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Bacterial enzymes – Hyaluronidase

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ABSTRACT

Bacterial enzyme 'Hyaluronidase' is a complex polysaccharide degrading enzyme that cleaves β-GlcNAc-(1→4) glycosidic linkage of Hyaluronate (HA) by β-elimination process. It is synthesized by a spectrum of gram-positive bacteria which serve as potential contributors to a multitude of infectious diseases in human beings. Especially, group A streptococcus bacteria (GAS) have evolved several orders of magnitude to attack the host organism and establish infection. Hyaluronidase led pathogenic/ infectious cycle is accomplished through a cascade of events where an escape from the host's immunity is very important. In this regard, a variety of factors are utilized by hyaluronidases which determine the successful bacterial penetration into hosts, like the use of substrate HA and/or it's enveloping capsule as energy source during HA lysis, genetic variation among the bacterial strains in the form of allelic polymorphisms, hyaluronidase enzyme structure-driven substrate binding properties etc. Previous studies have furnished better insights on nucleotide sequences of hyaluronidase genes and immunopathogenesis. However, for a better understanding of hyaluronidase association with bacteria and overall host-pathogen interaction, much investigation and literature support is still needed.

KEYWORDS

Bacteria;
Enzyme;
Hyalloronidase;
Pathogenic.

INTRODUCTION

Enzymes of certain pathogenic bacteria constitute special biochemical entities that often facilitate a link between the bacteria and the host organism. This mode of establishment is essential for completing the infection cycle and contributing to an adverse health outcome. One of the most successful candidates of such enzyme driven pathogenesis is Hyaluronidase or Hyaluronate lyase. (EC 4.2.2.1)[1]. These are polysaccharide degrading enzymes that mostly cleave β-GlcNAc-(1→4) glycosidic linkage of Hyaluronate (HA) by β-elimination process[2]. HA, the targeted substrate of Hyaluronidase, is a high molecular weight glycosaminoglycan polymer produced by Hyaluron synthases and is essential for maintaining the integrity of extracellular matrix[3].

The biology of HA is very important for a detailed functional understanding of hyaluronidase activity. HA is mainly localized in body tissues and fluids of higher organisms like umbilical cord, synovial fluid, cartilage, brain, and muscles with an equivalent proportion predominating in the skin region[4]. However, its presence in soft connective tissues has good significance. Hyaluronidase is functionally involved in biological processes with an increased role during embryogenesis, cell move-

ment, tissue repair, malignant transformation, and tissue turnover[5].

HYALURONIDASE SYNTHESIS

Hyaluronidases are chiefly produced by a wide range of gram positive bacteria. These are streptococci groups A, B, C and G[6], *Streptococcus pneumonia* and *Streptococcus constellatus*[7], *Streptococcus dysgalactiae*[8], and *Streptococcus uberis*[9]. Similarly, *Staphylococcus aureus* and *Staphylococcus hyicus* subsp. hyicus[10], *Clostridium perfringens* (Mu toxin)[11],*Clostridium difcile*[12], *Clostridium septicum* (Q toxin) and *Clostridium chauvoei*[13], *Propionibacterium acnes* and *Propionibacterium granulosum*[14]. *Streptomyces hyalurolyticus*, *Streptomyces coelicolor* and *Streptomyces griseus*[15].

Phage encoded hyaluronidases of group A streptococcal bacteria type also have a significant role in establishing the infection cycle. The examples include bacteriophages of *Streptococcus pyogenes*[16] and *Streptococcus equi*[17]. Hyaluronic acid or hyaluronan present in host cells is surrounded by a rigid capsular material. The diffuse spread of bacteria in host organism is determined by the utilization of host's HA and/or energy supplementing capsule of HA[18]. Bacteriophages take the assistance of hyaluronidase to penetrate the capsular material and get access to the cell surface of the host streptococcus[19].

Thus, bacteria of group A streptococcus (GAS) have evolved a special mechanism to escape the host's immune attack by hyaluronidases led catalytic degradation of HA that leads to bacterial infiltration in tissues and gradual distribution[20]. Hyaluronidase spreading factor, spnHL has been reported from *Streptococcus pneumoniae* that degrades hyaluronan by enzymatic beta-elimination process[21]. Greater the degradation of HA by hyaluronidases more will be the internalization of bacteria.

