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Review Article

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Proteomic Insights into Bovine Mastitis: Pathogenesis and Potential Biomarkers

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Introduction

It is a well-established fact that several contagious bacteria are the main etiological agents of mastitis. In addition to contagious pathogens, environmental microorganisms are also primary pathogens that survive and proliferate on the skin, in teat wounds, and in the mammary gland. Approximately 90% of mastitis cases are caused by different types of bacteria [1] hence, bacteria represent the major causative factor of mastitis.

Contagious Gram-positive bacteria, including Staphylococcus aureus, Streptococcus dysgalactiae, Streptococcus agalactiae, and Streptococcus uberis [2-5], as well as environmental Gram-negative bacteria such as Pseudomonas spp., Escherichia coli, and Klebsiella spp., are important pathogenic microorganisms responsible for mastitis (Hillerton and Berry, 2005).

Proteomic Insights into Bovine Mastitis

Once inside the teat canal, bacteria encounter the immune defense mechanisms of the udder, which attempt to eliminate the invading pathogens [6]. If elimination fails, the bacteria multiply within the tissue, adhere to host cells and extracellular matrix components, and are ultimately internalized into various milk-associated cells [7,8]. Fibronectin-binding proteins A and B are among the most important virulence factors facilitating bacterial invasion into host cells. Clumping factors A and B act as adhesion molecules that initiate infection. Ashraf et al. (2017) demonstrated that clumping factor A binds to Annexin A2, leading to bacterial invasion of epithelial cells.

Bacterial toxins, including hemolysins, leukotoxins, exfoliative toxins, enterotoxins, and toxic shock syndrome toxin-1, induce the release of chemoattractant cytokines such as tumor necrosis factor-α, interleukin-8, interleukin-1, prostaglandin F2α, oxygen free radicals, and acute-phase proteins. These mediators promote the recruitment of neutrophils to the site of infection [9]. Immune cells engulf and destroy pathogens through multiple pathways. However, the released inflammatory factors can damage both bacteria and epithelial cells, leading to the release of marker enzymes such as lactate dehydrogenase (LDH) and N-acetyl-β-D-glucosaminidase (NAGase). Most polymorphonuclear leukocytes (PMNs) undergo apoptosis, after which macrophages engulf and clear the remaining PMNs [10].

Sloughed-off mammary epithelial cells and dead leukocytes enter the milk, resulting in an increased somatic cell count (SCC). If the infection persists for an extended period, internal swelling within the mammary epithelium may occur, which is not externally detectable. Eventually, the milk alveoli become damaged, lose their functional and anatomical integrity, and ultimately lead to changes in milk quality [9].

In European countries, elevated SCC levels (>200,000 cells/mL) are considered an indicator of mastitis [11]. During mastitis, the concentrations of NAGase and LDH enzymes are also increased in milk. Mastitis can additionally be detected by changes in milk electrical conductivity or pH.

Recent advances in proteomic approaches, such as two-dimensional gel electrophoresis (2D-GE) and mass spectrometry (MS), have enabled the identification of novel mastitis biomarkers. Smolenski et al. (2007) used liquid chromatography–tandem MS and 2D-GE, followed by matrix-assisted laser desorption/

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ionization time-of-flight MS, to analyze individual protein spots in mastitic milk samples. A pathogen recognition protein and six chaperonins were identified in mastitic samples, indicating their potential as novel mastitis markers.

In another study, mastitis-infected animal tissues showed upregulation of κ-casein and downregulation of cytochrome c oxidase and annexin V [12] Estimation of inflammation-related enzymes may also be useful for mastitis detection, as these enzymes show a strong correlation with SCC. Haptoglobin concentrations have been reported to increase significantly in both milk and plasma during mastitis and are therefore considered a potential diagnostic marker for mastitis [13,14]. A new study shows that bacterial nanosomes play significant role for in mastitis [15].

Occlusion

Mastitis remains a major challenge in dairy production, with bacteria serving as the predominant etiological agents. Both contagious and environmental pathogens contribute to disease initiation and progression by colonizing the teat canal, evading host immune defenses, and establishing persistent intramammary infections. Interactions between bacterial virulence factors, including fibronectin-binding proteins, clumping factors, and toxins, and host mammary epithelial and immune cells drive bacterial adhesion, invasion, inflammation, and tissue damage.

