

Masters Thesis

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APPROVAL OF THESIS

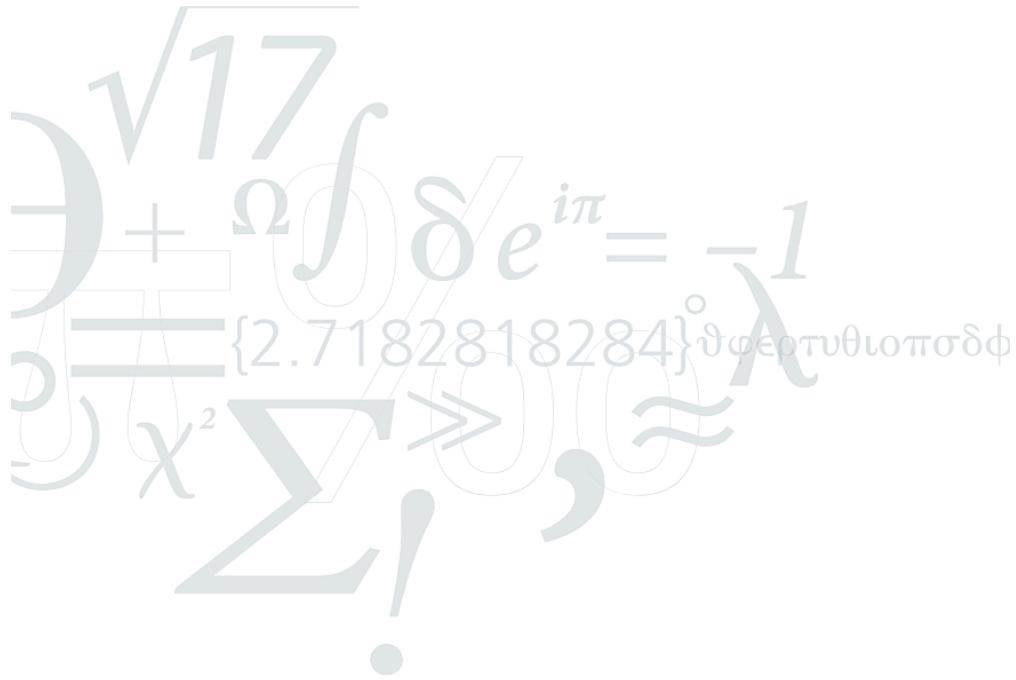
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Thesis Approval Date: Friday 27th June 2025

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STATEMENT OF THESIS ORIGINALITY

Declaration of Authorship

I, Miss Oriade Latifah Simpson, hereby declare that the present master's thesis is my own original work and has been written independently. This thesis has not been submitted, either in whole or in part, for the award of any academic degree or qualification at any other institution.

All sources of information and ideas that are not my own have been appropriately acknowledged and referenced. I affirm that this work complies with the ethical and academic standards required for submission at the Technical University of Denmark.

This thesis is submitted in partial fulfilment of the requirements for the Master's Programme at the Department of Health Technology, Technical University of Denmark.

Abstract

This section provides a concise summary of the research, including the central research question, the methodology employed, key findings and the main conclusions drawn from the analysis. The abstract does not exceed 500 words. It consists of 3 paragraphs each of which contains research problems and objectives research method and research results. The abstract is typed italicised.

The keywords related to the thesis are listed. (Write this at the end.)

Acknowledgements

First and foremost, I would like to express my deepest gratitude to my mother, Veronika Quintyne, for her unwavering support and encouragement throughout my academic journey. Her belief in me has been a constant source of strength.

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A detailed outline of all major sections and subsections, accompanied by page numbers for ease of navigation throughout the thesis.

Chapter I

INTRODUCTION

1.1 Background of the Problem

The rationale facts and observations that are important. The research problem and why the research problem is important and needs to be researched. Apply new knowledge from the program and present a piece of work that involves thinking. The subject should relate to the program and specific specialisation.

Set the scene and motivate the problem being studied. It describes a domain and indicates a problem in general terms.

What is the general area being addressed? What is the motivation for studying a particular problem?

What makes it worth the effort?

Is it a real problem in everyday life?

Is it a theoretical problem that is worth solving?

Would anyone care if I solved this?

1.2 Formulation of the problem

The situation or phenomenon that needs to be solved and requires an answer through thorough research and in depth thinking using scientific tools.

The research has a sense of clarity and authenticity and it is in line with the research objectives it is an important matter and worthy of research and it provides implications for empirical studies. It is supported by primary or secondary data. Based on the research problem research questions can be formulated.

1.3 Objective and Benefits of the Research

The research objectives reveals the results to be achieve through the research process. The research objective answers the research problem and reflects the scope of the research, the methods used and the expected results.

