TITLE PAGE

MECHANISM OF BACTERIAL TOXINS IN HUMAN CELL

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CERTIFICATION

This is to certify that this term paper titled "**MECHANISM OF BACTERIAL TOXINS IN HUMAN CELL**" was carried out by **DADA TOMIWA**, with matriculation number 16010101014. This project report meets the requirements governing the award of Bachelor of Science (B.Sc.) Degree in Microbiology department of Biological sciences of Mountain Top University, Ogun State, Nigeria and is approved for its contribution to knowledge and literary presentation.

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DECLARATION

I hereby declare that this project report written under the supervision of Dr. B. Opere is a product of my own research work. Information derived from various sources has been duly acknowledged in the text and a list of references provided. This research project report has not been previously presented anywhere for the award of any degree or certificate.

_____ _____

DADA, TOMIWA V. **Date**

DEDICATION

This project is dedicated to Almighty God that has helped me throughout my stay in Mountain Top University and for sparing my life till this moment.

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My sincere and utmost appreciation goes to my Lord and Redeemer, who in His infinite mercies has given me the wisdom, knowledge, assistance, support and protection to successfully complete this project.

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ABSTRACT

The primary target of bacteria toxins in the initiation of an infection is the cell, which is the functional unit and foundation of life. The multifactorial complexity of toxin and toxin producers brings about comparative and collaborative pathogenesis, of whose mechanism on a cellular level must be fully understood. All the toxins produced are either secreted out, called exotoxins (proteins), or are entrapped in the cell membrane, called endotoxins (lipopolysaccharides) and have been broadly categorized and discussed on this basis, for clarification.

CHAPTER ONE

1.0 INTRODUCTION

Bacteria toxins are soluble substances made up of small molecules or proteins within a living bacterial cell that alters normal metabolism of host cell on entry or contact, thereby resulting in an infectious disease in host or exerting a deleterious effect on the host cell (Wilson *et al*., 2015). Studies revealed them to be primary virulence factors which drive the underlying mechanisms of pathogenesis, responsible for the typical clinical features of bacterial disease (Rudkin *et al.,* 2017) therefore they have been implicated with diseases of global concerns, making them perhaps the most powerful toxins in existence and the most powerful poisons produced in the nature (Rudkin *et al.,* 2017)

Bacteria toxins have created proficient methodologies to modulate specific intracellular host cell targets and destabilize the immune system (Michel *et al.,* 2020). Although the multifactorial complexity of toxin and toxin producers virulence, poses a challenge in categorising of bacteria toxins (Sekhar, 2020) they have been categorized using fairly exhaustive parameters, according to the organism generating the toxin, organism susceptible to the toxin, secretion system used to release the toxin, tissue target type susceptible to the toxin, structure and domain architecture of the toxin etc

For the sake of clarification they have been broadly classified into endotoxin and exotoxin on the basis of their chemical composition (Todar, 2015). A bacterium can elucidate different types of toxins and even engage them simultaneously in its invasion and evasion of the human host cell (Ana *et al.,* 2016) hence a single infectious disease can result from the contribution of multiple toxins and other virulence factors (Aryal, 2020).

The regulation of synthesis and secretion of many bacterial toxins is tightly controlled by factors such as regulatory elements that are sensitive to environmental signals, such as the presence and absence of certain element, osmolality and temperature and the bacteria, while some bacteria inherently possess the genetic capability to generate toxins others acquire through processes of genetic exchange such as conjugation and transduction (Hernández-Cortez *et al.,* 2017)

CHAPTER TWO

2.0 SOURCES OF BACTERIA PRODUCING TOXINS

As a consequence bacteria ubiquitous nature, our interaction with them is ultimately unavoidable. While some interactions may be profitable others may be detrimental, like those with bacteria possessing the toxin virulence factor which is the underlying mechanism for pathogenesis, which mostly results in infectious disease (Lucas *et al.,* 2020). They gain access to human tissue and cells through two main types of routes: mucous surfaces inside the body (breaths of the gastrointestinal, digestive, reproductive and urinary tracts) or epithelial coverings outside the body (skin areas that could be undamaged or damaged due to bites of bugs, cuts / scrapes or other wounds) (Ribet *et al.*,2015). Generally microorganisms typically colonize host tissues in interaction with the external environment. (Todar, 2015) the external environment/or source includes but not limited to;

(i) Injection: a variety of routine medical procedures, such as tracheal intubation and catheterization of blood vessels and urethra, increase the risk of bacterial infection, the plastic devices used in these procedures are readily colonized by bacteria from skin, which integrate along the surface of the tube to infect deeper tissue or enter blood stream (Ko *et al.,* 2017).

(ii) Ingestion of contaminated food or water: FBDs are spread by food infected by pathogenic microorganisms with several virulence factors that offer them the aptness to stir up infection; certain bacterial genera can induce toxins directly in the meat, but other genera may create them once the intestine is colonized. Among the pathogens implicated with food borne disease that are as well adjudged to be toxigenic are Salmonella spp., V*ibrio parahaemolyticus, Vibrio cholerae, Staphylococcus aureus, Clostridium botulinum, Clostridium perfringens, Bacillus cereus, Listeria monocyotogenes.* By drinking and bathing in contaminated water and eating contaminated food, people may be exposed to bacterial toxins (Geneva, 2020).

(iii) Inhaling bacteria: inhaling contaminated droplets produced by breathing, talking, sneezing, coughing air or droplets of water (Pietrangelo, 2020).

