- Albanesi, D., Reh, G., Guerin, M. E., Schaeffer, F., Debarbouille, M., Buschiazzo, A., et al. (2013). Structural basis for feed-forward transcriptional regulation of membrane lipid homeostasis in Staphylococcus aureus. *PLoS Pathog* 9, e1003108. doi: 10.1371/journal.ppat.1003108.
- Bai, J., Zhu, X., Zhao, K., Yan, Y., Xu, T., Wang, J., et al. (2019). The role of ArlRS in regulating oxacillin susceptibility in methicillin-resistant Staphylococcus aureus indicates it is a potential target for antimicrobial resistance breakers. *Emerg Microbes Infect* 8, 503–515. doi: 10.1080/22221751.2019.1595984.
- Baker, J., Sengupta, M., Jayaswal, R. K., and Morrissey, J. A. (2011). The Staphylococcus aureus CsoR regulates both chromosomal and plasmid-encoded copper resistance mechanisms. *Environ Microbiol* 13, 2495–2507. doi: 10.1111/j.1462-2920.2011.02522.x.
- Balibar, C. J., Shen, X., and Tao, J. (2009). The Mevalonate Pathway of *Staphylococcus aureus*. *J Bacteriol* 191, 851–861. doi: 10.1128/JB.01357-08.
- Ballal, A., Ray, B., and Manna, A. C. (2009). sarZ, a sarA family gene, is transcriptionally activated by MgrA and is involved in the regulation of genes encoding exoproteins in Staphylococcus aureus. *J Bacteriol* 191, 1656–1665. doi: 10.1128/JB.01555-08.
- Beasley, F. C., Vinés, E. D., Grigg, J. C., Zheng, Q., Liu, S., Lajoie, G. A., et al. (2009). Characterization of staphyloferrin A biosynthetic and transport mutants in Staphylococcus aureus. *Mol Microbiol* 72, 947–963. doi: 10.1111/j.1365-2958.2009.06698.x.
- Bischoff, M., Entenza, J. M., and Giachino, P. (2001). Influence of a Functional *sigB* Operon on the Global Regulators *sar* and *agr* in *Staphylococcus aureus*. *J Bacteriol* 183, 5171–5179. doi: 10.1128/JB.183.17.5171-5179.2001.
- Bisognano, C., Kelley, W. L., Estoppey, T., Francois, P., Schrenzel, J., Li, D., et al. (2004). A recA-LexA-dependent pathway mediates ciprofloxacin-induced fibronectin binding in Staphylococcus aureus. *J Biol Chem* 279, 9064–9071. doi: 10.1074/jbc.M309836200.
- Biswas, L., Biswas, R., Nerz, C., Ohlsen, K., Schlag, M., Schäfer, T., et al. (2009). Role of the twin-arginine translocation pathway in Staphylococcus. *J Bacteriol* 191, 5921–5929. doi: 10.1128/JB.00642-09.

- Borisova, M., Gaupp, R., Duckworth, A., Schneider, A., Dalügge, D., Mühleck, M., et al. (2016). Peptidoglycan Recycling in Gram-Positive Bacteria Is Crucial for Survival in Stationary Phase. *mBio* 7, e00923-16. doi: 10.1128/mBio.00923-16.
- Bose, J. L., Daly, S. M., Hall, P. R., and Bayles, K. W. (2014). Identification of the Staphylococcus aureus vfrAB operon, a novel virulence factor regulatory locus. *Infect Immun* 82, 1813–1822. doi: 10.1128/IAI.01655-13.
- Boyle-Vavra, S., Yin, S., Jo, D. S., Montgomery, C. P., and Daum, R. S. (2013). VraT/YvqF Is Required for Methicillin Resistance and Activation of the VraSR Regulon in Staphylococcus aureus. *Antimicrob Agents Chemother* 57, 83–95. doi: 10.1128/AAC.01651-12.
- Cerca, N., Brooks, J. L., and Jefferson, K. K. (2008). Regulation of the Intercellular Adhesin Locus Regulator (icaR) by SarA, σ^B , and IcaR in Staphylococcus aureus. J Bacteriol 190, 6530–6533. doi: 10.1128/JB.00482-08.
- Chaffin, D. O., Taylor, D., Skerrett, S. J., and Rubens, C. E. (2012). Changes in the Staphylococcus aureus Transcriptome during Early Adaptation to the Lung. *PLoS ONE* 7, e41329. doi: 10.1371/journal.pone.0041329.
- Chastanet, A., Fert, J., and Msadek, T. (2003). Comparative genomics reveal novel heat shock regulatory mechanisms in Staphylococcus aureus and other Gram-positive bacteria. *Mol Microbiol* 47, 1061–1073. doi: 10.1046/j.1365-2958.2003.03355.x.
- Chatterjee, S. S., Joo, H.-S., Duong, A. C., Dieringer, T. D., Tan, V. Y., Song, Y., et al. (2013). Essential Staphylococcus aureus toxin export system. *Nat Med* 19, 364–367. doi: 10.1038/nm.3047.
- Cheung, A. L., Nishina, K., and Manna, A. C. (2008). SarA of *Staphylococcus aureus* Binds to the *sarA* Promoter To Regulate Gene Expression. *J Bacteriol* 190, 2239–2243. doi: 10.1128/JB.01826-07.
