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REVIEW ARTICLE

Bacteriophage Polysaccharide Depolymerases and Biomedical Applications

Jianlong Yan · Jiaoxiao Mao · Jianping Xie

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Abstract Polysaccharide depolymerase, a polysaccharide hydrolase encoded by bacteriophages (or 'phages'), can specifically degrade the macromolecule carbohydrates of the host bacterial envelope. This enzyme assists the bacteriophage in adsorbing, invading, and disintegrating the host bacteria. Polysaccharide depolymerase activity continues even within biofilms. This effectiveness means phages are promising candidates for novel antibiotic scaffolds. A comprehensive compendium of bacteriophage polysaccharide depolymerases has been compiled, together with their potential biomedical applications, such as novel antibiotics, adjuvants for antibiotics, bacterial biofilm disruptants, and diagnostic kits.

1 Introduction

Polysaccharides play important roles in bacterial structure and function such as growth and physiology. Thick macromolecular polysaccharide layers can be found among most bacteria. Polysaccharides largely include capsular polysaccharides (K antigens) and lipopolysaccharides (LPS) (O antigen) (usually present in Gram-negative bacteria), peptidoglycan, and free extracellular polysaccharides. These polysaccharides are involved in bacterial pathogenesis, biofilm formation, and protecting the bacteria against killing and phagocytosing. The polysaccharide structure varies significantly; at least 80 different capsular K antigens have been documented in *Escherichia coli* [1]. Bacteriophages (or 'phages') are viruses that parasitize bacteria, and can specifically kill or infect the host bacterium, including some pathogens. Bacteriophage bactericidal activity largely relies on their hydrolytic enzyme characteristics, such as endolysins, lysozymes, and some polysaccharide depolymerases. In this paper, we summarize bacteriophage polysaccharide depolymerases and their biomedical applications.

J. Yan · J. Mao · J. Xie (✉)
Institute of Modern Biopharmaceuticals, State Key Laboratory Breeding Base of Eco-Environment and Bio-Resource of the Three Gorges Area, Key Laboratory of Eco-environments in Three Gorges Reservoir Region, Ministry of Education, School of Life Sciences, Southwest University, Chongqing 400700, China
e-mail: georgex@swu.edu.cn; jianpingxie@vip.sina.com

J. Yan
e-mail: 519465867@qq.com

J. Mao
e-mail: 476275984@qq.com

2 The Constituents of Bacterial Polysaccharides

The pleiotropic bacterial polysaccharides can be divided into intracellular polysaccharides, structural polysaccharides, and extracellular polysaccharides or exopolysaccharides (EPS). Bacterial structural polysaccharides largely consist of a peptidoglycan layer and an LPS layer. Bacterial EPS are mainly bacterial capsular polysaccharides, located in the outer cell wall, such as alginates, polysialic acids (PSAs), and hyaluronic acid (HA) (see Table 1). These polysaccharides play important roles in maintaining the integrity of bacteria, and virulence.

3 Polysaccharides Represent a Barrier for Interactions between Bacteriophages and Bacteria

The specific interaction between bacteriophage and host involves five stages: adsorption, invasion, synthesis of

