Fagron AcneTest

Genetic awareness to personalize acne treatment

Fagron genomics

Patient name	**Example 2 Testing**
Date of birth	**05-05-2005**
Gender	**Male**

Sample code	**ACN00808AA**
Collection Date	**02-20-2023**
Received date	**02-24-2023**
Results date	**03-01-2023**
Requesting physician	**Development Testing**

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

IV. Complete Genetic Results

A list of the genotypes presented by the patient for each one of the 29 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	17
Gender	Male

BIOMETRIC DATA	
Weight (lbs)	175
Height (ft)	5 ft 11 ins
BMI	24.4

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	Yes
Cancer or neoplasia	No

SOCIAL HISTORY	
Exposure to sun and visible light	Yes
Physical activity	Yes
Intake of refined carbohydrate	Yes
Alcohol consumption	Yes

Patient personal information 2/2

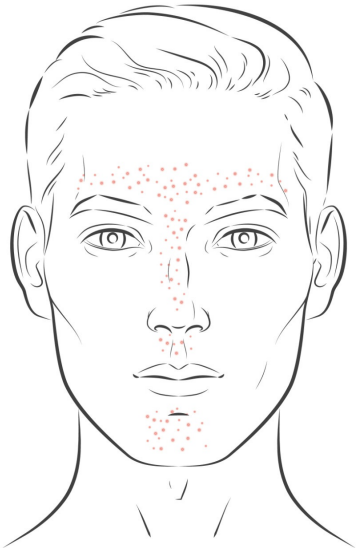
HISTORY OF PREVIOUS TREATMENTS	
Previous treatments	Retinoic acid, Soaps cleansing solutions,
Previous skin procedures	Glycolic acid (7-10 days)

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)	0
Idl (mg/dl)	
Triglycerides (mg/dl)	
Creatine kinase (CK) (U/L)	
Beta-human chorionic gonadotropin (Beta-HCG)	Negative

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	62.5%

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	20.37%

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	37.78%

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.

Antibiotics
• Azithromycin
• Doxycycline
• Clindamycin phosphate
• Dapsone (Topical)
• Dapsone
• Minocycline
• Minocycline
• Tetracycline
Retinoids
• Tazarotene
• Isotretinoin (Topical)
• Adapalene
• Isotretinoin (standard-dose treatment)
Antiandrogens
• Drospirenone
• Flutamide (topical)
• Spironolactone
Depigmenting agents
• Niacinamide
• Tranexamic acid
• Cysteamine
• Hydroquinone
• Kojic acid
• Azelaic acid
Antiparasitics
• Permethrin

Corticosteroids
• Prednisolone
Keratolytics
• Glycolic acid
• Mandelic acid
Antiinflammatory
• Acetylcysteine (N-Acetylcysteine)
• Benzoyl peroxide
Sebolytics
• N-Acetylcysteine
• Salicylic acid
• Zinc acetate
Vitamins
• Vitamin B6
• Vitamin E
Nutraceuticals
• Omega 3
• Levocarnitine

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).

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

- 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

3.1 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

IV.
Complete Genetic Results

A list of the genotypes presented by the patient for each one of the 29 SNPs analyzed to fully understand the relevant genetic profile of that patient regarding acne.

1. Skin Predisposition to Acne

Gene/Region	SNPiD	Genotype	RISK	DESCRIPTION
TGF-β2	rs1159268	AG	MEDIUM	Medium risk of severe acne
OVOL1	rs478304	TT	HIGH	High risk of severe acne
IL-1B	rs16944	GG	HIGH	Increased secretion of IL-1B, which is correlated to the pathogenesis of inflammation and acne
FST	rs38055	AG	MEDIUM	Medium risk of severe acne
MYC	rs4133274	AA	LOW	Low risk of severe acne in teenagers
TLR4	rs4986790	AA	HIGH	Normal risk of acne conglobata
TLR4	rs4986791	CC	HIGH	Normal risk of acne conglobata
CYP17A1	rs743572	AG	MEDIUM	Medium risk of increased sebum production and augmented acne severity