CHAPTER THREE

3.0 BACTERIA ADHESION, EVASION AND INVASION OF HUMAN HOST CELL

3.1 ADHESION

While some bacteria have broad tissue tropism and can invade several cell type/forms, most pathogenic bacteria specifically adhere to cell or tissue that promote their growth, to interact with them, examples include (Asadi *et al.*, 2018):

Streptococcus pyogenes, attaches to the Pharyngeal epithelium cell causing sore throat disease.

Streptococcus pneumonia, attaches to the mucosal epithelium cell causing Pneumonia disease.

Staphylococcus aureus, attaches to the mucosal epithelium cell causing various soft tissue infection.

Neisseria gonorrhoeae, attaches to the Urethral/cervical epithelium cell causing Gonorrhea.

3.2 EVASION

Direct damage to the host is a general mechanism used by pathogenic organisms to ensure infection and destruction of the host cell, (Emmanuel et al., 2019) hence the pathogenic organism should show explicit trademark that advance its development into a host cell, after it gains entrance into the host (David et al.,2015). This characteristic adds to their effectiveness and enables them to colonize a niche in host, attach to cells, evade the immune system, invade host cell and obtain nutrient from host. Pathogenic bacteria employ various tactics to evade the immune system. In other to escape immune detection, some bacteria (Varela-Chavez *et al.*, 2020):

1. **Modulate their cell surface** e.g. bacteria that cause meningitis (*Haemophilus influenzae, Escherichia coli K1*, and *Neisseria meningitidis)* rely extensively on capsules to promote their extracellular lifestyle within the host by preventing antibody and complement deposition and insertion (Ribet *et al.*,2015).
2. **Avoid immune surveillance** by camouflaging their surface or the infected cell such that it is not recognized by host surveillance systems, or dampen immune responses such that a complete immune response is avoided (Ali *et al.*, 2019).
3. **Vary immune dominant molecules** otherwise called antigenic variation, for circumventing humoral and cellular responses. Antigenic variation infers a single strain

specifically changing a subset of its antigens, either to sustain an ongoing infection or re-infect hosts even though the first infection was successfully cleared (Palmer *et al.*,2016)

4. **Subverting immune response Pathways,** Because of their size (1–3 microns), bacteria make particularly appropriate phagocytic targets. Several bacterial pathogens have developed ways of avoiding phagocytosis (Kaiser, 2020).

3.3 INVASION

After successfully evading the host immune system, the organism then invades the cell, some infect the cell without entering the host cells e.g. *V. cholerae* and *B. pertussis*, while the preferred niche for replication and survival for others are within the cytoplasm or intracellular compartments of particular host cells.(Bruce *et al.,* 2016) based on invasive properties they are classified into **Extracellular bacteria ,Facultative intracellular bacteria** and **Obligate intracellular bacteria** (Leon-Sicairos *et al.,* 2015**)**.

1. **Extracellular bacteria:** Extracellular bacterial pathogens do not penetrate cells in other to assail them rather they proliferate in the extracellular environment which is embellished with body fluids and nutrients. Some extracellular bacteria do not penetrate body tissues (e.g. *Vibrio cholerae*) rather adhere to epithelial surfaces and cause infection by emitting intense toxin. Extracellular bacteria do not have the capacity to survive the intracellular environment or to induce their own uptake by most host cells. Predominantly extracellular bacteria include; *Bacillus anthracis, Enterotoxigenic Escherichia coli, Haemophilus influenza, Mycoplasma spp, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pyogenes and Vibrio cholera* (Acharya, 2013).
2. **Intracellular Bacteria:** They enter the cells through phagocytosis or by the zipper mechanism of invasion, where they fool the host cell by binding with high partiality to a cell grip protein that the cell typically uses to cling to another cell or to the extracellular matrix, (Varela-Chavez,*et al.*,2020) the host cell then attempts to form a cell junction by spreading over the adhesive surface,but Since the bacterium is small relative to the host cell, the host cell's attempt to of the bacterium results in the phagocytic uptake of the bacterium.(Alberts *et al.*, 2016). Some intracellular bacteria can be cultured in the laboratory on microbiologic media (facultative) and others require living cells/animals (obligate) (Acharya, 2013).
3. **Facultative Intracellular Bacteria:** Facultative intracellular bacteria invade host cells when it provides a selective advantage.

(Acharya, 2013) intracellular bacteria are shielded from humoral antibodies and can only be eliminated by a cellular immune response. However these microorganisms should have specific components to shield them from the brutal climate of the lysosomal compounds experienced inside the cells. microbes that can enter and get by inside eukaryotic cells are protected from humoral antibodies and can be killed exclusively by a cell immune reaction, Examples include: *Legionella pneumophila*, *R. rickettsia*, *Mycobacterium tuberculosis*, *Listeria monocyotogenes*, *Salmonella* spp, Invasive *Escherichia coli*, *Neisseria* spp, *Brucella* spp and *Shigella* spp (Acharya, 2013).

Invasion can proceed by direct translocation of effector molecules into the host-cell cytosol using complex and specialized secretion systems when in direct engagement with surface host-cell receptors. Specifically, Type III and Type IV secretion systems to transport toxins with functional pathogenic components, promoting the modification of the plasma membrane architecture, prompting pathogen engulfment (Green et al., 2016).

Type III Secretion Systems: Type III secretion systems are characterized by the capacity to infuse a protein using critically structured protein appendages, directly from the bacterial cell to the eukaryotic cell. Certain species of pathogenic bacteria, including: *Salmonella*, *Shigella*, *Yersinia* and *Vibrio* exhibit type III secretion systems (Athina et al., 2015).

Type IV Secretion Systems: Type IV secretion systems are portrayed by the capacity to move secretory particles through a system like the bacterial conjugation machinery. The type IV emission frameworks can either emit or receive particles (Christie et al., 2016). The bacterial conjugation machinery permits move of hereditary (genetic material) material to happen through direct cell-to-cell contact or by an extension like contraption between the two cells. An example of a pathogenic bacterium that utilizes this secretion system is *Helicobacter pylori* (Salinas et al., 2019).