- Cirz, R. T., Jones, M. B., Gingles, N. A., Minogue, T. D., Jarrahi, B., Peterson, S. N., et al. (2007). Complete and SOS-mediated response of Staphylococcus aureus to the antibiotic ciprofloxacin. *J Bacteriol* 189, 531–539. doi: 10.1128/JB.01464-06.
- Coe, K. A., Lee, W., Stone, M. C., Komazin-Meredith, G., Meredith, T. C., Grad, Y. H., et al. (2019). Multi-strain Tn-Seq reveals common daptomycin resistance determinants in Staphylococcus aureus. *PLoS Pathog* 15, e1007862. doi: 10.1371/journal.ppat.1007862.

- Cosgrove, K., Coutts, G., Jonsson, I.-M., Tarkowski, A., Kokai-Kun, J. F., Mond, J. J., et al. (2007). Catalase (KatA) and Alkyl Hydroperoxide Reductase (AhpC) Have Compensatory Roles in Peroxide Stress Resistance and Are Required for Survival, Persistence, and Nasal Colonization in *Staphylococcus aureus*. *J Bacteriol* 189, 1025–1035. doi: 10.1128/JB.01524-06.
- Crosby, H. A., Schlievert, P. M., Merriman, J. A., King, J. M., Salgado-Pabón, W., and Horswill, A. R. (2016). The Staphylococcus aureus Global Regulator MgrA Modulates Clumping and Virulence by Controlling Surface Protein Expression. *PLoS Pathog* 12, e1005604. doi: 10.1371/journal.ppat.1005604.
- Crosby, H. A., Tiwari, N., Kwiecinski, J. M., Xu, Z., Dykstra, A., Jenul, C., et al. (2020). The Staphylococcus aureus ArlRS two-component system regulates virulence factor expression through MgrA. *Mol Microbiol* 113, 103–122. doi: 10.1111/mmi.14404.
- Dale, S. E., Doherty-Kirby, A., Lajoie, G., and Heinrichs, D. E. (2004a). Role of siderophore biosynthesis in virulence of Staphylococcus aureus: identification and characterization of genes involved in production of a siderophore. *Infect Immun* 72, 29–37. doi: 10.1128/IAI.72.1.29-37.2004.
- Dale, S. E., Sebulsky, M. T., and Heinrichs, D. E. (2004b). Involvement of SirABC in iron-siderophore import in Staphylococcus aureus. *J Bacteriol* 186, 8356–8362. doi: 10.1128/JB.186.24.8356-8362.2004.
- Das, S., Lindemann, C., Young, B. C., Muller, J., Österreich, B., Ternette, N., et al. (2016). Natural mutations in a *Staphylococcus aureus* virulence regulator attenuate cytotoxicity but permit bacteremia and abscess formation. *Proc. Natl. Acad. Sci. U.S.A.* 113. doi: 10.1073/pnas.1520255113.
- Ding, Y., Liu, X., Chen, F., Di, H., Xu, B., Zhou, L., et al. (2014). Metabolic sensor governing bacterial virulence in Staphylococcus aureus. *Proc Natl Acad Sci U S A* 111, E4981-4990. doi: 10.1073/pnas.1411077111.
- Dmitriev, A., Chen, X., Paluscio, E., Stephens, A. C., Banerjee, S. K., Vitko, N. P., et al. (2021). The Intersection of the Staphylococcus aureus Rex and SrrAB Regulons: an Example of Metabolic Evolution That Maximizes Resistance to Immune Radicals. *mBio* 12, e02188-21. doi: 10.1128/mBio.02188-21.
- Dubrac, S., Boneca, I. G., Poupel, O., and Msadek, T. (2007). New insights into the WalK/WalR (YycG/YycF) essential signal transduction pathway

- reveal a major role in controlling cell wall metabolism and biofilm formation in Staphylococcus aureus. *J Bacteriol* 189, 8257–8269. doi: 10.1128/JB.00645-07.
- Dubrac, S., and Msadek, T. (2004). Identification of genes controlled by the essential YycG/YycF two-component system of Staphylococcus aureus. *J Bacteriol* 186, 1175–1181. doi: 10.1128/JB.186.4.1175-1181.2004.
- Dunman, P. M., Murphy, E., Haney, S., Palacios, D., Tucker-Kellogg, G., Wu, S., et al. (2001). Transcription Profiling-Based Identification of *Staphylococcus aureus* Genes Regulated by the *agr* and/or *sarA* Loci. *J Bacteriol* 183, 7341–7353. doi: 10.1128/IB.183.24.7341-7353.2001.
- Elsholz, A. K. W., Gerth, U., and Hecker, M. (2010). Regulation of CtsR activity in low GC, Gram+ bacteria. *Adv Microb Physiol* 57, 119–144. doi: 10.1016/B978-0-12-381045-8.00003-5.
- Fagerlund, A., Granum, P. E., and Håvarstein, L. S. (2014). Staphylococcus aureus competence genes: mapping of the SigH, ComK1 and ComK2 regulons by transcriptome sequencing. *Mol Microbiol* 94, 557–579. doi: 10.1111/mmi.12767.
- Falord, M., Karimova, G., Hiron, A., and Msadek, T. (2012). GraXSR proteins interact with the VraFG ABC transporter to form a five-component system required for cationic antimicrobial peptide sensing and resistance in Staphylococcus aureus. *Antimicrob Agents Chemother* 56, 1047–1058. doi: 10.1128/AAC.05054-11.