GENETIC STUDIES ON HYALURONIDASE

Next, genetic studies have revealed the existence of hyaluronidase gene allelic polymorphism which is responsible for its genetic variation and host interacting mechanisms[22]. The gene for hyaluronidase enzyme named, hylA is widely distributed among a multitude of *Streptococcus pyogenes* strains; it encodes an 868 amino acid protein that has a size of 95941 Da[23]. In addition, nucleotide sequences of hyaluronidase genes have been determined. This encompasses eight bacterial hyaluronidase genes namely, *S. aureus* (U21221)[24], *Streptococcus agalactiae* (Y15903)[25], *S. pneumoniae* (L20670)[7], *S. griseus* (AB028210), *S. coelicolor* (AL031124), *P.acnes* (U15927)[26], *C. perfringens* (P26831)[11], *Proteus vulgaris* (1095454)[27] and *Bacteroides thetaiotaomicron* (L42367)[28]. Similarly, nucleotide sequences of bacteriophage hyaluronidases have also been determined. These include temperate phages that infect group A streptococci namely M19348 and U28144[16]. Hyaluronidases produced by various streptococcal bacteriophages vary with regard to size which may range from 36kDa to 160 kDa[1,16]. This molecular weight variation corresponds to known deduced amino acid sequence of hyaluronidases.

Hence, information obtained from sequence alignments and deduction could help in assessing the similarities or distant relationships among the members of bacterial hyaluronidases. For example, a high degree of similarity was shown by bacteriophage hyaluronidase genes when a region of collagen-like Gly-X-Y was found with a deletion or addition[16, 29].

ROLE IN INFECTION

Immunologic properties exhibited by hyaluronidases have been explored due to their better association with the temperate bacteriophages specific of M type of group A streptococci[30]. Thus, individuals infected with group A streptococci may have detectable antibodies to phage-encoded hyaluronidase in their serum[31].

STRUCTURAL PROPERTIES

In fact, the degrading potential of many pathogenic bacterial hyaluronidases is due to their en-

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larged cleft structure for harboring substrates like HA[21]. The cleft's structural integrity added to its localization in the helices and loops of twisted enzyme configuration permits' better substrate binding. Hyaluronidases of bacteria possess a four-domain structure that is fixed to the bacterial surface through covalent linkages to the cross bridges of peptidoglycan motifs[21, 32]. Most streptococcal hyaluronidases tend to follow a common hyalurunon degrading mechanism known as proton acceptance and donation (PAD)[21]. So, it is apparent that structure and mechanism are vital in favoring substrate binding.

CONCLUSION

In view of the above, it can be concluded that bacterial hyaluronidases are complicated and have much evolved from the structural and mode of action perspectives. Much research investigation is needed from biochemical assays to bioinformatic analysis to gain further insights.

REFERENCES

[1] R.Linhardt, P.Galliher, C.Cooney; Polysaccharide lyases, Appl.Biochem.Biotechnol., **12(2)**, 76-135 **(1986)**.

[2] E.Menzel, C.Farr; Hyaluronidase and its substrate hyaluronan: Cancer Lett., **131**, 1-3 **(1998)**.

[3] R.Stern; Hyaluronidases in cancer biology, Semin.Cancer Biol., **18**, 275-80 **(2008)**.

[4] T.F.Laurent; Hyaluronan, Jre.Faseb.J., **6**, 2397-2404 **(1992)**.

[5] K.Girish, K.Kemparaju; The magic glue hyaluronan and its eraser hyaluronidase: A biological overview, Life Sci., **80**,1921-43 **(2007)**.

[6] E.Gunther, J.H.Ozegowski, W.Kohler; Occurence of extracellular hyaluronic acid and hyaluronate lyase in streptococci of groups A, B, C, and G Zent.bl.Bakteriol., **285**, 64-73 **(1996)**.

[7] A.Berry, R.Lock, S.Thomas, D.Rajan, D.Hansman, J.Paton; Cloning and nucleotide sequence of the Streptococcus pneumoniae hyaluronidase gene and purification of the enzyme from recombinant Escherichia coli.Infect.Immun., **62**,1101-1108 **(1994)**.

[8] L.Calvinho, R.A.Almeida, S.P.Oliver; Potential virulence factors of Streptococcus dysgalactiae associated with bovine mastitis, Vet Microbiol, **61**, 93-110 **(1998)**.

[9] P.Schaufuss, R.Sting, W.Schaeg, H.Blobel; Isolation and characterization of hyaluronidase from Streptococcus uberis, Zent.bl.Bakt.Hyg., **271**, 46-53 **(1989)**.

[10] B.Skalka; Hyaluronidase test in the diagnosis of staphylococci, Vet Med (Prague), **30**, 373-378 **(1985)**.

[11] B.Canard, T.Garnier, B.Saint-Joanis, S.Cole; Molecular genetic analysis of the nagH gene encoding a hyaluronidase of Clostridium perfringens, Mol.Gen.Genet., **243**, 215-224 **(1994)**.

[12] S.Hafiz, C.Oakley; Clostridium diffcile: isolation and characterisitics, J.Med.Microbiol., **9**, 129-136 **(1976)**.

[13] T.Princewell, C.Oakley; Deoxyribonucelases and hyaluronidases of Clostridium septicum and Clostridium chauvoei.III. Relationship between the two organisms, C.L.Med.Lab.Sci., **33**, 118 **(1976)**.

