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Review Article

Revisiting the Journey of *Staphylococcus aureus*: From Invisible to Invasive

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Abstract

Staphylococcus aureus exhibits a dual lifestyle, transitioning from a commensal colonizer to pathogenic bacterium with the ability to cause cross-species infections and survive in variable environments. This adaptability is mainly driven by extensive genome plasticity facilitated by horizontal gene transfer (HGT). This review discusses major strain lineages (MSSA, MRSA, HA-MRSA, CA-MRSA and LA-MRSA), nasal colonization as key reservoir and outline the broad spectrum of diseases ranging from skin and soft tissue infections (SSTIs) to invasive conditions and toxin-mediated food poisoning. Advances in staphylococcal research including culture systems, molecular diagnostics, genomics, multi-omics approaches and *in vivo* infection models are reviewed with emphasis on their contributions to understand metabolism, virulence, resistance and host interactions. Additionally, highlighting the role of bacteriophages in HGT, therapy and genetic engineering via transduction. Collectively, this review summarizes research focused on all major dimensions of *S.aureus* biology, evolution and clinical relevance.

Keywords: *Staphylococcus aureus, Evolution, Biology, Pathogenesis, Genetic Tools*

Introduction

From an evolutionary perspective, the continual exchange of genetic material among pathogenic nonpathogenic and environmental bacteria serves as a central driver of genetic diversity. Horizontal gene transfer enables bacteria to rapidly acquire determinants of virulence, antibiotic resistance and metabolic genes, collectively expanding adaptive potential. This dynamic genetic fluidity has played a pivotal role in shaping bacterial pathogenicity and remains a major contributor to the global burden of infectious diseases, morbidity and mortality.

In this context, *Staphylococcus aureus* exemplifies remarkable adaptive refinement. Once regarded as a classical pyogenic bacterium of the 19th century, it has progressively evolved into a multidrug-resistant, pyrogenic-toxin producing pathobiont of the 21st century. This evolutionary trajectory reflects not only its ecological success but also extensive genome plasticity and regulatory flexibility [1]. Persistent global surveillance of staphylococcal infections has been instrumental in our understanding of evolution of diverse *Staphylococcus aureus* strains. Importantly, the clinically diverse infection profile of *Staphylococcus aureus* has catalyzed advances in staphylococcal research and diagnostics, leading to improved detection and strain characterization strategies [2,3].

This review brings together current understanding of *S.aureus* diversity, culture systems, experimental focus areas and *in vivo* models used to interrogate its ability to shift between pathogenic-commensal lifestyle plasticity as well as the different roles of bacteriophages.

Reservoir Association and Relevant Strains:

The trajectory from penicillin-susceptible (PEN^s) to resistance in *Staphylococcus aureus* illustrates how quickly selective pressure can reshape bacterial populations. Following methicillin deployment, resistance emergence highlights the organism's notable adaptive resilience under antibiotic pressure which led to the classification of *S.aureus* into methicillin-susceptible (MSSA) and methicillin-resistant (MRSA) groups.

Within clinical ecosystems, hospital-acquired MRSA (HA-MRSA) strains are most often associated with healthcare exposure, indwelling devices and immunocompromised hosts. Their defining feature is not just resistance, but in accumulation of multilayered antimicrobial defense, making them persistent contributors to bloodstream and device-associated infections [4].

Outside hospitals, community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) strains emerged independently, circulating among healthy individuals. These strains often carry elevated virulence and are strongly linked to skin and soft-tissue infections (SSTIs) [4].

Another branch of staphylococcal strains associated with animal farming and aquaculture form a livestock reservoir. Thus, suggested that they were no longer confined to human-associated settings. The ST398 (CC398) lineage is recognized as livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) with high pathogenicity and reservoir plasticity [5,6,7].

NCTC8325 (RN1) with its derivatives and Newman are the most frequently employed MSSA strains in laboratory studies. MRSA research commonly relies on representative lineages including pulse field gel electrophoresis (PFGE) type- USA100 (clonal complex 5 (CC5)) and USA200 (CC30). They are common HA/CA-MRSA subgroup strains however; among MRSA lineages the most comprehensively studied and dominant community-associated PFGE subtypes are USA300 (CC8) and USA400 (CC1) [8,9]. LA-MRSA CC398 and derivatives continue to serve as a key model for understanding zoonotic versatility [10,11].

Nasal Carriage Dynamics:

The most dominant colonization site of this bacterium is the host anterior nares. The colonization state is primarily asymptomatic, yet it retains the potential to progress towards subsequent bacterial infection. There are three phenotypes associated with nasal carriage- the intermittent phenotype carriers have nares sometimes colonized or uncolonized, the persistent phenotypes carriers form a smaller stable reservoir and non-carrier phenotype are in minority with undetectable traces of colonization [12].

