Fagron AcneTest

Genetic awareness to personalize acne treatment

Patient name	Demo Female Patient
Date of birth	05-09-1976
Gender	Female
Sample code	ACN00053AA
Sample date	25-05-2022
Report date	29-07-2022
Requesting physician	Demo Genomics
Requesting physician email	demo@genomics.com

Report Content

This report is structured into the following sections:

I. Clinical Questionnaire Data

Data entered in the clinical questionnaire for this patient.

II. Results Overview and Treatment

List of drugs recommended for acne treatment of this patient. Validated formulations will also be available here.

III. Detailed results

Genetics and clinical results will be combined into the following categories to improve the understanding of the acne presentation in this patient and guide treatment.

Results categories

- Skin Predisposition to acne
- Skin condition and inflammation
- Predisposition to hormone-related acne
- Nutritional advice

IV. Complete Genetic Results

A list of the genotypes presented by the patient for each one of the 60 SNPs analyzed to fully understand the relevant genetic profile of that patient regarding acne.

V. Genetics and Acne

Here we explain basic concepts of the influence of genetics in the treatment of acne and its sequalae.

I. Clinical Questionnaire Data

Data entered in the clinical questionnaire for this patient.

Patient personal information 1/2

PERSONAL DATA	
Age	46
Gender	Female

BIOMETRIC DATA	
Weight (Kg)	65
Height (cm)	166
BMI	23.6

MEDICAL HISTORY	
Systemic hypertension	No
Diabetes mellitus	No
Dyslipidemia	No
Liver disease	No
Endocrine disorders	No
Humor disorders	No
Personal or familial history of thromboembolic events	No
Cancer or neoplasia	No

GYNECOLOGICAL HISTORY	
Use of hormonal contraception	No
Polycystic ovary syndrome	No
Current pregnancy or intention of pregnancy	No
acn.global.hyperandrogenism	No

SOCIAL HISTORY	
Exposure to sun and visible light	No
Physical activity	No
Intake of refined carbohydrate	No
Alcohol consumption	No

Patient personal information 2/2

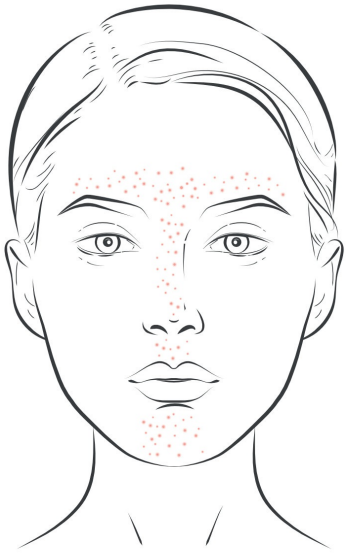
HISTORY OF PREVIOUS TREATMENTS	
Previous treatments	
Previous skin procedures	

LABORATORY EXAMINATION RESULTS	
Urea	
Aspartate transaminase (AST) (U/L)	
Alanine transaminase (ALT) (U/L)	
Alkaline Phosphatase (ALP) (U/L)	
Gamma-glutamyltransferase (GGT) (U/L)	
Total bilirubin (mg/dl)	
Total cholesterol (mmol/L)	
Idl (mg/dl)	
Triglycerides (mg/dl)	
Creatine kinase (CK) (U/L)	
Beta-human chorionic gonadotropin (Beta-HCG)	

Patient acne classification

Description of the method

Acne classification



Grade I
(comedogenic)

Grade II and III
(papular and pustular/inflammatory)

Grade IV
Grade IV (conglobata/nodulocystic)

Acne in an adult woman

II.
Results Overview and Treatment

List of drugs recommended for the acne treatment of this patient. Validated formulations will also be available here.