CHAPTER FOUR

4.0 TOXINOGENESIS OF BACTERIAL TOXIN IN HUMAN HOST CELL

Toxigenesis, the capacity to create toxins, is the underlying mechanism through which many pathogenic bacteria cause disease. In other for an infection to be established host cell must be directly damaged, which is made possible by toxins after successful cell invasion (Emmanuel *et al*., 2019). toxins are virulence factors that control host cell capacities to support microbial infections example when they cause the cells to lose membrane integrity, which can lead to necrosis, decreased cell viability, halt growth of cell, lyse the cell and even activate a genetic program of controlled cell death (apoptosis) (Tülay *et al*., 2018).

There are two types of bacterial toxins, on a chemical level, endotoxins and exotoxins (Ranjit *et al*., 2014).

4.1 ENDOTOXINS

They are integral component of the outer membrane of cell wall of gram negative bacteria, they are made of lipopolysaccharide (LPS) which serve précised purpose of protection of the organism and also mediate infections in host (Todar, 2015). In spite of their protective function in maintaining the integrity of the bacteria in face of cellular host defense strategies such as hydrophobic antibiotics, bile acids and antibiotics they are also key players in severe infections (Todar, 2015).

4.1.1 STRUCTURE OF ENDOTOXIN

The ability to successfully cause infections rely on their structural components, lipopolysaccharide is composed of, the hydrophilic lipid A and hydrophilic polysaccharide (O-region). In which they are both important for endotoxin biological activity (Sampath, 2018).

4.1.2 MECHANISM OF ACTION

The polysaccharide components (O antigens) stimulate the immune system i.e. it is the immunogenic component of the LPS while its toxicity function is correlated with the lipid component (Lipid A.) which acts as a lock and key with the lipid binding protein (LPB) which transfers it to the Toll like receptor 4 (TLR4), which then signals macrophages to secret pro-inflammatory cytokines and or (activates coagulation cascade or complement

cascade) (Sampath, 2018) resulting in a characteristic endotoxin shock and a series of physiological activity such as fever, physiologic stress (diarrhea, prostration) (Todar, 2015).

Examples of bacteria that employ endotoxins include; all gram negative bacteria, both pathogenic and non-pathogenic possess LPS as a component of their cell wall (Todar, 2015).

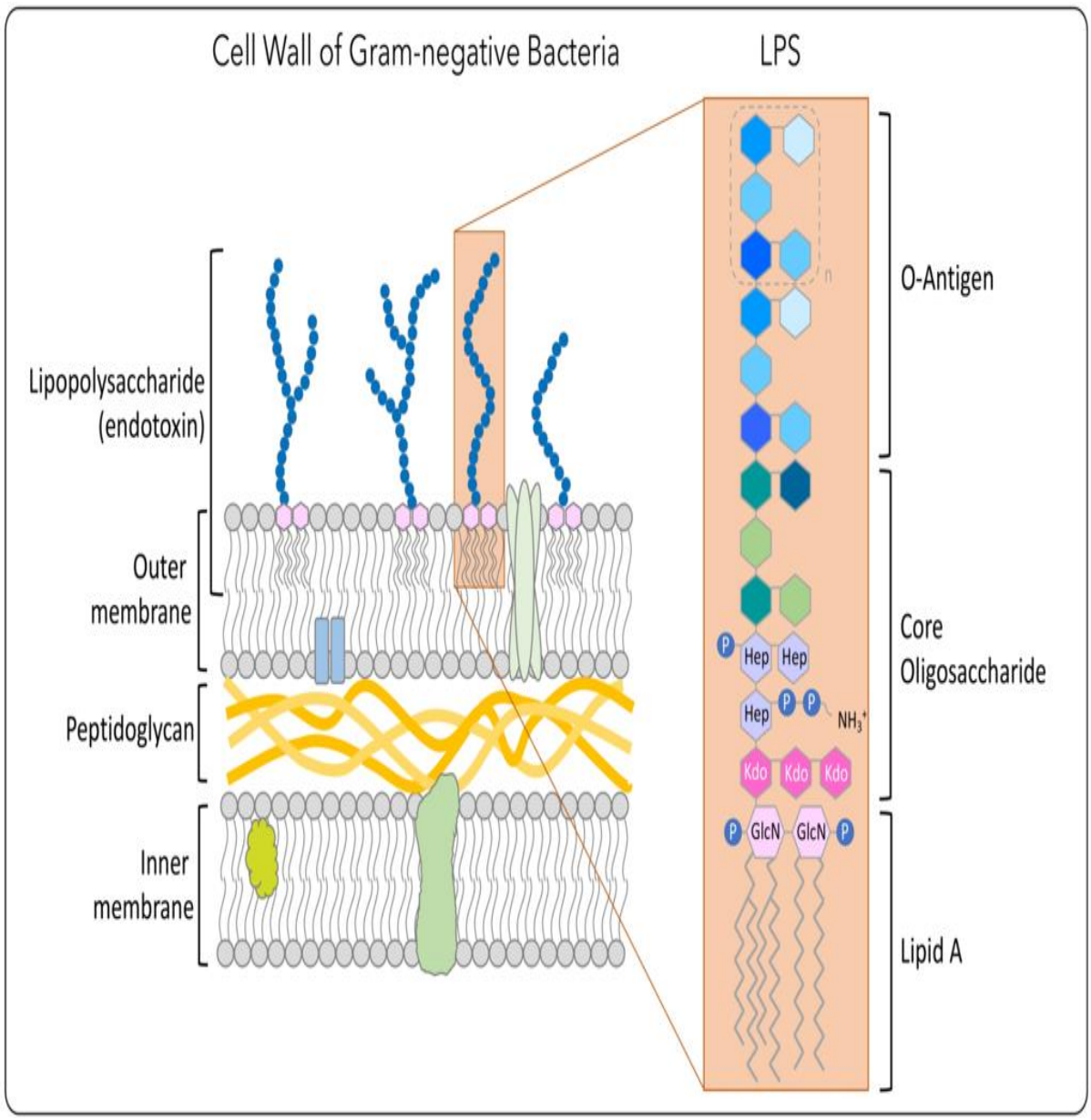

Figure 4.1: Structure of gram negative LPS and cell wall **Source:** AB Bioscience