Table 1 Components of bacterial extracellular polysaccharide

Bacterial polysaccharides	Bacterium	Structure and function
Structural polysaccharides		
PG	G^+ or G^-	Composed of a unit of disaccharides, *N*-acetyl glucosamine, and *N*-acetyl muramic acid, four peptide tails and peptide bridge; the component of the cell cytoskeleton, maintaining the stability of the cell; protecting bacterial cells from resisting outside pressure
LPS	G^-	Composed of O-polysaccharide, core-polysaccharide and lipid A; as the mammalian immune system birth one of the main targets of the enemy; serving as virulence factors of the pathogen; acting as congenital immune response receptor of ligands
Capsular polysaccharides		
Alginate	*Pseudomonas aeruginosa*, *Azotobacter vinelandii*	A linear polysaccharide, composed of aα-L-guluronate (G) and β-D-mannuronate; as an important virulence factor; inhibits nonopsonic phagocytosis by monocytes and neutrophils both in vitro and in vivo [2, 3]; enhances bacteria adhesion on airway epithelial cells and colonization rate in the respiratory tract; as a barrier of antibiotic penetration bacteria, decreases the uptake and early bactericidal effect of aminoglycosides [2]; inhibit the chemotaxis of polymorphonuclear leucocytes [4]; against IFN-γ-mediated killing by macrophages [5]; help to increase the viscoelastic properties of purulent CF airway secretions [6]
PSA	*Escherichia coli* K1, *Neisseria meningitidis* group B, *Mannheimia haemolytica* A2, *Moraxella nonliquefaciens*	Composed of 5-*N*-acetylneuraminic acid, 5-*N*-glycolylneuraminic acid, or deaminated neuraminic acid; as an important virulence factor to cause meningitis and sepsis; ability of making bacteria through the blood brain barrier; possess a poor immunogenicity; protect bacteria against complement-mediated cracking and opsonophagocytosis; play an important role in cell differentiation and development, organogenesis, neural plasticity, spatial learning, neural regeneration and malignancies; considered to be an oncofetal marker of a number of tumors
HA	*Streptococci*	Composed of a linear repetition of β-1-4-linked *N*-acetylglucosamine and D-glucuronic acid subunits; as a sole component of the capsule of group A *streptococci*; as an important of virulence factors; help to evade the human immune system

HA hyaluronic acid, *IFN* interferon, *LPS* lipopolysaccharide, *PG* bacterial peptidoglycan, *PSA* polysialic acids

phage macromolecular, assembly, and release. The adsorption of the phage and release of progeny phages play an important role in the bacteriophage infection process. The first barrier encountered by the bacteriophage is the polysaccharide structure of the bacterial surface, which represents a physical barrier for the phage (Fig. 1). Some bacteriophages can usurp the host bacteria surface polysaccharide to their advantage. Bacteriophage depolymerases are important in the disintegration of these polysaccharides.

4 Characteristics of the Bacteriophage that Encode Polysaccharide Depolymerase

4.1 Most Bacteriophages with Polysaccharide Depolymerases belong to *Caudovirales*

Bacteriophages are viruses of prokaryotes widespread in the biosphere. About 5,100 phages have been documented [7]. The phages are classified into 13 families and 30 genera, based on their shape, size, type of nucleic acid, and presence/absence of envelope or lipids in their structure. Most belong to the tailed bacteriophage, with an icosahedral head and a tail and double-stranded DNA. Tailed bacteriophages are estimated to outnumber their host species by a factor of ten [8]. Tailed bacteriophages are subdivided into three different families according to microscopic features of the tail morphology: the *Myoviridae*, the *Siphoviridae*, and the *Podoviridae*, reproducing Bradley groups A, B, and C, respectively [9, 10]. These three families make up the order *Caudovirales*, also referred to as tailed phages [11, 12]. The *Caudovirales* can recognize the surface receptor of the host and adsorb to the host surface by specifically digesting the surface polysaccharide of the host via tailed-associated protein. At present, most bacteriophages capable of degrading polysaccharides are virulent bacteriophages, while only very few are temperate bacteriophages. These bacteriophages belong to