1.4 Systematics of Writing

A brief description of the things in each chapter.

This thesis is submitted in fulfilment of the requirements for a master's degree in bioinformatics and serves as a demonstration of advanced research competences. It aims to exhibit the ability to define a clear research question, conduct a comprehensive review of the literature and apply appropriate research methodologies.

The objective of this study is to critically evaluate existing academic work in the field and to contribute new insights or perspectives that may advance scholarly understanding or have practical relevance.

The thesis presents an opportunity to dive deeply into a specific topic and enhance my expertise and understanding of that area. This process has also provided an opportunity for the development of academic communication skills, both written and oral, as a part of preparing, presenting and defending the thesis findings.

Through the formulation of a coherent research narrative and the integration of evidence based conclusions, this thesis seeks to generate original contributions with the chosen area of inquiry.

The master's thesis contributes original knowledge or insights to a specific discipline which can be beneficial for academic and practical applications.

Chapter II

LITERATURE REVIEW

Reviews existing research related to the topic, highlighting gaps that your study aims to address.

The literature review contains the theoretical basis and discussion of the results of previous similar studies. A framework of thought and hypothesis can also be put forward.

2.1 Theoretical Foundations and Previous Research

The theories supporting the hypothesis are said. The research problem has not been answered or solved satisfactorily.

What is the research context and discipline the thesis fits within?

Who has looked at this area before?

What is the state of the art of methods and solution to the problem?

What other work complements this research ?

2.2 Framework

The problems to be studied are explained. There is a research hypothesis. This explanation is included in the form of a schematic to clarify the purpose of the study. This is a series of thought arrangements about what should happen so the intended hypothesis arises.

2.4 Hypotheses | Problem Statement | Research Question

The hypothesis is a short statement that is concluded from the literature review and it is a temporary answer to the problem under study. The hypothesis is supported by theories or references from previous studies.

This is a statement of the hypothesis and problems. The hypothesis is the highest level problem or goal you are going to address.

The problems should be unambiguous. The importance of the problem should be mentioned if it was not already done so. You can develop a new approach for solving a well known problem or replicate a method in the literature.

Data Collection Method of Analysis

Hypothesis I: Analysing the genomic sequence of *Streptococcus pyogenes* (GAS) can reveal key virulence factors and their regulation mechanisms, providing insights into potential targets for vaccine development and therapeutic interventions.

Hypothesis II: Determine the structure of the M Protein?

The Skin

The Function of the Skin

The skin is the largest organ of the human body and is comprised of a diverse array of specialised cell types. It serves as a critical barrier that protects the internal organs from bacteria invasion, environmental pathogens, ultraviolet (UV) radiation and various biochemical agents. In addition to its protective role, the skin plays a fundamental part in thermoregulation by modulating body temperature and enabling adaptation to fluctuating environmental conditions. [1]

Furthermore, the skin facilitates the excretion of sweat, sebum, and metabolic waste products through its glandular structures [1]. It possesses wound-healing capabilities, allowing for the repair of abrasions, lacerations and other forms of tissue injury [1]. The subcutaneous fat layer functions as a mechanical cushion, providing shock absorption and an additional line of defence against infection [1].

The skin also contributes to endocrine function through its role in the synthesis of vitamin D upon exposure to UV radiation [1]. Additionally, it plays a vital sensory role, continuously transmitting information to the central nervous system regarding the external environment [2]. The skin is integrated with the nervous system to enable the perception of thermal stimuli, tactile sensations, and other sensory inputs essential for survival and interaction with the environment [1,2].

The Structure of the Skin

The skin is composed of three primary layers: the **epidermis**, the **dermis**, and the **hypodermis** (also known as the subcutaneous fat layer). Each layer performs specific functions essential to maintaining homeostasis, immunity and overall health.

The Epidermis

The **epidermis** is the outermost layer of the skin and is primarily composed of keratinocytes, which are specialised cells responsible for the synthesis of keratin, cytokines, growth factors and interleukins. This layer provides the first line of defence against environmental pathogens and is organised into four distinct strata, arranged from superficial to deep.

- *The Stratum corneum*
- *The Stratum granulosum*
- *The Stratum spinosum*
- *The Stratum basale* (also referred to as the *stratum germinativum* or the basal cell layer).

An illustrative representation of the epidermis is provided below [3].