LPS layer also referred to as the outer most layers found in the cell wall of gram negative bacteria. It is a characteristics trait specific to Gram negative bacteria. It is assembled in the plasma or inner membranes similar to the biosynthesis of the peptidoglycan.

4.2 EXOTOXINS

Exotoxins are toxins secreted by the bacteria i.e. it is discharged from bacterial cells, they may be secreted, or, similar to endotoxins, may be released during lysis of the bacteria hence their effect may be local or systemic and are expressed by both gram negative and gram positive bacteria, (Sagar, 2020) they are the most powerful human poisons known and retain high activity at very high dilutions (Kenneth, 2015). They are further classified into 3 types on the basis of their mechanism; Type I, Type II and Type III.19.

4.2.1 TYPE I EXOTOXINS

They are cell surface-active which bind to a receptor on the surface of the cell and stimulate intracellular signaling pathways. Two examples are super antigens and Heat-stable enterotoxins.

4.2.1.1 Super Antigens

They are unusual bacteria toxins that directly bind to class II major histocompatibility complex (MHC) molecules outside the peptide-binding groove. They do not enter the cell and are presented as unprocessed molecules to T cells carrying a T Pcell receptor (TcR). There, interactions with large numbers of T4-lymphocyte results in non-specific activation of 20% T-cells resulting in polyclonal T cell activation and massive cytokine release in the blood which can cause severe life threatening symptoms such as shock and multiple organ failures (Kaiser, 2020).

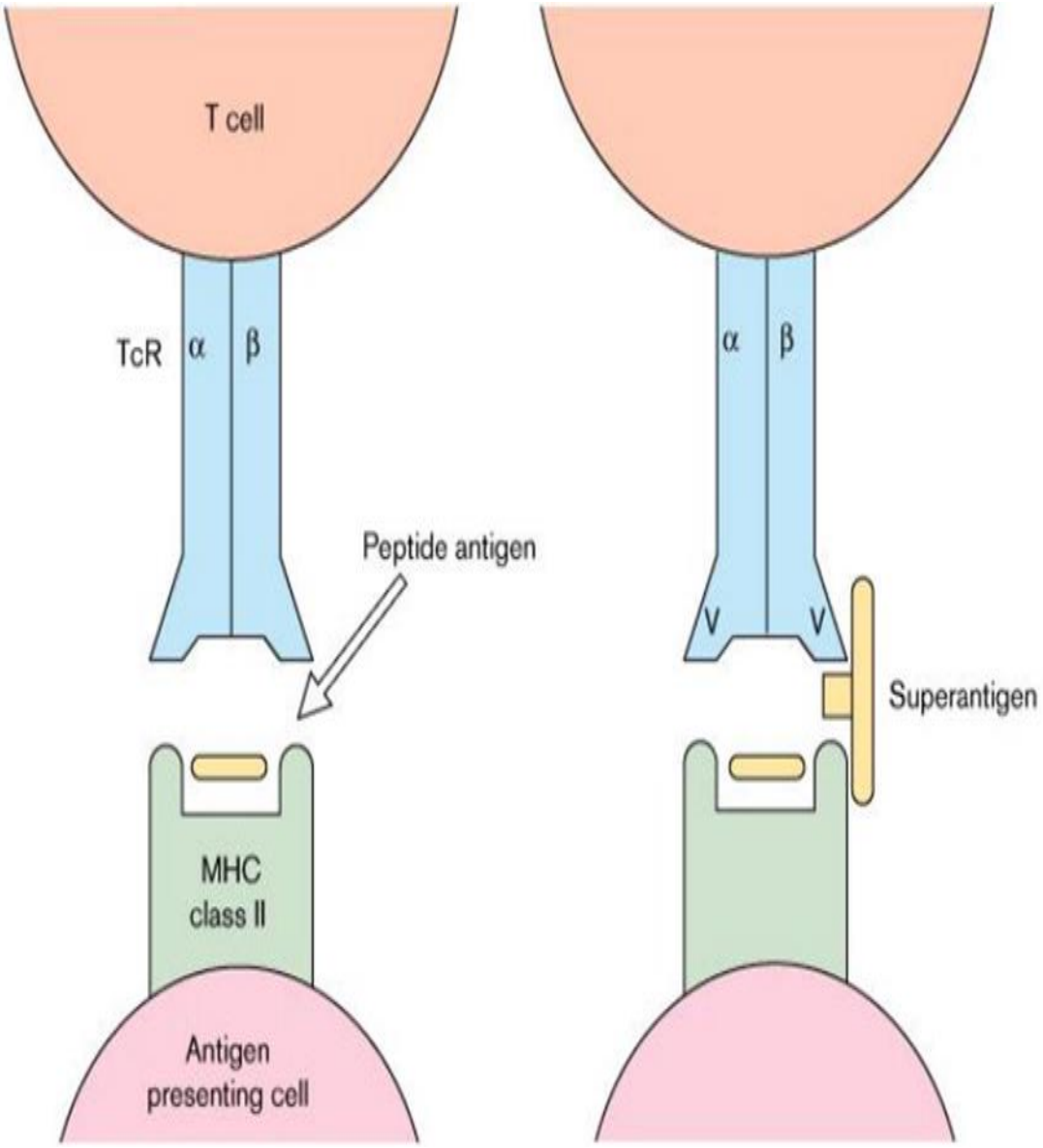

Figure 4.2: Super Antigens **Source:** Science direct.