- Falord, M., Mäder, U., Hiron, A., Débarbouillé, M., and Msadek, T. (2011). Investigation of the Staphylococcus aureus GraSR regulon reveals novel links to virulence, stress response and cell wall signal transduction pathways. *PLoS One* 6, e21323. doi: 10.1371/journal.pone.0021323.
- Figueiredo, T. A., Sobral, R. G., Ludovice, A. M., de Almeida, J. M. F., Bui, N. K., Vollmer, W., et al. (2012). Identification of Genetic Determinants and Enzymes Involved with the Amidation of Glutamic Acid Residues in the Peptidoglycan of Staphylococcus aureus. *PLoS Pathog* 8, e1002508. doi: 10.1371/journal.ppat.1002508.
- Frees, D., Chastanet, A., Qazi, S., Sørensen, K., Hill, P., Msadek, T., et al. (2004). Clp ATPases are required for stress tolerance, intracellular replication and biofilm formation in Staphylococcus aureus. *Mol Microbiol* 54, 1445–1462. doi: 10.1111/j.1365-2958.2004.04368.x.
- Friedman, D. B., Stauff, D. L., Pishchany, G., Whitwell, C. W., Torres, V. J., and Skaar, E. P. (2006). Staphylococcus aureus redirects central metabolism

- to increase iron availability. *PLoS Pathog* 2, e87. doi: 10.1371/journal.ppat.0020087.
- Fritsch, V. N., Loi, V. V., Busche, T., Sommer, A., Tedin, K., Nürnberg, D. J., et al. (2019). The MarR-Type Repressor MhqR Confers Quinone and Antimicrobial Resistance in Staphylococcus aureus. *Antioxid Redox Signal* 31, 1235–1252. doi: 10.1089/ars.2019.7750.
- Ghssein, G., Brutesco, C., Ouerdane, L., Fojcik, C., Izaute, A., Wang, S., et al. (2016). Biosynthesis of a broad-spectrum nicotianamine-like metallophore in *Staphylococcus aureus*. *Science* 352, 1105–1109. doi: 10.1126/science.aaf1018.
- Goncheva, M. I., Flannagan, R. S., Sterling, B. E., Laakso, H. A., Friedrich, N. C., Kaiser, J. C., et al. (2019). Stress-induced inactivation of the Staphylococcus aureus purine biosynthesis repressor leads to hypervirulence. *Nat Commun* 10, 775. doi: 10.1038/s41467-019-08724-x.
- Götz, F., and Mayer, S. (2013). Both terminal oxidases contribute to fitness and virulence during organ-specific Staphylococcus aureus colonization. *mBio* 4, e00976-00913. doi: 10.1128/mBio.00976-13.
- Gregory, P. D., Lewis, R. A., Curnock, S. P., and Dyke, K. G. (1997). Studies of the repressor (BlaI) of beta-lactamase synthesis in Staphylococcus aureus. *Mol Microbiol* 24, 1025–1037. doi: 10.1046/j.1365-2958.1997.4051770.x.
- Grossoehme, N., Kehl-Fie, T. E., Ma, Z., Adams, K. W., Cowart, D. M., Scott, R. A., et al. (2011). Control of Copper Resistance and Inorganic Sulfur Metabolism by Paralogous Regulators in Staphylococcus aureus. *Journal of Biological Chemistry* 286, 13522–13531. doi: 10.1074/jbc.M111.220012.
- Gustafsson, E., and Oscarsson, J. (2008). Maximal transcription of *aur* (aureolysin) and *sspA* (serine protease) in *Staphylococcus aureus* requires staphylococcal accessory regulator R (*sarR*) activity. *FEMS Microbiology Letters* 284, 158–164. doi: 10.1111/j.1574-6968.2008.01198.x.
- Hartmann, T., Zhang, B., Baronian, G., Schulthess, B., Homerova, D., Grubmüller, S., et al. (2013). Catabolite control protein E (CcpE) is a LysR-type transcriptional regulator of tricarboxylic acid cycle activity in Staphylococcus aureus. *J Biol Chem* 288, 36116–36128. doi: 10.1074/jbc.M113.516302.
- Heinrichs, J. H., Gatlin, L. E., Kunsch, C., Choi, G. H., and Hanson, M. S.

- (1999). Identification and characterization of SirA, an iron-regulated protein from Staphylococcus aureus. *J Bacteriol* 181, 1436–1443. doi: 10.1128/JB.181.5.1436-1443.1999.
- Henke, S. K., and Cronan, J. E. (2016). The Staphylococcus aureus group II biotin protein ligase BirA is an effective regulator of biotin operon transcription and requires the DNA binding domain for full enzymatic activity. *Mol Microbiol* 102, 417–429. doi: 10.1111/mmi.13470.
- Hiron, A., Falord, M., Valle, J., Débarbouillé, M., and Msadek, T. (2011). Bacitracin and nisin resistance in Staphylococcus aureus: a novel pathway involving the BraS/BraR two-component system (SA2417/SA2418) and both the BraD/BraE and VraD/VraE ABC transporters. *Mol Microbiol* 81, 602–622. doi: 10.1111/j.1365-2958.2011.07735.x.
- Hiron, A., Posteraro, B., Carrière, M., Remy, L., Delporte, C., La Sorda, M., et al. (2010). A nickel ABC-transporter of Staphylococcus aureus is involved in urinary tract infection. *Mol Microbiol* 77, 1246–1260. doi: 10.1111/j.1365-2958.2010.07287.x.