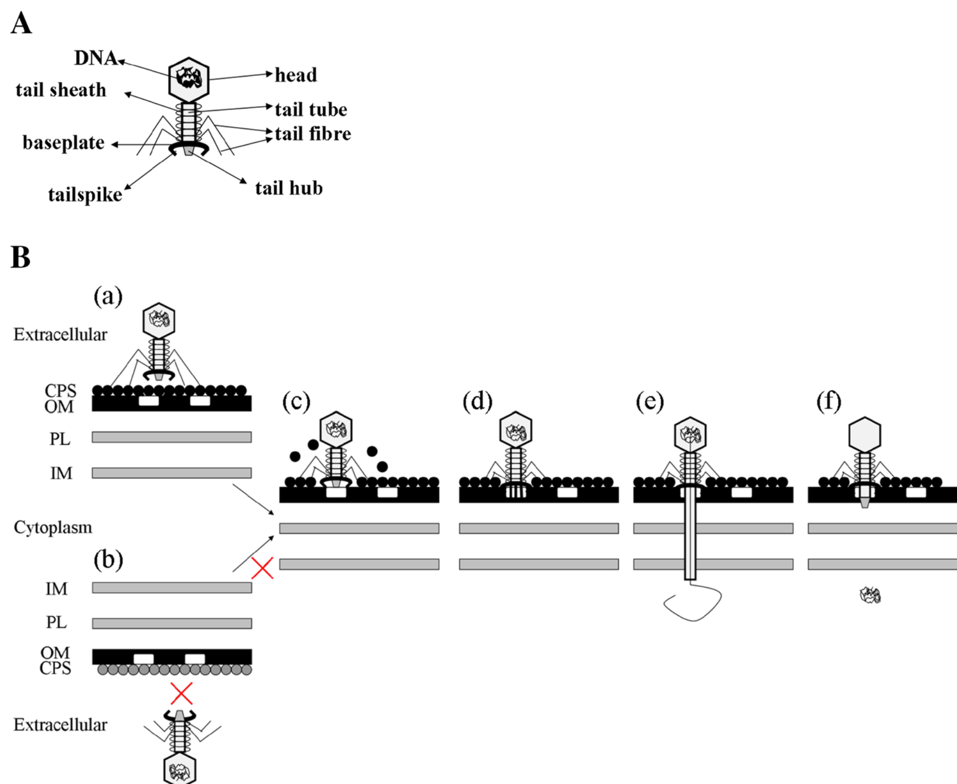

Fig. 1 The structure of a typical tailed bacteriophage (**a**) and the general model of bacteriophage infection (**b**). *a* Bacteriophage tail fibers come into contact with and recognize CPS on the cell surface. *b* When the bacterial CPS phage tail fiber does not recognize and digest the CPS, the phage does not bind to receptor on the cell surface. *c* The virus digests the CPS to reach the cell surface and *d* binds to a receptor on the cell outer membrane, causing the tail hub to open. *e* The phage tail tube forms a channel across the periplasmic space, thereby directing the viral DNA into the host cell cytoplasm. *f* After the viral genome has been completely internalized, the perisplamic tube seals to prevent leakage of cytoplasm, while the empty capsid remains on the cell surface. *CPS* capsule polysaccharides, *IM* inner membrane, *OM* outer membrane, *PL* peptidoglycan layer, the *black circle* and *gray circle* indicate CPS, the *white rectangle* indicates receptor on bacterial surface

Caudovirales (tailed-bacteriophage) or C group of bacteriophage.

4.2 Polysaccharide Depolymerase Protein is a Common Constituent of the Tail Structure of Bacteriophage

The virus particle of most studied tailed bacteriophages consists of an icosahedral capsid, or phage head, attached to the tail. The capsid shields a double-stranded DNA molecule, while the tail is responsible for specific adsorption/binding to host surface receptors and for efficient delivery of the phage genome across the bacterial cell envelope. Therefore, the tail apparatus of bacteriophages plays a key role in the tailed-bacteriophage infection of the host cell. Numerous studies have shown that activities of the tailed bacteriophage polysaccharide depolymerase is related to its tail structure. Tailspike proteins (TSPs) are components of the tail apparatus of many bacteriophages, and mediate the specific recognition of its bacterial host by binding to surface structures such as polysaccharides [13]. Additionally, many TSPs have endoglycosidase activity, hydrolyzing their polysaccharide receptors. TSPs identified to date include homotrimers consisting of an N-terminal capsid-binding domain, a central domain that binds/hydrolyzes the O-antigen region of bacterial surface LPSs, and a C-terminal region crucial for trimerization. A hallmark of TSPs is their high stability. TSPs, as well as their N-terminal truncated versions, are resistant to protease treatment, heat exposure, high concentrations of urea and sodium dodecyl sulfate (SDS), and can be reversibly unfolded in concentrated chemical denaturants [13, 14]. One well studied TSP is that of bacteriophage P22, which is a 215-kDa trimeric protein specifically recognizing several pathogenic *Salmonella* spp. including *Salmonella enterica* serovar *Typhimurium* [15, 16]. The P22 gene 9 protein forms the hexameric tailspike that recognizes the O-antigen of the host *Salmonella* LPS and harbors an endorhamnosidase activity, cleaving the α-(1 → 3) glycoside linkages between rhamnose and galactose and producing dimers of 2 O-antigen repeat units (RU) as the main product [17, 18]. φMR11, a siphovirus, was a candidate

therapeutic phage against *Staphylococcus aureus* infections. φMR11 gp61 is a tail-associated lytic factor involved in local cell-wall degradation [19].