Results Summary

Summary of the results generated by the genetic analysis

CATEGORY	DESCRIPTION	RESULT
Skin Predisposition to Acne	This patient presents medium predisposition to acne. Therefore, proper evaluation should be performed in order to proceed with treatment	41.67%

CATEGORY	DESCRIPTION	RESULT
Skin Condition and Inflammation	This patient presents low risk of an inflammatory profile related to the appearance of acne lesions and sequelae related to it	12.96%

CATEGORY	DESCRIPTION	RESULT
Predisposition to hormone-related acne	Patient presents low risk of presenting acne due to alterations in the metabolism and levels of hormones	31.11%

CATEGORY	DESCRIPTION	RESULT
Nutritional advice	This patient presents medium risk of nutrition-related alterations that might correlate with acne or its treatment, therefore, proper nutritional advice should be given so as to improve the treatment	38.49%

INDICATIONS

Low risk Medium risk High risk

Drug Efficacy Panel

This drug efficacy panel was generated by an automated qualitative pharmacogenetic algorithm that analyzes genetic data and relevant patient history to recommend the most appropriate active ingredients. A color scale from white to dark green (least to most recommended) lists the drugs recommended by the algorithm. Medications blocked due to intolerances or contraindications are shown in red.

Antibiotics
• Doxycycline
• Lymecycline
• Clindamycin HCl
• Minocycline
• Tetracycline
• Dapsone (Topical)
• Dapsone
Retinoids
• Isotretinoin (standard-dose treatment)
• Adapalene
• Isotretinoin (Topical)
Antiandrogens
• Chlormadinone (acetate)
• Spironolactone
• Cyproterone acetate
• Drospirenone
• Flutamide (topical)
Depigmenting agents
• Chromium (picolinate, chromium yeast)
• Niacinamide
• Azelaic acid
• Tranexamic acid
• Alpha-arbutin
• Ellagic acid
• Cysteamine
• Hydroquinone
• Kojic acid
Antiparasitics
• Permethrin
Corticosteroids
• Prednisolone

Keratolytics
• Benzoyl peroxide
• Glycolic acid
• Mandelic acid
Antiinflammatory
• Silymarin
• Acetylcysteine (N-Acetylcysteine)
• Phytic acid
• Enoxolone (18-beta-glycyrhetinic acid)
• Alpha-bisabolol
Sebolytics
• N-Acetylcysteine
• Zinc acetate
• Zinc pyrithione
Vitamins
• Vitamin E
• Vitamin B6
Probiotics
• Lactobacillus acidophilus
• Bifidobacterium bifidum
• Lactobacillus bulgaricus
• Lactobacillus plantarum
• Lactobacillus rhamnosus
Nutraceuticals
• Omega 3
• Gamma-linolenic acid (GLA) (Borage oil)
• Guggul (Commiphora mukul) dry extract
• Levocarnitine
• Silymarin extract

INDICATIONS

The intensity of the green indicates from less to more recommended, and those compounds we do not recommend range from white to red (red indicating less recommended).

Prescription Disclaimers

Antiandrogenic Treatment

The use of hormonal therapy might be related to the risk of thrombotic events. Caution should be applied when prescribing and following patients undergoing antiandrogenic therapy. Further clinical and laboratorial evaluation of the patient should be performed in order to mitigate that risk.

Antiandrogenic Treatment in Patients Undergoing Masculinizing Hormone Therapy

Currently, there are no guidelines directed to the transgender population, therefore, we must proceed with caution when beginning any antiandrogen treatments. It is important to not that the base of the acne treatment depends on the classification of the presented lesions, i.e. keratolytics for comedonian acne; fixed combinations and antibiotics (topical and oral) for inflammatory acne; and isotretinoin for severe cases. Medical decisions should be guided by individual patient assessment.

Formulations 1/3

A personalized formulation with suitable active ingredients and doses. The formulations below are composed of the validated combinations of molecules which are both active and safe to provide the best treatment possible for this patient.

Topical Treatment

Formula	
Adapalene	0.1% (w/w)
Benzoyl peroxide	2.5% (w/w)
Ethoxydiglycol	5.0% (w/w)
Cleoderm™, q.s	100%
Apply to the affected area once a day, at night.	

Formulations 2/3

A personalized formulation with suitable active ingredients and doses. The formulations below are composed of the validated combinations of molecules which are both active and safe to provide the best treatment possible for this patient.

Topical Treatment

Formula	
Flutamide (topical)	2% (w/w)
Alcoholic solution, q.s	100%
Apply to the affected area once a day, at night.	