Spectrum of Human Diseases:

The spectrum of *Staphylococcus aureus*-associated disease ranges from skin and soft-tissue infections (SSTIs) to life-threatening infective endocarditis, bacteremia (bloodstream infections- BSIs) and septic arthritis/osteomyelitis (bone and joint Infections-BJIs) [13]. These clinical manifestations have led to profound progress in research on *Staphylococcus aureus* pathogenesis, mechanisms of bacterial resistance, biofilm biology, genomic evolution and characterization of critical biosynthesis pathways [4]. The ability of *Staphylococcus aureus* to produce enterotoxin-mediated food poisoning (staphylococcal food poisoning- SFP) highlights its capacity for disease independent of invasion, particularly during inadequate food processing and storage [14].

Detection Approaches:

Laboratory and molecular approaches for *Staphylococcus aureus* identification encompass culture-based isolation [15], biosensor-enabled detection [16], antigen detection assays [17] and high-resolution genomic techniques [18,19]. Advances in molecular biology and microbial ecology have significantly expanded both diagnostic precision and therapeutic development strategies.

In table 1, the relevant features discussed about the *Staphylococcus aureus* biology are summarized for a quick reference.

Table1. An overview of *Staphylococcus aureus* Biology.

Reservoir-associated lineages	Representative strains	Nasal carriage	Spectrum of diseases	Detection approaches
MSSA, HA-MRSA, CA-MRSA, LA-MRSA	USA100, USA200, USA300, USA400, NM, ST398, NCTC8325	Intermittent, Persistent, Non-carriers	SSTIs, BSIs, BJIs, SFP	Culture-based Biosensor Antigen assay genomic

Staphylococcal Research:

Experimental Growth systems:

Staphylococcus aureus is a Gram-positive bacterium with optimal growth at 37℃ temperature and pH 7.4, typically forming visible colonies within 12-36 hours. Research employs diverse culture systems, including nutrient-rich media supporting robust growth [8], to defined minimal media to investigate metabolic dependency [20,21], to specialized biofilm-promoting systems that mimic infection state [22] and selective diagnostic media optimized for clinical detection [23].

Area of Research Interest:

***Metabolic plasticity**:*

The ability of *Staphylococcus aureus* to thrive in both nutrient-rich and nutrient-limited environments reflects a highly adaptable metabolic system. Key research areas include iron acquisition, carbohydrate and/or non-carbohydrate utilization as diverse carbon sources and reliance on exogenous fatty acids for its phospholipid layer [4,24-27].

Virulence factors and immune evasion:

Pathogenicity *Staphylococcus aureus* is not driven by a single determinant but by layered regulatory networks of metabolic genes, immune circumvention and production of virulence determinants. These systems collectively define its ability to transition from harmless colonizer to invasive pathogen [4, 25, 28-31].

***Bacterial Resistance to Antibacterial agents*:**

The progressive accumulation of resistance determinants has substantially reshaped the antibiotic susceptibility profile of *Staphylococcus aureus*. Resistance in *Staphylococcus aureus* arises through both acquired and adaptive mechanisms. Acquired resistance involves stable genomic changes, including spontaneous DNA mutations [32] or the horizontal gene transfer of mobile genetic elements like plasmids or transposons encoding resistance. Conversely, a temporary reprogramming of bacterial gene expression when exposed to antibacterial agent renders bacteria an adaptive resistance that dissipates when pressure is removed [33]. This dual strategy continues to challenge therapeutic control and drives ongoing efforts to restore susceptibility to antibiotics [4, 34, 35].

Experimental and Genomic Toolkits:

Whole-genome sequencing (WGS) provides a complete structural view of genetic potential [36], while the *Staphylococcus aureus* genome is understood as a mosaic of conserved core functions and variable accessory elements [37]. Functional interrogation now routinely employs WGS [38], random insertion of transposon across the genome (Tn-seq) [39,40] and clustered regularly interspaced short palindromic repeat (CRISPR)/Cas9 editing systems in *Staphylococcus aureus*, enabling precise dissection of gene function [41].

At the regulatory layer, RNA-Sequencing has uncovered a dense landscape of small RNAs in *Staphylococcus aureus*. These include multifunctional components of the transcriptionally active genome. The size of sRNA may extend beyond 500 nucleotides and in some cases may also encode short peptides highlighting both regulatory and coding potential. In *Staphylococcus aureus*, sRNAs are broadly categorized as cis-associated elements and trans-acting RNAs. Cis-associated regulation includes both cis-encoded antisense RNAs and regulatory regions within mRNAs (e.g., riboswitches), whereas trans-acting sRNA are encoded at distinct loci and act on distant targets. At the functional level, these non-coding RNAs fine tune gene expression through RNA-RNA or RNA-protein interactions. Collectively, these elements integrate metabolism, virulence and biofilm formation into a responsive regulator network [42-47].

