

UNLOCKING A PERSONALIZED MEDICINE APPROACH FOR ECZEMA TREATMENT

Submitted in partial fulfillment of the requirement for the award of Bachelor of
Technology degree in Biotechnology

Interdisciplinary Project

By

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INSTITUTE OF SCIENCE AND TECHNOLOGY

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BONAFIDE CERTIFICATE

This is to certify that this Project Report is the bonafide work of **Michelle Faustina Maria (41230033)**, **Nishita Cunchala (41230037)**, and **Shreya Ramesh (41230058)**, who carried out the project entitled **"A PERSONALIZED MEDICINE APPROACH FOR ECZEMA TREATMENT"** under the supervision from **Ms. S Haritha, Assistant Professor**, from January 2024 to April 2024.

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ABSTRACT

This project presents a precision medicine approach towards atopic eczema, focusing on targeting the FLG gene. The study utilizes a MATLAB program to identify mutations in the FLG gene, with the aim of tailoring treatment using specific concentrations of the biologic drug dupilumab that are ideal for each patient. The MATLAB program is designed to analyze the genetic makeup of individuals with atopic eczema, identifying specific mutations in the FLG gene associated with the condition. Based on these genetic findings, the program calculates and recommends personalized prescriptions that can effectively target the underlying causes of eczema. This personalized approach to treatment has the potential to improve therapeutic outcomes and minimize adverse effects by ensuring that patients receive the most appropriate and effective treatment for their specific genetic profile.

Keywords: Atopic eczema, FLG gene, dupilumab, personalized medicine, MATLAB

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LIST OF SYMBOLS AND ABBREVIATIONS

AE	Atopic Eczema
AD	Atopic Dermatitis
EASI	Eczema Area and Severity Index
FLG	Filaggarin gene
IL	Interleukin
GUI	Graphical User Interface
GWAS	Genome Wide Association Studies
PCR	Polymerase Chain Reaction
PM	Personalized medicine

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CHAPTER 1

INTRODUCTION

Atopic eczema, also known as atopic dermatitis, is a chronic inflammatory skin condition affecting millions worldwide. Despite various treatments, managing atopic eczema can be challenging due to varying treatment effectiveness among individuals. To address this, we propose a personalized medicine approach for atopic eczema treatment, leveraging a patient's unique genetic makeup and eczema phenotype characteristics to identify causative genes. By analyzing these genes and current research on atopic eczema, we aim to design a MATLAB program for optimal treatment regimens.

The rise in atopic eczema prevalence has led to a focus on skin barrier dysfunction as a key factor. Mutations in the filaggrin gene, inherited or acquired, can cause this dysfunction and are linked to atopic diseases. Individuals with atopic dermatitis have a compromised skin barrier, making them more prone to dryness, environmental triggers, and allergic reactions, contributing to inflammation and itching. This barrier defect may involve reduced ceramide levels, fatty molecules crucial for skin barrier function and water retention. Genetics play a well-defined role in atopic eczema, with the filaggrin (FLG) gene being a major risk factor. FLG mutations weaken the skin barrier, making it more susceptible to irritants and allergens. Environmental factors act as triggers that exacerbate these vulnerabilities, leading to skin barrier disruption and inflammation. Immune system dysregulation, specifically an overactive TH2-dominant response, further contributes to the inflammatory cascade in response to triggers. Symptoms of atopic eczema include itch (pruritus), sleep disturbance, dryness/roughness of the skin, bleeding, cracking, flaking, irritation, oozing, burning, changes in skin appearance, redness, scratching, rash, and stinging. Severity is classified based on disease activity, ranging from mild (limited involvement, manageable symptoms) to moderate (more extensive involvement, increased symptoms) to severe (widespread involvement, intense itching, oozing or crusting lesions).

The proposed MATLAB program aims to address these complexities by analyzing FLG gene mutations and incorporating current research on atopic eczema treatment, specifically incorporating the drug dupilumab. Dupilumab is a monoclonal antibody targeting IL-4R α , inhibiting IL-13 signaling and reducing pruritus. Clinical trials have shown its efficacy in improving AD symptoms, making it a promising treatment for atopic eczema, especially in cases of uncontrolled moderate-to-severe disease. The project seeks to unlock personalized medicine for eczema patients by utilizing MATLAB to analyze FLG gene mutations and optimize treatment with dupilumab. By tailoring treatment based on individual genetic profiles and clinical parameters, this approach aims to improve treatment outcomes and quality of life for individuals with atopic eczema.

CHAPTER 2

LITERATURE REVIEW

2.1 ATOPIC ECZEMA

A chronic, itchy skin condition called atopic eczema has become increasingly common in recent decades, affecting up to a quarter of school children and 10% of adults in developed countries. The rise in prevalence has led researchers to focus on skin barrier dysfunction as a key factor in eczema. Mutations in the filaggrin gene, which can be inherited, can cause this dysfunction and are linked to other atopic disease, (Sara J Brown, 2016). People with atopic dermatitis have a compromised skin barrier, making them more prone to developing dryness, irritation from environmental triggers, and allergic reactions. These factors contribute to inflammation and itching. This cause of the barrier defect may be a part of reduced levels of ceramides. Ceramides are fatty molecules that are found in the outermost layer of the skin. They play a vital role in maintaining the skin's barrier function and the prevention of excessive water loss through skin, (Logan Kolb & Sarah J. Ferrer-Bruker, 2020).

2.1.1 Causes of Eczema

Genetics play a well-defined role in the development of atopic eczema. Mutations in the filaggrin (FLG) gene, a critical protein for maintaining a healthy skin barrier, has been identified as a major risk factor. These mutations weaken the FLG protein's function, making the skin more susceptible to irritants and allergens, (Jayanta Gupta & David J margolis, 2020). Beyond genetics, environmental factors act as triggers that exacerbate existing vulnerabilities. Disruption of the skin barrier by irritants or allergens like dust, pollen can lead to flare-ups. Studies have shown various environmental triggers in AE pathogenesis emphasizing the importance of identifying individual triggers for effective management, (Logan Kolb & Sarah J. Ferrer-Bruker, 2020). Furthermore, research delves into the role of immune system dysregulation in atopic eczema. They

propose that individuals with atopic eczema have an overactive Th2-dominant immune response, leading to an exaggerated inflammatory cascade upon exposure to environmental triggers, (Jihyun Kim *et al.*, 2019).

2.1.2 Symptoms associated with Eczema

There are a variety of symptoms that are associated with atopic eczema. Itch, also known as pruritus, emerged as the most prevalent symptom, assessed in nearly all trials (289 out of 295, or 98%). Itch was measured either as a single, independent variable or incorporated into a broader symptom assessment tool. Sleep disturbance ranked as the second most commonly assessed symptom, reported in over half of the studies (181 out of 295, or 61%). Other symptoms were reported as less frequently that included dryness/roughness of the skin, bleeding, cracking, flaking, irritation, oozing, burning, changes in skin appearance, redness, scratching, rash and stinging, (L.A.A. Gerbens *et al.*, 2016).

2.1.3 Immunology of Atopic Eczema

Atopic eczema (AE) is a complex disease with several subtypes. These subtypes have different triggers and molecular compositions. While IgE levels are elevated in only a portion of patients, and mutations in the filaggrin gene are found in a small subset of patients of European ancestry, all subtypes of AE involve T cell mediated skin inflammation and skin barrier disruption. In AE, immune cells are recruited to damaged skin areas, releasing proinflammatory signals. In the acute phase, type 2, 17, and 22 helper T cells (T_H2 , T_H17 , T_H22) dominate, while the chronic phase is characterized by increased T_H1 activation along with T_H2 and T_H22 inflammation. Cytokines like TSLP, IL-25, and IL-33 promote the maturation of T_H2 cells and ILC2s, which produce the pro-inflammatory cytokine IL-13. IL-4 or IL-13 binding to the IL-4 receptor complex leads to JAK protein activation, which phosphorylates and activates STAT6 and STAT3, essential for skin-barrier function. This activation downregulates proteins crucial for the skin barrier, including filaggrin. Activation of STAT6 also increases periostin expression,

a protein that stimulates keratinocytes to produce TSLP. TH2 cells also express IL-31, which acts on keratinocytes to induce the release of IL-24, leading to decreased filaggrin production and skin barrier breakdown, (Newsom *et al.*, 2020).