[14] C.S.Cummins, J.L.Johnson; Priopionibacterium Orla-Jensen 1907, 337AL, In: Sneath PHA, ed, Bergey's Manual of Systematic Bacteriology, Los Angeles, United States: Williams and Wilkins,1346-1353 **(1986)**.

[15] T.Ohya, Y.Kaneko; Novel hyaluronidase from Streptomyces, Biochim.Biophys.Acta., **198**, 607-609 **(1970)**.

[16] W.L.Hynes, L.Hancock, J.J.Ferretti; Analysis of a second bacteriophage hyaluronidase gene from Streptococcus pyogenes: evidence for a third hyaluronidase involved in extracellular enzymatic activity, Infect Immun, **63**, 3015-3020 **(1995)**.

[17] J.F.Timoney, L.Pesante, C.Ernst; Hyaluronidase associated with a temperate bacteriophage of Streptococcus equi.In: Sclessinger D, Ed.; Microbiology., Washington, D.C.Unite States: American Society of Microbiology,145-146 **(1982)**.

[18] C.R.Starr, N.C.Engleberg; Role of hyaluronidase in subcutaneous spread and growth of group A streptococcus, Infect Immun, **74(1)**, 40 **(2006)**.

[19] J.R.Baker, S.Dong, D.G.Pritchard; The hyaluronan lyase of Streptococcus pyogenes bacteriophage H4489A, Biochem.J., **365(Pt 1)**,317-22 **(2002)**.

[20] A.M.Marciel, V.Kapur, J.M.Musser; Molecular population genetic analysis of a Streptococcus pyogenes bacteriophage-encoded hyaluronidase gene: recombination contributes to allelic variation, Microb Pathog, **22(4)**,209-17 **(1997)**.

[21] S.Li, S.J.Kelly, E.Lamani, M.Ferraroni, M.J.Jedrzejas; tructural basis of hyaluronan degradation by Streptococcus pneumonia hyaluronate lyase, EMBO J., **19(6)**,1228-4 **(2000)**.

[22] W.L.Hynes, A.R.Dixon, S.L.Walton, L.Aridgides The extracellular hyaluronidase gene (hylA) of Streptococcus pyogenes, FEMS.Microbiol.Lett., **184(1)**, 109-12 **(2000)**.

[23] J.R.Baker, S.Dong, D.Pritchard; The hyaluronan lyase of Streptococcus pyogenes bacteriophage H4489A, Biochem.J., **365(Pt 1)**, 317-22 **(2002)**.

[24] A.M.Farrell, D.Taylor, K.T.Holland; Cloning, nucleotide sequence determination and expression of the Staphylococcus aureus hyaluronate lyase gene, FEMS.Microbiol.Lett., **130**, 81-85 **(1995)**.

[25] K.Gase, J.Ozegowski, H.Malke; The Streptococcus agalactiae hylB gene encoding hyaluronate lyase: completion of the sequence and expression analysis, Biochim.Biophys.Acta., **1398**, 86-98 **(1998)**.

[26] B.Steiner, S.Romero-Steiner, D.Cruce, R.George; Cloning and sequencing of the hyaluronate lyase gene from Propionibacterium acnes, Can.J.Microbiol., **43**, 315-321 **(1997)**.

[27] N.Sato, M.Shimada, H.Nakajima, H.Oda, S.Kimura; Cloning and expression in Escherichia coli of the gene encoding the Proteus vulgaris chondroitin ABC lyase, Appl.Microbial.Biotechnol., **41**, 39-46 **(1994)**.

[28] Q.Cheng, M.Yu, A.R.Reeves, A.A.Salyers; Identification and characterization of a Bacteroides gene, csuF, which en- codes an outer membrane protein that is essential for growth on chondroitin sulfate, J.Bacteriol, **177**, 3721-3727 **(1995)**.

[29] A.Marciel, V.Kapur, J.Musser; Molecular population genetic analysis of a Streptococcus pyogenes bacteriophage encoded hyaluronidase gene: recombination contributes to allelic variation, Microb.Pathog., **22**, 209-217 **(1997)**.

[30] L.Benchetrit, L.Wannamaker, E.Gray; Immunological properties of hyaluronidases associated with temperate bacteriophages of group A streptococci, J.Exp.Med., **149**, 73-83 **(1979)**.

[31] S.A.Halperin, P.Ferrieri, E.D.Gray, E.L.Kaplan, L.W.Wannamaker; Antibody response to bacteriophage hyaluronidase in acute glomerulonephritis after group A streptococcal infection, J.Infect.Dis., **155**, 253-261 **(1987)**.

[32] D.J.Rigden, M.J.Jedrzejas; Genome-based identification of a carbohydrate binding module in Streptococcus pneumoniae hyaluronate lyase, Proteins, **52(2)**, 203-11 **(2003)**.