Review Article

Bacterial adhesion and manipulation of host membrane

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Abstract

Bacterial adhesion is the preliminary step in biofilm formation and colonization. Biofilms can be damaging equally to human life as well as industrial processes, such as causing infection, pathogen contamination, and slime formation, while being beneficial in bioprocesses and environmental technologies. The bacteria adhesion to surfaces recounts to such factors as surface charge and the characteristics of polymers on bacteria (prominent to formation of biofilms).Cell appendages such as proteinous nanofibers and polysaccharide chains have a significant function of bridging between cells and the substratum in conventional adhesion models, but sometimes cause deviation from the models of cell adhesion. Cell appendages are responsible for specific and nonspecific cell adhesion to biotic and abiotic surfaces.

Introduction

Among the most diverse single-celled living organism that thrives in a diverse environment and they have a wide variety of ecology, known as bacteria. To pathogenic bacteria which bound with different cellular organelles (Golgi apparatus, Endoplasmic reticulum, Nucleus, Mitochondrion) and secret toxin that cause the different course of infection. To the ease of colonization, bacteria have developed plenty of vivid cellular mechanisms to adhere with the host cell, change their physicochemical properties accordingly environment. Due to change in response at the time of surface attachment, can strike bacterial regulation, cellular respiration, metabolism, and process of colonization-pathogenesis.(1)

Bacteria instrument which is used for adhering and invading the cell are complex their range varies from single monomeric protein to highly specialized macro-molecules that work very fascinatingly they can be truly considered as the machine which is so small huge diversity of these type of machine relief us to evaluate and compare the behavior of pathogen is not simple by the knowledge which we were collected from the combination of tissue culture and laboratory studies. (2)

In this review, we provide an overview of the current understanding of how bacterial pathogens adhere with host membranes and what is the way these microorganisms exploit with the host cell, discuss the immune response after attached to the host cell. We focus on the role of the cytoskeleton, pathogen manipulation of host plasma membrane interaction with the cell membrane.

Chaperone-Usher Pili

For the many pathogens had studied in detail from Swedish group, Divulge that is E. coli bacteria, the children with critical kidney infection accumulate human RBC in P- blood group-specific mode and recognized the(1) sense organ

part like galα (1–4) gal represent in the series of glyco (glycoprotein).(3,5)

It was eventually that two adhesive characteristics were encrypted by two different pilus operons in uropathogenic E. coli, in the fim operon converted in type I pili- expressing mannose sensitivity hemagglutination and the Pap operon convert P or Pap pili manage for the interconnection with the di-galactoside unit in the P-blood group antigen. The pili of both two types were getting hetero-polymeric structures consisting or converted in only one pilus subunit protein, the pilus protein assembles up a stalk and in the distal end, have many small subunits. PapG and fim-H, there is a minor protein that denoted the actual adhesin. Both adhesins have two domains, a pilin domain helps in copolymerization, and a second carbohydrates-binding lecting domain. (6,7)

Pili and Fimbriae

Adhesive hairy organelles that elongate bacterial surfaces. During the time of bacterial conjugation, pili can be play the important role in the transfer of genetic material, to term "fimbria", described to pili, which role is immersed to attach bacteria to a surface. Escherichia Coli, only a Gram-negative organism in which earlier identified, scaffold-like rod anchored (filamentous surface) include to the outer membrane of bacteria and adhesin (bacterial adherence factor) which found scaffold's tip and provides ligation particularly. Pilus structure, first described in 1968, when Corynebacterium renale's structure looks like flexible rod due to electron microscopy study(8). Actinomyces, Ruminococcus, Enterococcus, Clostridia (species of streptococcus), are gram-positive bacteria in which pili have been seen (9)Assembly of pili in Gram-positive bacteria.(10,11), Pili in gram-positive pathogens with the help of electron microscopy. We have found two types of pili in Gram-positive bacteria which extend 70 nm and 500 nm in length, 1-2 nm in diameter which are found on the S. oralis, *S. gordonii*, and *streptococcus salivarius* surface (6). *S. pyrogenes*, *S. agalactiae*, *S. pneumoniae* are pathogenic streptococcus with 3-10 nm in diameter.

