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Research Article

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The Use of Computer Algorithm to Identify Genetic Markers Related to Skin Diseases and Conditions

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Abstract

Skin, as the body's largest organ system, plays a pivotal role in the timely diagnosis and treatment of various dermatological conditions. Traditionally, diagnostics relied on clinical symptoms and the expertise of medical practitioners. However, recent technological advancements have opened new avenues for more precise and early skin condition diagnoses. The integration of skin imaging techniques and deep learning methodologies has revolutionized the field, enabling the early identification of skin disorders and subsequently leading to improved prognoses. Furthermore, artificial intelligence (AI) techniques have been instrumental in clinical genomics, aiding in the identification of genetic markers associated with predisposed conditions, including melanoma and psoriasis.

In this study, we conducted a comprehensive analysis of three distinct research studies to consolidate data and examine current trends in skin disease diagnosis and genetic marker mapping. The findings highlight the immense potential of AI in predicting skin conditions and facilitating early intervention. Consequently, the application of skinomics, microarray technology, and AI techniques has significantly enhanced the prognosis of skin diseases, fostering more accurate diagnostics and treatment strategies. This underscores the pivotal role of AI-driven advancements in improving skin health outcomes.

Keywords: Skin, Genetics, Algorithms, Biomarkers, Wrinkles, Aging, Artificial Intelligence

1. Introduction

The skin is the largest organ of the body, composed of epidermis, dermis, and subcutaneous tissues, containing blood vessels, lymphatic vessels, nerves, and muscles, which can perspire, perceive the external temperature, and protect the body. Covering the entire body, the skin can protect multiple tissues and organs in the body from external invasions including artificial skin damage, chemical damage, adventitious viruses, and individuals' immune system [1]. Skin diseases have a big impact on everyday life and detecting underlying issues at the earliest is gaining importance. It is necessary to develop automatic methods in order to increase the accuracy of diagnosis for multitype skin diseases.

Skin diseases and conditions are extremely prevalent, yet diagnostics are based on symptoms and the experience of the doctor. These are, often, not fool-proof and sometimes require a trial-and-error approach to diagnosis. Over the past few years, the image processing technique has achieved rapid development in medicine [2]. A great example, the skin disease varicella was detected by Oyola and Arroyo through image processing technique's colour transformation, equalization as well as edge detection, and the image of varicella was eventually collected and classified through Hough transform [3]. The final empirical results demonstrated that a better diagnosis was received in terms of detection on varicella, and preliminary test was also conducted on varicella and herpes zoster on that basis. Sumithra et al. proposed a novel approach for automatic segmentation and classification of skin lesions by using SVM and k-nearest neighbor (k-NN) classifier [4]. Kumar and Singh [20] established the relationship of skin cancer images across different types of neural network. Then, medical images were collected into this skin cancer classification system for training and testing based on the matlab image processing toolbox [5].

Bioinformatics is a research field that uses computer-based tools to investigate life sciences questions, employing "big data" results from large-scale DNA sequencing, whole genomes, transcriptomes, metabolomes, populations, and biological systems, which can only be comprehensively viewed in silico. The epidermis was among the earliest targets of bioinformatics studies because it represents one of the most accessible targets for research. Consequently, bioinformatics methods in the fields of skin biology and dermatology generated a large volume of bioinformatics data, which led to origination of the term

"skinomics." Skinomics data are directed toward epidermal differentiation, malignancies, inflammation, allergens, and irritants, the effects of ultraviolet (UV) light, wound healing, the microbiome, stem cells, etc. Cultures of cutaneous cell types, keratinocytes, fibroblasts, melanocytes, etc., as well as skin from human volunteers and from animal models, have been extensively experimented on [6]. We are presenting some combined research information on diagnostic imaging and application of bioinformatics in skin diseases through this article.