The convergence of proteomic, metabolomic and transcriptomic is called multi-omics which has shifted *S. aureus* research towards system-level interpretation. This enables us to examine a coordinated biological network that defines metabolic state, virulence expression and environmental adaptation offering a deeper understanding of bacterial physiology and pathogenicity [48- 50].

Models and Therapy:

Animal Infections:

Because *S. aureus* occupies multiple anatomical and ecological niches, experimental infection models span a wide biological range. These *in vivo* models include abscesses formation [51], osteomyelitis [52-55], blood stream infections (BSIs) [56], pneumonia [57], endocarditis [58], mastitis [59], skin and soft tissue infections (SSTIs) [60] and biofilm associated systems [61-63]. These models are indispensable for evaluating efficacy of vaccines and therapeutic agents, with each model capturing a different dimension of bacterial adaptive pathogenic ability.

Bacteriophages:

Bacteria-eater “bacteriophages” was the term given by D’Herelle, who recognized their therapeutic potential in treating bacterial infections. The concept was based on the lytic life cycle of phages, during which they adsorb to the bacterial surface, introduce their genetic material, replicate within the host and lyse the bacterial cell. Despite this early promise, the antibiotics discovery and success overshadowed phage therapy.

Nevertheless, phages continued to play a significant role in bacterial evolution through generalized transduction, a form of horizontal gene transfer in which a random bacterial DNA fragment is mistakenly packaged into phage capsid and transferred to the new bacterial host, thereby promoting bacterial genome diversification. In addition to phages, plasmids, transposons and pathogenicity Islands contribute substantially to bacterial adaptability, antibiotic resistance and pathogenicity.

Recent studies demonstrate the dual role of bacteriophages in lysing resistant clinical isolates and facilitating HGT, while also serving as tools for genetic engineering via transduction, positioning them as key players in genetic manipulation, antimicrobial strategy development and bacterial evolutionary research [64-68].

In table 2, the key *Staphylococcus aureus* experimental and research strategies are compiled.

Table 2: An overview of Staphylococcal Research.

Experimental growth systems	Area of research interest	Experimental and genomic toolkits	Models and therapy
Nutrient-rich, chemically defined, biofilm-promoting, selective detection media	Metabolism Virulence resistance	WGS Tn-Seq CRISPR/Cas9 sRNA Multi-omics	Animal infections Bacteriophages

Conclusions

Staphylococcus aureus persist across diverse host niches, from the nutrient-variable environment of the anterior nares and skin to hostile deeper tissues during invasive infections. Its survival depends on constant fighting for nutrients, microbial communities, immune surveillance and antibiotic pressure. Rather than relying on fixed pathogenic traits, it reshapes through genetic plasticity, horizontal gene transfer and regulatory flexibility. Evolutionary flexibility allows it to be the most successful bacterial pathogen and important model for understanding bacterial pathogenesis and adaptation.

Conflict of Interest

The author declares no conflict of interest.

References

1. Deurenberg RH, Stobberingh EE. The evolution of Staphylococcus aureus. Infect Genet Evol. 2008 Dec;8(6):747-63. doi: 10.1016/j.meegid.2008.07.007. Epub 2008 Jul 29. PMID: 18718557.

2. Baede VO, David MZ, Andrasevic AT, Blanc DS, Borg M, Brennan G, Catry B, Chabaud A, Empel J, Enger H, Hallin M, Ivanova M, Kronenberg A, Kuntaman K, Larsen AR, Latour K, Lindsay JA, Pichon B, Santosaningsih D, Schouls LM, Vandenesch F, Werner G, Żabicka D, Žemličková H, Seifert H, Vos MC; MRSA Surveillance Worldwide Study Group (ISAC), the ESCMID Study Group for Nosocomial Infections (ESGNI), the ESCMID Study Group for Staphylococci and Staphylococcal Diseases (ESGS). MRSA surveillance programmes worldwide: moving towards a harmonised international approach. Int J Antimicrob Agents. 2022 Mar;59(3):106538. doi: 10.1016/j.ijantimicag.2022.106538. Epub 2022 Jan 26. PMID: 35091055.