They can produce more than one copy (multiple) with single pilin subunit, can function as adhesins Pili perform adhesion function while types IV pili, it plays mediate adhesion as well as complex function i.e. force-driven construction and these function provides to bacteria with forceful implement to build with host membrane (5).

Type I Pili

Brinton was the scientist who determined the type I pilus structure with the use of electron microscopy, X-Ray diffraction, and crystallography (12). (fim-A) a gene cluster which encoded adhesive organelles, the thickness of this gene have 6.9 nm and 1-2 micrometer in length rod-like helical composite structure, is attached to fim F to a fim G and adhesive fim H which 3nm wide (13). Type I pili are mostly found on E. coli strain which belongs around the Entero-bacteriaceae family, In UPEC, the pilus is the greatly usual kind where this cystitis (bladder infection) is remarkable (14). Typically, the bladder site is sterile in particular healthy the infection of the primary site of every urinary tract infections (UTIs), is more than 90% (9)From the flow of urine, in the urinary tract not capable the colonize bacteria and circumvent to fastly7 clearance in adhesin of UPEC to host cell. At the pick of pilus formation, the particular FimH adhesin accomplishes from the binding of specific to host cells. FimH has a two-domain both can be seen in an immunoglobulins (Ig), both are modified with an N- terminal receptor- binding domain and C- terminal pilin domain (15). The collapse of pilin- domain missing the 7th strand, so Ig like insufficient/incomplete, and also it has supplied by another subunit of pilin or chaperone FimC. Mannose-containing receptors added with FimH indicate by the host cell in more characters (16,17).

Type IV pili

Major pilin protein, Type IV pili (T4P) are polymers that are exposed to a large number of Gram-negative bacteria surface, were recently also recognized on Gram-positive bacteria (18–20). In Gram-negative bacteria, T4P mediates a

distinct type of locomotion called gliding motility and which are not dependent on flagella called twitching motility (20–22). In addition to motility, T4P carry out a multitude of functions, including adherence to eukaryotic cells, microcolony formation, DNA uptake, and protein secretion, and some even function as nanowires carrying electric current (23–26). T4P are polymerized from an inner membrane-bound pool of pilin monomers and are held together in the core of the pilus filament via hydrophobic interactions among the conserved N-terminal segments of the proteins (27–30). Beyond this common N-terminal segment, pilins can vary substantially in size and sequence, producing pili with unique surface features, interaction partners, and functions (18,20). The canonical T4P system is closely related to several other systems in bacteria and archaea. The type II secretion (T2S) system in Gram-negative bacteria, the competence systems (Com) for DNA uptake in Gram-positive bacteria (31), and archaeal flagella (recently renamed archaella (32) all have structural homologs of proteins found in T4P systems, including the major building blocks of the filament (22,33). The central proteins in all these systems in Gram-negative bacteria are (i) the major pilin subunit (including the archaeal flagellin), (ii) a prepilin peptidase that processes pilins to a mature form, (iii) an assembly ATPase, (iv) an inner membrane core protein, and (v) an outer membrane secretin channel. Conserved sequences within these proteins can be used to identify T4P and related systems in any organism for which the genome sequence has been determined. T4P was firstly described in the 1970s for *Pseudomonas aeruginosa* (34,35), and afterward were identified on many Gram-negative bacteria including human pathogens. Preliminarily they are considered to be exclusive to Gram-negative bacteria, in the architecture-based part of the assembly apparatus, which spans both bacterial membranes and intervening periplasm. Filaments resembling T4P were reported for *Streptococcus sanguinis* and *Clostridium difficile* (36,37), two Gram-positive pathogenic bacteria, but T4P-dependent twitching or gliding motility was not described. The availability of multiple-strain genome sequences for *Clostridium perfringens* led to the

identification of T4P gene products in that species and a realization that all of the clostridial species sequenced up to that time (2006) contained likely T4P-associated gene products (38). Since then, hundreds of more Gram-positive bacterial genomes have been sequenced and it is clear that T4P genes are almost universal in clostridia and also occur sporadically in other families.

