MEDINVITAgen

TEST AGEING 23.02.2015 Personal Report: JOE SAMPLE



MEDINVITAgen AGEING

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Welcome to your MEDINVITAgen AGEING analysis!

The skin is the largest organ of the body. An average man's skin covers more than 2 square yards and weighs 10 pounds. In just 1 square inch of skin there are approximately 30 million cells, 100 fat glands, 600 sweat glands, 65 hairs, numerous muscles, and thousands of nerve endings. The human skin ranges in thickness from 0.5 millimetre in the eyelid to more than 2 millimetres in the palms and soles.

- The skin performs a complex role in human physiology:
- Protects the rest of the body from toxins, injuries, the sun, and temperature extremes in the external environment
- Preserves the stability of the body's inner environment and keeps it in place
- Helps the body to regulate heat
- Communicates information about physical and emotional states
- Provides identification through unique finger- and sole-prints

The appearance, elasticity and ageing of skin is affected by both genes and environment and the way that they interact. Environmental features include diet, lifestyle, physical activity, sun exposure, etc. We also all have common genetic variants that affect processes important to our skin health however because genes do not act alone, by making suitable changes in diet, lifestyle, etc. we can exert some control over our apparent genetic destiny – with simple adjustments to our lives we can make significant improvements in our long term skin health, and even reduce / reverse effects of ageing that have already appeared.

Healthy skin, Healthy ageing, Anti-ageing

Areas covered by this test:

- Skin structure and ageing
- Oxidative Stress, Detoxification & Inflammation
- Advanced glycation end products (AGEs)
- Vascular tone & water retention

Skin health, blood & lymph circulation and conditions such as cellulite are interlinked at several levels. They involve complex processes that include microcirculation, local fat accumulation, hormonal factors, altered matrix metabolism, oxidative stress, inflammatory changes, and alterations in lymphatic drainage.

The panel provides information about the potential effect of your individual genetic variation on your overall skin health and well-being. Since we focus especially on research regarding gene x environment interactions the genetic information leads to specific personal modifications to your diet and lifestyle which can help with healthy skin ageing and prevent or combat processes such as cellulite, water retention, etc.

SKIN STRUCTURE

We have looked at genes associated with the generation and maintenance of skin structure.

Skin is "dynamic", it is constantly being broken down and rebuilt in response to external and internal stimuli (e.g. sunlight and metabolic oxidation).

Skin surface appearance is determined by the elasticity and resilience of the underlying protein fibre structure, mainly cross-linked collagen and elastin fibres. The genes we test include collagen, elastin and enzymes involved in the delicate remodelling process.

Variations in these genes can have small effects on this process which can have significant long-term consequences for skin ageing, but which can be ameliorated by taking protective measures.

OXYDATIVE STRESS, DETOXIFICATION & INFLAMMATION

These processes are normal features of everyday activity in the cell. Exposure to the sun increases generation of free radicals in the skin due to the activity of UV light on skin cells. Free radicals are also generated as part of the normal oxidative metabolic processes of energy production in the cell. Free radicals are extremely reactive molecules which can cause damage to all cellular components including DNA, proteins and lipids. The body has developed several protective mechanisms including enzymes which mop-up these free-radicals before they can cause their damage. We can also limit free-radical production by taking care over what we eat and by avoiding tobacco smoke (including passive smoking) and, as much as possible, environmental pollution.

With AGEING of MEDINVITAgen we have tested you for variations in several genes which are involved in these protective mechanisms. The variations may affect the efficiency of free-radical protection and specific advice for you on how to overcome this is given.

Inflammation is a normal function that is a vital part of many important processes such as wound healing, protection against infection and repairing damage caused by UV light. It is an extremely complex set of processes mediated in large part by various protein molecules called cytokines which may have either pro-inflammatory or anti-inflammatory actions. Many of the genes that produce these cytokines are polymorphic and the variations can affect the activity of the proteins leading to individual variations in inflammatory responses between different people.

Although having a protective role it is important that the inflammatory response is well controlled because over-inflammation can have consequences such as accelerated skin ageing. The inflammatory response can be modulated by nutrition and dietary supplementation, we have tested for variations in several cytokine genes and used the results to help to design appropriate protective measure unique for your particular make-up.

CARBOHYDRATE SENSITIVITY & GLYCATION

Individual genetic variation affects your sensitivity towards refined carbohydrates – an increased sensitivity coupled with over consumption of refined carbohydrates raises the likelihood of overweight and obesity.