3. Morris AK, Russell CD. Enhanced surveillance of Staphylococcus aureus bacteraemia to identify targets for infection prevention. J Hosp Infect. 2016 Jun;93(2):169-74. doi: 10.1016/j.jhin.2016.03.003. Epub 2016 Mar 22. PMID: 27107617.

4. Touaitia, R.; Mairi, A.; Ibrahim, N.A.; Basher, N.S.; Idres, T.; Touati, A. *Staphylococcus aureus*: A Review of the Pathogenesis and Virulence Mechanisms. *Antibiotics* **2025**, *14*, 470. https://doi.org/10.3390/antibiotics14050470

5. Oliveira R, Araújo D, Castro J, Nogueira T, Almeida G, Azevedo NF, Almeida C. Assessing host-adaptation of new sequence types of livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA). Microb Pathog. 2025 Dec;209:108042. doi: 10.1016/j.micpath.2025.108042. Epub 2025 Sep 15. PMID: 40962038

6. Oh WT, Jun JW, Giri SS, Yun S, Kim HJ, Kim SG, Kim SW, Han SJ, Kwon J, Park SC. *Staphylococcus xylosus* Infection in Rainbow Trout (*Oncorhynchusmykiss*) As a Primary Pathogenic Cause of Eye Protrusion and Mortality. Microorganisms. 2019 Sep 7;7(9):330. doi: 10.3390/microorganisms7090330. PMID: 31500280; PMCID: PMC6780347.

7. Vrbovská V, Sedláček I, Zeman M, Švec P, Kovařovic V, Šedo O, Laichmanová M, Doškař J, Pantůček R. Characterization of *Staphylococcus intermedius* Group Isolates Associated with Animals from Antarctica and Emended Description of *Staphylococcus delphini*. Microorganisms. 2020 Feb 1;8(2):204. doi: 10.3390/microorganisms8020204. PMID: 32024111; PMCID: PMC7074773.

8. Vitko NP, Richardson AR. Laboratory maintenance of methicillin-resistant Staphylococcus aureus (MRSA). Curr Protoc Microbiol. 2013 Feb;Chapter 9:Unit 9C.2. doi: 10.1002/9780471729259.mc09c02s28. PMID: 23408135; PMCID: PMC4070006.

9. King JM, Kulhankova K, Stach CS, Vu BG, Salgado-Pabón W. Phenotypes and Virulence among Staphylococcus aureus USA100, USA200, USA300, USA400, and USA600 Clonal Lineages. mSphere. 2016 Jun 8;1(3):e00071-16. doi: 10.1128/mSphere.00071-16. PMID: 27303750; PMCID: PMC4899884

10. Zheng L, Jiang Z, Wang Z, Li Y, Jiao X, Li Q and Tang Y (2023) The prevalence of Staphylococcus aureus and the emergence of livestock-associated MRSA CC398 in pig production in eastern China. Front. Microbiol. 14:1267885. doi: 10.3389/fmicb.2023.1267885

11. Silva V, Araújo S, Monteiro A, Eira J, Pereira JE, Maltez L, Igrejas G, Lemsaddek TS, Poeta P. *Staphylococcus aureus* and MRSA in Livestock: Antimicrobial Resistance and Genetic Lineages. Microorganisms. 2023 Jan 3;11(1):124. doi: 10.3390/microorganisms11010124. PMID: 36677414; PMCID: PMC9865216.

12. Kluytmans J, van Belkum A, Verbrugh H. Nasal carriage of Staphylococcus aureus: epidemiology, underlying mechanisms, and associated risks. Clin Microbiol Rev. 1997 Jul;10(3):505-20. doi: 10.1128/CMR.10.3.505. PMID: 9227864; PMCID: PMC172932.

13. Tong SY, Davis JS, Eichenberger E, Holland TL, Fowler VG Jr. Staphylococcus aureus infections: epidemiology, pathophysiology, clinical manifestations, and management. Clin Microbiol Rev. 2015 Jul;28(3):603-61. doi: 10.1128/CMR.00134-14. PMID: 26016486; PMCID: PMC4451395

14. Argudín MÁ, Mendoza MC, Rodicio MR. Food poisoning and Staphylococcus aureus enterotoxins. Toxins (Basel). 2010 Jul;2(7):1751-73. doi: 10.3390/toxins2071751. Epub 2010 Jul 5. PMID: 22069659; PMCID: PMC3153270.

15. Malhotra-Kumar S, Abrahantes JC, Sabiiti W, Lammens C, Vercauteren G, Ieven M, Molenberghs G, Aerts M, Goossens H; MOSAR WP2 Study Team. Evaluation of chromogenic media for detection of methicillin-resistant Staphylococcus aureus. J Clin Microbiol. 2010 Apr;48(4):1040-6. doi: 10.1128/JCM.01745-09. Epub 2010 Feb 17. PMID: 20164268; PMCID: PMC2849574.