2.1.4 Treatment of Eczema

Atopic eczema patients have a weakened skin barrier leading to dryness. This dryness can be managed through proper hydration. Mutations in the FLG gene, which reduces natural moisturizing factors which are common in AE. Hydration helps retain water, improve barrier function, and relieve itch. Emollients which are applied regularly (twice daily, including unaffected skin) and soon after bathing (within 3 minutes) are crucial. Lotions are preferred in warmer weather. Education on proper emollients is needed as many patients may not use enough. Wet dressing with emollients can be helpful for acute, oozing lesions to promote medication penetration, reduce infection risk and dry the oozing while protecting the skin from scratching, (Ji Hyun Lee *et al.*, 2015).

2.2 SEVERITY OF ECZEMA

This is a common classification based on overall disease activity. Mild eczema involves limited involvement (body surface area affected) with manageable symptoms like dryness and occasional itching. Moderate eczema presents with more extensive involvement and increased symptoms like redness, scaling, and frequent itching. Severe eczema is characterized by widespread involvement, intense itching disrupting sleep and daily activities, and potentially oozing or crusting lesions.

2.2.1 Symptoms for Severity

In mild eczema, the rash typically affects small areas of the body, often on the face (especially in infants) and hands and feet in adults. The most prominent symptom is dry, scaly skin, with a rough and flaky texture. Itching can be present, but it's usually

occasional and doesn't significantly disrupt sleep or daily activities. Redness might be noticeable, particularly on lighter skin tones.

As eczema progresses to moderate severity, the symptoms become more pronounced. The rash starts to affect larger areas of the body, potentially including the arms, legs, and torso. The dryness and scaling become more severe, with the skin appearing cracked and flaky. Itching becomes more frequent and intense, potentially interrupting sleep and leading to scratching that further irritates the skin. Redness becomes more prominent, especially on lighter skin tones, and bumps or papules might also be present. In long-standing cases of moderate eczema, persistent scratching can lead to a thickening and leathery texture of the skin, known as lichenification.

Severe eczema has a significant impact on both the skin and quality of life. The rash becomes widespread, potentially covering most or all of the body's surface. Itching becomes constant and severe, significantly disrupting sleep and daily activities. Scratching can break the skin, leading to oozing of fluids and crusting of lesions. The skin may appear very red, inflamed, and swollen. Chronic inflammation and scratching contribute to thickened, leathery skin. Broken and irritated skin becomes more susceptible to bacterial infections. Perhaps the most impactful aspect of severe eczema is the significant toll it takes on a person's well-being, affecting sleep, emotional health, and daily activities.

2.2.2 Methods for Severity Assessment

There are several methods for assessing the severity of atopic dermatitis. The SCORAD index is a widely used tool that considers both how widespread and severe the eczema is in different body regions. The SCORAD (Scoring Atopic Dermatitis) index is a widely used tool in research and clinical practice to assess the severity of atopic dermatitis (eczema). It combines objective clinical signs with subjective patient-reported symptoms to generate a total score reflecting disease activity. Each component is assigned a score based on its severity, and the individual scores are summed to generate a total SCORAD score (range 0-40). Higher scores indicate greater disease severity, (Oranje A. P. & Mahmoud Y. D. 2009). The SASSAD index, on the other hand,

focuses on the intensity of eczema at multiple body sites, without taking into account the total area affected. An earlier version of SASSAD, the Leicester score, assessed eczema in a larger number of body zones. The ADASI method utilizes color-coded body charts to assess the extent of eczema, but this approach may be difficult.

The Rajka and Langeland Scoring System is a simpler tool for assessing long-term severity, but it may not be sensitive to changes in eczema. Costa's Simple Scoring System (SSS) scores both the severity and location of eczema, but it can be complex to use. In contrast, the BCSS is a very simple scale that only assesses whether eczema is present or absent in specific body sites.

The ADASI assesses multiple eczema symptoms like redness, itching, and crusting, but there is limited data on its accuracy and reliability. The Skin Intensity Score (SIS) focuses on itching, redness, and thickened skin, and it has been shown to be related to markers of eczema activity. Finally, the ADAM is the newest method, but it has a complex scoring system that may not always be consistent between observers, (Carolyn Charman & Hywel Williams, 2000).

2.2.3 Eczema Area and Severity Index (EASI)

The Eczema Area and Severity Index (EASI) was developed in 1998 and later validated to meet the demands of investigators in need of a standardized evaluation tool for severity of atopic dermatitis (AD) signs in clinical studies. The EASI score is calculated using reference tables designed for both adults and children. Completing the assessment typically takes a trained investigator around 6 minutes. The result ranges from 0 (clear) to 72 (very severe), the EASI score categorizes eczema severity based on the sum of scores from four body regions: 0-1.0 (almost clear), 1.1- 7.0 (mild), 7.1- 21.0 (moderate), 21.1- 50.0 (severe), and >51.0 (very severe), (Jon M. Hanifin *et al.*, 2022).

Severity Score	Area Score							
Grade each sign on a scale: 0=clear/none 1=mild 2=moderate 3=severe	% Involvement	0	1-9%	10-29%	30-49%	50-69%	70-89%	90-100%
	Area Score	0	1	2	3	4	5	6

EASI Calculator (Adults)							
Body Region	Erythema (0-3)	Edema/Papulation (0-3)	Excoriation (0-3)	Lichenification (0-3)	Area Score (0-6)	Multiplier	Score
Head/Neck	(+)	+ +	+ +	+ +	x	x 0.1	
Trunk	(+)	+ +	+ +	+ +	x	x 0.3	
Upper Extremities	(+)	+ +	+ +	+ +	x	x 0.2	
Lower Extremities	(+)	+ +	+ +	+ +	x	x 0.4	
The final EASI score is the sum of the 4 region scores (0-72):							_____

EASI Calculator (Pediatrics < 8 years old)							
Body Region	Erythema (0-3)	Edema/Papulation (0-3)	Excoriation (0-3)	Lichenification (0-3)	Area Score (0-6)	Multiplier	Score
Head/Neck	(+)	+ +	+ +	+ +	x	x 0.2	
Trunk	(+)	+ +	+ +	+ +	x	x 0.3	
Upper Extremities	(+)	+ +	+ +	+ +	x	x 0.2	
Lower Extremities	(+)	+ +	+ +	+ +	x	x 0.3	
The final EASI score is the sum of the 4 region scores (0-72):							_____

EASI Score Interpretation					
Clear	Almost Clear	Mild	Moderate	Severe	Very Severe
0	0.1-1.0	1.1-7.0	7.1-21.0	21.1-50.0	50.1-72.0

Figure 2.2.1: EASI score assessment and calculation

2.3 BIOMARKERS FOR ECZEMA

Atopic dermatitis (AD), also referred to as eczema, varies from person to person, so it can not be treated with a traditional “one-size-fits-all” approach, (Czarnowicki *et al.*, 2019). Research is underway to explore additional eczema characteristics such as genetics. This research has helped identify biomarkers that have potential in diagnosis,

prediction of course of disease, risk of co-occurring conditions (such as food allergy or asthma), and guide treatment selection. The ability to classify AD based on genetics first emerged in 2009 with the development of a novel technique called Genome-Wide Association Studies, (Bin & Leung, 2016). This technique allows for the genetic screening of large numbers of individual patients to identify which genes are altered in populations with a specific disease compared to those without it. These studies were followed by others that sequenced the genetic material from individual AD patients to determine the altered genes. The findings of these studies demonstrate that genetic factors play a crucial role in the development of eczema and potential targets of therapeutic intervention, (Brown & Irwin McLean, 2009).

2.3.1 Inherited genes of eczema

It has been identified that children whose parents have eczema have a high risk of developing eczema as well, (Brown & Irwin McLean, 2009). A study involved 50 pedigrees with 231 individuals, all genotyped. Each family had at least two children with atopic eczema, with onset typically at 2.0 months and a median serum IgE level of 316 IU. Eczema prevalence varied among families, with some showing both parents affected and others only one parent affected. Analysis revealed significant allele sharing on chromosomes 5q31 and 11q13, with particular interest in the IL4 cluster on 5q31, known to regulate IgE levels. The study did not find evidence for a specific IL-4 receptor variant (Q576R) in atopic eczema. Results suggest a major atopy predisposition locus on 5q31, with different genes interacting with environmental factors to determine specific atopy manifestations, (Forrest *et al.*, 1999).