Streptococcus pyogenes

Belongs to gram-positive bacteria also called GAS (group A Streptococcus). This bacterial pathogen i.e. specific accommodate to the human host, is clinically vital, often caused RTI (respiratory tract infection) like strep throat (tonsillitis and pharyngitis). Pyoderma, superficial infection may be caused by group A streptococcus (GAS) (3).

Group A streptococcus in bacterial adherence

Variety of protein visualized in the surface of GAS cell as well as other macromolecules that make easy of the colonization of host membrane (reviewed in (4) Streptococcus adherence and colonization. At the beginning of adhesion, has time taking and hypothesized because of the two-step process, the high-affinity binding becomes more specific after weak interaction (39). In GAS, lipoteichoic acid moderated by weak hydrophobic interactions may confer earlier adherence to the host membrane (39). Some of the numerous proteins, adhesins are covalently attached through peptidoglycan by sortase enzyme to the cell surface, adhesins that permit GAS to colonize separated tissue lines (9,40,41).

M protein and its role in adherence

M protein has alpha-helical coiled-coil which diameter 60nm from the surface of bacteria (42), each of the monomers attached to the cell wall, and such process performed by the help sortase-A enzyme (40). EMM gene encrypted a protein is called M protein. Virulence factor, major surface protein combined and forms typing scheme of group A streptococcus. Four repeat regions (A-D) are composed of M protein which fluctuates in

amino acid composition as well as size. The antigenic diversity reveals appreciable reveal on the surface of N-terminus and the order of hypervariable A duplicate range more than 220 alternatives. The wide number of functions and molecules are interactions to the host membrane, have been M protein variants to assign (44,45,46).

M protein participates in adherence of GAS to host cells, which have to allow several verified studies. M1, M3, M5, M6, M18, and M24, these are multiple serotypes, have been denoting to put never- died cell lines to GAS adherence like HeP2 (3,39,44–47).

Mycobacterium tuberculosis

According to the world health organization (WHO), M tuberculosis is an extremely pathogenic microorganism, survey shows that during 2017-2018 it caused 1.3 million deaths worldwide. M. tuberculosis has difficulty in texture, his cell envelope consists of lipid, glycopolymers, glycolipids, protein, and polymers of mycolyl-arabinogalactan-peptidoglycan complex (16,48). It used our cell surface to join with EMC components as well as host surface receptors (49).

The cell envelope of *M. tuberculosis*

The covering of bacterial cell gives rigidity (mechanical), solute and protein are passes for transport, it protects itself from an adverse condition of environment & also plays the role of adherence to host cell receptor. The main four compositions of covering which lipid-rich) including Peptidoglycan, Arabinogalactan, Mycolic acid & capsule layers. These four compositions are above the plasma membrane (50–53).

Peptidoglycan (PG), made up of several units of Bita-1,4 linked N- glycolylmutramic acid (MurNGlyc) and N-acetylglusosamin (GlcNAc) constructing a mess like structure, this component is placed outside the plasma membrane. The MurGlyc unit bound through a lactyl bond liner

stem peptide of amino acids: L-Alanine (L-Ala), D-Glutamic acid (D-Glu), amidated Meso-diaminopimelic acid (meso-DAP) and D-alanine-D- alanine (D-Ala-D-Ala) (54–56). The terminal D- Ala is removed and the link is formed between meso-DAP of neighboring pentapeptide and the carboxylic group of D-Ala during the PG cross-linking(57). An additional non-classical cross-linking is observed in M. tuberculosis between meso-DAP in PG (58).

Arabinogalactan (AG), is a heteropolysaccharide of arabinose and galactose and AG layer placed above the PG layer. AG is covalently attached to PG's residue (10-12% of muramic acid) through the phosphodiester bond. In M. tuberculosis cell covering, large macropolymer which is constructive y PG and AG are placed between the plasma membrane and outer mycolic acid layer (Mycomembrane).