- Horsburgh, M. J., Clements, M. O., Crossley, H., Ingham, E., and Foster, S. J. (2001a). PerR controls oxidative stress resistance and iron storage proteins and is required for virulence in Staphylococcus aureus. *Infect Immun* 69, 3744–3754. doi: 10.1128/IAI.69.6.3744-3754.2001.
- Horsburgh, M. J., Ingham, E., and Foster, S. J. (2001b). In Staphylococcus aureus, fur is an interactive regulator with PerR, contributes to virulence, and Is necessary for oxidative stress resistance through positive regulation of catalase and iron homeostasis. *J Bacteriol* 183, 468–475. doi: 10.1128/JB.183.2.468-475.2001.
- Horsburgh, M. J., Wharton, S. J., Cox, A. G., Ingham, E., Peacock, S., and Foster, S. J. (2002). MntR modulates expression of the PerR regulon and superoxide resistance in Staphylococcus aureus through control of manganese uptake: Manganese uptake and oxidative stress in S. aureus. *Molecular Microbiology* 44, 1269–1286. doi: 10.1046/j.1365-2958.2002.02944.x.
- Ingavale, S. S., Van Wamel, W., and Cheung, A. L. (2003). Characterization of RAT, an autolysis regulator in Staphylococcus aureus. *Mol Microbiol* 48, 1451–1466. doi: 10.1046/j.1365-2958.2003.03503.x.
- Jefferson, K. K., Pier, D. B., Goldmann, D. A., and Pier, G. B. (2004). The teicoplanin-associated locus regulator (TcaR) and the intercellular

- adhesin locus regulator (IcaR) are transcriptional inhibitors of the ica locus in Staphylococcus aureus. *J Bacteriol* 186, 2449–2456. doi: 10.1128/JB.186.8.2449-2456.2004.
- Jeong, D.-W., Cho, H., Jones, M. B., Shatzkes, K., Sun, F., Ji, Q., et al. (2012). The auxiliary protein complex SaePQ activates the phosphatase activity of sensor kinase SaeS in the SaeRS two-component system of Staphylococcus aureus: SaePQ induces phosphatase activity of SaeS. Molecular Microbiology 86, 331–348. doi: 10.1111/j.1365-2958.2012.08198.x.
- Ji, Q., Zhang, L., Jones, M. B., Sun, F., Deng, X., Liang, H., et al. (2013). Molecular mechanism of quinone signaling mediated through S-quinonization of a YodB family repressor QsrR. *Proc Natl Acad Sci U S A* 110, 5010–5015. doi: 10.1073/pnas.1219446110.
- Jiang, Q., Jin, Z., and Sun, B. (2018). MgrA Negatively Regulates Biofilm Formation and Detachment by Repressing the Expression of *psm* Operons in Staphylococcus aureus. *Appl Environ Microbiol* 84, e01008-18. doi: 10.1128/AEM.01008-18.
- Joo, H.-S., Chatterjee, S. S., Villaruz, A. E., Dickey, S. W., Tan, V. Y., Chen, Y., et al. (2016). Mechanism of Gene Regulation by a Staphylococcus aureus Toxin. *mBio* 7, e01579-16. doi: 10.1128/mBio.01579-16.
- Jordan, M. R., Wang, J., Weiss, A., Skaar, E. P., Capdevila, D. A., and Giedroc, D. P. (2019). Mechanistic Insights into the Metal-Dependent Activation of Zn ^{II} -Dependent Metallochaperones. *Inorg. Chem.* 58, 13661–13672. doi: 10.1021/acs.inorgchem.9b01173.
- Kaatz, G. W., DeMarco, C. E., and Seo, S. M. (2006). MepR, a repressor of the Staphylococcus aureus MATE family multidrug efflux pump MepA, is a substrate-responsive regulatory protein. *Antimicrob Agents Chemother* 50, 1276–1281. doi: 10.1128/AAC.50.4.1276-1281.2006.
- Kaatz, G. W., McAleese, F., and Seo, S. M. (2005). Multidrug resistance in Staphylococcus aureus due to overexpression of a novel multidrug and toxin extrusion (MATE) transport protein. *Antimicrob Agents Chemother* 49, 1857–1864. doi: 10.1128/AAC.49.5.1857-1864.2005.
- Kaiser, J. C., King, A. N., Grigg, J. C., Sheldon, J. R., Edgell, D. R., Murphy, M. E. P., et al. (2018). Repression of branched-chain amino acid synthesis in Staphylococcus aureus is mediated by isoleucine via CodY, and by a leucine-rich attenuator peptide. *PLoS Genet* 14, e1007159. doi: 10.1371/journal.pgen.1007159.

- Kelliher, J. L., Radin, J. N., Grim, K. P., Párraga Solórzano, P. K., Degnan, P. H., and Kehl-Fie, T. E. (2018a). Acquisition of the Phosphate Transporter NptA Enhances Staphylococcus aureus Pathogenesis by Improving Phosphate Uptake in Divergent Environments. *Infect Immun* 86, e00631-17. doi: 10.1128/IAI.00631-17.
- Kelliher, J. L., Radin, J. N., and Kehl-Fie, T. E. (2018b). PhoPR Contributes to Staphylococcus aureus Growth during Phosphate Starvation and Pathogenesis in an Environment-Specific Manner. *Infect Immun* 86, e00371-18. doi: 10.1128/IAI.00371-18.
- Kinkel, T. L., Roux, C. M., Dunman, P. M., and Fang, F. C. (2013). The Staphylococcus aureus SrrAB Two-Component System Promotes Resistance to Nitrosative Stress and Hypoxia. *mBio* 4, e00696-13. doi: 10.1128/mBio.00696-13.
