation does not require any special diet recommendations.

CETP

These polymorphisms act on the circulating HDL concentration. CETP degrades HDL in to VLDL, and IDL/LDL. CETP shifts the LDL/HDL ratio towards LDL. CETP wild type is the active form, while polymorphisms [I 405 V]-and Taq1B [G279A] reduce CETP activity. They increase HDL concentration and reduce LDL and have also been linked to exceptional longevity.

Your genotype - homozygous wild type for the polymorphism I405 and heterozygous for G279A - is associated with a marginally reduced activity of CETP and rapid degradation of HDL. This yields in lower HDL-levels. Carriers of this constellation should increase their intake of polyphenols and exercise regularly.

FABP2

The analysed polymorphism provides information on the resorption of fat in the small intestine. Since fat has a high energy value, patients with increased fat resorption and insufficient physical activity run a particularly high risk of developing overweight.

Your homozygous wild type for the polymorphism A54 is not associated with increased fat resorption.

TEST NAME: LIPIDgen (12 SNPs)

ABCA1
ATP-binding cassette transporter ABCA1 (member 1 of human transporter sub-family ABCA) also known as the cholesterol efflux regulatory protein. This transporter is a major regulator of cellular cholesterol and phospholipid homeostasis. With cholesterol as its substrate, this protein functions as a cholesterol efflux pump in the cellular lipid removal pathway. Mutations in this gene have been associated with familial high-density lipoprotein deficiency.

Your homozygous wild type is associated with normal HDL-levels.

LPL
LPL stands for lipoprotein lipase. Fats are taken up from food and then reach the bloodstream where they stay for approx. one hour as emulsion in the blood. Lipase is responsible for splitting these fats. Three important polymorphisms are present for LPL all of which have an influence on lipase activity. Two of these polymorphisms, D9N and the N291S slow down lipase activity while one polymorphism increases fat degradation.

All alleles are present in wild type form and have no negative effect of lipid metabolism.

LDL-receptor (LDL-R AVA & LDL-R HINC)
The LDL receptor plays a crucial role in lipid metabolism. It is responsible for the uptake of lipoproteins into the cells. Mutations affecting the uptake into the cells are associated with familiar hypercholesterolaemia. The polymorphisms AvaI and HincII are analysed. Their clinical significance concerns familiar hypercholesterolaemia, very high LDL cholesterol and pronounced atherosclerosis.

Your homozygous wild type is not linked to high LDL concentrations with respect to LDL-receptor.

PPAR-gamma
PPAR-gamma plays a central role in signal transmission and has a great influence on insulin resistance and sugar metabolism (oral glucose tolerance). The factor also provides information on how you react to high sugar supply.

You have a heterozygous variant. This means that you have no increased predisposition for insulin resistance.

TEST NAME: LIPIDgen (12 SNPs)

4. Summary of interpretation

The present polymorphisms of ApoE, ApoA1 and ApoCIII are associated with negative influence on your lipid metabolism and will contribute to high levels of triglycerides, total and LDL-cholesterol.

You have a genetic predisposition for increased formation of small dense LDL particles.

The SNPs in ApoE and ApoA1 have a negative influence on your HDL value, the isolated heterozygous variant in G279A of the CETP gene may no contribute significant positive effects.

The genetic predisposition is expressed in the phenotype.

5. Therapy recommendations

Therapy goals:

1. Decrease of total and LDL-cholesterol level
2. Avoid formation of sdLDL
3. Stabilisation of triglycerides level
4. Increase of HDL level

This can be achieved by a change of diet.

In your case, a Mediterranean diet rich on fibres and polyphenols is ideal, under avoidance of olive oil or other monounsaturated fatty acids.

Nutrition should in general be "low fat". It is important, however, to supply a sufficient quantity of omega-3 fatty acids by fish and/or fish oil. Try to shift the ratio of omega-6 to omega-3 fatty acids to an optimum between 1 and 2 to avoid chronic inflammatory processes.

Intake of Niacin helps to lower total and LDL cholesterol, decrease small dense LDL particles and increase HDL values.

Reduce carbohydrate intake. The carbohydrate fraction of your food should have a low glycaemic index. In particular, you should avoid bread and bakery products with superfine flours and sweet beverages. The consumption of noodles, polished rice and potatoes should be restricted.

Reduce alcohol consumption.

Do sports. Light endurance training will lower the triglycerides and LDL values by simultaneous increase of HDL. Avoid anaerobic peak load which leads to formation of radicals/reactive oxygen species.

Supplementation with antioxidants should be considered.

Particularly recommended foods*:
Apple, aubergine, basil, bilberry, cauliflower, bean (broad), broccoli, button mushroom, cranberry, strawberry, fennel, garden cress, kale, halibut, herring, raspberry, ginger, currant, cod, cherry, salmon, lamb, leek, lavender, linseed, plum, cowberry, Brussels sprouts, red cabbage, hake, soybean, spinach, tea (green), tomato, vine leaves, courgettes, onion, cold water fish, olive oil
**if no type III food allergies or known intolerances exist.*

Foods to be avoided:
Eel, avocado, banana, cashew kernels, date, spelt, duck, peanut, sweet chestnut, goose, hazelnut, millet, carrot, potato, coconut, lab-fermented cheese, macadamia nut, maize, almond, cassava, nectarine, papaya, Brazil nut, parsnip, arrowroot, pistachio, rice, beetroot, pork, sunflower seeds, sweet potato, walnut, water melon, wheat, sausages, fat sauce, fried food, fast food, bakery, sweets, milk chocolate, pasta, bread, especially white bread, soft drinks, honey.

6. Further recommendation

Fatty acid Status

The evaluation of fatty acids is recommended. Omega 3 and Omega 6 fatty acids and their ratio measured in serum may contribute to inflammatory and atherogenic processes. According to the results dietary changes or supplementation with Omega 3 fatty acids may be reasonable to counteract your genetic constellation.

TEST NAME: LIPIDgen (12 SNPs)

Annex Definitions

Allele:
Every gene is present in "dimeric form", i.e. it consists of two parts each coming from a parent. If both genes are identical, they are called homozygous; if they are different, the gene is called heterozygous.

Wild type (wt/wt):
Wild type means the normal or reference type. It always has a homozygous form. It is assumed that this is the natural genotype found in nature which has prevailed during evolution. It is the most common genotype.

Heterozygous variants (wt/vt):
In case of a heterozygous variant, one allele is a genetic variant. In general, a heterozygous genotype has no or only minor effects on the enzymatic activity of the corresponding isoenzyme. An accumulation of heterozygous mutations of those isoenzymes belonging to the same family can have an important effect on the corresponding enzyme activity.

Homozygous variant (vt/vt):
In case of the homozygous variant, both alleles are in the form of the variant. A homozygous genotype shows a strongly reduced or increased enzyme activity - depending on the corresponding isoenzyme. In case of the genotype "zero" (0), a total loss of enzyme activity is present due to a gene deletion of both alleles.

Gene polymorphisms:
Variants of a gene, e.g. the different blood groups or eye colours. Changes in individual places within the gene (often, the exchange of a single element (nucleotide) is enough) may result in changes in the metabolism.