PATHWAY GENOMICS®

skinfit™
Healthy Skin From Within™

PHYSICIAN ORDERED GENETIC TEST REPORT
PROTECTED HEALTH INFORMATION
Dear Dr. Carlos Fig1,

SkinFit™ is a patent-pending precision skin-care genetic test report for medical professionals, outlining cosmetic and nutritional action-items for dermatological issues. This test, available for Physician order only, provides the results of a DNA test and relevant lifestyle information to help achieve healthier skin.

The purpose of this test is to provide information about how your patient’s genes affect their skin conditions. Pathway Genomic's SkinFit™ tests for over 70 different markers in 36 genes and provides a precision genetic report together with the latest, comprehensive, and scientifically advanced actionable topical and systemic skin-care information. This includes data on skin photoaging, texture, hydration, inflammation, oxidation, glycation, and skin nutrition. SkinFit™ was developed with input from your colleagues at major Dermatology and aging science research groups at Stanford, Berkeley, The Salk Institute, and New York University.

Based on the genetic testing results of your patient, we provide recommendations and multiple treatment options for the various skin phenotypes that you may take into consideration when providing consultations to your patients on diet, physical activity, or any medical treatments.

Pathway is here to help. If you have any questions or concerns regarding any aspect of this report, please contact our staff of genetic, dermatologic, or nutritional counselors by logging in to your Pathway Genomics account at www.pathway.com, or call us at (877) 505-7374.

Michael P. Nova MD
Chief Innovation Officer

REPORT INTERPRETATION GUIDE: The report has 3 important sections

Section 1: (Patient Results At A Glance) designed for the physician to view all genetic results in one place.

Section 2: (About Pages) contains information about the phenotypes tested on the left side, along with the patient results and treatment options on the right side.

Section 3: (Product Glossary) gives the ingredient and brand names associated with the possible treatment options.

NOTE: This test has not been evaluated by the FDA. This test is not intended to diagnose, treat, cure, or prevent any disease.
<table>
<thead>
<tr>
<th>PHENOTYPE NAME</th>
<th>GENETIC RESULTS</th>
<th>PAGE #</th>
<th>GENE/LOCUS</th>
<th>MARKER</th>
<th>GENOTYPE</th>
<th>GENE/LOCUS</th>
<th>MARKER</th>
<th>GENOTYPE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SKIN PHOTAGING</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WRINKLES AND COLLAGEN DEGRADATION</td>
<td>INCREASED RISK</td>
<td>P.8</td>
<td>MMP1</td>
<td>rs1799750</td>
<td>T/TC</td>
<td>STXBP5L</td>
<td>rs322458</td>
<td>T/T</td>
</tr>
<tr>
<td>TANNING RESPONSE</td>
<td>REDUCED</td>
<td>P.9</td>
<td>EXOC2</td>
<td>rs12201050</td>
<td>C/C</td>
<td>SLC24A5</td>
<td>rs1426654</td>
<td>A/A</td>
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<td></td>
<td></td>
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<td>C/T</td>
<td>TYR</td>
<td>rs1042602</td>
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<td>rs1126809</td>
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<td></td>
</tr>
<tr>
<td>SUN SPOTS (LENTIGINES)</td>
<td>INCREASED RISK</td>
<td>P.9</td>
<td>IRF4</td>
<td>rs12203592</td>
<td>C/T</td>
<td>MC1R</td>
<td>rs1805007</td>
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<td>G/G</td>
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<td>FRECKLES (EPHELIDES)</td>
<td>INCREASED RISK</td>
<td>P.10</td>
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<td>C/T</td>
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<td>TYR</td>
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<td>C/C</td>
<td>TYR</td>
<td>rs1393350</td>
<td>A/G</td>
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<td><strong>SKIN TEXTURE AND ELASTICITY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>CELLULITE</td>
<td>INCREASED RISK</td>
<td>P.10</td>
<td>ACE</td>
<td>rs4646994/</td>
<td>D/I</td>
<td>HIF1A</td>
<td>rs11549465</td>
<td>C/T</td>
</tr>
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<td>rs1799752</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>STRETCH MARKS (STRIAE DISTENSAE)</td>
<td>INCREASED RISK</td>
<td>P.11</td>
<td>ELN</td>
<td>rs7787362</td>
<td>T/T</td>
<td>SRPX</td>
<td>rs35318931</td>
<td>G/G</td>
</tr>
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<td></td>
<td></td>
<td>HMCN1</td>
<td>rs10798036</td>
<td>C/G</td>
<td>TMEM18</td>
<td>rs7594220</td>
<td>A/G</td>
</tr>
<tr>
<td><strong>VARICOSE VEINS</strong></td>
<td>INCREASED RISK</td>
<td>P.11</td>
<td>MTHFR</td>
<td>rs1801131</td>
<td>G/T</td>
<td>MTHFR</td>
<td>rs1801133</td>
<td>A/G</td>
</tr>
<tr>
<td><strong>SKIN INFLAMMATION AND ALLERGY RISK</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>ROSacea</td>
<td>INCREASED RISK</td>
<td>P.12</td>
<td>intergenic</td>
<td>rs763035</td>
<td>G/G</td>
<td>intergenic</td>
<td>rs111314066</td>
<td>A/A</td>
</tr>
<tr>
<td>CONTACT DERMATITIS</td>
<td>INCREASED RISK</td>
<td>P.12</td>
<td>FLG</td>
<td>rs61816761</td>
<td>G/G</td>
<td>FLG</td>
<td>rs558269137</td>
<td>CACTG/CACTG</td>
</tr>
<tr>
<td>GENERALIZED PSORIASIS</td>
<td>HIGH RISK</td>
<td>P.13</td>
<td>HLA-C</td>
<td>rs1265181</td>
<td>C/G</td>
<td>IL23R</td>
<td>rs2201841</td>
<td>A/A</td>
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<td></td>
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<td>rs12191877</td>
<td>C/T</td>
<td>MTHFR</td>
<td>rs1801133</td>
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<td>G/G</td>
<td>TNFAIP3</td>
<td>rs610604</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<td>rs20541</td>
<td>G/G</td>
<td>TNIP1</td>
<td>rs17728338</td>
<td>G/G</td>
</tr>
<tr>
<td>ECZEMA (ATOPIC DERMATITIS)</td>
<td>INCREASED RISK</td>
<td>P.13</td>
<td>FLG</td>
<td>rs1249insG</td>
<td>A/A</td>
<td>FLG</td>
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<td>G/G</td>
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<td>FLG</td>
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<td>C/G</td>
</tr>
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<td>CACTG/CACTG</td>
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<td>rs558269137</td>
<td>CACTG</td>
</tr>
</tbody>
</table>