- Kumaraswami, M., Schuman, J. T., Seo, S. M., Kaatz, G. W., and Brennan, R. G. (2009). Structural and biochemical characterization of MepR, a multidrug binding transcription regulator of the Staphylococcus aureus multidrug efflux pump MepA. *Nucleic Acids Res* 37, 1211–1224. doi: 10.1093/nar/gkn1046.
- Kuroda, M., Hayashi, H., and Ohta, T. (1999). Chromosome-determined zinc-responsible operon czr in Staphylococcus aureus strain 912. *Microbiol Immunol* 43, 115–125. doi: 10.1111/j.1348-0421.1999.tb02382.x.
- Lee, J.-H., Kim, N.-H., Winstel, V., Kurokawa, K., Larsen, J., An, J.-H., et al. (2015). Surface Glycopolymers Are Crucial for *In Vitro* Anti-Wall Teichoic Acid IgG-Mediated Complement Activation and Opsonophagocytosis of Staphylococcus aureus. *Infect Immun* 83, 4247–4255. doi: 10.1128/IAI.00767-15.
- Lei, M. G., Cue, D., Roux, C. M., Dunman, P. M., and Lee, C. Y. (2011). Rsp Inhibits Attachment and Biofilm Formation by Repressing *fnbA* in Staphylococcus aureus MW2. *J Bacteriol* 193, 5231–5241. doi: 10.1128/JB.05454-11.
- Lei, M. G., and Lee, C. Y. (2015). RbsR Activates Capsule but Represses the *rbsUDK* Operon in Staphylococcus aureus. *J Bacteriol* 197, 3666–3675. doi: 10.1128/JB.00640-15.
- Li, T., He, L., Song, Y., Villaruz, A. E., Joo, H.-S., Liu, Q., et al. (2016). AraC-Type Regulator Rsp Adapts Staphylococcus aureus Gene Expression to Acute Infection. *Infect Immun* 84, 723–734. doi: 10.1128/IAI.01088-15.
- Lindsay, J. A., and Foster, S. J. (2001). zur: a Zn(2+)-responsive regulatory

- element of Staphylococcus aureus. *Microbiology (Reading)* 147, 1259–1266. doi: 10.1099/00221287-147-5-1259.
- Loi, V. V., Busche, T., Tedin, K., Bernhardt, J., Wollenhaupt, J., Huyen, N. T. T., et al. (2018). Redox-Sensing Under Hypochlorite Stress and Infection Conditions by the Rrf2-Family Repressor HypR in Staphylococcus aureus. *Antioxid Redox Signal* 29, 615–636. doi: 10.1089/ars.2017.7354.
- Luebke, J. L., Shen, J., Bruce, K. E., Kehl-Fie, T. E., Peng, H., Skaar, E. P., et al. (2014). The CsoR-like sulfurtransferase repressor (CstR) is a persulfide sensor in Staphylococcus aureus. *Mol Microbiol* 94, 1343–1360. doi: 10.1111/mmi.12835.
- Luong, T. T., Dunman, P. M., Murphy, E., Projan, S. J., and Lee, C. Y. (2006). Transcription Profiling of the mgrA Regulon in Staphylococcus aureus. *J Bacteriol* 188, 1899–1910. doi: 10.1128/JB.188.5.1899-1910.2006.
- Luong, T. T., and Lee, C. Y. (2002). Overproduction of type 8 capsular polysaccharide augments Staphylococcus aureus virulence. *Infect Immun* 70, 3389–3395. doi: 10.1128/IAI.70.7.3389-3395.2002.
- Majerczyk, C. D., Dunman, P. M., Luong, T. T., Lee, C. Y., Sadykov, M. R., Somerville, G. A., et al. (2010). Direct targets of CodY in Staphylococcus aureus. *J Bacteriol* 192, 2861–2877. doi: 10.1128/JB.00220-10.
- Makhlin, J., Kofman, T., Borovok, I., Kohler, C., Engelmann, S., Cohen, G., et al. (2007). Staphylococcus aureus ArcR controls expression of the arginine deiminase operon. *J Bacteriol* 189, 5976–5986. doi: 10.1128/JB.00592-07.
- Manna, A. C., and Cheung, A. L. (2006). Expression of SarX, a negative regulator of agr and exoprotein synthesis, is activated by MgrA in Staphylococcus aureus. *J Bacteriol* 188, 4288–4299. doi: 10.1128/JB.00297-06.
- Manna, A. C., Ingavale, S. S., Maloney, M., van Wamel, W., and Cheung, A. L. (2004). Identification of *sarV* (SA2062), a New Transcriptional Regulator, Is Repressed by SarA and MgrA (SA0641) and Involved in the Regulation of Autolysis in *Staphylococcus aureus*. *J Bacteriol* 186, 5267–5280. doi: 10.1128/JB.186.16.5267-5280.2004.
- Manna, A., and Cheung, A. L. (2001). Characterization of *sarR*, a Modulator of *sar* Expression in *Staphylococcus aureus*. *Infect Immun* 69, 885–896. doi: 10.1128/IAI.69.2.885-896.2001.
- Masalha, M., Borovok, I., Schreiber, R., Aharonowitz, Y., and Cohen, G.

- (2001). Analysis of Transcription of the *Staphylococcus aureus* Aerobic Class Ib and Anaerobic Class III Ribonucleotide Reductase Genes in Response to Oxygen. *J Bacteriol* 183, 7260–7272. doi: 10.1128/JB.183.24.7260-7272.2001.