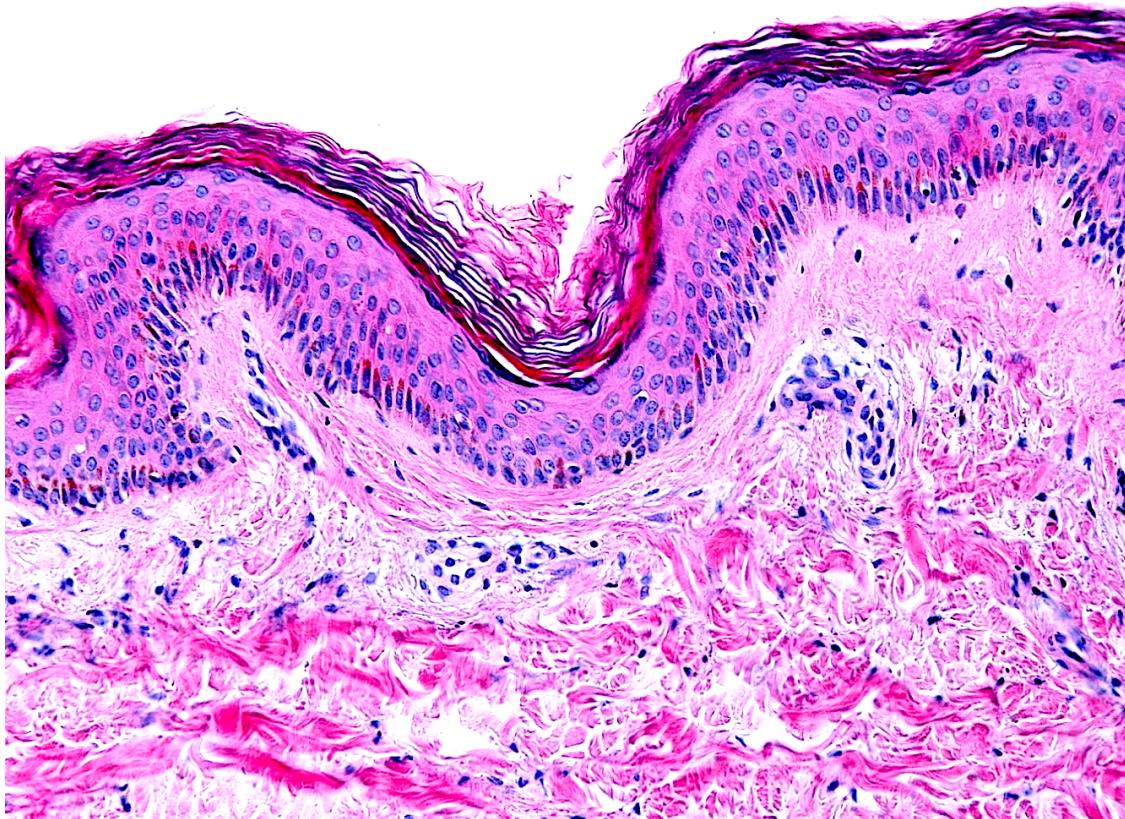


Figure 1: Structure of the epidermis with the different strata, resting on the dermis (Source: Shutterstock.com, Jose Luis Calvo, News Medical 2025)

The **stratum corneum** consists of *terminally differentiated* keratinocytes. Terminally differentiated cells exit the cell cycle as they can no longer divide. The keratinocytes become corneocytes in the stratum corneum. Corneocytes are non-viable, enucleated cells [4].

The corneocytes function to minimise transepidermal water loss and provide protection against mechanical and microbial damage. Keratin produced in the underlying layers accumulates in the corneocytes, which are eventually shed through a natural process known as desquamation.

The skin surface is interspersed with pores, which serve as conduits for the excretion of sweat and sebum via eccrine and sebaceous glands, respectively [2].

The **stratum spinosum**, or *prickle cell layer*, lies above the stratum basale and consists of keratinocytes connected by desmosomes, which provide structural support. In this layer, keratinocytes begin producing cytokeratins that form tonofibrils. Langerhans cells, involved in immune defence, are also present in this layer.

The **stratum granulosum** contains flattened keratinocytes that undergo terminal differentiation. Keratinocytes accumulate keratohyalin granules, involved in keratin aggregation, and lamellar bodies, which secrete lipids that form a barrier to water loss. Keratinocytes in this layer begin to lose their nuclei and organelles as they prepare for transformation into dead corneocytes of the uppermost layer ;the stratum corneum.

The **stratum basale** (or stratum germinativum) is the deepest layer of the epidermis and plays a central role in skin regeneration. This layer has mitotically active keratinocytes, which divide to replenish the upper layers. In addition to keratinocytes, several other specialised cells are found within this layer :

- **Melanocytes**, which produce melanin, the pigment responsible for skin colour and protection against ultraviolet (UV) radiation [4].
- **Langerhans Cells**, (LCs) a type of dendritic cell (DC) that originate from hematopoietic stem cells in the bone marrow. They have a role in immune surveillance by recognising antigens and initiating T-cell responses [4].
- **Merkel cells**, which are mechanoreceptors involved in the sensation of touch.
- **Dendritic cells**, which also play a defence role in the immune response as they differentiate into macrophages [4].