See Disclaimer(s) on page 3 of this report - Copyright 2016 © - All Rights Reserved. Patents Pending. · Protected Health Information · Laboratory Director: Nilesh Dharajiya, M.D. CLIA Number: 05D1092505 · 68465 sorrento valley blvd, Easton, NH 03785
**Assay Method**

SkinFit™ identifies 71 SNPs in 36 genes associated with skin health. DNA is isolated from blood or saliva and quantitated. Targeted regions are PCR amplified, enriched and sequenced by next-generation sequencing. Genotypes are reported for each SNP. The outcomes for each phenotype are calculated based on a proprietary weighted allele combinatorial algorithm. Cut off reporting thresholds (RT) are set based on the negative log of p-value for the strongest SNP GWAS-associations (high) and the weakest SNP associations (low). A "combined SNP weight (CSW) for each phenotype is calculated based on aggregation of all individual SNP weights, which are statistically significant from published GWAS studies (OR, CI and P-values) and SNP ranking on aggregated public databases (e.g. Phenotype-Genotype Integrator). Other factors may increase a phenotype CSW such as reproducibility in multiple qualified studies (i.e. studies which use large size and diverse cohorts as well as appropriate controls). Depending on which cut off RT a CSW passes the outcome will be as follows.

### Outcomes

- **High Risk** - if the CSW passes a high cut off RT
- **Increased Risk** - if CSW passes a low cut off RT but does not reach the high cut off RT
- **Normal Risk** - if CSW does not pass the low combinatorial cut off RT but it is a positive number.
- **Reduced Risk** - if CSW yields a negative number, which implies protection/advantage or a risk lower than normal.
- **Reduced** response or protection - if CSW passes a low cut off RT but does not reach the high cut off RT similar to the "Increased Risk" in other phenotypes.
- **Normal** response or protection - if CSW does not pass the low combinatorial cut off RT but it is a positive number.