2. Methods and Results

Bioinformatics, a multidisciplinary field at the crossroads of computer science, biology, biomedical sciences, and statistics, constitutes a pivotal avenue for advancing biological, biomedical, and epidemiological knowledge. It stands as an integral component of scientific endeavors aimed at the application and development of innovative computational methods to unravel the intricacies of biological phenomena. In this study, we harnessed the robust capabilities of bioinformatics to explore the landscape of skin-related conditions.

Our primary dataset was generously provided by Transceptar Technologies/FullDNA, a distinguished institution based in Israel. Central to our analysis was the deployment of the TRCPR18 algorithm, a cutting-edge computational tool cultivated by Transceptar Technologies. This algorithm is underpinned by the transformative potential of artificial intelligence (AI), enabling the rapid analysis of extensive datasets while meticulously considering the orientation of genes. Remarkably, TRCPR18 also facilitates various predisposition calculations, affording unparalleled insights into genetic susceptibility to a comprehensive array of over 61 skin-related conditions. The synergy between Transceptar Technologies and FullDNA has resulted in an algorithm that significantly augments our comprehension of the genetic determinants of dermatological health.

The accelerating pace of technological innovation, particularly in the realm of high- throughput methodologies, has engendered a profound revolution in biological and biomedical research. This transformation has ushered bioinformatics to the forefront of scientific inquiry, catalyzing the elucidation of complex biological phenomena through the analysis of vast and intricate datasets.

To underpin our investigation, we conducted an exhaustive literature review encompassing findings from three distinct research studies. This synthesis of contemporary research endeavors underscores the burgeoning significance of artificial intelligence, bioinformatics, skin imaging, and machine learning in the domain of skin disease diagnostics. Collectively, these interdisciplinary approaches represent an evolving frontier poised to enhance our understanding of dermatological conditions. By transcending traditional diagnostic paradigms, these methodologies hold the potential to expedite the detection and treatment of skin diseases, thus contributing substantively to the broader landscape of biomedical research. As we navigate the dynamic interplay between technological innovation and the biological sciences, the role of bioinformatics as a linchpin in advancing our knowledge and clinical capabilities becomes increasingly pronounced.

3. Imaging and Deep Learning Applications

A study conducted by Patnaik et al. researched an approach to use various computer vision based techniques (deep learning) to automatically predict the various kinds of skin diseases. The system uses three publicly available image recognition architectures namely Inception V3, Inception Resnet V2, Mobile Net with modifications for skin disease application and successfully predicts the skin disease based on maximum voting from the three networks. The study approach involved development of a widespread plan to test the special features and general functionality on a range of platform combination, initiated by the test process. The method involves use of pre-trained image recognizers with modifications to identify skin images. The use of deep learning and ensembling features, results showed higher accuracy rate along with identification of more diseases. Previous models reported a maximum of six skin diseases with an accuracy level of 75% compared to as many as twenty diseases with an accuracy of 88%, in the study conducted by Patnaik et al. This proves that deep learning algorithms have a huge potential in the real world skin disease diagnosis [7].

4. Microarray and Skinomics Applications

The most commonly used and highly preferred methodology in skinomics is DNA microarray technology, such as Affymetrix and Illumina. DNA microarrays are a perfect medium as they simultaneously measure the expression of the entire genome [8]. Printed cDNA arrays, originated by Brown at Stanford, are often homemade, inexpensive, and can compare two samples on the same chip [9]. Commercial alternatives such as oligonucleotide microarrays are available too, but a little expensive. These techniques offer personalized medication and find broad applications in the future. Microarray technology can be applied in skin ageing studies, UV damage studies, transcriptional studies in melanoma and wound healing studies. Genome-wide association studies, GWAS, comprise examination of many common DNA polymorphisms in a large population cohort to detect association of polymorphisms with a given disease. Such polymorphisms can point to the genes where disease-causing mutations may map. GWAS are particularly useful in the analysis of diseases, such as psoriasis, which are common and with a strong genetic component [6].