4.3 The 'Halo'

Bacteriophage polysaccharide-degrading capacity was first discovered in 1929. One feature of the bacteriophage is to form a circular bull's eye outside the plaque, termed the 'halo'. During the infection, the bacteriophage will produce some free depolymerases; both the infection process and the release of the phage progeny phase need such depolymerases. The presence of a halo indicates the capsule hydrolytic activity. The differential migration of the diffused depolymerases and the phage, which the latter is lagged, results in the development of a halo.

5 Bacteriophage Polysaccharide Depolymerases

Bacteriophage polysaccharide depolymerases are a specific hydrolytic enzyme that can use polysaccharides or polysaccharide derivatives as their substrate. Some typical depolymerases are listed.

5.1 Some Endolysins or Lysins are Polysaccharide Depolymerases

Bacteriophage-encoded lytic enzymes, such as endolysins or lysins, are produced by bacteriophages to digest the bacterial cell wall for bacteriophage progeny release. Depending on the enzymatic specificity, endolysins are divided into five main classes: *N*-acetylmuramidases (lysozymes), endo-β-*N*-acetylglucosaminidases, lytic transglycosylases, endopeptidases, and *N*-acetylmuramoyl-L-alanine amidases. Endo-β-*N*-acetylglucosaminidases, lytic transglycosylases, and *N*-acetylmuramidases act on the sugar moiety of the bacterial wall and can be categorized as polysaccharide depolymerases. But endopeptidases, which cleave the peptide moiety, and *N*-acetylmuramoyl-L-alanine amidases, which cut the amide bond connecting the glycan strand and peptide moieties, are not polysaccharide depolymerases.

5.2 Endorhamnosidase

Endorhamnosidase encoded by bacteriophages can specifically hydrolyze the bacterial outer membrane LPS. These bacteriophages largely infect Gram-negative bacteria. The first step of phage infection is the recognition mediated by the receptor of the host bacterium surface. Known receptors mediating bacteriophage recognition mainly include the protein receptors, LPS receptor, *pilus*, and flagella receptors, as well as the capsular polysaccharide receptors [20]. A common feature of bacteriophages attaching to the LPS O-chain is that their adsorption can result in polysaccharide chain-specific lyses [20]. Many depolymerase-encoding bacteriophages can absorb and degrade bacterial LPS (see Table 2). For example, bacteriophage HK620 specifically infect *E. coli* H, bacteriophage ε^{15}, P22, and Det 7 specifically infect *Salmonella*, and bacteriophage Sf6 specifically infect *Shigella*. All of these bacteriophages have been found to involve endorhamnosidase activities that degrade the bacterial LPS receptor [17, 21–24]. The HK620 tailspike has endo-*N*-acetylglucosaminidase activity and produces hexasaccharides of an O18A1-type O-antigen [21]. The activities of enzymes usually are associated with TSPs of bacteriophage. These TSPs form a very stable homotrimer, and the structure of the tailspike subunit can be divided into three parts: an amino-terminal head-binding domain, a central parallel-β-helix domain containing 13 complete right-handed β-helical turns, and a carboxy-terminal. The highly interwoven part is important for trimerization, thermostability, and the observed resistance to dissociation by SDS. The amino-terminal domain is thought to be flexibly attached to the other two parts, which together form a rigid unit; the flexibility of the short linker peptide may be important in the process of infection. The central β-helix domain binds to the O-antigen region of the bacterial cell surface LPS. It exhibits endorhamnosidase enzymatic activity, cleaving the O-antigen polysaccharide.