Formulations 3/3

A personalized formulation with suitable active ingredients and doses. The formulations below are composed of the validated combinations of molecules which are both active and safe to provide the best treatment possible for this patient.

Oral Treatment

Formula	
Silymarin	12 mg
Selenium yeast	200 mcg
N-Acetylcysteine	624 mg
DiluCap Hygro, q.s	30 capsules
One dose, once to twice a day.	

Oral Treatment

Formula	
Bifidobacterium bifidum	1 x 10^9 CFU
Lactobacillus acidophilus	1 x 10^9 CFU
Lactobacillus bulgaricus	1 x 10^9 CFU
Lactobacillus plantarum	1 x 10^9 CFU
Lactobacillus rhamnosus	1 x 10^9 CFU
Sachet excipient, q.s	1 Sachet
One dose, once at night.	

Prescriptions 1/3

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Signature of the prescribing physician	
Dr	Demo Genomics
Physician registration No.	demo
Signature	

Prescriptions 2/3

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Oral Treatment

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Bifidobacterium bifidum	1 x 10^9 CFU
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Lactobacillus plantarum	1 x 10^9 CFU
Lactobacillus rhamnosus	1 x 10^9 CFU
Sachet excipient, q.s	1 Sachet
One dose, once at night.	

Signature of the prescribing physician	
Dr	Demo Genomics
Physician registration No.	demo
Signature	

III.
Detailed results

Genetics and clinical results will be combined into the following categories to improve the understanding of the acne presentation in this patient and guide treatment.

1.1 Predisposition to severe acne

- Medium Risk -

ABOUT

Acne is a multifactorial inflammatory disease affecting the pilosebaceous follicles of the skin. As complex inflammatory mechanisms are key pathogenic factors in the development of acne, polymorphisms in genes related to the immune response will significantly impact the acne presentation in a patient. The type and severity of lesions may be substantially influenced by genetics.

Acne grading as well as the presence of inflammatory lesions influence the appearance of long-lasting consequences, e.g., scars and post-inflammatory hyperpigmentation. Therefore, being predisposed to severe acne might be a determining factor to early initiate specific treatment.

CATEGORY	DESCRIPTION	RESULT
Predisposition to severe acne	Genetic predisposition to presenting severe acne lesions.	**Medium Risk**

Medium Risk

This result indicates the patient has some predisposition to severe acne. The severity of lesions on the onset and genetic predisposition are essential determinants of sequelae, e.g., scars and hyperpigmentation, and relapse. Therefore, this patient should be carefully examined and, if adequate, earlier treatment should be prescribed.

INDICATIONS

Low risk Medium risk High risk

2.1 Predisposition to scars and hyperpigmentation

- Low Risk -

ABOUT

As acne is tightly related to inflammation, genetic markers predisposing to more exacerbated inflammation are often associated with lesions' appearance and long-lasting consequences.

The inflammatory immune system activates both melanocytes and fibroblasts production, and therefore, increased inflammatory response during acne development is likely to be associated with higher risk of sequelae (e.g, scars and hyperpigmentation).

CATEGORY	DESCRIPTION	RESULT
Predisposition to scars and hyperpigmentation	Genetic predisposition to exacerbated inflammation, resulting in being more prone to the formation of scars and hyperpigmentated areas	**Low Risk**

Low Risk

This result indicates the patient is at low risk for developing post-acne scars and hyperpigmented lesions. This patient is not likely to present scars or hyperpigmentation, so there is no necessity for further treatment unless clinical indication is present.

INDICATIONS

Low risk Medium risk High risk

2.2 Predisposition to increased sebum production

- Low Risk -

ABOUT

The production of sebum is one of the most widely known factors involved in the pathogenesis of acne. Although sebum is produced in response to several environmental stressors (physical and chemical insults), genetic factors might help to predict the patient predisposition to increased sebum production. Thus, treatment could be planned accordingly.

CATEGORY	DESCRIPTION	RESULT
Predisposition to increased sebum production	Genetic predisposition to increased activity and secretion of the sebaceous glands	**Low Risk**

Low Risk

This result indicates this patient is under low risk of increased sebum production, thus this patient is unlikely to present sebum as an important cause of acne. However, clinical data should be taken into consideration.

