ACNE Solutions

Smart DNA – Acne Profile

Doctor report

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Fagron Acnetest
Laboratory teste processed by IVD Medical Device Algorithm

REF FGMS-Acne

Fagron Genomics,
SRN: ES-MF-000001092
C/ de les Cosideres, 150
08226 Terrassa, Barcelona (Spain)

Patient name	SmartSalem Test Patient
Date of birth	03-03-1973
Gender	Male
Sample code	ACN02021AA
Received in laboratory	03-07-2024
Genetic results date	03-07-2024
Requesting physician	SmartSalem test doctor
Requesting physician email	testsmartsalemdoctor@mail.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	51
Gender	Male

BIOMETRIC DATA	
Weight (Kg)	73
Height (cm)	175
BMI	23.8

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

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

Patient personal information 2/2

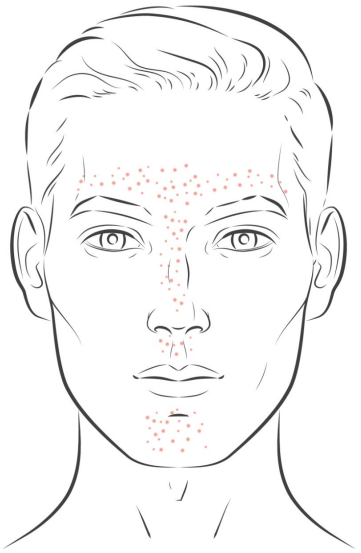
History of previous treatments	
Retinoic acid	No
Benzoyl peroxide	No
Azelaic acid, salicylic acid or glycolic acid	No
Fixed combinations	No
Sunscreen	No
Skin tonic, astringent, micellar water, make-up remover	No
Soaps	No
Excessive soap or cleansing solution	No
Antimicrobials	No
Isotretinoin	No
Antiandrogens	No
Probiotics	No
Previous skin procedures	No

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)	
ldl (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)

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	59.38%

CATEGORY	DESCRIPTION	RESULT
Skin Condition and Inflammation	This patient presents medium risk of an inflammatory profile related to the appearance of acne lesions and sequelae related to it	41.11%

CATEGORY	DESCRIPTION	RESULT
Predisposition to hormone-related acne	Patient presents medium risk of presenting acne due to alterations in the metabolism and levels of hormones	46.67%

INDICATIONS

Low risk Medium risk High risk

Results Summary

Summary of the results generated by the genetic analysis

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	42.78%

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.

Retinoids	
• Tretinoin	100%
• Adapalene	100%
• Isotretinoin (standard-dose treatment)	
Antibiotics	
• Erythromycin	100%
• Clindamycin HCl	100%
• Minocycline	37.5%
• Metronidazole	
• Dapsone (Topical)	
• Dapsone	
• Doxycycline	
• Minocycline	
• Tetracycline	
Antiandrogens	
• Chlormadinone (acetate)	
• Cyproterone acetate	
• Spironolactone	
Depigmenting agents	
• Azelaic acid	43.7%
• Tranexamic acid	39.4%
• Hydroquinone	25%
• Kojic acid	25%
• Niacinamide	25%
Antiparasitics	
• Ivermectin	
Corticosteroids	
• Clobetasol propionate	

Keratolytics	
• Glycolic acid	28.4%
• Mandelic acid	17.9%
Antiinflammatory	
• Phytic acid	75%
Sebolytics	
• Acetylcysteine (N-Acetylcysteine)	83.3%
• Zinc acetate	
• Zinc pyrithione	
Vitamins	
• Vitamin E	75%
• Vitamin B6	25%
Probiotics	
• Lactobacillus acidophilus	7.8%
Nutraceuticals	
• Levocarnitine	50%
• Chromium (picolinate, chromium yeast)	47%
Moisturizing	
• Hyaluronic acid	40%

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	0.3 %
Erythromycin	5 %
Azelaic acid	15 %
Cleoderm, q.s.	100%

Apply on the affected skin once a day according to medical indication.

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	
Acetylcysteine (N-Acetylcysteine)	5 %
Fitalite, q.s.	1000

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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	
Minocycline	2 %
Vitamin E	400 UI
DiluCap PSD, q.s.	30 capsules
Take one capsule daily according to medical indication and final dosing. Isotretinoin and antibiotics should be taken taking into consideration their specific recommendations.	