Within the **stratum basale** UV radiation stimulates the conversion of provitamin D_3 into pre-vitamin D_3 that initiates the cutaneous synthesis of vitamin D. Subsequent hydroxylation in the liver and kidneys leads to the production of the active form of vitamin D [4].

The epidermis is not only a structural barrier but also a site of pathological relevance. Several dermatological and systemic conditions occur in this layer including **seborrhoeic dermatitis** (dandruff), **psoriasis**, **atopic dermatitis** (eczema), melanoma, **acne vulgaris** , **actinic keratosis** and pressure ulcers (decubitus ulcers) [2].

The Dermis

The dermis is the middle layer of the skin, situated beneath the epidermis, and serves as the primary site of structural and functional support. It contains many essential components including blood vessels such as capillaries [4], lymphatic vessels, sweat glands, sebaceous glands, hair follicles, nerve endings, and specialised sensory receptors. The dermis is primarily composed of **collagen** and **elastin**, two fibrous proteins that confer tensile strength and elasticity, respectively.

The dermis is subdivided into two distinct layers:

- **The papillary dermis**, the superficial layer, which is composed of loose connective tissue and contains capillaries and sensory neurons.
- **The reticular dermis**, the deeper layer, composed of dense irregular connective tissue rich in collagen and elastin fibres, glands, hair follicles, and larger blood vessels.

The dermis contains sweat glands, sebaceous glands, blood vessels, lymphatic vessels, and other structures critical to skin function. These glands play essential roles in thermoregulation, lubrication, and excretion. The eccrine glands are responsible for sweat production, while the sebaceous glands secrete sebum to maintain skin hydration and barrier function. Both are embedded within the dermal layer and are regulated by hormonal and neural signals.

The dermis contains sweat glands, sebaceous glands, blood vessels, lymphatic vessels, and other structures critical to skin function. These glands play essential roles in thermoregulation, lubrication, and excretion. The eccrine glands are responsible for sweat production, while the sebaceous glands secrete sebum to maintain skin hydration and barrier function. Both are embedded within the dermal layer and are regulated by hormonal and neural signals.

Fibroblasts, the predominant cell type in the dermis, are responsible for synthesising collagen proteins, and other components of the extracellular matrix, which maintains the structural framework of connective tissues. In addition to their structural role, fibroblasts are actively involved in **wound healing** through production of signalling molecules and matrix proteins [5].

Collagen is the most abundant protein in the human body and is found not only in the skin but also in muscles, bones, tendons, ligaments, blood vessels, internal organs and the gastrointestinal lining [6]. The primary amino acids in collagen include glycine, proline and hydroxyproline, which assemble into a characteristic triple-helix structure to form collagen fibrils. The biosynthesis of this structure requires several cofactors, including **vitamin C, zinc, copper and manganese** [6].

Among the specialised mechanoreceptors in the dermis are Meissner's corpuscles and Pacinian corpuscles, which detect mechanical stimuli such as touch, pressure, and vibration. These corpuscles are multicellular structures (of multiple cell types) consisting of a sensory nerve ending surrounded by specialised Schwann cells.

The vascular network within the dermis plays a crucial role in thermoregulation by adjusting blood flow in response to temperature changes [4]. The nerve endings transmit sensory information such as touch, pain, and temperature [4]. Dermal immune cells contribute to the inflammatory response following injury or infection.

The dermis contains a diverse population of cells, including fibroblasts, immune dendritic cells, macrophages, T lymphocytes, mast cells, innate lymphoid cells, neutrophils, eosinophils, and natural killer cells, neuronal cells and endothelial cells [7].

Among the immune cells, T lymphocytes are predominantly located in close proximity to blood vessels, vessels, hair follicles and sweat glands within the dermis. Subsets of T cells perform distinct immunological functions: **Th1 cells** secrete cytokines that enhance the capacity of other immune cells to target and eliminate pathogens; however, dysregulation of Th1 activity may contribute to the development of autoimmune disorders [7]. **Th2 cells** are primarily involved in the mediation of allergic responses. **Th17 cells** play a crucial role in defending against bacterial and fungal infections and are implicated in the pathogenesis of inflammatory skin diseases such as eczema and psoriasis.

In contrast, **regulatory T cells (Tregs)** modulate immune responses by suppressing excessive inflammation through the release of inhibitory signals and by eliminating over-active immune cells, thereby maintaining immune homeostasis with the dermis [7].