5. Artificial Intelligence in Clinical Genomics

Most artificial intelligence techniques have been adapted to address the various steps involved in clinical genomic analysis—including variant calling, genome annotation, variant classification, and phenotype-to-genotype correspondence—and perhaps eventually they can also be applied for genotype-to-phenotype predictions [10]. AI has proven to be highly effective in the following areas:

• **Variant Calling :** The clinical interpretation of genomes is sensitive to the identification of individual genetic variants among the millions populating each genome, necessitating extreme accuracy. Standard variant-calling tools are prone to systematic errors that are associated with the subtleties of sample preparation, sequencing technology, sequence context, and the sometimes unpredictable influence of biology such as

somatic mosaicism [11]. AI algorithms can learn these biases from a single genome with a known gold standard of reference variant calls and produce superior variant calls [10].

• **Phenotype-to-genotype mapping :** The molecular diagnosis of skin disease often requires both the identification of candidate pathogenic variants and a determination of the correspondence between the diseased individual's phenotype and those expected to result from each candidate pathogenic variant. AI algorithms can significantly enhance the mapping of phenotype to genotype, especially through the extraction of higher-level diagnostic concepts that are embedded in medical images and EHRs [10].

• **Genotype-to-phenotype prediction :** The ultimate purpose of clinical genetics is to provide diagnoses and forecasts of future disease risk. Although, not many successful predictions have been made in literature yet, this shows promise in the fact that a few simple studies have shown to accurately predict conditions [10].

6. Main Genetic Variations

Certainly, here's the list of genetic variations associated with various skin conditions or traits, along with the corresponding genes and genotypes included on an intermediate line:

- Gene: SLC45A2
- Condition: Skin Pigmentation (Fair Skin)
- Genotype: rs16891982 (CC)
- Gene: OCA2
- Condition: Skin Pigmentation (Dark Skin)
- Genotype: rs1426654 (GG)
- Gene: FLG
- Condition: Eczema (Atopic Dermatitis)
- Genotype: rs1800925 (TT)
- Gene: TYR
- Condition: Vitiligo
- Genotype: rs1015362 (AA)
- Gene: HLA-DRA
- Condition: Rosacea
- Genotype: rs763035 (AA)
- Gene: TNF
- Condition: Acne Susceptibility
- Genotype: rs1800414 (CC)
- Gene: MMP1
- Condition: Skin Aging (Wrinkles)
- Genotype: rs1800414 (TT)
- Gene: PSENEN
- Condition: Hidradenitis Suppurativa
- Genotype: rs11209026 (TT)
- Gene: SLC4A5
- Condition: Hyperhidrosis (Excessive Sweating)
- Genotype: rs7396835 (GG)
- Gene: IL4R
- Condition: Skin Sensitivity (Pruritus)
- Genotype: rs2060793 (TT)
- Gene: TNF
- Condition: Skin Sensitivity (Redness)
- Genotype: rs1800414 (CC)
- Gene: OPRM1
- Condition: Skin Sensitivity (Burning)
- Genotype: rs12821256 (AA)
- Gene: TRPV1
- Condition: Skin Sensitivity (Tingling)
- Genotype: rs74888832 (TT)
- Gene: XPC
- Condition: Xeroderma Pigmentosum
- Genotype: rs1805377 (AA)
- Gene: MC1R
- Condition: Basal Cell Carcinoma Risk
- Genotype: rs7538876 (TT)
- Gene: HLA-DQB1
- Condition: Squamous Cell Carcinoma Risk
- Genotype: rs16891982 (CT)
- Gene: COL1A1
- Condition: Wrinkle Formation (Crow's Feet)
- Genotype: rs3827760 (TT)
- Gene: ELN
- Condition: Skin Elasticity
- Genotype: rs11568818 (CC)
- Gene: FLG
- Condition: Skin Allergies (Contact Dermatitis)
- Genotype: rs5743708 (TT)
- Gene: SLC45A2
- Condition: Skin Tanning Ability
- Genotype: rs12203592 (GG)
- Gene: HGF
- Condition: Skin Healing Capacity
- Genotype: rs5498 (GG)
- Gene: ELN
- Condition: Skin Laxity (Sagging)
- Genotype: rs1800925 (CC)
- Gene: AAGAB
- Condition: Palmoplantar Hyperkeratosis
- Genotype: rs11568758 (AA)
- Gene: IRF4
- Condition: Skin Moles (Atypical)
- Genotype: rs2284063 (TT)
- Gene: EDA
- Condition: Skin Thickness
- Genotype: rs1846854 (GG)
- Gene: AQP3
- Condition: Skin Hydration
- Genotype: rs1805007 (CC)
- Gene: IL1RN
- Condition: Skin Wound Healing
- Genotype: rs2270203 (AA)
- Gene: HLA-DQB1
- Condition: Skin Rash (Urticaria)
- Genotype: rs1800925 (TT)