The outer covering of cell and host interaction

The cell envelope of M. tuberculosis is very complicated, it contains vivid ingredients such as myloic acid, protein carbohydrates, and other constituents like the matrix of peptidoglycan. Following research works of (59,60) proved that the mycobacterial cell wall consists of a large number of proteins (528 proteins). In M. tuberculosis 24.62% are involved in the procedure of macromolecule genesis and breakdown, 7.58% are implemented in cell procedure, and more efficient 35.23% are equate small molecule by metabolism, 19.13% hypotheticals proteins are maintenance and rest 13.45% unknown protein (59,60). Few proteins are like host cells which used in adhesion are rapidly identified and divided into three major groups respectively: - (i) single protein order surface protein, (ii) a group which doesn't have single peptide order, and (iii) transmembrane protein.

Colonization of host surface

 The surface area of about 300-400 square meters is covered by the representation of urogenital mucosa, digestive & respiratory. These areas are approximately 200 times fold larger than that of

the skin surface and with the help of bacteria among sites are constitute. A smooth muscles thin layer, the loose connective tissue of lamina propria, and an epithelium layer these above three layers are contained in the mucosa. The pathogenic bacteria and symbiotic both are aggregated on these surfaces to build frontline resistance. The level of resistance occurs by different defenses instead, the bacteria has many kinds of profile for adhesion to their surface of proliferating & epithelial surface. (61).

Bacterial entry into host cells

The zipper mechanism & the trigger mechanism both are used to rearrange the membrane of different kinds morphologically. This mechanism goes through the duration of bacterial cells entering a cell. In the earlier case, the bacterium compact enfolds the membrane. The interaction between a bacterial surface protein and its receptor on the host cell. The escape of bacteria pathogens from the internalization vacuole to replicate therein and the cytosol. A bacterium involves two major conquering proteins like internal in and I nib and this bacterium is the listeria monocyte gene (62,63).

The I nib mainly interact with Met, while internal in a bind to adhesion molecule cell E-cadherin growth factor receptor is hepatocyte during the entry, the modification of E-cadherin successive posttranslational around phosphorylation, ubiquitination (64), These modification goes through as well as Met (44). The critical for the entry of DRMs in the plasma membrane (65). In the starting bulking of E-cadherin, DRMs and their component (cave Olin) are critical, and needed for the entry process in a host cell that performed E-cadherin, in the I nib- mediated the DRMs play the role entry occurs at the end stage i.e., the activation of Rac in downstream of P13 kinase activation (65).

The entry in cell the lipid & DRMs works raft has been very other pathogens demonstrate involving R. conorii, rubella aborts us (66), & chlamydia is a special strain (67). The entry of Listeria is currently in the paradigm that the cadherin used

for the large object as bacteria & also plays the role in the internalization of small particles (44). With the entry of Listeria & a series of reactions, cadherin-mediated endocytosis is needed. It recruitment actin shift & needed for bacterial entry (44). The emerging of new techniques/methods in internalization sites deserve & fast invention. The mechanism of the second well studied is the trigger mechanism that is an apparition of big no. Of member is role at the bacterial site. In the bacterium, the structure is finally in a small macro pinocytosis entry site. Salmonella & Shigella are the best examples of trigger mechanisms in paradigms (68).

Direct bacterial interaction with the host plasma membrane

Bacterial pathogens perform various mechanisms attached to the plasma membrane, gram-positive and gram-negative bacteria both have pili, and they have extracellular matrix components like glycoprotein receptor or glycoprotein (69). They have some other factor that allows bacteria to attached or interact with the host membrane, streptococcus pyrogens is a gram-positive bacteria which have fibronectin and collagen-binding protein which help pathogen to interact with the host plasma membrane to interact with the host membrane it includes surface-associated adhesins which present on bacterial surface when multimeric pilus is absent and auto transporter (YadA) protein which binds collagen, laminin, and fibronectin (70,71).

EPEC (enteropathogenic *Escherichia coli*) EHEC (enterohaemorrhagic) has a unique mechanism, is used to attach with the host plasma membrane in which T3SS and TiR (type three secretion system, translocated intinin receptor) are used. Vivid actin polymerization signal development by EHEC TiR and EPEC, EHEC TiR consist a tyrosine residue (Y474) on C- terminal tail, when host adaptor protein (NcK) through its (Src) homology 2 domain (72).