5.3 Alginate Lyase

Alginate lyses have been isolated from various sources, such as marine algae, marine mollusks, fungi, bacteria, bacteriophages, and viruses [27]. Furthermore, alginate lyases have also been detected in certain bacteriophages that are specific for *Pseudomonas aeruginosa* [28, 29] and *Azotobacter vinelandii* [30], and a lyase gene was recently found to be associated with a *Chlorella* virus [31]. Based on their different substrate specificities, alginate lyases, as an alginate-depolymerization enzyme, are classified into three groups: the first type is specific for G block guluronate lyase, the second type for M block mannuronate lyase, and the third type is bifunctional for both G and M blocks [27, 32]. Moreover, they are also grouped into three types based on their molecular masses: small (25–30 kDa), medium (around 40 kDa), and large [27] (>60 kDa) lyases. Thus, alginate lyases show a wide molecular diversity. Alginic acid polysaccharide depolymerase produced by bacteriophages is mainly a proteolytic enzyme that degrades alginate and polymers of alginate capsular polysaccharide. It can break the glycosidic bond in alginate and alginate capsular polysaccharide produced by pathogenic bacteria by β-elimination reaction. These enzymes help the

Table 2 Some known endorhamnosidase

Name	Bacteriophage	Virus family	Accession	Size	References
Endorhamnosidase	Det7	Myovirus	CAO78738.1	708aa	[23]
Endorhamnosidase	P22	Podoviridae	AAM81383.1	667aa	[17]
Endorhamnosidase	Sf6	Podoviridae	AAD33394.2	623aa	[14]
Endo-N-acetylglucosaminidase	Bacteriophage HK620	Podoviridae	2VJI_A	600aa	[21]
Endorhamnosidase	Bacteriophageε^{15}	Podoviridae	–	–	[22]
Endogalactoseaminidase	Bacteriophageφ1	UN	–	–	[25]
Endomannosidase	BacteriophageΩ8	UN	–	–	[26]

UN unknown, '–' indicates protein not cloned and expressed

phage penetrate the acetylated poly (M)-rich EPS produced by host bacteria. The phage lyases have endolytic activity on their respective host EPS, and molecular masses ranging from 30 to 42 kDa, and optima pH are between 7.5–8.5. The alginate lyase gene from a *Chlorella* virus has recently been cloned and sequenced. This 39-kDa enzyme shows weak homology to SP2, the mannuronate lyase from Trachinus *cornutus* has a pH optimum of 10.5, and requires Ca^{2+} for enzyme activity [31]. Moreover, PT-6 was *a P. aeruginosa*-specific phage belonging to the Podoviridae family C1. The enzyme can reduce the viscosity of four alginate preparations and release uronic acid-containing fragments from the polymers [29].

5.4 Endosialidase

Sialidase is a specific hydrolase-degrading PSA. Three different types of sialidases are distinguished, based on the mode of cleavage reaction [33]: (i) exosialidases (exo-α-sialidase, neuraminidase), which remove terminal sialic acid moieties from glycosyl conjugates, typically belonging to the family of retaining glycosidases, which act using a two-step double-displacement mechanism via a covalent glycosyl-enzyme intermediate [34, 35]; (ii) anhydrosialidases are a special exosialidase that release 2,7-anhydro-a-*N*-acetylneuraminate in an elimination reaction from the non-reducing end [36]; (iii) endosialidases (endo-a-sialidase, endoNF) is a glycosyl hydrolase that specifically cleaves a 2,8-linkage of PSA instead of the promiscuous cleavage by exosialidases and anhydrosialidases. EndoNF has recently been described as an inverting sialidase [37]. Since endosialidases can cleave PSA composed of either 5-*N*-acetylneuraminic acid (Neu5Ac) or 5-*N*-glycolylneuraminic acid (Neu5Gc)—two derivatives of sialic acid in a 2,8-linkage, endosialidases have also been called 'endo-*N*-acyl-neuraminidases' [38]. All known endosialidases so far are specialized TSPs of bacteriophages infecting encapsulated *E. coli* strains. Six endosialidase genes have been cloned and expressed as functional proteins from *E. coli* phages K1A, K1E, K1F, 63D, K1-5, and prophage CUS-3 (see Table 3).The proteins encoded by these genes share a common architecture, including three domains: (i) an N-terminal capsid-binding domain is required to anchor the endosialidase tailspike to the phage particle. This domain varies in length in different phages and is dispensable for enzymatic activity [39, 40]; (ii) a highly conserved central catalytic domain comprises the polySia binding and cleavage activities; (iii) a short C-terminal domain (CTD) that functions as an intramolecular chaperone and is released from the matured enzyme [39, 41]. The CTD is required for proper folding of the catalytic part.