Although the host immune response is essential for pathogen clearance, excessive inflammation leads to epithelial injury, increased somatic cell counts, and deterioration of milk quality. Persistent infections cause irreversible structural and functional damage to mammary alveoli, resulting in significant economic losses. Conventional diagnostic indicators such as SCC, NAGase, LDH, milk conductivity, and pH are useful but lack sensitivity for early or pathogen-specific detection.

Recent proteomic advances have enabled identification of novel biomarkers, including pathogen recognition proteins, chaperonins, κ-casein, annexin V, cytochrome c oxidase, and haptoglobin. Emerging evidence on nanosomes [16,17] further highlights new diagnostic and therapeutic opportunities for effective mastitis control.

References

1. Lassa H, Kubiak J, Małkińska-Horodyska M. Antibiotic susceptibility of the bacteria most often isolated from clinical mastitis in cows. Życie Weterynaryjne. 2013. 88: 651-653.
2. Crispie F, Alonso-Gómez M, O'Loughlin C, Klostermann K, Flynn J, et al. Intramammary infusion of a live culture for treatment of bovine mastitis: effect of live lactococci on the mammary immune response. Journal of Dairy Research. 2008. 75: 374-384.
3. Zadoks RN, Middleton JR, Mc Dougall S, Katholm J, Schukken YH. Molecular epidemiology of mastitis pathogens of dairy cattle and comparative relevance to humans. Journal of mammary gland biology and neoplasia. 2011. 16: 357-372.
4. Bi Y, Wang YJ, Qin Y, Vallverdu RG, Garcia JM, et al. Prevalence of bovine mastitis pathogens in bulk tank milk in China. PLoS One. 2016. 11: p.e0155621.
5. Abebe R, Hatiya H, Abera M, Megersa B, Asmare K. Bovine mastitis: prevalence, risk factors and isolation of Staphylococcus aureus in dairy herds at Hawassa milk shed, South Ethiopia. BMC Veterinary Research. 2016. 12: 270.
6. Sordillo LM, Streicher KL. Mammary gland immunity and mastitis susceptibility. J. Mammary Gland Biol. Neoplasia. 2002. 7: 135-146.
7. Almeida RA, Matthews KR, Cifrian E, Guidry AJ, Oliver SP. Staphylococcus aureus invasion of bovine mammary epithelial cells. Journal of Dairy Science. 1996. 79: 1021-1026.
8. Hebert A, Sayasith K, Sénéchal S, Dubreuil P, Lagacé J. Demonstration of intracellular Staphylococcus aureus in bovine mastitis alveolar cells and macrophages isolated from naturally infected cow milk. FEMS microbiology letters. 2000. 193: 57-62.
9. Zhao X, Lacasse P. Mammary tissue damage during bovine mastitis: causes and control. J. Anim. Sci. 2008. 86: 57-65.
10. Paape MJ. The bovine neutrophil: structure and function in blood and milk. Vet. Res. 2003. 34. 597-627.
11. Schukken YH. Monitoring udder health and milk quality using somatic cell counts. Vet. Res. 2003. 34: 579-596.
12. Yang Y. Proteomic analysis of mammary tissues from healthy cows and clinical mastitic cows for identification of diseaserelated proteins. Vet. Res. Commun. 2009. 33: 295-303.
13. Gronlund U. Haptoglobin and serum amyloid A in milk and serum during acute and chronic experimentally induced Staphylococcus aureus mastitis. J. Dairy Res. 2003. 70: 379-386.
14. Hiss S. Haptoglobin concentrations in blood and milk after endotoxin challenge and quantification of mammary Hp mRNA expression. J. Dairy Sci. 2004. 87: 3778-3784.
15. Kumar J, Sharma P, Onteru S K, Singh D. Small milk extracellular vesicles potentiate β-lactam antibiotic activity for combating pathogenic Staphylococcus aureus. Journal of Drug Delivery Science and Technology. 2025. 106952.
16. Antibiotic Resistance. 2019.
17. Smolenski G. Characterisation of host defence proteins in milk using a proteomic approach. J. Proteome Res. 2003. 6: 207-215.