16. Ceylan Koydemir H, Külah H, Özgen C, Alp A, Hasçelik G. MEMS biosensors for detection of methicillin resistant Staphylococcus aureus. Biosens Bioelectron. 2011 Nov 15;29(1):1-12. doi: 10.1016/j.bios.2011.07.071. Epub 2011 Aug 4. PMID: 21856144.

17. Kim JK, Yun HY, Kim JS, Kim W, Lee CS, Kim BG, Jeong HJ. Development of fluorescence-linked immunosorbent assay for rapid detection of Staphylococcus aureus. Appl Microbiol Biotechnol. 2024 Dec;108(1):2. doi: 10.1007/s00253-023-12836-2. Epub 2023 Dec 28. PMID: 38153552.

18. Mairi A, Ibrahim NA, Idres T, Touati A. A Comprehensive Review of Detection Methods for *Staphylococcus aureus* and Its Enterotoxins in Food: From Traditional to Emerging Technologies. Toxins (Basel). 2025 Jun 23;17(7):319. doi: 10.3390/toxins17070319. PMID: 40711131; PMCID: PMC12298662.

19. Hwang KY, Kwon SH, Jung SO, Namkoong K, Jung WJ, Kim JH, Suh KY, Huh N. Solid phase DNA extraction with a flexible bead-packed microfluidic device to detect methicillin-resistant Staphylococcus aureus in nasal swabs. Anal Chem. 2012 Sep 18;84(18):7912-8. doi: 10.1021/ac3016533. Epub 2012 Aug 30. PMID: 22908991.

20. Machado H, Weng LL, Dillon N, et al. Strain-Specific Metabolic Requirements Revealed by a Defined Minimal Medium for Systems Analyses of *Staphylococcus aureus*. Applied and Environmental Microbiology. 2019 Nov;85(21):e01773-19. DOI: 10.1128/aem.01773-19. PMID: 31471305; PMCID: PMC6803309.

21. Razvi F, Burke TL, Shinde D, Ahn J, Thomas VC, Sadykov M, Fey PD. Growth and acetate metabolism of *Staphylococcus aureus* in defined medium. Appl Environ Microbiol. 2025 Nov 19;91(11):e0155425. doi: 10.1128/aem.01554-25. Epub 2025 Oct 16. PMID: 41099525; PMCID: PMC12628684.

22. Redfern J, Cunliffe AJ, Goeres DM, Azevedo NF, Verran J. Critical analysis of methods to determine growth, control and analysis of biofilms for potential non-submerged antibiofilm surfaces and coatings. Biofilm. 2024 Feb 27;7:100187. doi: 10.1016/j.bioflm.2024.100187. PMID: 38481762; PMCID: PMC10933470.

23. Kim, HJ., Oh, SW. Performance comparison of 5 selective media used to detect *Staphylococcus aureus* in foods. *Food Sci Biotechnol* **19**, 1097–1101 (2010). https://doi.org/10.1007/s10068-010-0155-2

24. Onyango, Laura A., Alreshidi, Mousa M., Adaptive Metabolism in Staphylococci: Survival and Persistence in Environmental and Clinical Settings, Journal of Pathogens, 2018, 1092632, 11 pages,

2018. https://doi.org/10.1155/2018/1092632

25. Wong Fok Lung, T.; Prince, A. Consequences of Metabolic Interactions during *Staphylococcus aureus* Infection. *Toxins* **2020**, *12*, 581. https://doi.org/10.3390/toxins12090581

26. Delekta PC, Shook JC, Lydic TA, Mulks MH, Hammer ND. Staphylococcus aureus Utilizes Host-Derived Lipoprotein Particles as Sources of Fatty Acids. J Bacteriol. 2018 May 9;200(11):e00728-17. doi: 10.1128/JB.00728-17. PMID: 29581406; PMCID: PMC5952394.

27. Hammer ND, Skaar EP. Molecular mechanisms of Staphylococcus aureus iron acquisition. Annu Rev Microbiol. 2011;65:129-47. doi: 10.1146/annurev-micro-090110-102851. PMID: 21639791; PMCID: PMC3807827.

28. Arumugam P, Kielian T. Metabolism Shapes Immune Responses to Staphylococcus aureus. J Innate Immun. 2024;16(1):12-30. doi: 10.1159/000535482. Epub 2023 Nov 28. PMID: 38016430; PMCID: PMC10766399.