2.3.2 Biomarkers involved in eczema

Variants in several candidate genes, including those encoding interleukin (IL)-4, the IL-4 receptor, and IL-13, have been studied in relation to eczema pathogenesis due to their roles in epidermal and immune function. However, the most strongly associated

gene is filaggrin (FLG), which plays a crucial role in skin barrier development and maintenance. Loss-of-function mutations in FLG are present in up to 10% of the general population and are associated with ichthyosis vulgaris, a dry skin disorder. These mutations are also found in up to 40% of patients with moderate-to-severe atopic eczema, significantly increasing the risk for eczema. This highlights the substantial impact of FLG mutations on eczema risk, demonstrating a strong effect for a single gene in a complex trait, (Brown, 2016). Other genes identified to be associated with atopic eczema are listed in the figure below:

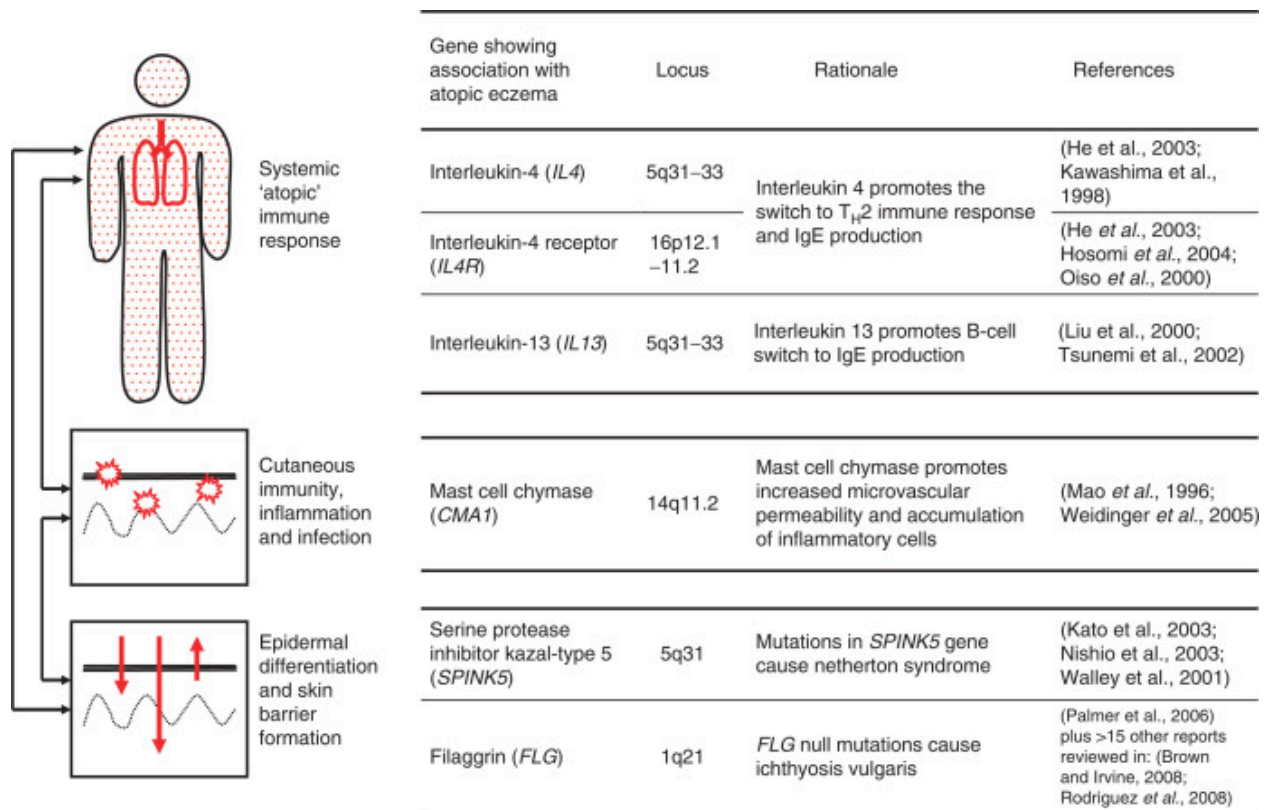


Figure 2.3.1 Genes associated with atopic eczema

Out of all the genes identified, FLG has been titled as the “strongest candidate so far” for genetic factors associated with eczema. Filaggrin is known for its role in skin barrier function. The FLG gene encodes profilaggrin, a protein that is processed into

filaggrin peptides, crucial for forming the skin's barrier and inhibiting the entry of microbes and allergens. FLG mutations, particularly R501X and 2282del4, are strongly linked to eczema, found in about 9% of Europeans. These mutations increase the risk of early onset, persistent, and severe eczema, as well as other atopic conditions like asthma. Clinical signs like palmar hyperlinearity and keratosis pilaris are indicators of FLG mutations. Overall, FLG is considered a major factor in the development of atopic eczema and related conditions, (Brown & Irwin McLean, 2009).

2.4 CURRENT MEDICATIONS FOR AE

While there is currently no cure for eczema, there are numerous treatments available, with more in development. Treatment options vary based on the type and severity of eczema, and not all treatments work the same for everyone. These can include lifestyle changes, over-the-counter remedies, and prescription medications. Common treatments include: emollients (moisturizers), topical corticosteroids, antihistamines, calcineurin inhibitors, PDE4 inhibitors, janus kinase (JAK) inhibitors, and other steroids. In some cases, prescription injectables known as biologics may be used. Biologics are highly targeted therapies that use human DNA to treat diseases at the immune system level.

2.4.1 Prescription Treatments for Eczema

Prescription treatment refers to medications or therapies that are prescribed by a healthcare provider to treat a specific medical condition. These treatments are not available over-the-counter and require a prescription from a licensed healthcare professional, such as a doctor or nurse practitioner.

2.4.1.1 JAK inhibitor

Several small-molecule JAK inhibitors, including baricitinib, abrocitinib, and upadacitinib, are being actively studied for the treatment of moderate to severe atopic

dermatitis (AD). These inhibitors target JAK proteins, which, when activated, stimulate the expression of inflammatory mediators. Baricitinib is an oral inhibitor of JAK1 and JAK2. In clinical trials, a higher proportion of subjects achieved significant improvements in AD symptoms with baricitinib compared to placebo. Abrocitinib is a selective inhibitor of JAK1, a significantly higher proportion of subjects on abrocitinib achieved improvement in AD symptoms compared to placebo. Upadacitinib is a selective inhibitor of JAK1. In a clinical phase trial, a higher percentage of subjects receiving upadacitinib achieved significant improvements in AD symptoms compared to placebo. Thus, JAK inhibitors show promise in treating AD, with varying levels of efficacy and safety profiles. Ongoing research aims to further understand their potential in managing this skin condition, (Newsom *et al.*, 2020). Cibinqo (abrocitinib) and Rinvoq (upadacitinib) are oral JAK1 inhibitors recently FDA-approved for refractory moderate to severe AD in adults and children aged 12 years and older. They are recommended when other systemic drugs, including biologics, are ineffective or not advised.

2.4.1.2 Topical calcineurin inhibitors

Topical calcineurin inhibitors (TCIs) are nonsteroidal medications that help manage eczema symptoms by preventing certain immune cells from becoming activated, thereby reducing redness, itching, and inflammation. Two TCIs available are tacrolimus ointment (Protopic®) and pimecrolimus cream (Elidel®). Tacrolimus is FDA-approved for moderate to severe atopic dermatitis in children aged 2-15 years and adults, while pimecrolimus is approved for mild to moderate atopic dermatitis in adults and children aged 2 years and older. TCIs can be applied to sensitive areas such as the face, eyelids, genitals, or skin folds, where topical steroids may not be preferred.

2.4.1.3 Topical PDE4 inhibitors

Phosphodiesterase 4 (PDE4) is an enzyme involved in the production of inflammatory cytokines within immune cells. These cytokines play a role in the normal immune response, but when triggered erroneously, they can lead to inflammation seen

in diseases like atopic dermatitis. Blocking PDE-4 inhibits the production of these cytokines, which can help reduce inflammation. Crisaborole (Eucrisa®) is an FDA-approved topical PDE4 inhibitor for mild to moderate atopic dermatitis in adults and children aged 3 months and older.