- Mazmanian, S. K., Ton-That, H., Su, K., and Schneewind, O. (2002). An iron-regulated sortase anchors a class of surface protein during Staphylococcus aureus pathogenesis. *Proc Natl Acad Sci U S A* 99, 2293–2298. doi: 10.1073/pnas.032523999.
- McGavin, M. J., Arsic, B., and Nickerson, N. N. (2012). Evolutionary blueprint for host- and niche-adaptation in Staphylococcus aureus clonal complex CC30. *Front Cell Infect Microbiol* 2, 48. doi: 10.3389/fcimb.2012.00048.
- Michalik, S., Depke, M., Murr, A., Gesell Salazar, M., Kusebauch, U., Sun, Z., et al. (2017). A global Staphylococcus aureus proteome resource applied to the in vivo characterization of host-pathogen interactions. *Sci Rep* 7, 9718. doi: 10.1038/s41598-017-10059-w.
- Morrissey, J. A., Cockayne, A., Brummell, K., and Williams, P. (2004). The Staphylococcal Ferritins Are Differentially Regulated in Response to Iron and Manganese and via PerR and Fur. *Infect Immun* 72, 972–979. doi: 10.1128/IAI.72.2.972-979.2004.
- Morrissey, J. A., Cockayne, A., Hill, P. J., and Williams, P. (2000). Molecular cloning and analysis of a putative siderophore ABC transporter from Staphylococcus aureus. *Infect Immun* 68, 6281–6288. doi: 10.1128/IAI.68.11.6281-6288.2000.
- Nguyen, T., Kim, T., Ta, H. M., Yeo, W. S., Choi, J., Mizar, P., et al. (2019). Targeting Mannitol Metabolism as an Alternative Antimicrobial Strategy Based on the Structure-Function Study of Mannitol-1-Phosphate Dehydrogenase in Staphylococcus aureus. *mBio* 10, e02660-18. doi: 10.1128/mBio.02660-18.
- O'Gara, J. P. (2007). ica and beyond: biofilm mechanisms and regulation in Staphylococcus epidermidis and Staphylococcus aureus. *FEMS Microbiol Lett* 270, 179–188. doi: 10.1111/j.1574-6968.2007.00688.x.
- Olson, M. E., King, J. M., Yahr, T. L., and Horswill, A. R. (2013). Sialic acid catabolism in Staphylococcus aureus. *J Bacteriol* 195, 1779–1788. doi: 10.1128/JB.02294-12.
- Oriol, C., Cengher, L., Manna, A. C., Mauro, T., Pinel-Marie, M.-L., Felden, B., et al. (2021). Expanding the Staphylococcus aureus SarA Regulon to Small RNAs. *mSystems* 6, e00713-21. doi: 10.1128/mSystems.00713-21.

- Oskouian, B., and Stewart, G. C. (1990). Repression and catabolite repression of the lactose operon of Staphylococcus aureus. *J Bacteriol* 172, 3804–3812. doi: 10.1128/jb.172.7.3804-3812.1990.
- Ouyang, Z., Zheng, F., Chew, J. Y., Pei, Y., Zhou, J., Wen, K., et al. (2019). Deciphering the activation and recognition mechanisms of Staphylococcus aureus response regulator ArlR. *Nucleic Acids Res* 47, 11418–11429. doi: 10.1093/nar/gkz891.
- Pagels, M., Fuchs, S., Pané-Farré, J., Kohler, C., Menschner, L., Hecker, M., et al. (2010). Redox sensing by a Rex-family repressor is involved in the regulation of anaerobic gene expression in Staphylococcus aureus: Redox sensitive gene regulation in S. aureus. *Molecular Microbiology* 76, 1142–1161. doi: 10.1111/j.1365-2958.2010.07105.x.
- Peng, H., Shen, J., Edmonds, K. A., Luebke, J. L., Hickey, A. K., Palmer, L. D., et al. (2017). Sulfide Homeostasis and Nitroxyl Intersect via Formation of Reactive Sulfur Species in Staphylococcus aureus. *mSphere* 2, e00082-17. doi: 10.1128/mSphere.00082-17.
- Peschel, A., Otto, M., Jack, R. W., Kalbacher, H., Jung, G., and Götz, F. (1999). Inactivation of the dlt operon in Staphylococcus aureus confers sensitivity to defensins, protegrins, and other antimicrobial peptides. *J Biol Chem* 274, 8405–8410. doi: 10.1074/jbc.274.13.8405.
- Popella, P., Krauss, S., Ebner, P., Nega, M., Deibert, J., and Götz, F. (2016). VraH Is the Third Component of the Staphylococcus aureus VraDEH System Involved in Gallidermin and Daptomycin Resistance and Pathogenicity. *Antimicrob Agents Chemother* 60, 2391–2401. doi: 10.1128/AAC.02865-15.
- Poupel, O., Moyat, M., Groizeleau, J., Antunes, L. C. S., Gribaldo, S., Msadek, T., et al. (2016). Transcriptional Analysis and Subcellular Protein Localization Reveal Specific Features of the Essential WalKR System in Staphylococcus aureus. *PLoS ONE* 11, e0151449. doi: 10.1371/journal.pone.0151449.