INDICATIONS

Low risk Medium risk High risk

2.3 Predisposition to skin sensitivity

- Low Risk -

ABOUT

Acne treatment might severely impact the skin condition potentially leading to sensitivity and red-ness. These issues may affect patient adherence as well as treatment result. Therefore, knowing beforehand the patient predisposition to skin sensitivity represents an important tool to guide the therapeutic decision, especially regarding topical treatment.

CATEGORY	DESCRIPTION	RESULT
Predisposition to skin sensitivity	Predisposition to sensitivity to drugs applied topically to the skin.	**Low Risk**

Low Risk

This result indicates this patient presents low risk of having a sensitive skin.

INDICATIONS

Low risk Medium risk High risk

3.1 Predisposition to acne due to hormonal alteration

- Low Risk -

ABOUT

Hormonal profile is determined by several factors, including sex, age, nutrition, and medication intake. Nevertheless, the hormones balance (e.g., production and metabolism) is highly dependent on the patient's genetic factors. Therefore, the patient genetic predisposition to acne is largely related to the genetic balance of hormone homeostasis.

CATEGORY	DESCRIPTION	RESULT
Predisposition to acne due to hormonal alteration	Genetic predisposition to presenting acne due to alterations in the hormonal levels, which should be treated accordingly.	**Low Risk**

Low Risk

This patient presents low risk of acne due to hormonal changes.

INDICATIONS

Low risk Medium risk High risk

3.2 Predisposition to polycystic ovary syndrome

- Medium Risk -

ABOUT

Polycystic ovary syndrome is a highly inherited condition affecting women, and the presence of signs of hyperandrogenism (e.g.,acne) is one of the diagnostic criteria. Therefore, genetic predisposition to polycystic ovary syndrome should also be considered during the acne diagnosis and treatment.

Nutritional management has been considered an important tool to control the polycystic ovary syndrome. Hypocaloric diets aimed at weight loss have been shown to improve free testosterone levels, menstrual cycle alterations, acne, and overall quality-of-life.

CATEGORY	DESCRIPTION	RESULT
Predisposition to polycystic ovary syndrome	Predisposition of developing polycystic ovary syndrome, thus presenting acne	**Medium Risk**

Medium Risk

This patient presents medium risk of polycystic ovary syndrome. The detection of this condition would allow the early treatment of acne.

INDICATIONS

Low risk Medium risk High risk

Nutritional advice

General information

Nutrition plays a vital role in the development of acne and several clinical markers related to the appearance of lesions. Lipidemia and glycemia correlate tightly to the sebaceous glands' functioning and the skin's inflammatory milieu. Maintaining a healthy and balanced diet is very relevant to mitigating the predisposition to acne and treating the condition.

Furthermore, biochemical alterations might be expected during the treatment with oral retinoids, so proper nutritional management should be indicated. In this sense, a personalized nutritional evaluation might mitigate these effects.

The nutritional plan must be designed taking to account the patient genetic predisposition to biochemical alterations, e.g. insulin levels and carbohydrate metabolism, either pre-existing or derived from the treatment with isotretinoin.

4.1 Predisposition to retinoid-related hyperlipidemia

- Medium Risk -

ABOUT

As retinoids bind to nuclear receptors, they alter the expression of several genes. Therefore, oral retinoid therapy might directly impact the blood levels of lipoproteins, potentially affecting the patient health status. During this therapeutic approach, some genetic markers might indicate an augmented predisposition to present hyperlipidemia or dyslipidemia. Therefore, nutritional therapy is recommended.

CATEGORY	DESCRIPTION	RESULT
Predisposition to retinoid-related hyperlipidemia	Genetic predisposition to presente higher cholesterol levels during therapy with retinoids	**Medium Risk**

Medium Risk

This result indicates this patient presents medium risk of developing hyperlipidemia due to the treatment with oral retinoids. Caution should be applied when prescribing and following this patient, nutritional management might be necessary.

INDICATIONS

Low risk Medium risk High risk

4.2 Lipid metabolism

- Medium Risk -

ABOUT

The lipoproteins and triglycerides blood concentrations are highly influenced by genetic factors. Considering the important role of these biochemical markers in the development of acne, proper nutritional followup of patients with increased risk of hyperlipidemia is needed. In addition, the early detection of this patients might diminish the long-lasting acne consequences.