Several conditions originate within the dermis, including wrinkles (due to collagen degradation), cellulitis (a bacterial skin infection), dermoid cysts (which may contain hair or teeth), sebaceous cysts, and dermatofibromas.

An illustrative representation of the dermis containing sweat glands, sebaceous glands, blood vessels, lymphatic vessels is shown below[8].

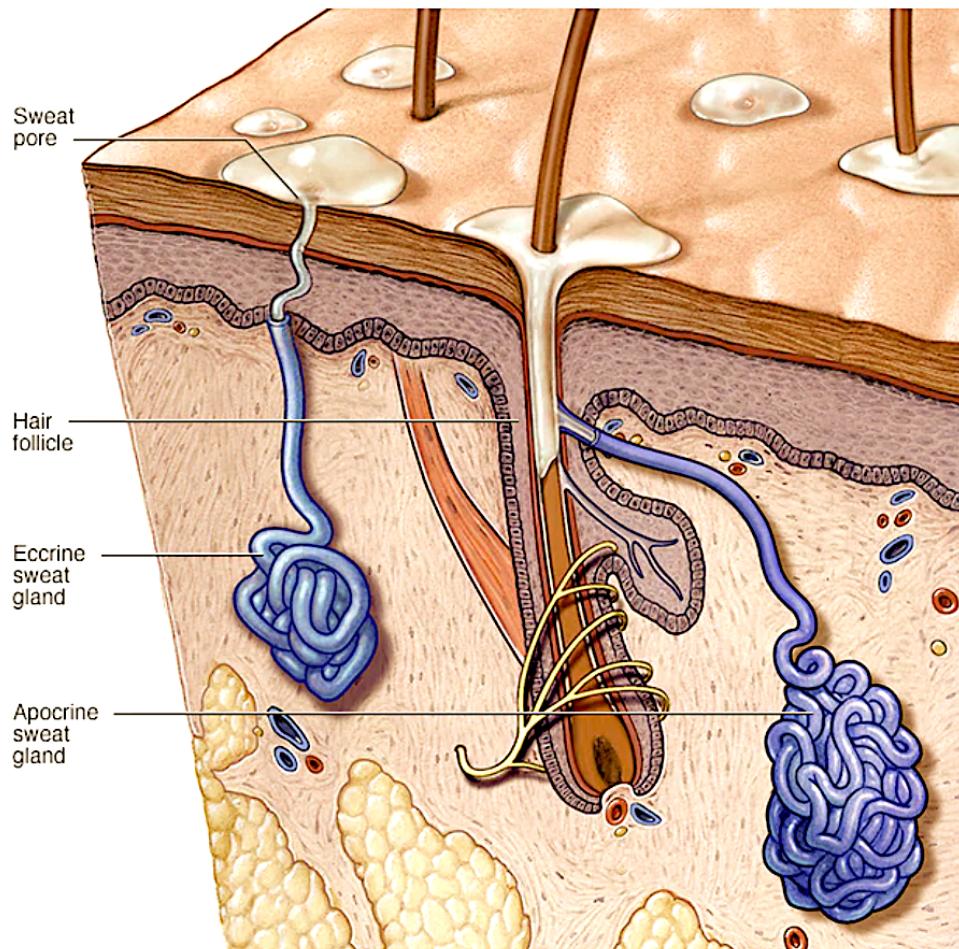


Figure 2: Eccrine & sebaceous glands in the dermis (Source: Mayo Foundation, 2025)

The Hypodermis

The **hypodermis**, also known as the subcutaneous layer of fat, lies beneath the dermis and primarily consists of adipose tissue. This layer is composed of lipocytes that function to insulate the body, maintain thermoregulation, and serve as an energy reserve. The hypodermis also plays a crucial role in absorbing mechanical shock and protecting underlying muscles and organs.

Structurally, the hypodermis includes the following key components:

- Fibroblasts: Cells responsible for the production of collagen [9]. They also regulate the immune response to producing cytokines and chemokines [7].

- Adipose tissue: Specialised are fatty tissues composed of lipocytes [9]
- Connective tissue: A network of collagen and elastin fibres that support and anchors, and gives structure to other tissues[9].
- Blood vessels: Including arteries, veins and capillaries that supply the skin with oxygen rich blood and nutrients, while facilitating thermoregulation [9].
- Lymphatic vessels: Structures involved in maintaining fluid homeostasis and transporting lymph, a fluid containing immune cells and waste products[9].
- Hair follicles: Structures that anchor individual hair shafts and are associated with sebaceous glands and nerve endings.
- Nerve fibres: Sensory neurons the body's sense of position and movement in space.

The hypodermis functions as a supportive and protective layer and has important vascular, immune and sensory roles.