Carbohydrate sensitivity can also result in higher levels of glycaemia, glycation, an increased probability of developing insulin resistance and eventually type 2 diabetes. These processes also contribute to the development of non-enzymatic modification of proteins in the formation of advanced glycation end products (AGEs) which are implicated as detrimental in various processes important for skin health, vascular tone, cellulite and physiological ageing.

Once formed, AGEs tend to gravitate toward dermal collagen and elastin. Common symptoms of skin with glycation issues include premature ageing, such as wrinkling and sagging; weakened elastin and collagen; and a reduced ability for skin to quickly rehabilitate. The presence of AGEs also make the skin more vulnerable to oxidative stress, smoking and UV exposure.

The total state of oxidative stress on the healthy body, and the accumulation of AGErelated damage is proportional to the dietary intake of refined carbohydrates which is also affected by individual genetic sensitivity to these macromolecules. AGEs affect nearly every type of cell and molecule in the body, and are thought to be one factor in ageing and some age-related chronic diseases.

They are also believed to play a causative role in the vascular complications of diabetes mellitus. They have a range of pathological effects, including increasing vascular permeability, inhibition of vascular dilation by interfering with nitric oxide, oxidising LDL, increasing inflammation and enhancing oxidative stress.

VASCULAR TONE & WATER RETENTION

Vascular tone is the contractile activity of vascular smooth muscle cells in the walls of small arteries and arterioles and is the major determinant of the resistance to blood flow through the circulation. Thus, vascular tone plays an important role in the regulation of blood pressure and the distribution of blood flow between and within the tissues and organs of the body. When this tone is normal, the blood vessels are considered to be functioning at optimal levels.

Reduced nitric oxide production has been linked to vascular tone which appears to improve when diet is rich in omega-3 fatty acids, irrespective of genotype but is thought to be even more critical for those with impaired endothelial function as associated with individuals with the NOS3 variation. Cold-water fatty fish (salmon, halibut, mackerel, tuna) and their oils are excellent sources of omega-3 fats. Plant sources include canola oil, flaxseed, walnuts, and their oils.

The ACE gene codes for an enzyme that has a key role in cardiovascular health because it is closely involved in the regulation of the processes of vasoconstriction and vasodilation. The ACE gene contains an "Insertion/Deletion" polymorphism (allele "I" = Insertion; allele "D" = Deletion), that influences enzyme activity. The gene AGT (Angiotensinogen) is involved in the regulation of blood flow, blood pressure and electrolyte balance. ACE and AGT play a key role in the maintenance of cardiovascular homeostasis because they are important in the regulation of vasoconstriction and dilation. Recent studies have linked these genes to salt-sensitive increases in blood pressure.

RESULTS

Gene	Variant	Result		Effect
SKIN STRUCTURE:				
MMP1	rs495366 (A/G)	AG	*	You carry a copy of the G version of the gene which may cause increased collagen breakdown
MMP3	rs3025058 (-/A)	5A/ 6A	*	You carry a copy of the 5A version of the gene which may cause increased collagen breakdown
COL1A1	rs1800012 (G/T)	TT	**	You carry two copies of the T allele and this variation
				leads to increased production of collagen $\alpha 1$ relative
				to collagen α 2, altering the ratios of fibre types which can affect skin integrity.
ELN	rs2071307 (A/G)	GG		Espressione normale
OXYDATIV	E STRESS & INFL	AMMATIC	DN:	
SOD2	rs4880 (C/T)	CC	**	increased dietary antioxidants
CAT	rs1001179 (C/T)	СТ	*	The T allele is associated with lower levels of the enzyme catalase
GPX1	rs1050450 (C/T)	CC		Normal expression
NQO1	rs1800566 (C/T)	CC		Normal expression
EPHX	rs1051740 (T/C)	ΤT	**	Higher activity: reduce grilled meat. Try to reduce exposure to external pollutants such as cigarette smoke and urban pollution (do not carry out strenuous exercise (e.g. jogging) in polluted outdoor areas).
GSTM1	INS/DEL	DEL	**	Increase consumption of allium and cruciferous to several servings per week. Reduce exposure to pollutants
GSTT1	INS/DEL	INS	**	Increase consumption of allium and cruciferous to several servings per week. Reduce exposure to pollutants
IL6	rs1800795 (G/C)	GG		Normal expression
TNF	rs1800629 (G/A)	GG		Normal expression
CARBOHY	DRATE SENSITIV	ITY & GL	YCAT	ION
ACE	rs4341 (I/D)	ID	*	Limit intake of refined carbohydrates and sugars –
PPARG	rs1801282 (C/G)	CC	**	Glycemic load < 70/day Fibers: 30 g/day
TCF7L2	rs7903146 (C/T)	CC		
ADRB2	rs1042713 (A/G)	GG	**	
FTO	rs9939609 (A/T)	TT		
FABP2	rs1799883 (C/T)	CT	*	
HYPERTEN	SION AND VAS	CULAR TO	ONE	
ACE	rs4341 (I/D)	ID	*	Sensitive to salt, <1,600 mg / day sodium (4g salt)
AGT	rs699 (C/T)	CC	**	
NOS3	rs1799983 (G/T)	GT	*	T allele: associated with lower levels of NO
BDKRB2	rs1799722 (C/T)	TC	*	Intermediate expression