Prescriptions 1/3

Topical Treatment

Formula	
Adapalene	0.3 %
Erythromycin	5 %
Azelaic acid	15 %
Cleoderm, q.s.	100%

Apply on the affected skin once a day according to medical indication.

Signature of the prescribing physician	
Dr	
Physician registration No.	
Date	

Address	Signature

Prescriptions 2/3

Topical Treatment

Formula	
Acetylcysteine (N-Acetylcysteine)	5 %
Fitalite, q.s.	1000

.

Signature of the prescribing physician	
Dr	
Physician registration No.	
Date	

Address	Signature

Prescriptions 3/3

Oral Treatment

Formula	
Minocycline	2 %
Vitamin E	400 UI
DiluCap PSD, q.s.	30 capsules
Take one capsule daily according to medical indication and final dosing. Isotretinoin and antibiotics should be taken taking into consideration their specific recommendations.	

Signature of the prescribing physician	
Dr	
Physician registration No.	
Date	

Address	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.
Skin Predisposition to Acne

1.1 Predisposition to severe acne

- High 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.	High Risk

High Risk

This result indicates the patient is predisposed to presenting 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, appropriate treatment should be started earlier for this patient.

INDICATIONS

Low risk Medium risk High risk

1.
Skin Predisposition to Acne

1.2 Risk of acne in teenagers

- Medium Risk -

ABOUT

Acne is particularly prevalent among adolescents, reflecting a high correlation between the onset of puberty and the onset of acne. During puberty, there's an increase in sebum production, a crucial factor in acne development. After the late teen years or early adulthood, the incidence of acne typically declines. The genetic influence also plays a significant role in the manifestation of acne during adolescence, contributing to its high occurrence in this population.

CATEGORY	DESCRIPTION	RESULT
Risk of acne in teenagers	Predisposition to develop acne in the adolescence	Medium Risk

Medium Risk

This patient demonstrates a moderate genetic risk of developing acne during adolescence; therefore, it is advisable to seek appropriate dermatological management. Such proactive care could enhance the outcome and diminish the likelihood of significant, long-lasting sequelae.

INDICATIONS

Low risk Medium risk High risk

1.
Skin Predisposition to Acne

1.3 Risk of acne conglobata

- High Risk -

ABOUT

Acne conglobata is an uncommon, extremely inflammatory, and severe form of acne vulgaris, which typically affects adult males and demonstrates a chronic, persistent course. It is characterized by the presence of grouped comedones, nodules, abscesses, and interconnected draining sinus tracts. Genetic predispositions, particularly variations in the gene of the Toll-Like Receptor 4 (TLR4), have been associated with this condition. TLR4 is instrumental in mediating the immune response against Propionibacterium acnes, the bacteria implicated in acne. Variations in the TLR4 gene can alter this inflammatory response, potentially exacerbating inflammation and making certain individuals more susceptible to acne conglobata.

CATEGORY	DESCRIPTION	RESULT
Risk of acne conglobata	Genetic Predisposition: Protection or risk for acne conglobata	High Risk

High Risk

This patient does not carry protective alleles within the TLR4 gene, which is involved in the response to bacteria implicated in acne. This genetic profile increases the propensity for developing acne conglobata.

INDICATIONS

Low risk Medium risk High risk

1.
Skin Predisposition to Acne

1.4 Predisposition to acne relapse

- Medium Risk -

ABOUT

Refractory acne, typified by persistent relapses, has been linked to a genetic predisposition. Genetic factors may affect the severity of the acne, how it responds to treatment, and the likelihood of relapses. Recent advancements in proteomics have also highlighted the role of genes involved in inflammation, wound healing, and tissue remodelling, such as myeloperoxidase, lactotransferrin, and neutrophil elastase inhibitor in the pathogenesis of acne. Particularly, the resistin gene (RETN) has been found to influence considerably the proability of relapses after treating acne. The continuous exploration of the genetic landscape of acne will be key to understanding the biological mechanisms underlying refractory acne and in the development of effective therapeutic strategies.