Streptococcus pyogenes

Streptococcus pyogenes: Taxonomy, Morphology & Clinical Relevance

Streptococcus pyogenes is a Gram-positive, anaerobic bacterium commonly referred to as Group A Streptococcus (GAS) [11].

The Gram-positive nature is due to a thick peptidoglycan layer in its cell wall, which retains the crystal violet stain.

Structurally, *S.pyogenes* is characterised by its beta-hemolytic activity, meaning it causes complete lysis of red blood cells on blood agar plates. Morphologically, the cells are small, spherical, and typically arranged in chains, a feature that distinguishes them from other bacterial species [11].

Taxonómically, *S.pyogenes* is classified as follows:

- **Domain:** *Bacteria*
- **Kingdom:** *Bacillati*
- **Phylum:** *Bacillota*
- **Class:** *Bacilli*
- **Order:** *Lactobacillales*
- **Family:** *Streptococcaceae*
- **Genus:** *Streptococcus*
- **Species:** *S.pyogenes* [11]

As a highly adaptable pathogen, *S.pyogenes* is capable of causing a wide range of clinical diseases, from mild superficial infections to severe invasive conditions. Its chain-like cellular arrangement and distinct beta-hemolytic properties are key identifiers in both clinical and microbiological contexts.

Infection of Human Skin

Streptococcus pyogenes is a significant pathogen responsible for a wide spectrum of clinical diseases. Prompt diagnosis and treatment of *S.pyogenes* infections are critical due to the organism's capacity to cause both superficial and systemic illnesses.

Skin infections caused by *S.pyogenes* range from localised conditions such as impetigo to more severe and invasive diseases, including necrotising fasciitis, a life-threatening infection of the deep dermal and subcutaneous tissues [11].

In addition to skin infections, *S.pyogenes* is known to cause pharyngitis, pneumonia, scarlet fever, acute post-streptococcal glomerulonephritis, and the autoimmune condition rheumatic fever. In chronic cases, *S.pyogenes* may also contribute to the development of rheumatic heart disease.

Virulence Factors of Streptococcus pyogenes

Virulence factors are molecules produced by pathogens that facilitate infection, survival and damage within the host. *S.pyogenes* expresses a diverse array of virulence factors that enable its pathogenicity, immune system invasion, and tissue invasion [11].

1. **Capsules** The bacterium produces a capsule that protects it from being engulfed by the host immune cells.
2. **Adherence Factors** Adherence factors (Adhesins), including lipoteichoic acid (LTA) and fibronectin-binding proteins help the bacterium to attach to host epithelial cells and tissues.