SKIN STRUCTURE

We have looked at genes associated with the generation and maintenance of skin structure. Skin is "dynamic" it is constantly being broken down and rebuilt in response to external and internal stimuli (e.g. sunlight and metabolic oxidation). Skin surface appearance is determined by the elasticity and resilience of the underlying protein fibre structure, mainly cross-linked collagen and elastin fibres. The genes we test for include collagen, elastin and enzymes involved in the delicate remodelling process. Variations in these genes can have small effects on this process which can have significant longterm consequences for skin ageing, but which can be ameliorated by taking protective measures.

Gene	Result	Effect	
MMP1	GG	The variation leads to increased expression of the enzyme which may cause increased collagen breakdown. Various antioxidants such as astaxanthin have been shown to reduce MMP1 expression and can be useful for maintaining skin health.	
MMP3	5A/6A	MMP3, like MMP1, is involved in collagen turnover, you have one copy of the 5A version of the gene which is associated with increased collagen breakdown	
COLIAI	тт	 You carry two copies of the T allele and this variation leads to increased production of collagen α 1 relative to collagen α 2, altering the ratios of fibre types which can affect skin integrity. The A allele is associated with reduced elasticity and distensibility, especially after middle-age, from around 50 yrs old 	
Eln	AA		

- You carry two copies of the T allele and this variation leads to increased production of collagen α1 relative to collagen α 2, altering the ratios of fibre types which can affect skin integrity.
- Avoid tobacco smoke, including passive. If you live in a polluted urban area try to get out regularly
- Always use a good quality UV screen when in sunlight
- It is important that you consume foods rich in vitamin C as this can help with maintain production of collagen.
- Keep your skin hydrated

OXYDATIVE STRESS, DETOXIFICATION AND INFLAMMATION

The gene SOD2 codes for an enzyme called manganese superoxide dismutase. This enzyme is important in protecting the cell environment from internally generated oxidative free radicals, especially those generated during energy production. Each cell in the body during normal metabolism generates large quantities of free radicals; these are highly reactive species which can damage cell components such as lipid membranes, proteins and DNA. However they are rapidly removed by the several protective mechanisms, one of which involves SOD2. Together with catalase (CAT) and glutathione peroxidase (GPX, a selenoprotein), these enzymes constitute a primary defense against oxidative stress.

Free radicals are considered by many scientists to be involved in the ageing process. The coenzyme Q10 reductase (NQO1) enzyme converts coenzyme Q10 (ubiquinone) to its reduced form, ubiquinol, which scavenges free radicals in the mitochondria and lipid membranes. Individuals with a SNP in the NQO1 gene have slower reduction of ubiquinone to ubiquinol, resulting in very low blood and tissue levels of this key antioxidant. CoQ10-depleted skin tissue may be particularly more prone to the damage by free radicals because of its constant exposure to environmental oxidants such as sunlight and pollution.

EPHX1 codes for an enzyme that is involved in Phase I (activation) of removing toxins, such as carcinogens from food and smoke. GSTM1 & GSTT1 (glutathione S-transferases) are involved in phase II of the detoxification process by which toxins are removed from the body (via the conjugation of toxic molecules with glutathione, facilitating their elimination). According to genetic variation the enzyme activity is either present (Insertion or "I") or absent (Deletion or "D").

Both IL6 and TNF are cytokines involved in the inflammatory process as part of the body's normal immune response and genetic in these genes variation (IL-6-174 G/C and TNF-308 G/A) affects the amounts of cytokines produced.