29. Chambers HF, Deleo FR. Waves of resistance: Staphylococcus aureus in the antibiotic era. Nat Rev Microbiol. 2009 Sep;7(9):629-41. doi: 10.1038/nrmicro2200. PMID: 19680247; PMCID: PMC2871281

30. Otto M. Basis of virulence in community-associated methicillin-resistant Staphylococcus aureus. Annu Rev Microbiol. 2010;64:143-62. doi: 10.1146/annurev.micro.112408.134309. PMID: 20825344.

31. Tristan A, Ferry T, Durand G, Dauwalder O, Bes M, Lina G, Vandenesch F, Etienne J. Virulence determinants in community and hospital meticillin-resistant Staphylococcus aureus. J Hosp Infect. 2007 Jun;65 Suppl 2:105-9. doi: 10.1016/S0195-6701(07)60025-5. PMID: 17540252.

32. Foster TJ. Antibiotic resistance in Staphylococcus aureus. Current status and future prospects. FEMS Microbiol Rev. 2017 May 1;41(3):430-449. doi: 10.1093/femsre/fux007. PMID: 28419231.

33. Brdová D, Ruml T, Viktorová J. Mechanism of staphylococcal resistance to clinically relevant antibiotics. Drug Resist Updat. 2024 Nov;77:101147. doi: 10.1016/j.drup.2024.101147. Epub 2024 Aug 31. PMID: 39236354.

34. Leonard FC, Markey BK. Meticillin-resistant Staphylococcus aureus in animals: a review. Vet J. 2008 Jan;175(1):27-36. doi: 10.1016/j.tvjl.2006.11.008. Epub 2007 Jan 9. PMID: 17215151.

35. Li T, Zeng F, Zhang J, Zhang Y, Yin W. Reversing Antibiotic Resistance: Strategies From Adjuvants to Innovative Therapeutics. Microbiologyopen. 2026 Feb;15(1):e70233. doi: 10.1002/mbo3.70233. PMID: 41691452; PMCID: PMC12906665.

36. Giulieri, S.G., Leroi, M., Daniel, D. *et al.* A multi-hospital, clinician-initiated bacterial genomics programme to investigate treatment failure in severe *Staphylococcus aureus* infections. *Nat Commun* **16**, 4869 (2025). https://doi.org/10.1038/s41467-025-60045-4

37. Malachowa N, DeLeo FR. Mobile genetic elements of Staphylococcus aureus. Cell Mol Life Sci. 2010 Sep;67(18):3057-71. doi: 10.1007/s00018-010-0389-4. Epub 2010 Jul 29. PMID: 20668911; PMCID: PMC2929429.

38. Price J, Gordon NC, Crook D, Llewelyn M, Paul J. The usefulness of whole genome sequencing in the management of Staphylococcus aureus infections. Clin Microbiol Infect. 2013 Sep;19(9):784-9. doi: 10.1111/1469-0691.12109. Epub 2013 Jan 18. PMID: 23331482.

39. Santiago M, Matano LM, Moussa SH, Gilmore MS, Walker S, Meredith TC. A new platform for ultra-high density Staphylococcus aureus transposon libraries. BMC Genomics. 2015 Mar 29;16(1):252. doi: 10.1186/s12864-015-1361-3. PMID: 25888466; PMCID: PMC4389836.

40. Fey PD, Endres JL, Yajjala VK, Widhelm TJ, Boissy RJ, Bose JL, Bayles KW. A genetic resource for rapid and comprehensive phenotype screening of nonessential Staphylococcus aureus genes. mBio. 2013 Feb 12;4(1):e00537-12. doi: 10.1128/mBio.00537-12. PMID: 23404398; PMCID: PMC3573662.

41. Liu Q, Jiang Y, Shao L, Yang P, Sun B, Yang S, Chen D. CRISPR/Cas9-based efficient genome editing in Staphylococcus aureus. Acta Biochim Biophys Sin (Shanghai). 2017 Sep 1;49(9):764-770. doi: 10.1093/abbs/gmx074. PMID: 28910979.

42. Tomasini A, François P, Howden BP, Fechter P, Romby P, Caldelari I. The importance of regulatory RNAs in Staphylococcus aureus. Infect Genet Evol. 2014 Jan;21:616-26. doi: 10.1016/j.meegid.2013.11.016. Epub 2013 Nov 27. PMID: 24291227.

43. Rochat T, Bohn C, Morvan C, Le Lam TN, Razvi F, Pain A, Toffano-Nioche C, Ponien P, Jacq A, Jacquet E, Fey PD, Gautheret D, Bouloc P. The conserved regulatory RNA RsaE down-regulates the arginine degradation pathway in Staphylococcus aureus. Nucleic Acids Res. 2018 Sep 28;46(17):8803-8816. doi: 10.1093/nar/gky584. PMID: 29986060; PMCID: PMC6158497.