CATEGORY	DESCRIPTION	RESULT
Predisposition to acne relapse	Predisposition to present acne refractory to treatment	Medium Risk

Medium Risk

This patient presents a few alleles associated to increased risk of the acne presentation being refractory to treatment.

INDICATIONS

Low risk Medium risk High risk

2.
Skin Condition and Inflammation

2.1 Predisposition of developing keloids

- High Risk -

ABOUT

Keloids, benign growths of dermal fibroblasts, result from an abnormal wound healing process where fibrous tissue overgrows beyond the original wound. This is driven by imbalances in the extracellular matrix and influenced by alterations in growth factors, collagen turnover, and tension alignment. The development of keloids has a strong genetic component, with the ASAH1 and FOXL2 genes implicated in their pathogenesis. Variants in ASAH1 and changes in FOXL2 expression contribute to the genetic predisposition to keloids, affecting their incidence, severity, and treatment response. These hyperproliferative scars commonly affect young adults across all ethnicities, albeit with varying incidence rates. The genetic understanding of keloids could lead to improved treatment strategies for this often-recurrent and treatment-resistant condition.

CATEGORY	DESCRIPTION	RESULT
Predisposition of developing keloids	Genetic predisposition to developing keloids after skin damage	High Risk

High Risk

This patient demonstrates a high genetic propensity for keloid formation. This indicates a significantly increased risk of extensive scarring in response to acne, underscoring the need for comprehensive dermatological care, proactive scar prevention, and possibly more aggressive treatment strategies.

INDICATIONS

Low risk Medium risk High risk

2.
Skin Condition and Inflammation

2.2 Predisposition to increased inflammatory response related to acne development

- High Risk -

ABOUT

The genetic predisposition to alterations in the inflammatory response plays a crucial role in the pathogenesis of acne. Variations in specific genes, including the Toll-Like Receptor 4 (TLR4) gene, can alter the body's immune response to Propionibacterium acnes, a bacterium implicated in acne. Furthermore, variations in specific interleukin (IL) genes, such as IL-1B and IL-10, as well as Tumour Necrosis Factor-alpha (TNF-α), Transforming Growth Factor-beta 2 (TGF-β2), and Wingless-type MMTV integration site family, member 10A (WNT10A) genes, could predispose individuals to an exacerbated inflammatory response. This heightened inflammation can contribute to increased severity of acne. A comprehensive understanding of these genetic influences offers a more sophisticated perspective on acne pathogenesis, underscoring the potential for personalised treatment strategies for individuals genetically predisposed to severe acne manifestations.

CATEGORY	DESCRIPTION	RESULT
Predisposition to increased inflammatory response related to acne development	Genetic predisposition to altered control of inflammation mechanisms	**High Risk**

High Risk

The patient presents a high genetic risk associated with alterations in the inflammatory response related to acne. Due to the inherent role of inflammation in the onset and severity of acne, immediate initiation of treatment with retinoids, if clinically appropriate, is strongly suggested to manage potential exacerbations.

INDICATIONS

Low risk Medium risk High risk

2.
Skin Condition and Inflammation

2.3 Predisposition to scars and hyperpigmentation

- Medium 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 equelae (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	Medium Risk

Medium Risk

This result indicates the patient is at medium risk for developing post-acne scars and hyperpigmented lesions. Early treatment and lightning agents are recommended.

INDICATIONS

Low risk Medium risk High risk

2.
Skin Condition and Inflammation

2.4 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.
Skin Condition and Inflammation

2.5 Predisposition to skin sensitivity

- Medium 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.	Medium Risk

Medium Risk

This result indicates this patient presents medium risk of having a sensitive skin, , and thus, there might be increased predisposition to presenting redness and sensitivity skin when using topical treatment.

INDICATIONS

Low risk Medium risk High risk

3.
Predisposition to hormone-related acne

3.1 Predisposition to acne due to hormonal alteration

- Medium 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.	Medium Risk

Medium Risk

This patient presents medium risk of acne due to hormonal changes. The knowledge of the patient hormone levels is recommended in order to provide a better and personalized care.