Gene	Result	Effect
SOD2	CC	**
CAT	CT	*
GPX1	СС	
NQO1	СС	

Gene	Result	Effect
EPHX1	TT	**
GSTM1	DEL	**
GSTT1	INS	**
IL6	GG	
TNF	GG	

You carry two copies of the EPHX1 which codes for a higher activity enzyme which can lead to increased production of reactive intermediates during the detoxification process. You have the D (deleted) version of both the GSTM1 & GSTT1 genes which means neither enzyme is produced.

• Your genetic test results indicate the possibility of a reduced capacity to neutralise free radicals. Dietary anti-oxidants are very

important sources of protection from free radicals and other types of oxidative stress. In order to support your body's own protection mechanism it is important for you to ensure that you reach your goals for vitamins A, C and E and selenium.

- With your genetic results it is advisable to limit your consumption of grilled or smoked meat to 1-2 servings per week.
- You can compensate increasing the cruciferous vegetable consumption to at least 3-4 servings per week.

NUTRIENT	YOUR RECOMMENDED DAILY INTAKE
Vitamin A	5,000 IU / 1,500 μg day
Beta carotene	7 mg /day
Vitamin C	250 mg/ day
Vitamin E	15 IU / 13.5 mg / day
Cruciferous vegetables	3-4 servings per week
Omega-3	1.6 g / day
Alpha Lipoic Acid	150 mg / day

HYPERTENSION AND VASCULAR TONE

The ACE gene codes for an enzyme that is closely involved in the regulation of the processes of vasoconstriction and vasodilation. The ACE gene contains an "Insertion/Deletion" polymorphism (allele "I" = Insertion; allele "D" = Deletion), that influences enzyme activity. Recent studies have demonstrated and association between the genotypes I/D and I/I and dietary salt sensitivity affecting blood pressure.

Angiotensinogen is involved in the regulation of blood flow, blood pressure and electrolyte balance. Angiotensin (a small peptide formed by the action of renin and ACE on angiotensinogen) is part of the renin-angiotensin system. ACE and AGT play a key role in the maintenance of cardiovascular homeostasis because they are important in the regulation of vasoconstricition and dilation. Recent studies have linked these genes to salt-sensitive increases in blood pressure.

NOS3 produces nitric oxide (NO), a cell signaling molecule implicated in vascular smooth muscle relaxation and plays a key role in the regulation of vascular tone, peripheral resistance and has vasoprotection by suppressing platelet aggregation, leukocyte adhesion and smooth muscle cell proliferation.

Bradykinin is one of the peptides known as kinins. This peptide has been recognized as a significant vasodilator and may influence edema. Bradykinin is an endothelial dependent vasodilator and acts via the Bradykinin B2 receptor (BDKRB2). It is associated with vasodilation and blood pressure control. Efficiency of muscular contraction and cell hydration. The C allele is associated with lower receptor mRNA expression and is associated with increased thirst and fluid loss.

Gene	Result	Effect
ACE	ID	*
AGT	CC	**
NOS3	GT	*
BDKRB2	TC	*

Your genetic tests reveals that you have the "I/I" and Met/Thr genotype and therefore a possible predisposition to hypertension and maybe water retention when salt (specifically sodium) consumption is excessive. You are advised to limit your salt intake to a maximum of 4g/day (about ³/₄ of a teaspoon salt), equivalent to about 1.6g/day sodium. The GT version of the NOS3 gene is associated with lower levels of NO which can affect endothelial structure and long term skin health. The effect of this variation is aggravated by tobacco smoke, overweight and low physical activity. Omega-3 fatty acids have been shown to improve endothelial function, reducing vasoconstriction, especially in carriers of the T (Asp) allele.. The BDKRB2 TC genotype is associated with an intermediate expression, it will not have much effect on its own because NOS3 is normal and the ACE gene does not carry the D allele

Why Is Salt (Sodium) Important For Your Health?

Salt is made up of sodium and chloride. It's the sodium content that's of most concern because it can cause high blood pressure in those genetically-susceptible. Historically, government agencies have stressed the importance of reducing sodium intake at or below 2300 milligrams (mg) per day. This amount of sodium translates as 1 teaspoon of salt per day and includes all the salt we add to our foods and the prepared foods we consume. In general, our commercial foods tend to be highly salted for flavor and it's a good idea for all of us to be aware of how much salt we ingest on a daily basis. However, for those susceptible to salt-sensitive high blood pressure, it's essential to cut back on salt and its sodium content.

- Taste your food before salting it. You may not need the extra salt!
- Know where the hidden salt in foods is. Assume most convenience foods are high in salt content.
- Consider adding herb mixes to your food to enhance the flavor of your food without adding salt.

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