5.5 Hyaluronidases

HA lyase is a glucosaminidase that can degrade glycosaminoglycan family high-molecular-weight polysaccharides. Hyaluronidases are produced by a variety of organisms, including mammals, insects, leeches, and bacteria [48]. In terms of their enzymatic mechanisms, hyaluronidases are divided into 'true' hyaluronidases of eukaryotic origin that cleave the glycosidic β-1- 4 linkage using a substrate-assisted acid-base catalytic mechanism [49] and hyaluronate lyases of bacterial origin that hydrolyze the same linkage via a β-elimination mechanism [50]. Besides these well-known sources, phage-encoded hyaluronidases from *Streptococcus pyogenes* and *Streptococcus equi* have also been identified [51] (see Table 4). *S. pyogenes* is an HA-encapsulated group A Streptococci that is known to have bacteriophage sequences in its genome [52]. The hyaluronate lyase, HylP2, is the bacteriophage hyaluronidase present in the *S. pyogenes* strain 10403 [53]. Another hyaluronidase, HylP1, has been isolated and characterized from the prophage sequences of *S. pyogenes* strain SF370.1 [54]. The *S. equi* prophage-encoded hyaluronate lyases SEQ2045 are hyaluronan-specific and are thought to be primarily involved in the degradation of the hyaluronan capsule of streptococci during bacteriophage infection [55]. These bacteriophage hyaluronidases are lyases, catalyzing through a β-elimination mechanism similar to the bacterial hyaluronidases. The phage hyaluronidase recognizes hyaluronan as its only substrate. Its main function is to assist the phage to

Table 3 Some known endosialidases

Name	Bacteriophage	Bacteriophage family	Accession	Size	References
endoNA	K1A	Podoviridae	ABP02011.1	811aa	[42]
endoNE	K1E	Podoviridae	CAA85449.2	811aa	[43]
endoNF	K1F	Podoviridae	AAZ73001.1	1064aa	[44, 45]
endoN63D	63D	Siphoviridae	ADA82273.1	984aa	[46]
endoNK1-5	K1-5	Podoviridae	AAG59822.1	811aa	[47]
			AAG59821.1	632aa	
endoNK1	CUS-3	Prophage	CAJ29292.1	981aa	[40]

penetrate the HA capsule surrounding the host cells of this phage and hence gain access to the cell surface of the host *Streptococcus* [53]. At the primary sequence level, the CAZy classification [56] places the eukaryotic hyaluronidases into glycoside hydrolase family 56 and the bacterial hyaluronate lyases into polysaccharide lyase families 6, 8, and 16, the last family exclusively comprising streptococcal bacteriophage and prophage members.

5.6 Other Polysaccharide Depolymerases

Phage polysaccharide depolymerases other than those mentioned above have also been found. K5 lyase A (KflA) is a TSP encoded by a K5A coliphage, which cleaves K5 capsular polysaccharide, a glycosaminoglycan with the RU -4)-βGlcA-(1,4)-αGlcNAc(1-, displayed on the surface of *E. coli* K5 strains [60]. Moreover, virus K2 hydrolyses capsule of *Aerobacter aerogenesis* using glucane hydrolase splitting α1,3-bond between galactose residues [61].

6 The Application of Polysaccharide Depolymerase

6.1 Bacteriophage Polysaccharide Depolymerases for Antibiotics

Polysaccharides are important integral components of bacteria. Therefore, bacteriophage polysaccharide depolymerases might be good starting point for improved antibiotics. Fire blight caused by *Erwinia amylovora* is the most destructive bacterial disease of pear and apple. In order to improve fire blight resistance in apples, *E. amylovora* phage phi-Ea1 h gene encoding an EPS depolymerase was transferred into apple *scion cv* via an *Agrobacterium tumefaciens*-mediated leaf disk transformation system using a binary vector [62]. Resistance to *E. amylovora* was evaluated by in vitro infection of leaves as well as by inoculation of ex vitro apple plants in the greenhouse. The φV10 TSP recognizes and degrades the O157 LPS [63].