- Pragman, A. A., Ji, Y., and Schlievert, P. M. (2007). Repression of *Staphylococcus aureus* SrrAB Using Inducible Antisense *srrA* Alters Growth and Virulence Factor Transcript Levels. *Biochemistry* 46, 314–321. doi: 10.1021/bi0603266.
- Pragman, A. A., Yarwood, J. M., Tripp, T. J., and Schlievert, P. M. (2004). Characterization of Virulence Factor Regulation by SrrAB, a Two-Component System in *Staphylococcus aureus*. *J Bacteriol* 186,

- 2430-2438. doi: 10.1128/JB.186.8.2430-2438.2004.
- Purves, J., Cockayne, A., Moody, P. C. E., and Morrissey, J. A. (2010). Comparison of the regulation, metabolic functions, and roles in virulence of the glyceraldehyde-3-phosphate dehydrogenase homologues gapA and gapB in Staphylococcus aureus. *Infect Immun* 78, 5223–5232. doi: 10.1128/IAI.00762-10.
- Qian, Z., Yin, Y., Zhang, Y., Lu, L., Li, Y., and Jiang, Y. (2006). Genomic characterization of ribitol teichoic acid synthesis in Staphylococcus aureus: genes, genomic organization and gene duplication. *BMC Genomics* 7, 74. doi: 10.1186/1471-2164-7-74.
- Rapun-Araiz, B., Haag, A. F., De Cesare, V., Gil, C., Dorado-Morales, P., Penades, J. R., et al. (2020). Systematic Reconstruction of the Complete Two-Component Sensorial Network in Staphylococcus aureus. *mSystems* 5, e00511-20. doi: 10.1128/mSystems.00511-20.
- Ray, A., Edmonds, K. A., Palmer, L. D., Skaar, E. P., and Giedroc, D. P. (2020). Staphylococcus aureus Glucose-Induced Biofilm Accessory Protein A (GbaA) Is a Monothiol-Dependent Electrophile Sensor. *Biochemistry* 59, 2882–2895. doi: 10.1021/acs.biochem.0c00347.
- Reed, J. M., Olson, S., Brees, D. F., Griffin, C. E., Grove, R. A., Davis, P. J., et al. (2018). Coordinated regulation of transcription by CcpA and the Staphylococcus aureus two-component system HptRS. *PLoS One* 13, e0207161. doi: 10.1371/journal.pone.0207161.
- Reed, S. B., Wesson, C. A., Liou, L. E., Trumble, W. R., Schlievert, P. M., Bohach, G. A., et al. (2001). Molecular characterization of a novel Staphylococcus aureus serine protease operon. *Infect Immun* 69, 1521–1527. doi: 10.1128/IAI.69.3.1521-1527.2001.
- Roberts, C. A., Al-Tameemi, H. M., Mashruwala, A. A., Rosario-Cruz, Z., Chauhan, U., Sause, W. E., et al. (2017). The Suf Iron-Sulfur Cluster Biosynthetic System Is Essential in Staphylococcus aureus, and Decreased Suf Function Results in Global Metabolic Defects and Reduced Survival in Human Neutrophils. *Infect Immun* 85, e00100-17. doi: 10.1128/IAI.00100-17.
- Rodionov, D. A., Mironov, A. A., and Gelfand, M. S. (2002). Conservation of the biotin regulon and the BirA regulatory signal in Eubacteria and Archaea. *Genome Res* 12, 1507–1516. doi: 10.1101/gr.314502.
- Ruiz-Villafán, B., Cruz-Bautista, R., Manzo-Ruiz, M., Passari, A. K., Villarreal-Gómez, K., Rodríguez-Sanoja, R., et al. (2022). Carbon catabolite

- regulation of secondary metabolite formation, an old but not well-established regulatory system. *Microb Biotechnol* 15, 1058–1072. doi: 10.1111/1751-7915.13791.
- Sadykov, M. R., Windham, I. H., Widhelm, T. J., Yajjala, V. K., Watson, S. M., Endres, J. L., et al. (2019). CidR and CcpA Synergistically Regulate Staphylococcus aureus cidABC Expression. *J Bacteriol* 201, e00371-19. doi: 10.1128/JB.00371-19.
- Safo, M. K., Zhao, Q., Ko, T.-P., Musayev, F. N., Robinson, H., Scarsdale, N., et al. (2005). Crystal structures of the BlaI repressor from Staphylococcus aureus and its complex with DNA: insights into transcriptional regulation of the bla and mec operons. *J Bacteriol* 187, 1833–1844. doi: 10.1128/JB.187.5.1833-1844.2005.
- Satiaputra, J., Eijkelkamp, B. A., McDevitt, C. A., Shearwin, K. E., Booker, G. W., and Polyak, S. W. (2018). Biotin-mediated growth and gene expression in Staphylococcus aureus is highly responsive to environmental biotin. *Appl Microbiol Biotechnol* 102, 3793–3803. doi: 10.1007/s00253-018-8866-z.
- Sause, W. E., Balasubramanian, D., Irnov, I., Copin, R., Sullivan, M. J., Sommerfield, A., et al. (2019). The purine biosynthesis regulator PurR moonlights as a virulence regulator in *Staphylococcus aureus*. *Proc. Natl. Acad. Sci. U.S.A.* 116, 13563–13572. doi: 10.1073/pnas.1904280116.
- Schlag, S., Fuchs, S., Nerz, C., Gaupp, R., Engelmann, S., Liebeke, M., et al. (2008). Characterization of the Oxygen-Responsive NreABC Regulon of *Staphylococcus aureus*. *J Bacteriol* 190, 7847–7858. doi: 10.1128/JB.00905-08.