Interaction with cell organelles (Golgi and Golgi derived vesicles)

Gram-negative bacteria which causes various infection site, bacteria like *C. trachomatis* (an obligate gram-negative bacteria). Chlamydia has two phases of life cycle lifestyle i.e. it shows a diphasic lifestyle. Cells impute a defensive elementary body of bacterium that undergoes differentiates into a replicative form that is called the reticulate body, and demonstrate inclusion (replication vacuole) (73). The establishment of replication vacuole needs a range of host cells as well as bacterial factors. On taking and inclusion formation (within two hours of uptake), an inclusion membrane protein that is known as bacterial effector protein insert and mutate the membrane of the vacuole. (74).

In a cell infected with chlamydia, the Golgi body (attached with chlamydia containing replication vacuole/ MOT) is segmented into ministacks because of golgin-84 cleavage. This Golgi fragmentation is vital for lipid accession by the inclusion because it allows the transfer of sphingomyelin precursor (ceramide) into inclusion. (75).

PI metabolism impedes chlamydia in PI4 metabolism number of proteins participates. In the Golgi complex, a lipid that superiorly restrains, are engaged to inclusion. These lower proteins, PI4KIIα, and 1(OCRL1) of oculocerebrorenal syndrome include Arf1, where consumption decreases the number of infections progeny and inclusion formation (76). (OCRL1 hydrolyzes) PI (4,5)P2 to P14P, P14KIIα phosphorylates PI to PI4P, and Arf 1 participates in recruiting PI4Ks and PI- binding protein to the Golgi (46,76).

Diversity of intracellular compartments used for bacterial replication

After entry into the cell, there is three main class of division in which intracellular bacteria can replicate. The first class corresponds to which bacteria that have an acidic pH and also contain hydrolytic enzymes is constituted by lysosome-like vacuoles. The second compartment, vacuole

situated within a cell (intracellular) and non-acidic in nature i.e. intracellular nonacidic vacuole that does not fuse to the lysosome, usually alters the structure by the pathogen. The third corresponds to the cytosol of the cell where some invader or pathogen can exist after exiting from the internalization vacuole.

There is a known widely example of an intracellular bacterium (coxiella burnetti, agent of a Q fever) that can survive in an intracellular lysosomal-like compartment (68,77).

Coxiella burnetti can proficiently replicate in the lysosome-like compartment as well as pathogens used this mechanism for their survival in this type of vacuole are not properly understood (77).

The diversity of non-acidic intracellular vacuoles, occupy the bacteria (pathogenic), additive to vacuoles as like lysosomal vacuole (68). These vacuoles are differentiated by these bacteria particularly and alternately the proteic and lipidic complexity or compartment of host vacuolar with their interaction and trafficking. Salmonella, as an example, after internalization in vacuoles occupied that under acidification but do not behave like lysosomal. T3ss of salmonella play a precious role in alternation and secreted several effectors in these salmonella-containing vacuoles. Some especially secreted effectors across the vacuolar membrane alternate the actin cytoskeleton regulating pathogen virulence and these vacuole surrounding by allowing the polymerization of actin basket.

Conclusion

Bacteria have evolved an exceedingly large and diverse array of adhesion and invasion molecules that enable them to exploit a variety of host-cell surface components and occupy different niches within the human body. Recent major advances were concerned with the biogenesis, structure, and assembly of earlier known invasins, pili, type III secretion systems, fimbriae, and new adhesive structures which surprisingly been discovered in Gram-positive bacteria such as streptococci, emphasizing the diversity of the approaches used

by pathogenic bacteria to adhere and colonize their hosts.

In several cases, it is challenging to assign to a given protein an invasin versus an adhesin function, as several invasins are frequently working as adhesins. The critical issue is that how contact is made, as for various membrane organizations, bacterial pathogens and the existence of micro-domains seem to administer key events in the internalization process. The future challenge will be to comprehend how bacteria synchronize in space-time, the different effectors' expression, and how the cell counters to this hostility. Understanding cells behavior in presence of a pathogen could also offer crucial answers to more universal questions in cell biology.

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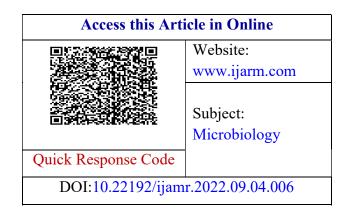
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