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

GENETIC DATA APPROVED BY
Fagron Genomics Laboratory

2. Skin Condition and Inflammation

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

Gene/Region: part of the patient's DNA affected by the possible variation;
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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

GENETIC DATA APPROVED BY
Fagron Genomics Laboratory

3. Predisposition to hormone-related acne

Gene/Region	SNPiD	Genotype	RISK	DESCRIPTION
MYEF2	rs1426654	AA	LOW	Normal melanin production
CYP19A	rs700518	CT	MEDIUM	Altered aromatase activity, leading to medium increase in testosterone levels. Might correlate to medium increase in sebum production
CYP17A1	rs743572	AG	MEDIUM	Medium risk of increased sebum production and augmented acne severity

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

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4. 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	Genotype	RISK	DESCRIPTION
HLA-B*51:01	rs2442736	GG	LOW	No elevated risk of hypersensitivity to clindamycin
HLA-B*13:01	rs2844573	AA	HIGH	Predisposition of hypersensitivity to dapsone in Asian populations

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 29 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.

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

METHODOLOGY AND LIMITATIONS: Testing for genetic variation/mutation on listed genes was performed using Real-Time PCR with TaqMan® allele-specific probes on the QuantStudio 12K Flex. All genetic testing is performed by GX Sciences, 805 Las Cimas Pkwy, Suite 430, Austin TX, 78746. This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Test results do not rule out the possibility that this individual could be a carrier of other mutations/variations not detected by this gene mutation/variation panel. Rare mutations surrounding these alleles may also affect our detection of genetic variations. Thus, the interpretation is given as a probability. Therefore, this genetic information shall be interpreted in conjunction with other clinical findings and familial history. Patients should receive appropriate genetic counseling to explain the implications of these test results. The analytical and performance characteristics of this laboratory-developed test (LDT) were determined by GX Sciences' laboratory pursuant to Clinical Laboratory Improvement Amendments (CLIA) requirements. CLIA #: 45D2144988 Laboratory Director: James Jacobson, PhD DISCLAIMER: This test was developed and its performance characteristics were determined by GX Sciences. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA and qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. rsIDs for the alleles being tested were obtained from the dbSNP database. DISCLAIMER: Report contents and report recommendations are created based on the consultation, advice, and direction of Dr. Kendal Stewart, Medical Director for GX Sciences. Sole responsibility for the proper use of the information on the GX Sciences report rests with the user, or those professionals with whom the user may consult. Report contents and report recommendations are intended to be informational only. Report contents and report recommendations are not intended and should not be interpreted to make claims regarding the use, efficacy, or safety of products, formulas, and/or services listed herein. Only a doctor or other appropriately licensed health care professional, as a learned intermediary, can determine if a formula, product, or service described herein is appropriate for a specific patient. Sole responsibility for the proper use of the information on the GX Sciences report rests with the user, or those professionals with whom the user may consult. DISCLAIMER: These products are not approved by the Food and Drug Administration and are not intended to diagnose, treat, cure, or prevent disease. These recommendations are for informational purposes only and an individual is not required to use such products. These are recommendations only and do not replace the advisement of your healthcare practitioner. This test is NOT for diagnostic purposes. It may identify general health risks that are associated with genetic variations but does NOT indicate a propensity for or susceptibility to any illness, disease, impairment, or other disorders, whether physical or mental.

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 29 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.

References

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2. Guo, Z., Huang, Y., Gong, L., Gan, S., Chan, F., Gu, C., Xiang, S. and Wang, S., 2018. Association of androgen deprivation therapy with thromboembolic events in patients with prostate cancer: a systematic review and meta-analysis. Prostate Cancer and Prostatic Diseases, 21(4), pp.451-460.
3. Lu, Y., Huang, C., Yeh, H., Hong, J., Chang, C., Muo, C., Chung, S., Yang, T., Jaw, F. and Chung, C., 2019. Associations between Peripheral Thromboembolic Vascular Disease and Androgen Deprivation Therapy in Asian Prostate Cancer Patients. Scientific Reports, 9(1).

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