Conventional protein antigens are handled by B cell and a peptide of the protein antigen is introduced to its coordinating antigen-explicit CD4 T cell via MHC-II-peptide, TCR Super antigens are not prepared intracellular instead they bind to the class II MHC molecules as intact macromolecules forming a tri-molecular complex as they bind to the outside of the peptide-antigen restricting section.

Examples of super antigens include:

1. **Toxic shock syndrome toxin-1 (TSST-1):** They are generated by some strains of *Staphylococcus aureus*, causes toxic shock syndrome (TSS) by signaling the excessive cytokine production by the immune system which leads to fever, rash, and shock.

2. S**treptococcal pyrogenic exotoxin (Spe):** produced by scarlet fever strains of *Streptococcus pyogenes*. They are cytotoxic and pyrogenic, with enhanced lethal effects they also add to cytokine-actuated incendiary harm. SPEs are liable for causing streptococcal toxic shock syndrome (STSS) where excessive cytokine production leads to rash fever, and triggering the shock cascade. The SPEs also is responsible for causing necrotising fasciitis, an infection that can obliterate the tissue covering the muscle (the fascia skin, fat, and). SPE B is also a precursor for a cysteine protease that can destroy muscles tissue. (Gary, 2020)

3. **Staphylococcal enterotoxins (SE):** They are produced by many strains of *Staphylococcus aureus.* These exotoxins cause staphylococcal food poisoning. The stimulation of the vagus nerve in the stomach lining that causes vomiting is due to excessive inter-leukin 2 (II-2) production, the side effects also includes fever, nausea, vomiting and diarrhoea (Gary, 2020).

4.2.1.2 Heat-stable Enterotoxins

ETEC enterotoxins are produced by entero toxigenic E. coli (ETEC). They are able to withstand heat treatment at 100 ℃. , they recognize distinct receptors on the cell surface and consequently influence distinctive intracellular flagging pathways For example, STa enterotoxins bind and activate membrane-bound guanylate cyclase, leading the intracellular accumulation of cyclic GMP and effects on several signaling pathways. This results in lead loss of electrolytes and water from intestinal cells (Sagar, 2020). It is amongst of the most common causes of traveler's diarrhea (Gary, 2020).

4.2.2 TYPE II EXOTOXINS

They are membrane damaging toxins which exhibit haemolysin or cytolysin activity in vitro in other to lyse the host targeted cells for intracellular delivery of bacterial factors, nutrients or for phagossomal escape (Ferdinand *et al*., 2013). At low concentrations of toxin, the effect

may be subtle such that cell lysis. Would be absent and modulation of host cell signal transduction may be observed.

Membrane-damaging toxins are divided into two categories, the channel-forming toxins, which sometimes function as enzymes affectting membrane

4.2.2.1 Channel-forming / pore forming toxins

The mechanism involves the recognition and binding to a specific receptor causing them to associate with the target membrane and form multimers, as they are water soluble they then undergo a conformational change leading to a pore formation in the membrane of the target host cell (David *et al.,* 2020).

Pore forming toxins are further divided into two; **Cholesterol-dependent cytolysins** and **RTX toxins**

1. **Cholesterol-dependent cytolysins**

Formation of pores by cholesterol-dependent cytolysins (CDC) is dependent on the presence of cholesterol in the target cell. The size of the pores ranges from 25nm to 30 nm in diameter. All CDCs are secreted by the type II secretion system; the exception is pneumolysin, which is released from the cytoplasm of Streptococcus pneumoniae when the bacteria lyse **(**Kristin *et al.,* 2015**)**.

2. **RTX toxins**

RTX toxins can be identified by the presence of a specific tandemly repeated nine-amino acid residue sequence in the protein (González-Bullón *et al.,* 2020).

Pore-forming toxins (PFTs) are the most widely recognized bacterial cytotoxic proteins and are needed for destructiveness in countless significant pathogens, examples but not limited to the following (Ferdinand *et al*., 2013);

Streptococcus pneumonia, it produces pneumolysin in vivo during its infection and is required for virulence in pneumonia, meningitis, otitis media, and bacteraemia,

Streptococcus pyogenes **(GAS)**, it produces streptolysin which are important virulence factors in GAS that cause skin and other soft tissue diseases (e.g., impetigo, pharyngitis, erysipelas, and cellulitis) during the early stages of infection.

Staphylococcus aureus, it possess, α-hemolysin, γ-hemolysins, leukocidin which it employs in its infections soft tissue and including fatal sepsis and necrotizing fasciitis,

Escherichia coli, it possesses hemolysin A and cytolysin A, with which Diarrheagenic *E. coli* such as enterohemorrhagic *E. coli* (EHEC) causes diarrhea, hemorrhagic colitis, and hemolytic-uremic syndrome (Ferdinand *et al.*, 2013).

As proteins, many bacterial toxins resemble enzymes, catalytically, exhibiting specific actions. The substrate (in the host) may be a component of tissue cells, organs or body fluid. One example is the α toxin of *C. perfringens*, which causes gas gangrene; α toxin has phospholipase activity (Oda *et al.*, 2015).