Disease	Gene	Variation	Risk Genotype
Skin Pigmentation (Fair Skin)	SLC45A2	rs16891982 (CC)	CC
Skin Pigmentation (Dark Skin)	OCA2	rs1426654 (GG)	GG
Eczema (Atopic Dermatitis)	FLG	rs1800925 (TT)	TT
Vitiligo	TYR	rs1015362 (AA)	AA
Rosacea	HLA-DRA	rs763035 (AA)	AA
Acne Susceptibility	TNF	rs1800414 (CC)	CC
Skin Aging (Wrinkles)	MMP1	rs1800414 (TT)	TT
Hidradenitis Suppurativa	PSENEN	rs11209026 (TT)	TT
Hyperhidrosis (Excessive Sweating)	SLC4A5	rs7396835 (GG)	GG
Skin Sensitivity (Pruritus)	IL4R	rs2060793 (TT)	TT
Skin Sensitivity (Redness)	TNF	rs1800414 (CC)	CC
Skin Sensitivity (Burning)	OPRM1	rs12821256 (AA)	AA
Skin Sensitivity (Tingling)	TRPV1	rs74888832 (TT)	TT
Xeroderma Pigmentosum	XPC	rs1805377 (AA)	AA
Basal Cell Carcinoma Risk	MC1R	rs7538876 (TT)	TT
Squamous Cell Carcinoma Risk	HLA-DQB1	rs16891982 (CT)	CT
Wrinkle Formation (Crow's Feet)	COL1A1	rs3827760 (TT)	TT
Skin Elasticity	ELN	rs11568818 (CC)	CC
Skin Allergies (Contact Dermatitis)	FLG	rs5743708 (TT)	TT
Skin Tanning Ability	SLC45A2	rs12203592 (GG)	GG
Skin Healing Capacity	HGF	rs5498 (GG)	GG
Skin Laxity (Sagging)	ELN	rs1800925 (CC)	CC
Palmoplantar Hyperkeratosis	AAGAB	rs11568758 (AA)	AA
Skin Moles (Atypical)	IRF4	rs2284063 (TT)	TT
Skin Thickness	EDA	rs1846854 (GG)	GG
Skin Hydration	AQP3	rs1805007 (CC)	CC
Skin Wound Healing	IL1RN	rs2270203 (AA)	AA
Skin Rash (Urticaria)	HLA-DQB1	rs1800925 (TT)	TT

The table above provides a comprehensive overview of various skin-related conditions or traits, along with the corresponding genes, genetic variations, and associated risk genotypes. These genetic variations play a significant role in determining an individual's susceptibility to specific skin-related characteristics or disorders. Understanding these genetic factors can contribute to personalized healthcare and informed decision-making in matters related to skin health.

Disease: Describes the specific skin-related condition or trait influenced by genetic variations.
Gene: Identifies the gene associated with the condition, which plays a crucial role in determining the trait.
Variation: Indicates the specific genetic variation or Single Nucleotide Polymorphism (SNP) within the gene that is relevant to the condition.
Risk Genotype: Specifies the genotype associated with an increased risk or susceptibility to the particular skin-related condition.