44. Manna AC, Leo S, Girel S, González-Ruiz V, Rudaz S, Francois P, Cheung AL. Teg58, a small regulatory RNA, is involved in regulating arginine biosynthesis and biofilm formation in Staphylococcus aureus. Sci Rep. 2022 Sep 2;12(1):14963. doi: 10.1038/s41598-022-18815-3. PMID: 36056144; PMCID: PMC9440087.

45. McKellar, S.W., Ivanova, I., Arede, P. *et al.* RNase III CLASH in MRSA uncovers sRNA regulatory networks coupling metabolism to toxin expression. *Nat Commun* **13**, 3560 (2022). https://doi.org/10.1038/s41467-022-31173-y

46. Desgranges E, Barrientos L, Herrgott L, Marzi S, Toledo-Arana A, Moreau K, Vandenesch F, Romby P, Caldelari I. The 3'UTR-derived sRNA RsaG coordinates redox homeostasis and metabolism adaptation in response to glucose-6-phosphate uptake in Staphylococcus aureus. Mol Microbiol. 2022 Jan;117(1):193-214. doi: 10.1111/mmi.14845. Epub 2021 Nov 25. PMID: 34783400.

47. Schilcher K, Horswill AR. Staphylococcal Biofilm Development: Structure, Regulation, and Treatment Strategies. Microbiol Mol Biol Rev. 2020 Aug 12;84(3):e00026-19. doi: 10.1128/MMBR.00026-19. PMID: 32792334; PMCID PMC7430342

48. Liu J, Li Y, Liu H, Yan S, Jia H, Yang Y, Hu W, Wang J, Li W, Xue H, Zhao X, Li L, Liu P. 2026. Expression patterns of core metabolic genes and elevated intracellular ROS confer drug tolerance in Staphylococcus aureus. Microbiol Spectr 14:e01868-25. https://doi.org/10.1128/spectrum.01868-25

49. Mujchariyakul W, Walsh CJ, Giulieri S, Cramond C, LêCao K, Stinear TP, Howden BP, Guérillot R, Hachani A. 2026. Integrated multi-omics reveals coordinated Staphylococcus aureus metabolic, iron transport, and stress responses to human serum. mSystems 11:e01183-25. https://doi.org/10.1128/msystems.01183-25

50. Rose WE, Sauer J. 0. Unlocking the secret to Staphylococcus aureus survival in serum. mSystems 0:e01813-25.https://doi.org/10.1128/msystems.01813-25

51. Enriquez KT, Skaar EP. The anatomy and molecular inventory of Staphylococcus aureus abscesses. Trends Microbiol. 2026 Mar 24:S0966-842X(26)00031-4. doi: 10.1016/j.tim.2026.02.005. Epub ahead of print. PMID: 41881696.

52. Beenken KE, Campbell MJ, Reyes-Pardo H, O'Brien CA, Smeltzer MS. 0. Mechanistic insights into the pathogenesis and therapeutic recalcitrance of Staphylococcus aureus osteomyelitis. Clin Microbiol Rev 0:e00259-25.https://doi.org/10.1128/cmr.00259-25

53. Song, M., Sun, J., Lv, K. et al. A comprehensive review of pathology and treatment of staphylococcus aureus osteomyelitis. Clin Exp Med 25, 131 (2025). https://doi.org/10.1007/s10238-025-01595-1

54. Power ME, Olson ME, Domingue PA, Costerton JW. A rat model of Staphylococcus aureus chronic osteomyelitis that provides a suitable system for studying the human infection. J Med Microbiol. 1990 Nov;33(3):189-98. doi: 10.1099/00222615-33-3-189. PMID: 2250289.

55. Li K, Chen Y, Lin Y, Zhang G, Su J, Wu X, Cheng C, Wang Y, Yu B, Zhang X. PD-1/PD-L1 blockade is a potent adjuvant in treatment of Staphylococcus aureus osteomyelitis in mice. Mol Ther. 2023 Jan 4;31(1):174-192. doi: 10.1016/j.ymthe.2022.09.006. Epub 2022 Sep 14. PMID: 36104974; PMCID: PMC9840119.

56. Nwofor OV, Leipold A, Chen Q, Geffers R, Saliba A-E, Goldmann O and Medina E (2026) Zone-specific hepatocytes orchestrate the early onset of host immune defenses during Staphylococcus aureus bloodstream infection. Front. Immunol. 17:1776887. doi: 10.3389/fimmu.2026.1776887

57. Duan W, Qin F, Wu D, Dai Y. Diphenyl pyrimidine exhibits protective effect on Staphylococcus aureus pneumonia in rat model by targeting NLRP3 expression. Microb Pathog. 2021 Dec;161(Pt A):105168. doi: 10.1016/j.micpath.2021.105168. Epub 2021 Aug 31. PMID: 34478857.