CATEGORY	DESCRIPTION	RESULT
Lipid metabolism	Predisposition to present hyperlipidemia regardless of retinoid therapy	Medium Risk

Medium Risk

This result indicates medium predisposition to increased levels of cholesterol and triglycerides. Nutritional management is advised.

INDICATIONS

Low risk Medium risk High risk

4.3 Carbohydrate metabolism

- Medium Risk -

ABOUT

The carbohydrates metabolism is influenced by genetic factors. For example, higher glucose serum concentrations, through several pathways (e.g., IGF-I receptor and insulin receptor), might lead to increased sebum production and inflammation in the skin. Therefore, proper nutritional management is recommended during acne treatment.

CATEGORY	DESCRIPTION	RESULT
Carbohydrate metabolism	Genetic predisposition. To presenting altered gycemia and carbohydrate metabolism	**Medium Risk**

Medium Risk

This patient has increased risk of higher serum levels of glucose. Nutritional management is recommended.

INDICATIONS

Low risk Medium risk High risk

4.4 Food allergy

- Medium Risk -

ABOUT

Food allergy often clinically manifests as skin lesions due to changes of the immunological environment (e.g., presence of cytokines typical of the inflammatory process) of the skin. Although food allergy does not directly cause acne, it might be related to its manifestation. Therefore, reducing the intake of an allergenic food might be beneficial in the treatment of acne.

CATEGORY	DESCRIPTION	RESULT
Food allergy	Genetic predisposition to presenting food allergy, which might ellicit skin manifestations	Medium Risk

Medium Risk

This patient presents some genetic markers of the predisposition to food allergy. It is advised to provide nutritional counseling in order to determine and eliminate potential allergens.

INDICATIONS

Low risk Medium risk High risk

IV.
Complete Genetic Results

A list of the genotypes presented by the patient for each one of the 60 SNPs analyzed to fully understand the relevant genetic profile of that patient regarding acne.

1. Skin Predisposition to Acne

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
OVOL1	rs478304	G>A	A	TT	HIGH	High risk of severe acne
TLR4	rs4986791	T>C	C	CC	HIGH	Normal risk of acne conglobata
TLR4	rs4986790	G>A	A	AA	HIGH	Normal risk of acne conglobata
IL-1B	rs16944	A>G	G	AA	LOW	Normal levels of IL-1B
CYP17A1	rs743572	A>G	G	AG	MEDIUM	Medium risk of increased sebum production and augmented acne severity
TGF-β2	rs1159268	G>A	A	GG	LOW	Low risk of severe acne
MYC	rs4133274	A>G	G	AA	LOW	Low risk of severe acne in teenagers
FST	rs38055	G>A	A	GG	LOW	Low risk of severe acne

Gene/Region: part of the patient's DNA affected by the possible variation;
SNPiD: Scientific identification for the genetic alteration;
Transition: Nucleotide alteration;
Risk allele: Nucleotide that confers a particular deleterious condition for the patient;
Genotype: Combination of nucleotides the patient presents in each copy of that gene or region
RISK: Category of risk related to that genotype
DESCRIPTION: a brief explanation of the phenotypic consequences related to the genotype presented by the patient

2. Skin Condition and Inflammation

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
WNT10A	rs74333950	G>T	T	TG	MEDIUM	Medium risk of acne related to inflammation
Non-genic region	rs873549	T>C	C	CT	MEDIUM	Medium predisposition of keloid formation
PIK3R1	rs10515088	A>G	G	AG	MEDIUM	Medium predisposition to increased sebum production
IRF4	rs12203592	C>T	T	CC	LOW	Low risk of skin sensitivity
MTA3	rs17030203	T>G	G	TT	LOW	Low risk of skin sensitivity
RETN	rs1862513	C>G	G	CC	LOW	Low predisposition to severe acne, increased sebum production and acne relapse
RETN	rs3745367	G>A	A	GG	LOW	Low predisposition to severe acne, increased sebum production and acne relapse
IL-10	rs1800896	T>C	C	TC	MEDIUM	Somewhat decreased secretion of IL-10, which might impair inflammation control leading to post-inflammatory hyperpigmentation
MYEF2	rs1426654	A>G	G	AA	LOW	Normal melanin production
FLG	rs7927894	C>T	T	CT	MEDIUM	Medium risk for skin sensitivity and risk of atopy
TNF-α	rs1800629	G>A	A	GG	LOW	Normal production of TNF-α and low predisposition to hyperpigmentation
FOXL2	rs1511412	G>A	A	GG	LOW	Low predisposition of keloid formation in asian populations