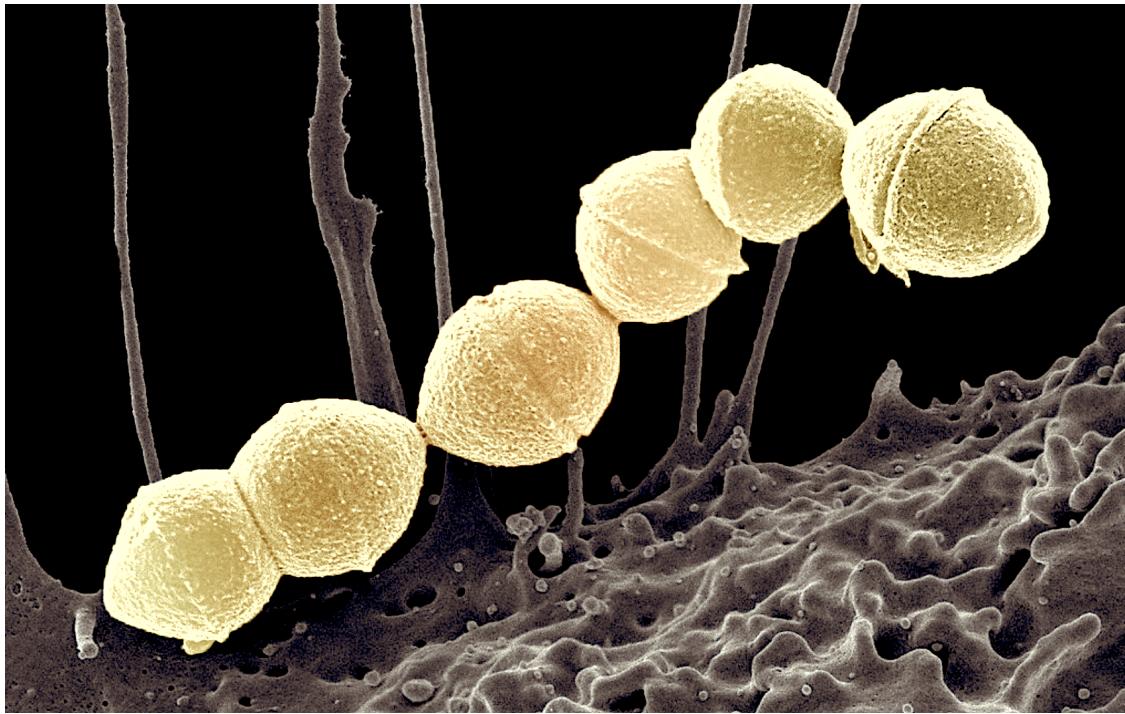


Figure 3: *Streptococcus pyogenes* (Source:National Institute of Allergy and Infectious Diseases (NIAID), Flickr, December 29, 2022)

3. Surface Proteins Surface proteins such as M protein and related members (e.g. Mrp and Enn) play crucial roles in immune evasion. These proteins have variable antigens which allow the pathogen to avoid recognition by the host immune system.

4. Enzymes *S.pyogenes* secretes several enzymes that degrade host tissues and promote bacterial invasion. These include:

- **Streptokinase:** Converts plasminogen to plasmin, aiding in the breakdown of fibrin blood clots.
- **Hyaluronidase:** Degrades hyaluronic acid in connective tissue, facilitating bacterial spread.
- **DNases:** Break down extracellular DNA.

5. Toxins *S.pyogenes* produces streptolysins (SLO and SLS), exotoxins that lyse red blood cells and other host cells. Additionally, streptococcal pyrogenic exotoxins (SPEs) are super-antigens that activate T cells and induce a massive immune response. At least three distinct SPEs have been identified [11].

The M Protein

The M protein is a major virulence factor encoded by the emm gene family, which is present in all *S.pyogenes* strains [10]. These surface-anchored proteins are involved in adherence, immune evasion, and resistance to phagocytosis.

The M protein is considered one of the most important virulence factors.

- **Structure:** The M protein is a coiled-coil molecule anchored in the bacterial membrane, with a highly variable N-terminal region responsible for antigenic diversity.
- **Function:** It interferes with opsonisation and complement activation, making it a key player in immune system evasion. The M-protein changes surface antigens to make it harder for the host to recognise the pathogen.

- **Variants:** M-related proteins such as Mrp and Enn, along with fibronectin-binding proteins, are also expressed and contribute to pathogenicity.

F proteins

F proteins are another group of surface adhesins produced by *S.pyogenes*. These include fibrinogen-binding and fibronectin-binding proteins, which facilitate tight adherence to host tissues and are critical in the early stages of infection.

Streptolysins and Exotoxins

- Streptolysin O (SLO) and Streptolysin S (SLS) are cytolytic toxins that cause hemolysis and contribute to tissue damage during infection.
- Streptococcal pyrogenic exotoxins (SPEs) are potent super-antigens activate T cells and stimulate a massive immune response, often leading to severe systemic symptoms.

Lipoteichoic Acid and Vaccine Targets

Lipoteichoic acid is a key surface molecule involved in adherence and immune activation, and it is under investigation as a potential target for vaccine development [11].

Antimicrobial Resistance

S.pyogenes also harbours genes associated with antimicrobial resistance. Notable among these are:

- **lmrP:** Encodes a multidrug efflux pump
- **tetM and tetL:** Confer resistance to tetracyclines.
- **tgfT:** involved in resistance to specific antimicrobial agents [13].

These resistance genes highlight the need for continuous surveillance and prudent use of antibiotics in treating *S.pyogenes* infections.

Biofilm Formation and Quorum Sensing in *Streptococcus pyogenes*

Biofilms are structured microbial communities encased within a self-produced extracellular matrix. In *Streptococcus pyogenes*, biofilm formation facilitates communication between cells and contributes to bacterial survival, particularly under host immune response and exposure to antibiotics. This communication is mediated by a mechanism known as quorum sensing, which regulates gene expression in response to cell density.

In *S.pyogenes*, one of the key quorum sensing pathways involved in biofilm development is the Rgg2/3 pathway. This pathway controls the expression of genes involved in biofilm formation through the modulation of short hydrophobic peptides, which act as quorum sensing pheromones, also referred to as autoinducers.

Short hydrophobic peptides are initially synthesised in an immature form within the bacterial cell. To become functionally active, these peptides undergo a two-step processing mechanism. First, an intracellular metalloprotease enzyme processes the SHPS. Subsequently, they undergo further processing in the extracellular environment to reach their mature, biologically active form.

The specific transport mechanism responsible for the SHP export and the identity of the extracellular processing factor(s) remain to be elucidated.