2.4.2 Biologics

Biologic drugs, also known as prescription injectables, are highly targeted therapies that use human DNA to treat diseases at the immune system level. These medications, taken subcutaneously or intravenously, contain proteins derived from living tissues or cells cultured in a lab. Biologics for atopic eczema block specific interleukins (ILs) from binding to their receptors, calming the immune system and reducing inflammation. Dupixent® (dupilumab) is the only biologic approved by the FDA for moderate to severe atopic dermatitis in adults and children aged 6 months and older when topical treatments are ineffective or not recommended, (Ratchataswan *et al.*, 2021).

2.4.2.1 Anti-OX40 antibody

The anti-OX40 antibody, also known as GBR 830, is a humanized monoclonal IgG1 antibody that targets the OX40 costimulatory molecule (CD134). OX40 is crucial for T-cell expansion and is expressed on activated antigen presenting cells and endothelium. In a phase IIa clinical trial in adults, the treatment group showed reduced epidermal hyperplasia compared to baseline at 29 days ($p < 0.01$) and 71 days ($p < 0.001$), while the placebo group did not. Levels of IL-31, CCL11, CCL17, and TSLP were decreased in the treatment group compared to baseline by 71 days ($p < 0.001$). However, IL-4, IL-13, IL-17a, and IL-22 levels were not altered after treatment with GBR830. (Newsom *et al.*, 2020).

2.4.2.2 Treatments targeting Interleukin-31

Nemolizumab (CIM331) is a monoclonal antibody that binds to the IL-31 receptor α component, preventing IL-31 from acting on neurons and reducing the sensation of pruritus (itching). Phase III clinical trials are ongoing for nemolizumab in atopic dermatitis (AD) patients. In a 12-week phase II trial with a 64-week extension, nemolizumab showed a significant decrease in pruritus compared to placebo. By 64 weeks, subjects receiving nemolizumab at different doses achieved sustained improvement in pruritus and a high proportion achieved an EASI-75 (75% improvement in Eczema Area and Severity Index). In a phase IIb trial, nemolizumab also showed promising results, with a higher proportion of subjects achieving an IGA (Investigator's Global Assessment) score of 0 or 1 and EASI-75 compared to placebo by week 24.

2.4.2.3 Treatments targeting Interleukin-13 or its receptors

IL-13 is a key target in atopic dermatitis (AD) treatment, as its increased levels correlate with disease severity. Three monoclonal antibody treatments targeting IL-13—dupilumab, tralokinumab, and lebrikizumab—have shown promise for refractory AD. Dupilumab, this antibody binds to IL-4R α , inhibiting IL-13 signaling and reducing pruritus. Clinical trials have demonstrated its efficacy in improving AD symptoms, with a higher proportion of patients achieving success compared to placebo. Tralokinumab is a monoclonal antibody that neutralizes IL-13. In a phase IIb trial, tralokinumab significantly reduced Eczema Area and Severity Index (EASI) scores compared to placebo. Lebrikizumab, another IL-13 antibody, inhibits the dimerization of IL-13 receptors. In the phase II trial, lebrikizumab demonstrated efficacy in improving EASI scores, with a higher proportion of patients achieving EASI-50 and EASI-75 compared to placebo.

2.5 MATLAB

MATLAB is both a powerful environment for numerical computing and a capable programming language. While it offers a core set of tools, its strength lies in matrix manipulation, data analysis, and visualization. This is for those who want to delve

deeper, additional toolkits are available, but they come at an extra cost. This is known to be a popular computing program for engineers and data analysis. It offers a user-friendly environment for complex calculations, with additional toolboxes available for specific needs. Beyond its computational power, MATLAB excels in data visualization. Users can easily create clear and informative graphs and tables without extensive coding knowledge. This makes it ideal for those without a strong statistical background, allowing them to understand and present their data effectively. This easy visualization extends to complex data analysis, making MATLAB valuable for businesses that need to analyze and communicate large datasets, (Ceyhun Ozgur *et al.*, 2021).

2.5.1 Process of MATLAB

Several key elements contribute to MATLAB's functionality as a computational platform. At its core lies the interactive environment, offering a command window for user input, a workspace for variable management, and an editor and visualization area for program development and data exploration, (Prautzsch H *et al.*, 2013). This user - friendly interface fosters an iterative workflow where users can test commands, observe results, and refine their approach. Furthermore, MATLAB's language foundation revolves around matrices and arrays, enabling a natural representation of mathematical concepts for data manipulation and problem-solving in scientific fields, (Allaire J *et al.*, 2014). Beyond these core aspects, MATLAB offers a vast library of built-in functions encompassing mathematical operations, data analysis, and signal processing tasks. The ability to create custom scripts and functions further extends MATLAB's capabilities, allowing users to automate repetitive tasks and develop specialized tools for their specific needs. Finally, MATLAB's strength in data visualization empowers researchers to create informative graphs and plots, aiding in data comprehension and the identification of relationships within databases.

2.5.2 Application of MATLAB

MATLAB has become an indispensable tool for biologists due to its robust capabilities in various areas. Some of the applications of them include data analysis and modeling. Biological research often involves complex datasets from experiments or simulations. MATLAB excels at handling large datasets, performing statistical analyses like regression and hypothesis testing, and fitting curves to experimental data. A prime example is a study by Lin *et al.* (2017) who employed MATLAB to analyze gene expression data, identifying key genes involved in antibiotic resistance in bacteria, (Lin Y *et al.*, 2017). Similarly, Silva *et al.* (2010) leveraged MATLAB's modeling capabilities to simulate population dynamics of the *Aedes aegypti* mosquito, a vector of Dengue fever, (Silva *et al.*, 2010).

Biological imaging techniques like microscopy generate vast amounts of image data. MATLAB provides powerful tools for image processing, segmentation (separating objects from background), and feature extraction. For instance, Xie *et al.* (2008) used MATLAB to analyze confocal microscopy images of neurons, measuring neurite outgrowth, a crucial aspect of neural development, (Xie *et al.*, 2008).

Bioinformatics plays a vital role in modern biology, dealing with the analysis of large biological databases like DNA and protein sequences. MATLAB offers functionalities for sequence alignment, motif discovery and phylogenetic analysis. For example, Li *et al.* implemented a MATLAB-based algorithm for protein secondary structure prediction, a fundamental step in understanding protein function.

2.6 DNA EXPLORATION: ADVANCED TECHNIQUES

2.6.1 Introduction to Genetic testing

Genetic testing is a type of medical test that identifies changes in chromosomes, genes or proteins. Gene tests seek the abnormalities in DNA taken from a person's blood, body fluids or tissues. The tests search for large mistakes such as a gene that has a section missing or added. Other tests look for small changes within the DNA. Other mistakes that can be found include genes that are too active, genes that are turned off, or those that are lost entirely. Genetic tests examine a person's DNA in a

variety of ways. They are all designed to identify differences between the gene being tested and what would be a normal version of the same gene.

2.6.2 Strategies to obtain genetic material from patients for diagnosis

There are various techniques available in the present to obtain genetic material from patients for performing diagnosis. A few of them are Molecular testing, Biochemical testing, and Chromosomal testing. These approaches aim to extract DNA or RNA samples containing genetic information relevant to the patient's condition. Additionally, advancements in technology have led to innovative approaches such as liquid biopsies, enabling the detection of genetic material in bodily fluids like blood or urine. Overall, these strategies play a crucial role in diagnosing genetic disorders, guiding treatment decisions, and advancing personalized medicine.

2.6.3 Types of genetic tests

There are numerous tests available to obtain genetic material from patients relevant to their condition, some of them are Newborn screening, Diagnostic testing, Carrier testing, Prenatal testing, Pre-implantation testing, Predictive testing, Forensic testing etc.

2.6.4 Genetic tests that are performed in the case of Atopic Eczema

- Skin Biopsy: A small sample of affected skin tissue can be collected through a biopsy procedure. This method allows for the extraction of genetic material directly from the affected area, providing valuable insights into the molecular mechanisms underlying eczema.
- Blood Draw: Peripheral blood samples can be collected from patients with eczema to isolate DNA for genetic analysis. This non-invasive method is

commonly used in research studies and clinical settings to investigate genetic factors associated with the condition.

- **Saliva Collection:** Saliva contains buccal epithelial cells that can be used to extract DNA for genetic testing. Saliva collection kits are convenient and minimally invasive, making them suitable for use in both research and clinical practice to study the genetic basis of eczema.
- **Swabbing:** Buccal swabs or oral brushes can be used to collect cells from the inside of the cheek for genetic analysis. This method is simple, painless, and well-tolerated by patients, making it a preferred option for obtaining genetic material from individuals with eczema, especially children.
- **Hair Follicle Sampling:** Hair follicles contain DNA that can be extracted for genetic testing. Plucking a few hairs from the scalp or other affected areas can provide sufficient genetic material for analysis, offering a non-invasive alternative for obtaining genetic samples in patients with eczema.