### Risks & Limitations

The purpose of this test is to provide information about how a tested individual's genes affect their skin conditions and nutritional choices. Tested individuals should not change their diet, physical activity, or any medical treatments they are currently using based on genetic testing results without consulting their personal health care provider. Tested individuals may find that their experience is not consistent with Pathway's selected peer-reviewed scientific research findings of relative improvement for the study group(s). The science in this area is still developing and many personal health factors affect skin health. Since subjects in the scientific studies referenced in this report may have had personal health and other factors different from those of tested individuals, results from these studies may not be representative of the results experienced by tested individuals. Further, some recommendations may or may not be attainable, depending on the tested individual's physical ability or other personal health factors. A limitation of this testing is that most scientific studies have been performed in Caucasian populations only. The interpretations and recommendations are done in the context of Caucasian studies, but the results may or may not be relevant to tested individuals of different or mixed ethnicities. The association between genetic variant and the information within this report is an active area of scientific research, and future scientific discoveries might alter our understanding of how this information is related to nutrition and skin care treatments.

Based on test results and other medical knowledge of the tested individual, health care providers might consider additional independent testing, or consult another health care provider or genetic counselor.

Pathway Genomics is a CLIA-certified (Clinical Laboratory Improvement Amendments of 1988) and CAP-accredited (College of American Pathologists) laboratory with standard and effective procedures in place for handling samples. However, laboratory error can occur, which might lead to incorrect results. Examples include, but are not limited to, a sample or DNA mislabeling or contamination, failure to obtain an interpretable report, and any other operational laboratory error. Sometimes Pathway's laboratory may not be able to obtain an interpretable result for a particular SNP. Sometimes it is not possible to obtain a testing result for a particular variant or marker due to circumstances beyond Pathway's control, in which case it may not be possible for Pathway to conclusively report on a genetic change that might cause or be predictive of a condition. This may mean that Pathway cannot report results for a particular health trait or condition, carrier status result, drug response, or other phenotype. Pathway may re-test a sample in order to obtain these results, but upon re-testing the results may still not be obtained. As with all medical laboratory testing, there is a small chance that the laboratory could report false positive or false negative results. A false positive result means that a genotype is reported as being present when it is actually not present. A false negative result means that a genotype is not reported as being present when it actually is present. A tested individual may wish to pursue further testing to verify any results.
The following pages contain information about the skin phenotypes on the left side, along with your patient's result on the right side. For the tested phenotypes, multiple available treatment options are listed as a reference.

These recommendations can be taken in consideration together with the patient's medical history when you make individual recommendation for your patient.

A Product Glossary is provided at the end of the report for Physician Use.
SKIN PHOTOAGING

Photoaging refers to aging of the skin as a result of exposure to ultraviolet (UV) radiation over a person’s lifetime. Although photoaging is affected by extrinsic (environmental) factors like gravity or smoking, all skin is susceptible to photoaging with UV exposure. Intrinsic factors, including skin pigmentation and genetics, can also affect the individual’s response to extrinsic factors, thus affecting the degree and type of potential photoaging. Different types of skin, for example, respond differently to tanning, impacting the likelihood of developing sun spots or freckles, while vitamins and nutrition can affect collagen production and the ability of skin cells to repair damage sustained from UV exposure. The best defense against photoaging is to understand individual risk factors, maintain proper nutrition and limit UV exposure.

WRINKLES AND COLLAGEN DEGRADATION

Wrinkles can range in severity from fine lines to deep furrows in the skin. Wrinkling is a sign of skin aging and is caused by both intrinsic factors (e.g. genetics, hormonal state and skin pigment) and environmental factors (e.g. the passage of time, gravity, chronic ultraviolet exposure, alcohol abuse and smoking) (1). These factors can cause damage to skin cells and breakdown of supportive structures called collagen in the dermis of the skin (2,3). Wrinkling tends to occur after the age of 30, and deep wrinkling is more likely to occur in individuals with darker skin (1).

Genetic variants in the MMP1 and STXBP5L genes have been associated with increased susceptibility to severe wrinkling (1,3).

PATIENT RESULTS & TREATMENT OPTIONS

INCREASED RISK

Based on the patient’s genetics, the risk of developing skin wrinkles is considered INCREASED.

ORAL: Antioxidants, such as vitamin C + E, zinc, alpha-lipoic acid, green tea, resveratrol, proanthocyanidins (French marine bark), soy isoflavones, carotenoids, such as lycopene, beta-carotene and vitamin A (also isoretinoin), have shown considerable efficacy as oral supplementation for skin health (4-12). In addition, botanicals red ginseng, chlorophyll, aloe and algae astaxanthin all improve skin integrity (13-16). Hyaluronic acid peptides + glucosamine + CoQ10 are newer oral products that have been shown to significantly improve skin photoaging damage (17).