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.
Nutritional advice

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.
Nutritional advice

4.2 Lipid metabolism

- High 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	High Risk

High Risk

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

INDICATIONS

Low risk Medium risk High risk

4.
Nutritional advice

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.
Nutritional advice

4.4 Food allergy

- Low 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	Low Risk

Low Risk

This patient does not present genetic markers analysed that predispose to food allergy.

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.

1.1 Predisposition to severe acne

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
CYP17A1	rs743572	A>G	G	AA	LOW	Low risk of increased sebum production
TGF-β2	rs1159268	G>A	A	AA	HIGH	High risk of severe acne
FST	rs38055	G>A	A	AG	MEDIUM	Medium risk of severe acne
OVOL1	rs478304	G>T	T	TT	HIGH	High risk of severe acne
IL-1B	rs16944	A>G	G	GA	MEDIUM	Somewhat increased secretion of IL-1B, which is correlated to the pathogenesis of inflammation and acne
TLR4	rs4986790	G>A	A	AA	HIGH	Absence of protection against acne conglobata
TLR4	rs4986791	T>C	C	CC	HIGH	Absence of protection against acne conglobata
HLA-DRA	rs763035	A>G	G	GG	HIGH	High predisposition to acne rosacea

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

1.3 Risk of acne conglobata

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
TLR4	rs4986790	G>A	A	AA	HIGH	Absence of protection against acne conglobata
TLR4	rs4986791	T>C	C	CC	HIGH	Absence of protection against acne conglobata

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

1.4 Predisposition to acne relapse

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
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

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

2.1 Predisposition of developing keloids

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
FOXL2	rs1511412	G>A	A	GG	LOW	Low predisposition of keloid formation in asian populations
Non-genic region	rs873549	T>C	C	CC	HIGH	High predisposition of keloid formation

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

2.2 Predisposition to increased inflammatory response related to acne development

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
TGF-β2	rs1159268	G>A	A	AA	HIGH	High risk of severe acne
IL-1B	rs16944	A>G	G	GA	MEDIUM	Somewhat increased secretion of IL-1B, which is correlated to the pathogenesis of inflammation and acne
WNT10A	rs74333950	G>T	T	TT	HIGH	Increased risk of acne related to inflammation

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

2.3 Predisposition to scars and hyperpigmentation

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
WNT10A	rs74333950	G>T	T	TT	HIGH	Increased risk of acne related to inflammation
FOXL2	rs1511412	G>A	A	GG	LOW	Low predisposition of keloid formation in asian populations
Non-genic region	rs873549	T>C	C	CC	HIGH	High predisposition of keloid formation
TNF-α	rs1800629	G>A	A	GG	LOW	Normal production of TNF-α and low predisposition to hyperpigmentation
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

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

2.4 Predisposition to increased sebum production

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
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
PIK3R1	rs10515088	A>G	G	AA	LOW	Low predisposition to increased sebum production

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

2.5 Predisposition to skin sensitivity

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
FLG	rs7927894	C>T	T	TT	HIGH	Increased skin sensitivity and risk of atopy
IRF4	rs12203592	C>T	T	CC	LOW	Low risk of skin sensitivity
MTA3	rs17030203	T>G	G	TT	LOW	Low risk of skin sensitivity

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

3.1 Predisposition to acne due to hormonal alteration

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
CYP19A	rs700518	T>C	C	CC	HIGH	Altered aromatase activity, leading to increased testosterone levels. Might correlate to increased sebum production
MYEF2	rs1426654	A>G	G	AA	LOW	Normal melanin production
CYP17A1	rs743572	A>G	G	AA	LOW	Low risk of increased sebum production

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RISK: Category of risk related to that genotype
DESCRIPTION: a brief explanation of the phenotypic consequences related to the genotype presented by the patient

4.1 Predisposition to retinoid-related hyperlipidemia

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
RXR	rs10918169	C>G	G	GG	HIGH	Increased risk of familial hyperlipidemia, caution should be applied when prescribing retinoids
RXR	rs2651860	C>A	A	AC	MEDIUM	Medium risk of familial hyperlipidemia
RXR	rs283696	C>T	T	CC	LOW	Low risk risk of familial hyperlipidemia