2.6.5 Similar Sampling Strategies in other Allergic and Autoimmune Diseases

Some similar existing strategies to attain genetic material from patients with other diseases, such as psoriasis, involve a range of techniques that are made relevant to each condition's specific characteristics. For psoriasis, skin biopsies are usually used to collect affected tissue samples for genetic analysis, providing insights into the genetic factors contributing to the disease's development and progression. Blood is also drawn-out to isolate the DNA from peripheral blood samples, allowing researchers to look for genetic variations associated with psoriasis susceptibility and treatment response. Additionally, saliva collection and buccal swabs provide non-invasive methods for obtaining genetic material from patients, allowing large-scale genetic studies and personalized medicine approaches for psoriasis management. Furthermore, hair follicle sampling has emerged as a promising technique for genetic analysis in

psoriasis research, offering a convenient and minimally invasive techniques of collecting DNA samples from affected individuals. These strategies play a crucial role in advancing our understanding of the genetic basis of psoriasis and informing personalized treatment strategies tailored to patients' genetic profiles.

2.7 PERSONALIZED MEDICINE

2.7.1 Introduction to Personalized medicine

Personalized medicine serves for diseases based on individuals' specific traits and is supported by budding technologies such as DNA sequencing and proteomics, revealing significant inter-individual differences in disease processes. Progressed by the aim to improve treatment efficacy by considering individual differences, personalized medicine is rooted from historical precedents and experiences to guide its implementation. Recent successes and setbacks highlight both the potential and challenges of personalized medicine.

2.7.2 Motivation for Personalized medicine

The motivation for personalized medicine comes from the realization of limitations present in traditional one-size-fits-all approaches to treatment. These standard methods often overlook the diverse biological and genetic factors that contribute to individual variations in disease susceptibility, progression, and response to treatment. By altering medical interventions to each patient's unique traits, personalized medicine holds the potential to address several challenges in healthcare. It identifies the variability in treatment response among patients, ensuring that conciliation is optimized for everyone's specific requirements and conditions.

Eczema, being a complex and multifactorial condition, often exhibits significant variability in presentation and treatment response among patients. Personalized medicine provides a promising solution by altering interventions to each patient's unique attributes, including genetic predispositions, immune profiles, and environmental

triggers. By identifying specific molecular pathways and biomarkers associated with eczema subtypes, personalized medicine holds the potential to overcome challenges such as treatment resistance, adverse drug reactions, and variability in treatment response. Overall, the motivation for personalized medicine is its ability to revolutionize healthcare by providing more effective, efficient, and personalized treatment strategies customized to the individual patient.

2.7.3 Current State of Personalized Medicine

The present scenario of personalized medicine displays its progressing applications across various fields of clinical practice, including oncology, pharmacogenomics, and rare diseases. In oncology, personalized medicine has enhanced the scenario of cancer treatment by enabling targeted therapies tailored to the genetic mutations and molecular profiles of individual tumors. Pharmacogenomics uses gene information to optimize drug selection and dosing, reducing the risk of adverse drug reactions and improving treatment outcomes. In the case of eczema, PM is emerging as a promising approach to better understanding and management of the condition. Research efforts have focused on identifying genetic markers and molecular pathways associated with eczema susceptibility, severity, and treatment response. By using this knowledge, clinicians can develop personalized treatment plans made to each patient's unique genetic profile and clinical characteristics. For example, individuals with mutations in the filaggrin gene, a known risk factor for eczema, may benefit from targeted therapies aimed at restoring skin barrier function. Moreover, it offers hope for patients with rare diseases by facilitating accurate diagnosis, targeted therapies, and improved management strategies tailored to their specific genetic abnormalities.

2.7.4 Future Directions

The future of personalized medicine has great possibilities for growth and expansion, with innovative approaches that can revolutionize healthcare delivery. One

main area of development is precision prevention, which focuses on identifying and mitigating individual risk factors for disease before symptoms manifest. Predictive modeling is another key aspect of future directions in personalized medicine for eczema. By leveraging genetic, environmental, and lifestyle data, precision prevention strategies aim to tailor interventions to each person's unique risk profile, ultimately reducing the burden of disease on populations. Additionally, the integration of artificial intelligence (AI) and big data analytics holds immense potential in advancing personalized medicine research and practice for eczema.

In the envisioned future of personalized medicine (PM), the public is empowered with control over their health-related data, enabling input, monitoring, and access. Accessible and reliable sources of medical information making sure that individuals can make knowledgeable decisions about their health. Simultaneously, health providers are equipped to navigate this area, easily merging health information and research results into standard clinical practice. Multidisciplinary teams collaborate to make clinical decisions, with healthcare education enhancing the interdisciplinary aspects of PM. Close relations between clinicians and researchers aid the rapid growth and implementation of PM solutions. Within healthcare systems, equitable access to PM services is ensured, with resources allocated in alignment with societal values. Secure data flow from citizens to regulatory authorities and research entities is established, ensuring privacy and safety. Utilization of personal data from electronic health records enables more efficient PM, while harmonized solutions address data privacy and security concerns. Ultimately, this future foster economic value by establishing a balanced ecosystem where investment, profit, and shared benefits for citizens coexist. Telemedicine and mobile solutions further promote PM and contribute to economic growth, creating new job opportunities within healthcare systems.

2.7.5 Integration of MATLAB in Personalized Medicine

Integrating MATLAB into personalized medicine for dosage optimization holds promise in improving treatment outcomes. MATLAB's computational power can analyze

patient-specific data, like genetic profiles and clinical parameters, to develop personalized dosage algorithms. By simulating drug behavior in the body and considering factors like age and genetics, MATLAB can predict optimal dosages that maximize efficacy while minimizing adverse effects. Its machine learning tools can identify optimal dosage strategies for different patient populations, adapting to changing needs. Integration with other tools and databases enables comprehensive analysis, empowering healthcare providers to make informed, personalized treatment decisions. Overall, MATLAB facilitates tailored treatment strategies that enhance patient care in personalized medicine.

2.8 INHERITANCE PATTERNS OBSERVED IN AE

Research has shown that genetic factors play an important role in the development of atopic eczema. Studies have shown, those individuals with a family history of atopic eczema or other atopic diseases, such as asthma and allergic rhinitis, are more likely to develop the condition themselves. Additionally, genome-wide association studies (GWAS) have identified specific genetic variations associated with an increased risk of atopic eczema. A 2015 study found that the chance of inheriting eczema is approximately 75%^{Trusted Source}. Genes carry information that contains instructions to make proteins. Every person will have two copies of each gene, one from each parent. A person may inherit mutated genes from one or both of their parents, which increases their chance of developing eczema. Certain genes, such as CARD11, KIF3A, and FLG, have been involved in the development of atopic eczema. Mutations in the CARD11 gene, essential for lymphocyte function, weaken the immune system and may lead to eczema. Studies have identified five CARD11 mutations associated with the condition. Additionally, genetic variations in KIF3A, involved in protein binding and transport, contribute to a weakened skin barrier, increasing water loss and eczema risk. FLG gene mutations, affecting Pro filaggrin and filaggrin protein production, are strongly linked to eczema, with 20–30% of patients exhibiting FLG mutations. Eczema severity is often heightened in individuals with mutations in both copies of the FLG gene. These findings suggest that atopic eczema can be inherited, with certain genetic

predispositions increasing susceptibility to the condition. However, it's important to note that genetics alone may not fully determine an individual's risk of developing atopic eczema, as environmental factors also play a significant role in its onset and severity. Therefore, research into the inheritance patterns of atopic eczema involves understanding the complex interplay between genetic and environmental factors in disease development.