PROCEDURE: For moderate-extensive skin photoaging, many dermatology groups are now using fractional non-ablative/ablative resurfacing or Q-switched laser treatments for removing skin wrinkling or other photo-damage issues (18-23). Radiofrequency and ultrasound therapies have also shown the ability to tighten the skin (24,25). In addition, common alternatives used are wrinkle-relaxing injections (Botox®) and soft tissue filler treatments (26,27).

TOPICAL: Sunscreens (SPF 30+, UV/IR protection) and antioxidant cream or serums, vitamin C + E, CoQ10, green tea + ginko, resveratrol, alpha-lipoic acid, coffee/cherry fruit and many others are baseline defenses for the patient’s skin type (28-35). Subsequent treatments are exfoliation, moisturization and line reduction with retinoids (vitamin A, tretinoin, isoretinoin, retinol, retinyl palmitate and retinyl proprionate + niacinamide), hydroxy acids and DMAE/dimethylaminoethanol (36-46). Hyaluronic acids are increasingly popular skin-firming and plumping agents (47,48). There are topical formulations that provide skin health benefits by reducing cellular structural damage, such as products containing synthetic peptides (e.g argireline + aloe), multiple peptides (+/- urea) and collagen peptides. In addition, there are newer topical products containing growth factors, (e.g. TGF + FGF), DNA repair enzymes and stem cells (49-59).

Refer to Product Glossary A on page 21 of this report
E - Skin Oxidation Protection

Niacinamide: NOW Foods®

Topical:
- Ascorbic acid/Vitamin C: Isabis™ Formulae, SkinCeuticals®
- Apple stem cells + Urea + Peptides: Ureadin Fusion®/ISDIN®
- Astaxanthin: Madre Labs®
- Kinetin: Gentle Rejuv/Obagi®
- Resveratrol + Vitamin E + Baicalin: Resveratrol B E/ SkinCeuticals®
- Vitamin C + E: C E Ferulic/SkinCeuticals®

F - Skin Glycation

Oral:
- Niacinamide: NOW Foods®

Topical:
- Carnosine: Lineless/Dr. Brandt®, Bio Lifting/Chantecaille®
- Niacinamide: InstaNatural®, Olay®, Metacell Renewal B3/ SkinCeuticals®
- Silibinin + Alpha-Lipoic acid: Revitalizing Night Crème/Aubrey Organics
- Truffles/Mushrooms: ReNutriv/Estee Lauder®, Truffle Therapy™
- Serum/Skin&Co Roma®

G - Skin Nutritional Needs

Topical:
- Vitamin A:
  - Vitamin A Plus Serum/ MyChelle®, Vitamin A Serum Regenerate/ Skin Inc.®, Dermalogica®
- High Potency Vitamin A: Perricone MD®, SkinCeuticals®, Alpha-H®
- Retinol: Obagi®, Exuviance®
- Vitamin B2: B6, Olay®
- Vitamin B6:
  - Combination products: Burt's Bees®, Vitamin C Serum
  - Rebalance/Skin Inc.®, Total Effects 7/Olay®
- B6 Spray: Urban Decay®
- Vitamin B12:
  - Maxasorb™ B12/Vita Sciences, Vitacream B12®, C-Serum®
  - Seaweed Filtrate/Repechage®
- Vitamin C:
  - Isabis™ Formulae®, ViolàVe®, 90210 Naturals®, goPure®, 100% Pure®
- Vitamin D:
  - PureLx®
- Vitamin E:
  - Vitamin E + Vitamin C + Hyaluronic acid: Body Shop®, Skin Inc.®, goPure®, 100% Pure®
- Folate-Folic Acid:
  - Folate + Creatine: Thin to Thick®/JĀSÖN®, Neutrogena Naturals®
  - Omega-3, Omega-6:
  - Omega 3+6: Global Beauty®, Olay®
References

The scientific studies referenced in this report are provided below and can be found at www.pubmed.gov. All cited articles are published in peer-reviewed journals, U.S. government, or medical associations websites. PubMed is a service managed by the National Institutes of Health (NIH), a part of the U.S. Department of Health and Human Services, and it tracks more than 19 million citations for biomedical articles and scientific research.

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46. Tadini KA et al. Pharmazie 64, 818-22 (2009), PMID 20095140.