6.2 Biofilm Disruptants

Most bacteria can grow in biofilm, which is the aggregate of microorganisms and their extracellular polysaccharide matrix products [64], in some stages. Bacteria within biofilm are difficult to manage as the unique structure of biofilm renders the bacteria impervious to drugs and inaccessible to conventional host immunity [65, 66]. Biofilm polysaccharides also protect the bacteria against the majority of phages. It is interesting that bacteriophages can produce polysaccharide depolymerases that degrade the extracellular polysaccharide matrix of the biofilm [66, 67]. Therefore, phages can use the specific polysaccharide depolymerase to degrade the extracellular polysaccharide matrix of the biofilm and gain access to the bacterial

Table 4 Some known hyaluronidases

Name	Bacterium or bacteriophage	Bacteriophage family	Accession	Size	References
hylP	*Streptococcus pyogenes* phage H4489A	n.d.(prophage)	AAA98101.1	371aa	[57, 58]
HylP1	*Streptococcus* phage 370.1	Siphoviridae	AAK33657.1	337aa	[54]
HylP2	*Streptococcus* phage 370.3	n.d. (prophage)	AAK33900.1	372aa	[59]
HylP3	*S. pyogenes* M1 GAS	n.d. (prophage)	AAK34249.1	370aa	[59]
SEQ2045	*Streptococcus equi*	n.d. (prophage)	YP_002747260	372aa	[55]
HylP2	*S. pyogenes phage* H10403	n.d. (prophage)	AAA86895.1	337aa	[53]
HA Lyase	*Streptococcal* phage-encoded tail-fiber	n.d. (prophage)	2C3F_A	358aa	[54]

n.d. not divided

surfaces [67]. Phages have proven able to remove *Proteus mirabilis*, *E. coli*, *Streptococcus suis*, *Klebsiella pneumoniae*, *P. aeruginosa*, and other bacteria formations of biofilm [68–70]. T4 phage can infect and replicate within *E. coli* biofilms and disrupt the morphology of the biofilm by killing bacterial cells [71]. KPO1K1, a depolymerase producing lytic bacteriophage, can specifically infect *K. pneumoniae* B5055, which is an opportunistic pathogen frequently associated with nosocomial infections. KPO1K2 treatment alters the structure of the *K. pneumoniae* B5055 biofilm matrix and decreases the size of the micro-colony [72]. KPO1K2 alone can significantly eradicate older biofilms, and its action is primarily depolymerase mediated; the purified depolymerase showed optimum activity at 37 °C and pH 7.0 [73].

6.3 Antibiotic Adjunctive Agent

The increasing incidence of drug-resistant isolates necessitates novel measures to control pathogens. *P. aeruginosa* is one of the most important opportunistic human pathogens, especially for cystic fibrosis. Alginate produced by mucoid strains of *P. aeruginosa* not only can act as a barrier to prevent antibiotic penetration [3], but also decreases the uptake and early bactericidal effect of aminoglycosides by blocking the diffusion of positively charged hydrophilic drugs [74]. Alginate lyase from phages can facilitate the diffusion of aminoglycoside drugs [75] to overcome the biofilm [76]. Combining antibiotics with alginate lyase can effectively kill *P. aeruginosa* within biofilms [77]. Alginate lyase biofilm dispersing and antibiotic synergy are catalysis independent [78]. This combined administration of polysaccharide depolymerase and antibiotics represents promising measures to combat drug resistance and biofilm-related infection.

6.4 As a Diagnostic Agent

Poly (sialic acid) units of the neural cell adhesion molecule (polySia) is an oncofetal marker for several tumors [79, 80]. PolySia favors the growth and metastasis of malignant neural cells by escaping the immune system [81]. The very same polySia is the constituent of the capsule of bacteria causing meningitis and septicemia. The polySia favors the pathogenesis of bacterial infections by conferring serum resistance and escape from immune defense due to the well-tolerated host-mimicking capsule [82, 83]. A new conceptual polySia mimic antibody, namely green fluorescent protein (GFP), fused with a catalytically inactive endosialidase known to bind but not degrade PSA, can efficiently and specifically detect PSA in the developing brain, neuroblastoma cells, and bacteria causing meningitis [84]. This represents a new aspect to harnessing phage enzymes for diagnostics.

7 Concluding Remarks

Polysaccharide on the bacterial surface represents an evolutionary tactic to empower bacteria with resistance to stress and virulence. Measures to destroy this polysaccharide can be involved in effective novel approaches to combat pathogens. Phage-encoded polysaccharide depolymerase can provide an alternative for improved antibiotics and diagnostic tools.

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