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3. Predisposition to hormone-related acne

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
THADA	rs12478601	T>C	C	CT	MEDIUM	Medium predisposition of polycystic ovary syndrome and increased severity of symptoms of this condition
FSHR	rs2268361	T>C	C	CT	MEDIUM	Medium predisposition of polycystic ovary syndrome
THADA	rs13429458	C>A	A	AC	MEDIUM	Medium predisposition of polycystic ovary syndrome and increased severity of symptoms of this condition
CYP17A1	rs743572	A>G	G	AG	MEDIUM	Medium risk of increased sebum production and augmented acne severity
MYEF2	rs1426654	A>G	G	AA	LOW	Normal melanin production
CYP19A	rs700518	T>C	C	CT	MEDIUM	Altered aromatase activity, leading to medium increase in testosterone levels. Might correlate to medium increase in sebum production
LHCGR	rs13405728	G>A	A	AA	HIGH	High predisposition of polycystic ovary syndrome
FSHR	rs2349415	C>T	T	CC	LOW	Low predisposition of polycystic ovary syndrome

Gene/Region: part of the patient's DNA affected by the possible variation;
SNPiD: Scientific identification for the genetic alteration;
Transition: Nucleotide alteration;
Risk allele: Nucleotide that confers a particular deleterious condition for the patient;
Genotype: Combination of nucleotides the patient presents in each copy of that gene or region
RISK: Category of risk related to that genotype
DESCRIPTION: a brief explanation of the phenotypic consequences related to the genotype presented by the patient

4. Nutritional advice

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
SOAT1	rs404818	C>T	T	CC	LOW	Low risk of acne related to cholesterol levels; increased risk of atherosclerosis
ARAP1	rs9667947	T>C	C	TT	LOW	Low risk of DM2
HNF1A-AS1	rs2650000	C>A	A	CC	LOW	Low predisposition of increased LDL levels
C11orf30/LRRC32	rs2212434	C>T	T	CT	MEDIUM	Normal risk of food allergy
RXR	rs2651860	C>A	A	AC	MEDIUM	Medium risk of familial hyperlipidemia
RXR	rs10918169	C>G	G	GG	HIGH	Increased risk of familial hyperlipidemia
ABCG8	rs6544713	C>T	T	CC	LOW	Low predisposition of increased LDL levels
APOE	rs4420638	G>A	A	AA	HIGH	High predisposition of increased LDL levels, risk of DM2, and increased insulin levels
ODZ4	rs7103693	C>T	T	CC	LOW	Low risk for altered fasting glucose
FLG-AS1	rs12123821	C>T	T	CC	LOW	Normal risk of food allergy
TM6SF2	rs58542926	T>C	C	CC	HIGH	High predisposition of increased LDL levels
RXR	rs283696	C>T	T	CC	LOW	Low risk risk of familial hyperlipidemia
SERPINB7	rs12964116	A>G	G	AA	LOW	Normal risk of food allergy
FTO	rs8050136	C>A	A	AA	HIGH	Increased risk of DM2 and increased fasting glucose
GHRL	rs27647	T>C	C	CT	MEDIUM	Medium risk of decreased satiety, which might lead to altered insulin resistance. Acne risk might be increased
RXR	rs1128977	G>A	A	GG	LOW	Low risk risk of familial hyperlipidemia
IL-13	rs1295686	T>C	C	CC	HIGH	Increased risk of food allergy
FABP2	rs1799883	C>T	T	CT	MEDIUM	Medium sensitivity to refined carbohydrates
PNPLA3	rs738409	G>C	C	CC	HIGH	Increased risk of acne, hypertrygliceridemia, and steatosis

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SNPiD: Scientific identification for the genetic alteration;
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5. Pharmacogenetics

ABOUT

Pharmacogenetics analyzes the genetic variants that might impact the response to drugs. Response to drugs might vary due to alterations in enzymes involved in the metabolism and drug concentration, i.e., pharmacokinetic processes, and in the very molecular mechanism of the drug, namely pharmacodynamic.