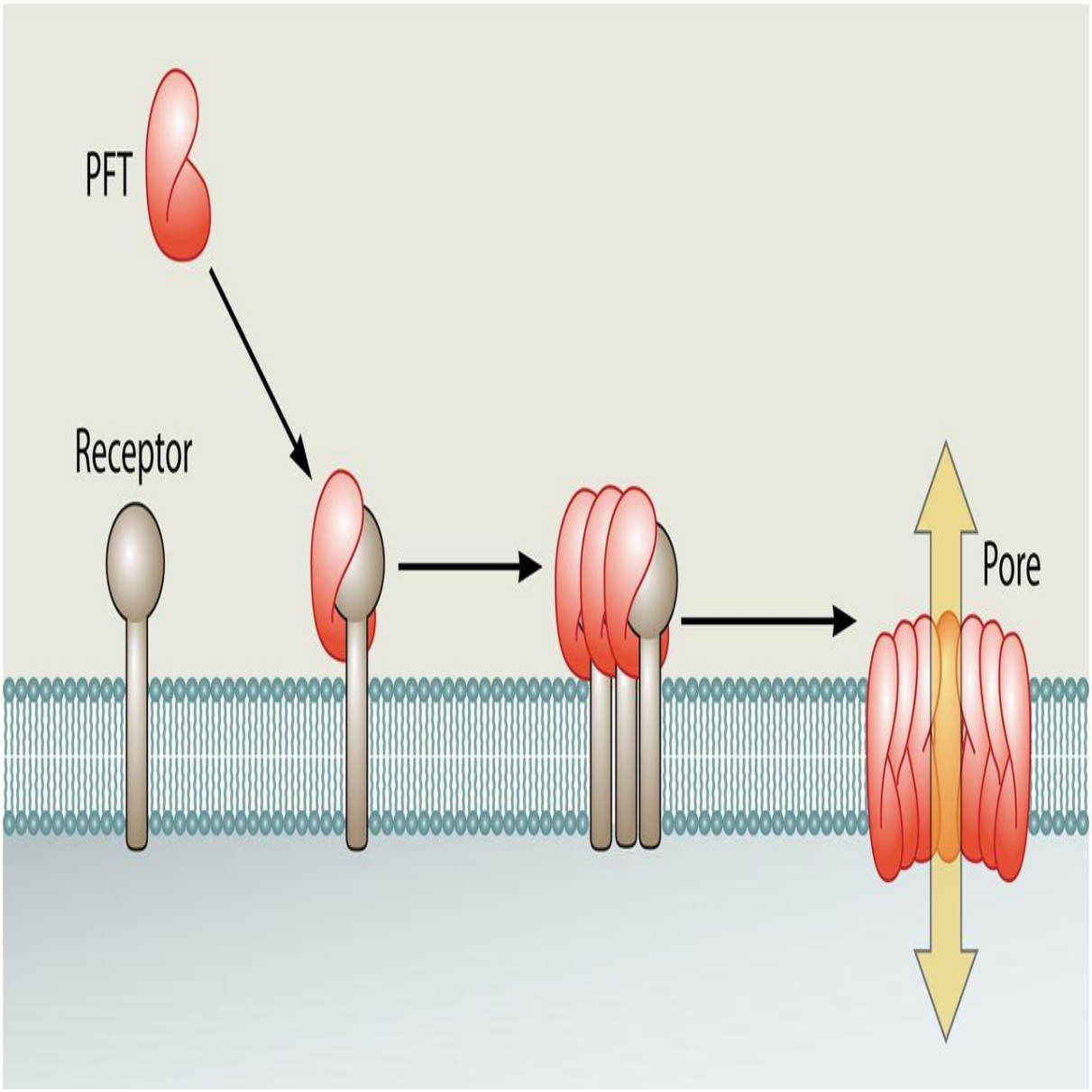

Figure 4.3: Schematic representation of the pore formation in pore-forming toxins (PFTs) **Source:** NCBI.

Soluble PFTs are recruited to the host membrane by protein receptors and/or specific interactions with lipids (for example, sphingomyelin for actinoporins or sterols for cholesterol-dependent cytolysins (CDCs),Upon membrane binding, the toxins concentrate and start the oligomerization process which results in the formation of a transmembrane pore with different architecture, stoichiometry, size and conduction features.

4.2.3 TYPE III EXOTOXINS

Here, bacteria deliver toxins directly from their cytoplasm to the cytoplasm of the target cell through a needle-like structure or The 'B'-subunit (binding) of the AB toxins attaches to target regions to receptor molecules on cell membranes surface, the 'A'-subunit (active) then enters through the membrane and possesses enzymatic function that affects internal cellular bio-mechanisms, by which they remove the ADP-ribosyl group from the co-enzyme NAD and covalently attach to to some host cell protein, hence interfering with the functions in a particular host cell thereby damaging the cell, the damage it brings about is dependent on what host functions it alters (Gary, 2020).

Examples of AB toxins;

1. **Diphtheria exotoxin**: They are produced by *Corynebacterium diphtheria*. It is produced as single polypeptide chain. The function of the protein is divided into two parts: subunit A, which possess the enzymatic activity for elongation factor-2 EF-2), inhibition, which is involved in host protein synthesis and subunit B, which binds to the membrane of the susceptible host cell. EF-2) (Kaiser, 2020). The B subunit consists of the T (translocation) domain region which enters into the endosome membrane by binding to the receptor mediating endocytosis, the pH drops to about 5 In the vesicle allowing the unfolding of the A and B chains, exposing the hydrophobic regions of both the A and B chains that can insert into the vesicle membrane to secure the release of the enzymatic component into the cytoplasm. The outcome is openness of the A chain to the cytoplasmic side of the membrane. There, decrease and proteolytic cleavage delivers the A chain in the cytoplasm. The A piece is delivered as an all-encompassing chain however recovers its dynamic (enzymatic) globular conformation in the cytoplasm. The A chain catalyzes the ADP ribosylation of elongation factor-2 (EF-2) NAD to elongation factor (EF-2) which inactivates its function in protein synthesis resulting in cell death. Cells of the throat are

initially killed by the toxin. The toxin is also released into the blood where it damages internal organs and can lead to organ failure (Kenneth, 2015).