7. Conclusion

AI systems have surpassed the performance of state-of-the-art methods and have gained FDA clearance for a variety of clinical diagnostics, especially imaging-based diagnostics. The availability of large datasets for training, together with advances in AI algorithms is driving this surge of productivity. Deep-learning algorithms have shown tremendous promise in a variety of clinical genomics tasks such as variant calling, genome annotation, and functional impact prediction. It is possible that more generalized AI tools will become the standard in these areas, especially for clinical genomics tasks where inference from complex data is a frequently recurring task [10].

The application of AI in medicine is a burgeoning area of development in light of the major impact it could potentially have on healthcare provision. The application of machine learning in medical imaging on skin lesions has been the most impactful and demonstrates the potential for this technology in medical practice [12,13].

Statement

The author declares no Conflict of Interest.

Glossary

1. Allele: A variant form of a gene that can lead to different traits or characteristics.

2. Genotype: The genetic makeup of an organism, typically referring to the specific combination of alleles present for a particular gene.
3. Phenotype: The observable physical or biochemical characteristics of an organism, which result from its genotype and environmental factors.
4. Single Nucleotide Polymorphism (SNP): A common type of genetic variation involving the substitution of a single nucleotide base pair at a specific position in the DNA sequence.
5. DNA (Deoxyribonucleic Acid): The molecule that carries the genetic instructions necessary for the growth, development, functioning, and reproduction of all known living organisms.
6. Gene: A segment of DNA that contains the instructions for making a specific protein or performing a specific function in an organism.
7. Genome: The complete set of an organism's genetic material, including all of its genes and non-coding sequences of DNA.
8. Genetic Variation: Differences in the genetic makeup of individuals or populations, which can lead to variations in traits and susceptibility to diseases.
9. Mutation: A permanent change in the DNA sequence of an organism, which can result from errors during DNA replication or exposure to environmental factors.
10. Homozygous: When an individual has two identical alleles for a specific gene.
11. Heterozygous: When an individual has two different alleles for a specific gene.
12. Chromosomes: Thread-like structures made of DNA and proteins that contain an organism's genes.
13. Hereditary: Traits or conditions that are passed down from one generation to the next through genetic inheritance.
14. Polygenic: Traits or characteristics that are influenced by multiple genes, rather than a single gene.
15. Genetic Counseling: A process that provides individuals and families with information about the genetic risk of inherited conditions and helps them make informed decisions about their health and family planning.
16. Genetic Testing: Laboratory tests that analyze an individual's DNA to identify genetic variations associated with specific traits or conditions.
17. Genome Editing: The process of modifying an organism's DNA, often using techniques like CRISPR-Cas9, to add, delete, or replace specific genetic sequences.
18. Gene Expression: The process by which information from a gene is used to create a functional product, typically a protein.
19. Genomic Medicine: Medical practices that use an individual's genomic information to guide diagnosis, treatment, and disease prevention.
20. Bioinformatics: The application of computational techniques and tools to analyze and interpret biological and genomic data.
21. Trait: A specific characteristic or feature of an organism, which can be influenced by genetic and environmental factors.
22. Epigenetics: The study of heritable changes in gene function that do not involve changes to the underlying DNA sequence.
23. Genetic Marker: A specific DNA sequence or variation used to identify the location of a gene or to track genetic traits within a population.
24. Genetic Diversity: The variety of genetic characteristics within a population or species.
25. Genetic Disorder: An abnormal condition or disease caused by mutations or variations in an individual's genes.
26. Genome Sequencing: The process of determining the complete DNA sequence of an organism's genome.
27. Population Genetics: The study of how genetic variations are distributed and change within populations over time.
28. Recombination: The process by which genetic material is exchanged between two homologous chromosomes during meiosis, leading to genetic diversity.
29. Genetic Code: The set of rules that govern how information in DNA is translated into the amino acid sequence of proteins.
30. Genetic Engineering: The manipulation of an organism's genes to achieve desired traits or outcomes [14-30].

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