The patient's genetic predisposition to respond to the main drugs involved in acne treatment significantly alters the treatment of this and other conditions. Here you will find a summary of the recommendations of this patient regarding pharmacogenetics of the essential drugs. Note that those are not necessarily drugs used in the same pharmacotherapy.

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
CYP3A4*11	rs28988604	G>A	A	GG	LOW	Normal activity of CYP3A4
HLA-B*13:01	rs2844573	A>C	C	AC	MEDIUM	Predisposition of hypersensitivity to dapsone in Asian populations
CYP3A4*20	rs67666821	TTTTT>TTTT	TTTT	TTTTTTTTT	LOW	Normal activity of CYP3A4
HLA-DRB1	rs701829	C>T	T	CC	LOW	No elevated risk of hypersensitivity to dapsone in Asian populations
HLA-B*51:01	rs2442736	G>C	C	GG	LOW	No elevated risk of hypersensitivity to clindamycin
RXR	rs2651860	C>A	A	AC	MEDIUM	Medium risk of familial hyperlipidemia
CYP2C9*8	rs7900194	G>A	A	GG	LOW	Normal activity of CYP2C9
CYP2C9*2	rs1799853	C>T	T	CC	LOW	Normal activity of CYP2C9
RXR	rs10918169	C>G	G	GG	HIGH	Increased risk of familial hyperlipidemia
CYP3A5	rs776746	T>C	C	CC	HIGH	Higher CYP3A5 activity, generating faster clearance of drugs metabolised by this enzyme. Retinoids are potentially affected by this alteration.
CYP3A4*2	rs2737418	C>A	A	CC	LOW	Normal activity of CYP3A4, metabolism of erythromycin is normal
CYP2C9*3	rs1057910	A>C	C	CA	MEDIUM	Medium decrease in activity of the CYP2C9 enzyme was shown, generating slower clearance of drugs metabolised by CYP2C9, dapsone is potentially affected by this alteration
CYP2C9*5	rs28371686	C>G	G	CC	LOW	Normal activity of CYP2C9
OATP1B1	rs4149056	T>C	C	CT	MEDIUM	Medium decrease in activity of the OATP1B1, reducing transport of several drugs. Erythromycin pharmacokinetics might be affected
CYP3A4*22	rs35599367	G>A	A	GG	LOW	Normal activity of CYP3A4, metabolism of erythromycin is normal
RXR	rs283696	C>T	T	CC	LOW	Low risk risk of familial hyperlipidemia
ABCC2	rs717620	T>C	C	CT	MEDIUM	Somewhat higher activity of the ABCC2 enzyme, as it is know to be involved in the metabolism of erythromycin, it might reduce its serum concentration

V.
Genetics and Acne

Basic concepts of the influence of genetics in the treatment of acne and its sequalae.

Fagron AcneTest

is a pharmacogenetics-centered algorithm considering the genetic predisposition to skin features to guide and improve acne treatment.

Why use the Genetic approach in the treatment of acne?

Although acne is a disease commonly treated with success in the dermatological practice, the type of treatment and stage at which this approach is taken influence the outcome. Late treatment of some types of acne will make the patient prone to scar tissue formation and other long-lasting sequelae, e.g., post-inflammatory hyperpigmentation. The prescription of adequate treatment promptly is essential to achieve better results, avoiding the necessity for lengthier and costly treatments.

Despite being a frequent disease with typical onset during the teenage years, the pathogenetic aspects of acne may be strongly influenced by genetics. Approximately 81% of the biological factors related to acne are influenced by genetics. Furthermore, the genetic influence in the hormone metabolism may be part of the pathogenesis of acne in the adult woman. As an example, considering the influence of the immune response in acne, genetic variations in genes related to inflammation are essential in predicting the severity of acne and the probability of the essential sequelae.