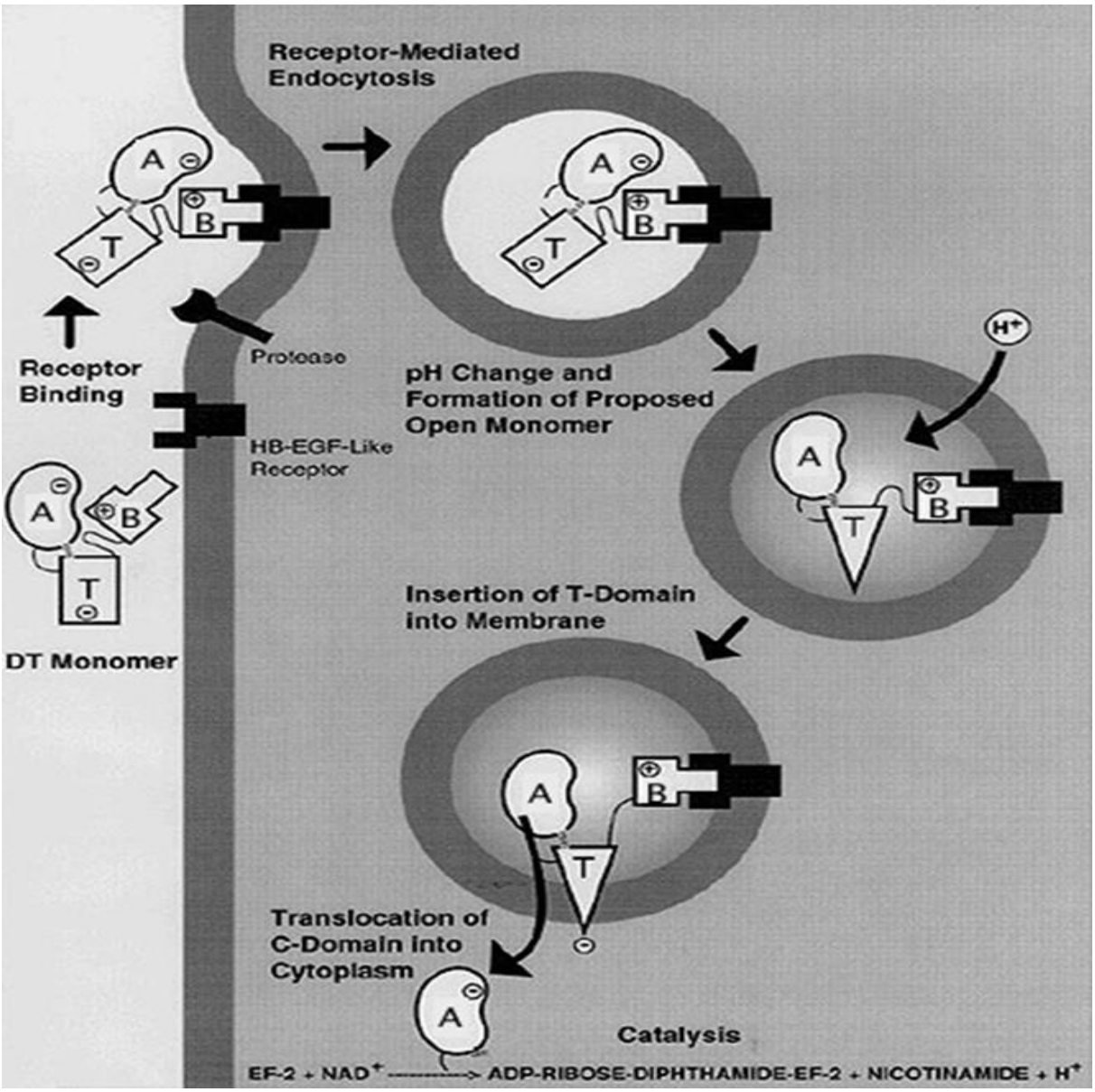

Figure 4.4: Schematic depiction of the mechanism of diphtheria toxin entry into eukaryotic cell cytosol

Source: Bacteriology.

Diphtheria toxin attaches to its cell surface receptor and is then internalized into the endosomal vesicles. The trans membrane domain of the toxin undergoes a spontaneous dynamic reorganization and enters the membrane by forming a pore through which it delivers the C-domain to the cytosol. Once refolded into a functioning compliance, the C-domain catalyzes the ADP-ribosylation of elongation factor.