The Rgg2/3 pathway is essential for biofilm maturation and plays a central role in *S.pyogenes* pathogenesis, particularly in facilitating persistent infections by enhancing resistance to host immune defences and antimicrobial agents.

MELANOMA

Neural Crest Cells

The most important growth factors that regulate the development of melanocytes from neural crest cells (NCCs) include Endothelins, Stem cell factor (SCF), which is the ligand for the c-Kit receptor, and Wnt proteins and Neuregulin-1 (NRG1) which is a key growth factor.

NRG1 is also important in: Nervous system: Promotes development of Schwann cells (which form the myelin sheath), supports neuron growth, and synaptic plasticity. Heart: Regulates the development of heart muscle and blood vessels. Repair processes: Involved in healing after injury, especially in nerve and heart tissue. Neuregulin-1 (NRG1) = A key growth factor. Acts via: ErbB receptors. Also important for: Nervous system and heart development.

Other key signaling pathways involved in melanocyte development include: The MAPK (mitogen-activated protein kinase) pathway

MAPK stands for Mitogen-Activated Protein Kinase. It's a signalling pathway , a series of protein interactions inside a cell, that responds to external signals (like growth factors) and tells the cell what to do.

In melanocyte development, the MAPK pathway helps control cell survival (preventing cell death, Proliferation (making more cells), Differentiation (developing into mature melanocytes).

The MAPK pathway is activated when growth factors like Stem Cell Factor (SCF) bind to receptors such as c-Kit on the surface of melanoblasts. This triggers a chain reaction inside the cell that leads to activation of proteins like ERK, which then move to the nucleus and turn on specific genes needed for melanocyte development and melanin production.

Chapter III

RESEARCH METHODS

3.1 Types and Sources of Data

3.2 Methods of Collecting Data

3.3 Methods of Analysis This section describes the techniques of analysis and the mechanism for using tools in research.

The job is to translate the problems into research goals and briefly indicate how you will solve the problem and which method you will use to solve it.

It is important to have clear goals.

You have to accomplish your goals in the thesis.

Chapter IV

RESULTS AND ANALYSIS

Presents the findings of the research often with charts and graphs to illustrate data. The GUI created look like this, but I have to get it to scan the image properly, and also take in the real time data correctly.

4.1 Data Analysis

This is the results of the data processing according to the analytical tools and techniques.

Where do you get your data?

Complete genome sequences of the type strain of *S. pyogenes* (NCTC 8198T = CCUG 4207T) are available in DNA Data Bank of Japan, European Nucleotide Archive, and GenBank under the accession numbers LN831034 and CP028841.[33]

https://www.ncbi.nlm.nih.gov/nuccore/NZ_CP028841.1

<https://www.ncbi.nlm.nih.gov/protein/XDR38324.1?report=fasta>

XDR38324.1 M-related protein Mrp Streptococcus pyogenes MSKRNPNKHYSRKLKTGTASVAVALTVLGT-GLANTTDVKADLSTQENPRVTKAREEALEEVLRSDYGS VRAALAGSYRKNLQLENTIKQKDKEFLSKVLDEAKKYRESS-DKYKQEIGQLKAAAEEAQKALDALN NKNKQISDLTNENAQLKEAIEGYVQTIQNASREIAKQQELAAAK-SLEAKNAEIEALKQQDASKTEIA KLQSEAETLENLLGSAKRELTDLQAKLDTATAEKAKLESQVTTLLENLL-GSAKRELTDLQAKLDAANAEKE KLQSQAAALEKQLEATKKELADLQAKLAATNQEKEKLEAEAKALKEQLAKQAEE-LAKLKADKASGAQKPD TKPGNKEVPTRPSQRTNTNKAPMAQTKRQLPSTGEETTPFFTAALTVIASAGVLALKREEN

Where do you analyse it?

Can you do this yourself?

4.2 Interpretations

4.3 Implications or Perspectives 4.4 Impact - Innovation and Application

You should summarise what you expect to be the most important find is or contributions. What to you do about the problem you have identified.

CHAPTER V

CONCLUSION

4.1 Conclusion

The conclusion is a brief presentation of what has been obtained from the discussion. Summarises the key findings and their importance offering final thoughts on the research.

4.2 Limitations

The limitations of the study describe the weaknesses and shortcomings found after analysis and interpretations of the results.

4.3 Suggestion

Suggestions for future research.

Describes the research design, methods used for data collection and analysis and justifies the chosen approach.

Interprets the results, linking them back to the research questions and existing literature, discussing implications, limitations and future research directions.

Appendices

Supplementary material, such as raw data, questionnaires or additional charts that are relevant to the thesis but not critical in the main sections.

Bibliography

Lists all the sources cited in the thesis in a consistent format.

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