CHAPTER 3

AIM AND OBJECTIVE

3.1 AIM

- Proposal aims to identify specific genes responsible for a patient's eczema for highly targeted and effective treatment plans.
- This approach improves patient outcomes by reducing trial-and-error approaches and minimizing unnecessary medication use.
- Use of MATLAB program for treatment prediction offers efficiency and potentially faster customization based on latest research.
- Developing and validating the accuracy of genetic tests to pinpoint causative genes is crucial for this approach

3.2 OBJECTIVE

- Atopic eczema (AE), or atopic dermatitis, is a common skin condition characterized by dry, itchy, cracked, inflamed skin.
- Approximately 1 in 10 people will develop eczema in their lifetime.
- Main treatments for AE include emollients (moisturizers), topical corticosteroids, and antihistamines.
- These treatments offer some relief but provide a generalized approach, challenging the treatment of varying severities of AE.
- Proposal to develop a personalized medicine approach for AE treatment.
- This approach leverages a patient's unique genetic makeup to identify causative genes contributing to their specific eczema phenotype (severity and characteristics).
- By analyzing these genes, the goal is to design a computational program using MATLAB to predict optimal treatment regimens for individual patients aligned with current research on AE therapeutics.

CHAPTER 4

MATERIALS AND METHODOLOGY

4.1 PATIENT SAMPLE COLLECTION AND MUTATION ANALYSIS

Genomic DNA extracted from mouthwash samples using standard methods and was subjected to mutation analysis for the FLG gene mutations R501X and 2282del4. For the R501X mutation, the presence of the mutation was screened using a new NlaIII restriction enzyme site created by the mutation, following a previously described method (Smith *et al.*, 2006). Additionally, genotyping for the R501X mutation was performed using a TAQMAN-based allelic discrimination assay (Palmer *et al.*, 2006). For the 2282del4 mutation, an 811 bp PCR fragment of genomic DNA was amplified using forward primer RPT1P7 and reverse primer RPT2P1 (Smith *et al.*, 2006). The 2282del4 mutation creates a new DraIII restriction enzyme site, which was utilized to screen samples for this mutation. Moreover, genotyping for the 2282del4 mutation was conducted by sizing a fluorescent-labeled PCR fragment on an Applied Biosystems 3100 or 3730 DNA sequencer (Palmer *et al.*, 2006).

Table 4.1: Oligonucleotide sequences of primers for PCR target regions of FLG gene

Genome region	Primer direction	Nucleotide sequence 5'–3'
2282delACTG	direct	TGGTAGTCAGGCCACTGACAGTG
	reverse	GGTGACCAGCCTGTCCATGG
R501X	direct	GACCTATTACCGATTGCTCGTGG
	reverse	GGACGTTTCAGGGTCTTCCTCT

4.2 DUPILUMAB (DUPIXENT®)

Atopic dermatitis commonly presents with dry, itchy skin, often starting in infancy and potentially persisting into adulthood. While the exact cause remains elusive, a

combination of genetics, like mutations in the filaggrin gene, and environmental factors such as pollutants are thought to contribute. The telltale signs of AD can vary depending on age, with redness, swelling, and scaly patches appearing on the face, limbs, and flexural areas in children, and hands and feet in adults. Fortunately, there are ways to manage this condition. During inactive periods, consistent use of thick moisturizers helps prevent flare-ups. When flare-ups occur, characterized by heightened dryness, itching, and inflammation, treatment involves topical medications like steroids or calcineurin inhibitors, alongside identifying and avoiding triggers like irritants and allergens.

Dupilumab offers a targeted approach to managing Atopic Dermatitis by interrupting the inflammatory cycle at its source. This medication acts as a specialized antibody that binds to interleukin-4 (IL-4) and interleukin-13 (IL-13), key players in the inflammatory response. By blocking these interleukins, Dupilumab effectively hinders the release of various inflammatory molecules, including those responsible for itching and allergic reactions. While the precise mechanism by which Dupilumab translates to symptom relief remains under investigation, its ability to neutralize these inflammatory signals is likely the root cause of its effectiveness. This pharmacological section delves deeper into the technical aspects of Dupilumab's action within the body. It details how the drug is absorbed and distributed throughout the system, reaching peak concentration within a week of the initial dose. The dosing frequency is then adjusted to maintain consistent levels in the bloodstream, maximizing its therapeutic effect. Furthermore, the passage explores how the body eliminates Dupilumab, providing a comprehensive picture of the drug's pharmacokinetic profile.

Clinical trials tested Dupilumab's effectiveness in over 2,100 adults with severe eczema unresponsive to usual treatments. Three studies compared Dupilumab injections to placebo, with one also including topical steroids. After 16 weeks, significantly more patients on Dupilumab achieved clear or almost clear skin, along with substantial improvement in eczema and itch scores. This treatment also led to reduced anxiety, depression symptoms, better sleep, and improved quality of life for patients.

Standard Dosage: Adults: Initial dose of 600mg (two 300mg injections) followed by 300mg every other week.

Table 4.2: The effect of Dupilumab drug

	Dupilumab Monotherapy				Dupilumab + Topical Steroids	
	Trial 1 (SOLO 1)		Trial 2 (SOLO 2)		Trial 3	
	Placebo	Dupilumab	Placebo	Dupilumab	Placebo + TCS	Dupilumab + TCS
IGA score 0 or 1	10%	38%	9%	36%	12%	39%
EASI-75 ⁺	15%	51%	12%	44%	69%	23%
Peak pruritus numerical-rating scale (NRS) score (> 4-point improvement)	12%	41%	36%	10%	20%	59%

EASI = Eczema Area and Severity Index; IGA = Investigator's Global Assessment; TCS = topical corticosteroids.

⁺An improvement from baseline of at least 75% on the Eczema Area and Severity Index.

4.3 COMBINATION OF MATLAB AND PYTHON

The combination of MATLAB and Python played a pivotal role in the development of our program for determining drug dosages tailored to different eczema mutations. MATLAB's robust numerical computation capabilities were harnessed to implement complex algorithms for interpreting genetic data and calculating optimal drug dosages. Leveraging MATLAB's computational power allowed us to efficiently handle the intricate mathematical models required for this task. Meanwhile, Python's extensive libraries for data manipulation and visualization complemented MATLAB's strengths, providing additional flexibility and functionality. By integrating MATLAB scripts with Python using appropriate interfaces, such as MATLAB Engine for Python, we seamlessly exchanged data between the two languages, enabling a cohesive workflow. This synergy between MATLAB and Python enabled us to harness the strengths of each language, resulting in a comprehensive program that delivers accurate and personalized drug dosage recommendations for eczema patients based on their specific genetic mutations.

4.4 PROGRAM FOR DETERMINING THE DRUG DOSAGES

To develop a program for determining drug dosages tailored to specific eczema mutations such as RX501 single mutation, RX501 double mutation, 2284del4 single mutation, and 2284del4 double mutation, we employed a combination of MATLAB and Python scripting languages. We gathered genetic data on eczema mutations from reliable sources and structured it into a suitable format for analysis. This included information on mutation types, patient characteristics, and corresponding drug

responses. MATLAB was utilized for its powerful numerical computation capabilities. We developed algorithms to interpret the genetic data and calculate optimal drug dosages based on mutation types. This involved implementing mathematical models that consider mutation severity, patient-specific factors, and drug efficacy profiles.

While MATLAB excels in numerical computation, Python offers extensive libraries for data manipulation and visualization. To leverage the strengths of both languages, we integrated MATLAB scripts with Python using appropriate interfaces such as MATLAB Engine for Python. This allowed seamless data exchange and enhanced the overall functionality of the program. Depending on the project requirements, we designed a user-friendly interface using MATLAB's GUI development tools or Python frameworks like Tkinter or PyQt. This interface facilitated easy input of patient data and mutation types, and provided intuitive displays of calculated drug dosages.

Rigorous testing procedures were conducted to validate the accuracy and reliability of the program. We employed synthetic datasets representing diverse mutation scenarios, as well as real-world patient data where available, to assess the performance of the algorithms across different use cases.

Continuous optimization efforts were made to enhance the efficiency and robustness of the program. This involved fine-tuning algorithm parameters, optimizing computational workflows, and addressing any identified limitations or bottlenecks.

Comprehensive documentation was prepared to aid users in understanding the program functionality, input requirements, and interpretation of results. Once finalized, the program was deployed for practical use, either as a standalone application or as a component within a broader healthcare system.

4.5 CODE GENERATED FOR THE PROGRAM

A combination of MATLAB and Python programming languages were used for the creation of our dosage determining program.

Initially the code was made using Python, by using the advantage of its extensive libraries for data handling and processing. Through python, we constructed the initial logic for interpreting genetic data and calculating drug dosages tailored to eczema mutations.