58. Hanses F, Roux C, Dunman PM, Salzberger B, Lee JC. Staphylococcus aureus gene expression in a rat model of infective endocarditis. Genome Med. 2014 Nov 3;6(10):93. doi: 10.1186/s13073-014-0093-3. PMID: 25392717; PMCID: PMC4228149.

59. Tong J, Hou X, Cui D, Chen W, Yao H, Xiong B, Cai L, Zhang H, Jiang L. A berberine hydrochloride-carboxymethyl chitosan hydrogel protects against Staphylococcus aureus infection in a rat mastitis model. Carbohydr Polym. 2022 Feb 15;278:118910. doi: 10.1016/j.carbpol.2021.118910. Epub 2021 Nov 18. PMID: 34973731.

60. Xie X, Zhong R, Luo L, Lin X, Huang L, Huang S, Ni L, Chen B, Shen R, Yan L, Duan C. The infection characteristics and autophagy defect of dermal macrophages in STZ-induced diabetic rats skin wound Staphylococcus aureus infection model. Immun Inflamm Dis. 2021 Dec;9(4):1428-1438. doi: 10.1002/iid3.492. Epub 2021 Oct 14. PMID: 34647429; PMCID: PMC8589369.

61. Wang Y, Cheng LI, Helfer DR, Ashbaugh AG, Miller RJ, Tzomides AJ, Thompson JM, Ortines RV, Tsai AS, Liu H, Dillen CA, Archer NK, Cohen TS, Tkaczyk C, Stover CK, Sellman BR, Miller LS. Mouse model of hematogenous implant-related Staphylococcus aureus biofilm infection reveals therapeutic targets. Proc Natl Acad Sci U S A. 2017 Jun 27;114(26):E5094-E5102. doi: 10.1073/pnas.1703427114. Epub 2017 Jun 12. PMID: 28607050; PMCID: PMC5495257.

62. O'Gara JP. ica and beyond: biofilm mechanisms and regulation in Staphylococcus epidermidis and Staphylococcus aureus. FEMS Microbiol Lett. 2007 May;270(2):179-88. doi: 10.1111/j.1574-6968.2007.00688.x. Epub 2007 Apr 10. PMID: 17419768.

63. Abdul Hamid, A.I., Nakusi, L., Givskov, M. et al. A mouse ear skin model to study the dynamics of innate immune responses against Staphylococcus aureus biofilms. BMC Microbiol 20, 22 (2020). https://doi.org/10.1186/s12866-019-1635-z

64. Rossi CC, Teixeira FCOB, Silva GCD, Pereira MF, Giambiagi-deMarval M. Staphylococcal phages as agents of evolution and innovation: From gene flow to next-generation therapeutics. Genet Mol Biol. 2026 Feb 9;49(suppl 1):e20250131. doi: 10.1590/1678-4685-GMB-2025-0131. PMID: 41677000; PMCID: PMC12895238.

65. Hatoum-Aslan A. The phages of staphylococci: critical catalysts in health and disease. Trends Microbiol. 2021 Dec;29(12):1117-1129. doi: 10.1016/j.tim.2021.04.008. Epub 2021 May 21. PMID: 34030968; PMCID: PMC8578144.

66. Krausz KL, Bose JL. Bacteriophage Transduction in Staphylococcus aureus: Broth-Based Method. Methods Mol Biol. 2016;1373:63-8. doi: 10.1007/7651_2014_185. PMID: 25646607.

67. Firth N, Jensen SO, Kwong SM, Skurray RA, Ramsay JP. Staphylococcal Plasmids, Transposable and Integrative Elements. Microbiol Spectr. 2018 Nov;6(6):10.1128/microbiolspec.gpp3-0030-2018. doi: 10.1128/microbiolspec.GPP3-0030-2018. PMID: 30547857; PMCID: PMC11633639.

68. Łubowska N, Grygorcewicz B, Kosznik-Kwaśnicka K, Zauszkiewicz-Pawlak A, Węgrzyn A, Dołęgowska B, Piechowicz L. Characterization of the Three New Kayviruses and Their Lytic Activity Against Multidrug-Resistant Staphylococcus aureus. Microorganisms. 2019 Oct 18;7(10):471. doi: 10.3390/microorganisms7100471. PMID: 31635437; PMCID: PMC6843549.