2. **Cholera exotoxin (choleragen), produced by *Vibrio cholera*:** The exotoxin catalyzes ADP-ribosylation of host cell protein Gs that turns the synthesis of a metabolic regulator molecule called cyclic AMP (cAMP) on and off, causing synthesis to stay turned on. Producing High levels of cAMP which prevents the intestinal epithelial cells from taking in sodium from the lumen of the intestines hence stimulating large secretion of chloride. Water and other electrolytes. This causes loss of fluids, diarrhoea, and severe dehydration (Ferdinand *et al*., 2013).
3. **Pertussis exotoxin, produced by *Bordetella pertussis***: The pertussis exotoxin catalyzes the ADP-ribosylation of the host cell protein Gi leading to high intracellular levels of cAMP. Disrupting vital cellular function. The high levels of cAMP results in increased respiratory secretions and mucous production and coughing In the respiratory epithelium,. In the case of phagocytes, excessive cAMP results in decreased phagocytic activities. In the blood, the toxin results in increased sensitivity to histamine. This can result in hypotension increased capillary permeability and shock. It may also act on neurons resulting in encephalopathy (Ferdinand *et al*., 2013).
4. **Shiga toxin produced by species of Shigella and enterohemorrhagic *Escherichia coli* (EHEC) such as such as E. coli O157:H7**: This toxin is an A-B toxin, it cleaves host cell rRNA preventing the attachment of charged tRNAs and stopping host cell protein synthesis. The shiga toxin also enhances the release of cytokines such as Il-1 and TNF-is also responsible for a complication of shigellosis and *E. coli* O157:H7 infection called hemolytic uremic syndrome by damaging the blood vessel (Ferdinand et al., 2013) (Ferdinand *et al.*, 2013)

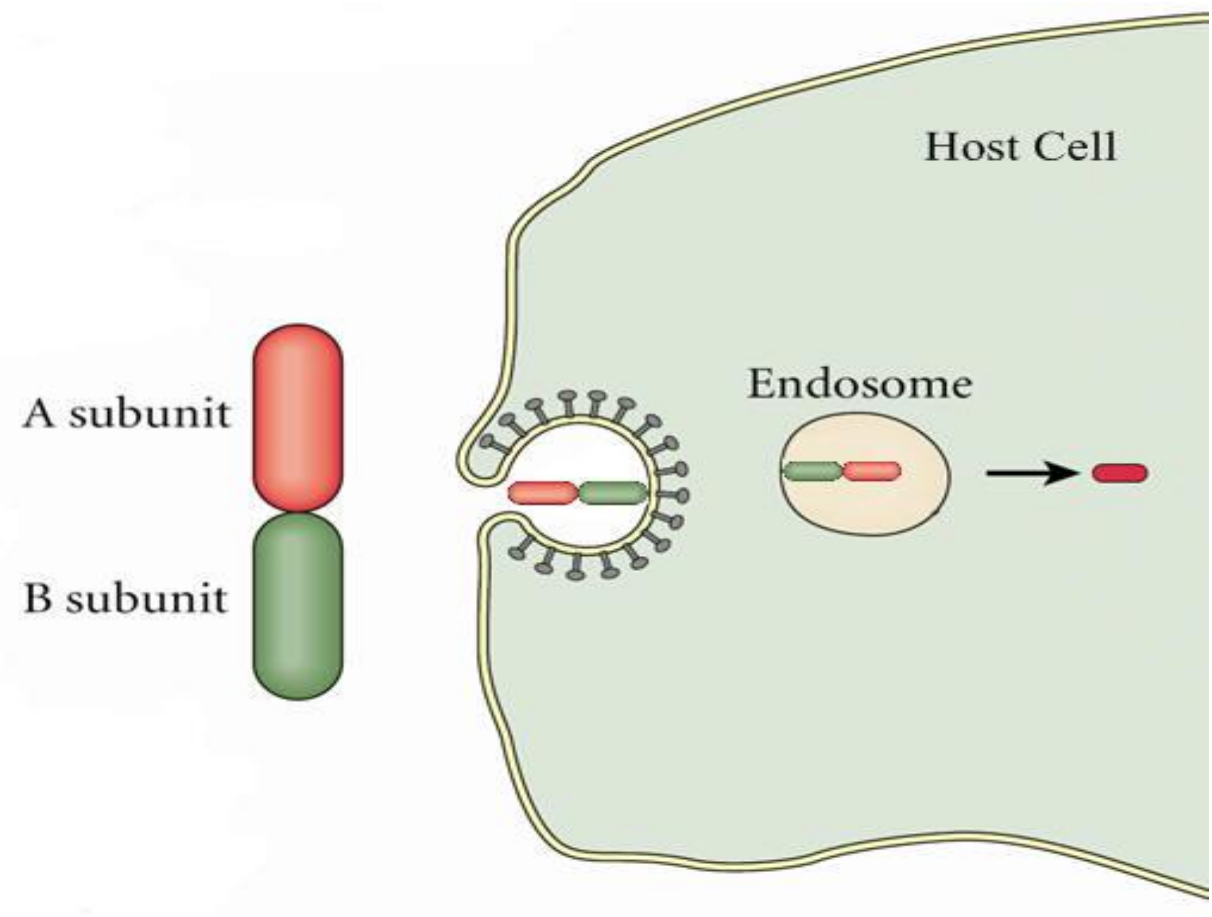

Figure 5.1: General mechanism of A-B toxin **Source:** pathogen profile dictionary

A-B toxins, the B segment ties to the host cell through its collaboration with explicit cell surface, The toxin is acquired through endocytosis, Once inside the vacuole, the A segment (dynamic part) isolates from the B segment and the A segment accesses the cytoplasm.

CHAPTER FIVE

CONCLUSION

Healthy humans are colonized and co-exist with over 100 trillion bacteria, which outnumber human cells by about 10–100-fold, while commensal organisms may provide the host with a number of benefits (e.g. contributing to metabolism or shaping immune competence), pathogenic gram positive and negative bacteria utilize well-structured molecular weapons such as toxins, by which they exhibit diverse biological activities during infection. The infective potential of pathogenic toxin producing bacteria relies on by both general and highly specific, time-dependent local host and environmental factors, as well as by the ecological status of the micro biome, causing disease by directly damaging host cell and interrupting or hyper stimulating many essential functions and pathways of eukaryotic cells.