What is evaluated?

Besides a comprehensive clinical evaluation algorithm, the patient is genotyped for 60 single nucleotide polymorphisms. With that genetic profile, we generate information on 1) skin predisposition, i.e., how the patient is predisposed to acne, inflammation, scars, and hyperpigmentation; 2) pharmacogenetics, patient-specific response to medication; 3) predisposition to hormone-related acne; 4) nutritional correlation.

By genetically testing the patients, doctors are able to deeply understand underlying pathophysiological mechanisms. The AcneTest allows acquiring information that would not be possible by the clinical approach. Therefore, dermatologists will be able to make better-informed decisions and provide personalized treatment.

What is pharmacogenetics?

One of the main aims of the test is to provide information on the response to drugs employed in acne treatment. For that purpose, we use the concept of pharmacogenetics. As a result, pharmacogenomics may be considered the center of personalized medicine; thus, further studying and applying pharmacogenomics leads to a better understanding of the patient and the possibility of delivering customized treatment. Furthermore, pharmacogenetic knowledge allows for better treatment adherence and improves results in refractory cases.

We may approach pharmacogenetics initially by considering two main targets: 1) variations on genes of proteins involved in the metabolism of the specific drug; 2) variations on genes of molecular targets, e.g., receptors. Considering the first target, i.e., metabolism, certain enzymes are involved in either the activation or the degradation of one or several drug molecules. Thus, genomic variants yielding more or less active enzymes will determine the pharmacokinetics of this molecule, i.e., the variation of concentration over time.

Considering the range of drugs used in acne treatment, the decision among those molecules for therapy may benefit from having precise genetic information from the patient. With that knowledge, the physician is able to choose a precise molecule and its dose. Therefore, a more effective treatment, with less side-effects is possible.

How else genetics impacts the acne treatment?

The genetic predisposition increased to inflammation markers is correlated to the clinical presentation of inflammatory acne and, therefore, to the sequalae following the lesions. Patients with the predisposition to inflammatory severe acne might be treated precociously to avoid further complications.

Some patients might also have the genetic predisposition to higher glycemia or lipidemia, therefore, providing nutritional recommendation to control those biochemical parameters will aid in treating acne.

Furthermore, hormonal disbalances are key factors in the development of acne in the adult woman. Genetics allows an early understanding of patient hormones metabolism and, therefore, allows the early implementation of the antiandrogenic treatment.

Legal disclaimer

Fagron Genomics, S.L.U carries out genetic tests upon request by healthcare professionals, in relation to biological samples from patients obtained by the healthcare professional. Our tests do not replace a medical consultation, nor do they make up a diagnostic or treatment, nor should they be interpreted this way. Only healthcare professionals can interpret the results of said tests, based on their knowledge of the clinical records of the patients and other relevant factors and, under their responsibility, give a diagnostic or prescribe treatment to the patient. We decline all responsibility derived from the use and interpretation of the results of our tests by the solicitant healthcare professional. Fagron Genomics, S.L.U expressly reserves any legal actions in case of an inappropriate, negligent or incorrect use or interpretation of the results of our tests. It is the responsibility of the healthcare professional who requests a test to guarantee to the patient the appropriate genetic advice as foreseen by Law 14/2007, of 3rd July, of biomedical research. As Fagron Genomics, S.L.U does not have access to the personal identifiable information about the patient from whom the sample comes, it is the responsibility of the requesting healthcare professional to comply with the applicable data protection Laws and regulations.

Methodology

How was this test performed?

DNA was extracted from the buccal swab sample provided and was analyzed by our clinical analysis laboratory. DNA was extracted using the KingFisher Flex® robotic extraction system (Thermo Fisher Scientific). The study of the genetic variants was carried out using a custom-designed microfluidic card to measure for the chemiluminescent detection of each of them using TaqMan® technology. TaqMan® technology for genotyping testing is proven and widely used in clinical and research settings. The sensitivity (detection limit) of this study is 99%.

We analyze 60 SNPs related to the pathogenesis, predisposition, and treatment of acne.

This report has been generated by a validated automatic reporting algorithm under the responsibility of Fagron Genomics S.L.U.

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