The code was made such that the PCR result is provided as the input by the front end and the output generated would be the provision of recommended dosages that are applicable for the type of eczema mutation the patient has been diagnosed with. Once the code was successful in python, the same code was modified according to the MATLAB language, and the code was generated for our application.

As our project progressed it became evident that MATLAB's specialized tools for numerical computation and algorithm development could enhance the performance and efficiency of the program. The python code was adapted to MATLAB, ensuring compatibility with MATLAB's syntax and conventions. Once the MATLAB code was finalized, it was integrated into the project and MATLAB's runtime environment was utilized to execute the code and generate precise drug dosage recommendations based on eczema mutations.

Code of input code generator in Python:

```
def assess_patient_by_pcr(pcr_result):
    if pcr_result == "RX501 - single mutation":
        easi_score_classification = "Mild Eczema"
        drug_concentration = "Low concentration"
        administration_frequency = "Once daily"
    elif pcr_result == "RX501 - double mutation":
        easi_score_classification = "Moderate to Severe Eczema"
        drug_concentration = "Medium concentration"
        administration_frequency = "Twice daily"
    elif pcr_result == "2282DEL4 - single mutation":
        easi_score_classification = "Moderate Eczema"
        drug_concentration = "Medium concentration"
        administration_frequency = "Twice daily"
    elif pcr_result == "2282DEL4 - double mutation":
        easi_score_classification = "Severe Eczema"
        drug_concentration = "High concentration"
        administration_frequency = "Three times daily"
    else:
```

```

easi_score_classification = "Unknown"
drug_concentration = "Not determined"
administration_frequency = "Not determined"

return easi_score_classification, drug_concentration, administration_frequency

# Getting PCR result from user input
pcr_input = input("Enter the PCR result ")

# Call function to assess patient based on PCR result
result_classification, drug_conc, admin_freq = assess_patient_by_pcr(pcr_input)

# Output the result
print("\nEczema classification:", result_classification)
print("Concentration of drug:", drug_conc)
print("Frequency of administration:", admin_freq)

```

The program operates based on the PCR results of the patient, specifically identifying whether the mutation is RX501 single mutation, RX501 double mutation, 2284del4 single mutation, 2284del4 double mutation.

Upon receiving this input, the program utilizes predefined algorithms and computational models to determine the optimal drug dosage for eczema treatment tailored to the specific mutation type. Once the calculations are complete the program generates a recommendation for the required dosage, providing precise guidance for the treatment regime.

Code of input code generator in MATLAB:

The screenshot shows the MATLAB IDE with the 'assess_patient_by_pcr' function code. The code is as follows:

```

1 function [easi_score_classification, drug_concentration, administration_frequency] = assess_patient_by_pcr(pcr_result)
2     if strcmp(pcr_result, 'RX501 - single mutation')
3         easi_score_classification = 'Mild Eczema';
4         drug_concentration = 'Low concentration';
5         administration_frequency = 'Once daily';
6     elseif strcmp(pcr_result, 'RX501 - double mutation')
7         easi_score_classification = 'Moderate to Severe Eczema';
8         drug_concentration = 'Medium concentration';
9         administration_frequency = 'Twice daily';
10    elseif strcmp(pcr_result, '2282DEL4 - single mutation')
11        easi_score_classification = 'Moderate Eczema';
12        drug_concentration = 'Medium concentration';
13        administration_frequency = 'Twice daily';
14    elseif strcmp(pcr_result, '2282DEL4 - double mutation')
15        easi_score_classification = 'Severe Eczema';
16        drug_concentration = 'High concentration';
17        administration_frequency = 'Three times daily';
18    else
19        easi_score_classification = 'Unknown';
20        drug_concentration = 'Not determined';
21        administration_frequency = 'Not determined';
22    end
23 end
24
25 % Getting PCR result from user input
26 pcr_input = input('Enter the PCR result ', 's');

```

Figure 4.5.1 MATLAB code for determining drug dosage

The screenshot shows the MATLAB IDE with the main script code. The code is as follows:

```

24
25 % Getting PCR result from user input
26 pcr_input = input('Enter the PCR result ', 's');
27
28 % Call function to assess patient based on PCR result
29 [result_classification, drug_concentration, admin_frequency] = assess_patient_by_pcr(pcr_input);
30
31 % Output the result
32 fprintf('\nEczema classification: %s\n', result_classification);
33 fprintf('Concentration of drug: %s\n', drug_concentration);
34 fprintf('Frequency of administration: %s\n', admin_frequency);
35

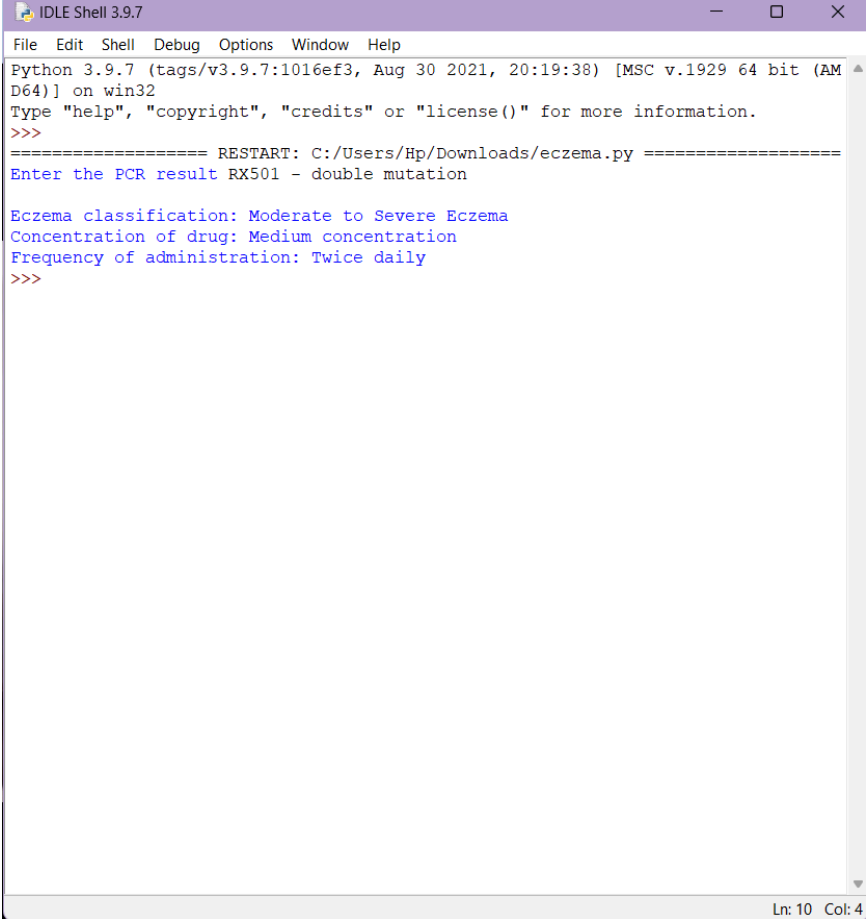
```

Figure 4.5.2 MATLAB code for determining drug dosage

CHAPTER 5

RESULTS AND DISCUSSION

5.1 OUTPUT GENERATED USING PYTHON



The image shows a screenshot of a Python IDLE Shell window. The window title is "IDLE Shell 3.9.7". The menu bar includes "File", "Edit", "Shell", "Debug", "Options", "Window", and "Help". The shell displays the following text:

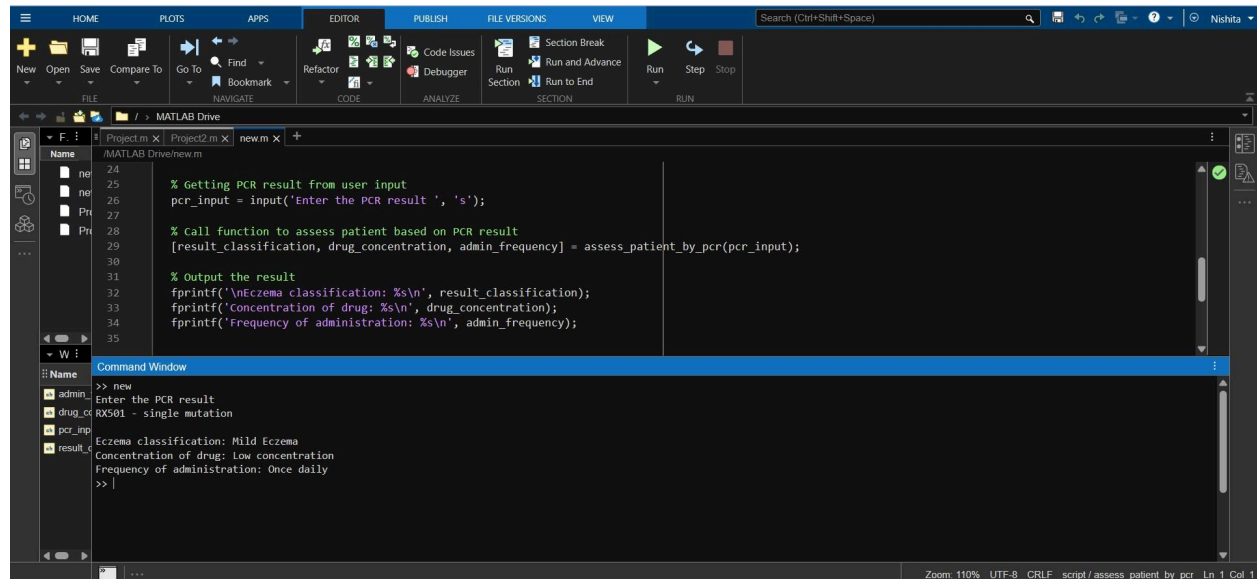
```
Python 3.9.7 (tags/v3.9.7:1016ef3, Aug 30 2021, 20:19:38) [MSC v.1929 64 bit (AMD64)] on win32
Type "help", "copyright", "credits" or "license()" for more information.
>>>
===== RESTART: C:/Users/Hp/Downloads/eczema.py =====
Enter the PCR result RX501 - double mutation

Eczema classification: Moderate to Severe Eczema
Concentration of drug: Medium concentration
Frequency of administration: Twice daily
>>>
```

The status bar at the bottom right indicates "Ln: 10 Col: 4".

Figure 5.1.1 Output obtained in Python

5.2 OUTPUT GENERATED USING MATLAB



The image shows the MATLAB IDE interface. The main editor window displays a script with the following code:

```
24  
25 % Getting PCR result from user input  
26 pcr_input = input('Enter the PCR result ', 's');  
27  
28 % Call function to assess patient based on PCR result  
29 [result_classification, drug_concentration, admin_frequency] = assess_patient_by_pcr(pcr_input);  
30  
31 % Output the result  
32 fprintf('\nEczema classification: %s\n', result_classification);  
33 fprintf('Concentration of drug: %s\n', drug_concentration);  
34 fprintf('Frequency of administration: %s\n', admin_frequency);  
35
```

The Command Window at the bottom shows the execution output:

```
>> new  
admin: Enter the PCR result  
drug_Cf RX501 - single mutation  
pcr_inp  
result: Eczema classification: Mild Eczema  
Concentration of drug: Low concentration  
Frequency of administration: Once daily  
>> |
```

Figure 5.2.1 Output obtained in MATLAB

Mutations in the FLG gene are closely associated with eczema, with specific mutations like R501X and 2282del4 being particularly linked to the condition. The FLG gene encodes filaggrin, a protein crucial for forming the skin's barrier and inhibiting the entry of microbes and allergens. When the FLG gene is mutated, the production of filaggrin is affected, leading to a weakened skin barrier that allows allergens and irritants to penetrate the skin more easily. This can result in the development of eczema.

Having a double mutation in the FLG gene is associated with more severe cases of eczema compared to having a single mutation or no mutation. While FLG mutations themselves do not directly regulate the activity of interleukins (ILs) like IL-4 and IL-13, which are overproduced in eczema, the compromised skin barrier caused by FLG deficiency can influence how the immune system responds. Studies suggest that skin lacking proper filaggrin might be more sensitive to the effects of IL-4 and IL-13, leading to a more pronounced inflammatory response. Therefore, FLG mutations and IL activity play somewhat independent but interconnected roles in the development and severity of eczema, with FLG mutations affecting the skin barrier and IL activity contributing to inflammation and immune system activation in the skin.

PCR analysis determined whether the patient had a single or double mutation of R501X or 2282del4 for the FLG gene. By using the result obtained from the PCR analysis about the type of mutation present in the eczema patient, a program was created to provide tailored drug dosage recommendations. The MATLAB program developed in this study encompasses four distinct scenarios based on the presence of single or double mutations in the R501X or 2282del4 genes, as determined by PCR analysis. For each scenario, the program calculates the classification of eczema severity, the optimal concentration of drug required for the patient, and the recommended frequency of administration. The calculated ranges aim to target the skin barrier effectively and indirectly reduce interleukin (IL) activity. It is important to note that the ranges provided in the program are based on assumptions due to the lack of access to clinical data studies specifically addressing this aspect of treatment optimization. While past research has explored the link between FLG mutations and atopic eczema, as well as the effectiveness of dupilumab in treating the condition, your project offers a unique approach. Our focus is on personalized medicine, using a MATLAB program to analyze individual FLG mutations and recommend tailored concentrations of dupilumab for each patient. This goes beyond past decisions about dupilumab use and leverages automation for a more precise treatment approach.

The future of personalized medicine for eczema holds immense potential for revolutionizing healthcare delivery. Precision prevention strategies, focusing on identifying and mitigating individual disease risk factors before symptoms manifest, are set to reduce disease burden. Predictive modeling, utilizing genetic, environmental, and lifestyle data, aims to tailor interventions to each person's unique risk profile. Integration of artificial intelligence (AI) and big data analytics will further advance personalized medicine research and practice. In this envisioned future, individuals will have control over their health data, empowering informed decision-making, while healthcare providers seamlessly integrate research into practice. Multidisciplinary teams will collaborate, and healthcare education will emphasize interdisciplinary aspects. Equitable access to personalized medicine services will be ensured, with secure data flow and privacy measures in place. Electronic health records will enable more efficient personalized medicine, fostering economic value and job creation in healthcare.

CHAPTER 6

SUMMARY AND CONCLUSION

The integration of MATLAB and Python programming has been instrumental in creating a program capable of determining optimal drug dosages tailored to specific eczema mutations. By analyzing the genetic makeup of patients with eczema, particularly mutations in the FLG gene, this approach aims to provide more targeted and effective treatment plans. Mutations in the FLG gene, such as R501X and 2282del4, are closely associated with eczema, impacting the production of filaggrin, a crucial protein for skin barrier formation. This can lead to a weakened skin barrier, allowing allergens and irritants to penetrate more easily, thus contributing to the development of eczema. Having a double mutation in the FLG gene is associated with more severe cases of eczema compared to having a single mutation or no mutation. While FLG mutations themselves do not directly regulate the activity of interleukins (ILs) like IL-4 and IL-13, which are overproduced in eczema, the compromised skin barrier caused by FLG deficiency can influence how the immune system responds. Studies suggest that skin lacking proper filaggrin might be more sensitive to the effects of IL-4 and IL-13, leading to a more pronounced inflammatory response. The program's ability to predict ideal drug concentrations based on genetic data represents a significant advancement in eczema treatment, potentially reducing the need for trial-and-error approaches, minimizing unnecessary medication use, and avoiding cases of over- or underdosing. Future work will focus on further refining the program, including a larger range of subsets, and conducting clinical trials to validate its effectiveness in real-world settings. The future of personalized medicine is poised for transformative growth, with innovative approaches that can revolutionize healthcare. Precision prevention, focusing on identifying and mitigating individual disease risk factors before symptoms appear, is a key area of development. Predictive modeling, which uses genetic, environmental, and lifestyle data to tailor interventions, aims to reduce disease burden. Integration of artificial intelligence (AI) and big data analytics is set to revolutionize personalized medicine research and practice. In this future vision, individuals have control over their health data, enabling

informed decision-making. Accessible medical information empowers individuals, while healthcare providers seamlessly integrate research into practice.

Ultimately, our research proposes a personalized medicine approach for the treatment of atopic eczema, focusing on leveraging the unique genetic makeup of each patient to design optimal treatment regimens. By analyzing specific genes associated with eczema severity and characteristics, we aim to develop a computational program using MATLAB to predict personalized drug dosages. This approach offers a promising avenue for improving patient outcomes by reducing trial-and-error approaches and minimizing unnecessary medication use. The combination of MATLAB and Python proved to be instrumental in developing a comprehensive program that delivers accurate and personalized drug dosage recommendations for eczema patients based on their specific genetic mutations.

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