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

4.2 Lipid metabolism

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
SOAT1	rs404818	C>T	T	TT	HIGH	Increased risk of acne related to cholesterol levels; increased risk of atherosclerosis
HNF1A-AS1	rs2650000	C>A	A	AC	MEDIUM	Medium predisposition of increased LDL levels
ABCG8	rs6544713	C>T	T	CT	MEDIUM	Medium 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
TM6SF2	rs58542926	T>C	C	CC	HIGH	High predisposition of increased LDL levels
RXR	rs1128977	G>A	A	AG	MEDIUM	Medium risk of familial hyperlipidemia

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

4.3 Carbohydrate metabolism

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
ARAP1	rs9667947	T>C	C	TC	MEDIUM	Medium risk of DM2
ODZ4	rs7103693	C>T	T	CT	MEDIUM	Medium risk for altered fasting glucose
FTO	rs8050136	C>A	A	AC	MEDIUM	Medium risk of DM2 and increased fasting glucose
FABP2	rs1799883	C>T	T	CT	MEDIUM	Medium sensitivity to refined carbohydrates

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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

4.4 Food allergy

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
C11orf30/LRRC32	rs2212434	C>T	T	CT	MEDIUM	Normal risk of food allergy
FLG-AS1	rs12123821	C>T	T	CC	LOW	Normal risk of food allergy
SERPINB7	rs12964116	A>G	G	AA	LOW	Normal risk of food allergy
GHRL	rs27647	T>C	C	TT	LOW	Low risk of alterations satiety
IL-13	rs1295686	T>C	C	CC	HIGH	Increased risk of food allergy

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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

5 Pharmacogenetics

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
Genetics of the antibiotics in the acne therapy						
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
CYP2C9*8	rs7900194	G>A	A	GG	LOW	Normal activity of CYP2C9
CYP3A4*2	rs2737418	C>A	A	CC	LOW	Normal activity of CYP3A4, metabolism of erythromycin is normal
CYP3A4*11	rs28988604	G>A	A	GG	LOW	Normal activity of CYP3A4
CYP3A4*20	rs67666821	GTTTT>GTTTT	GTTTT	TTTTTTTTTT	LOW	Normal activity of CYP3A4
CYP3A4*22	rs35599367	G>A	A	GG	LOW	Normal activity of CYP3A4, metabolism of erythromycin is normal
HLA-B*13:01	rs2844573	A>C	C	AA	HIGH	Predisposition of hypersensitivity to dapsone
HLA-DRB1	rs701829	C>T	T	CC	LOW	No elevated risk of hypersensitivity to dapsone
HLA-B*51:01	rs2442736	G>C	C	GG	LOW	No elevated risk of hypersensitivity to clindamycin
Genetics of the retinoids in the acne therapy						
RXR	rs10918169	C>G	G	GG	HIGH	Increased risk of familial hyperlipidemia, caution should be applied when prescribing retinoids
RXR	rs1128977	G>A	A	AG	MEDIUM	Medium risk of familial hyperlipidemia
RXR	rs2651860	C>A	A	AC	MEDIUM	Medium risk of familial hyperlipidemia
RXR	rs283696	C>T	T	CC	LOW	Low risk risk of familial hyperlipidemia

Gene/Region: part of the patient's DNA affected by the possible variation;
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DESCRIPTION: a brief explanation of the phenotypic consequences related to the genotype presented by the patient

5 Pharmacogenetics

Gene/Region	SNPiD	Transition	Risk allele	Genotype	RISK	DESCRIPTION
Genetics of the keratolytics in the acne therapy						
RETN	rs3745367	G>A	A	GG	LOW	Low predisposition to severe acne, increased sebum production and acne relapse
CYP17A1	rs743572	A>G	G	AA	LOW	Low risk of increased sebum production
PIK3R1	rs10515088	A>G	G	AA	LOW	Low predisposition to increased sebum production
FLG	rs7927894	C>T	T	TT	HIGH	Increased skin sensitivity and risk of atopy
IRF4	rs12203592	C>T	T	CC	LOW	Low risk of skin sensitivity
MTA3	rs17030203	T>G	G	TT	LOW	Low risk of skin sensitivity

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;
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V.
Genetics and Acne

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

Smart DNA – Acne Profile

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.

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.

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