- Schmidt, K. A., Manna, A. C., and Cheung, A. L. (2003). SarT Influences *sarS* Expression in *Staphylococcus aureus*. *Infect Immun* 71, 5139–5148. doi: 10.1128/IAI.71.9.5139-5148.2003.
- Seidl, K., Goerke, C., Wolz, C., Mack, D., Berger-Bächi, B., and Bischoff, M. (2008). Staphylococcus aureus CcpA affects biofilm formation. *Infect Immun* 76, 2044–2050. doi: 10.1128/IAI.00035-08.
- Seidl, K., Müller, S., François, P., Kriebitzsch, C., Schrenzel, J., Engelmann, S., et al. (2009). Effect of a glucose impulse on the CcpA regulon in Staphylococcus aureus. *BMC Microbiol* 9, 95. doi: 10.1186/1471-2180-9-95.
- Shang, Y., Wang, X., Chen, Z., Lyu, Z., Lin, Z., Zheng, J., et al. (2020). Staphylococcus aureus PhoU Homologs Regulate Persister Formation

- and Virulence. Front Microbiol 11, 865. doi: 10.3389/fmicb.2020.00865.
- Singh, R., and Ray, P. (2014). Quorum sensing-mediated regulation of staphylococcal virulence and antibiotic resistance. *Future Microbiol* 9, 669–681. doi: 10.2217/fmb.14.31.
- Singh, V. K., Utaida, S., Jackson, L. S., Jayaswal, R. K., Wilkinson, B. J., and Chamberlain, N. R. (2007). Role for dnaK locus in tolerance of multiple stresses in Staphylococcus aureus. *Microbiology (Reading)* 153, 3162–3173. doi: 10.1099/mic.0.2007/009506-0.
- Singh, V. K., Xiong, A., Usgaard, T. R., Chakrabarti, S., Deora, R., Misra, T. K., et al. (1999). ZntR is an autoregulatory protein and negatively regulates the chromosomal zinc resistance operon znt of Staphylococcus aureus. *Mol Microbiol* 33, 200–207. doi: 10.1046/j.1365-2958.1999.01466.x.
- Skaar, E. P., and Schneewind, O. (2004). Iron-regulated surface determinants (Isd) of Staphylococcus aureus: stealing iron from heme. *Microbes Infect* 6, 390–397. doi: 10.1016/j.micinf.2003.12.008.
- Soutourina, O., Poupel, O., Coppée, J.-Y., Danchin, A., Msadek, T., and Martin-Verstraete, I. (2009). CymR, the master regulator of cysteine metabolism in Staphylococcus aureus, controls host sulphur source utilization and plays a role in biofilm formation. *Mol Microbiol* 73, 194–211. doi: 10.1111/j.1365-2958.2009.06760.x.
- Speziali, C. D., Dale, S. E., Henderson, J. A., Vinés, E. D., and Heinrichs, D. E. (2006). Requirement of Staphylococcus aureus ATP-binding cassette-ATPase FhuC for iron-restricted growth and evidence that it functions with more than one iron transporter. *J Bacteriol* 188, 2048–2055. doi: 10.1128/JB.188.6.2048-2055.2006.
- Stauff, D. L., Torres, V. J., and Skaar, E. P. (2007). Signaling and DNA-binding activities of the Staphylococcus aureus HssR-HssS two-component system required for heme sensing. *J Biol Chem* 282, 26111–26121. doi: 10.1074/jbc.M703797200.
- Strandén, A. M., Roos, M., and Berger-Bächi, B. (1996). Glutamine synthetase and heteroresistance in methicillin-resistant Staphylococcus aureus. *Microb Drug Resist* 2, 201–207. doi: 10.1089/mdr.1996.2.201.
- Tavares, A. C., Fernandes, P. B., Carballido-López, R., and Pinho, M. G. (2015). MreC and MreD Proteins Are Not Required for Growth of Staphylococcus aureus. *PLoS ONE* 10, e0140523. doi: 10.1371/journal.pone.0140523.

- Torres, V. J., Stauff, D. L., Pishchany, G., Bezbradica, J. S., Gordy, L. E., Iturregui, J., et al. (2007). A Staphylococcus aureus regulatory system that responds to host heme and modulates virulence. *Cell Host Microbe* 1, 109–119. doi: 10.1016/j.chom.2007.03.001.
- Voyich, J. M., Vuong, C., DeWald, M., Nygaard, T. K., Kocianova, S., Griffith, S., et al. (2009). The SaeR/S Gene Regulatory System Is Essential for Innate Immune Evasion by *Staphylococcus aureus*. *J INFECT DIS* 199, 1698–1706. doi: 10.1086/598967.
- Wang, R., Braughton, K. R., Kretschmer, D., Bach, T.-H. L., Queck, S. Y., Li, M., et al. (2007). Identification of novel cytolytic peptides as key virulence determinants for community-associated MRSA. *Nat Med* 13, 1510–1514. doi: 10.1038/nm1656.
- Waters, N. R., Samuels, D. J., Behera, R. K., Livny, J., Rhee, K. Y., Sadykov, M. R., et al. (2016). A spectrum of CodY activities drives metabolic reorganization and virulence gene expression in Staphylococcus aureus. *Mol Microbiol* 101, 495–514. doi: 10.1111/mmi.13404.
- Weaver, A. J., Peters, T. R., Tripet, B., Van Vuren, A., Rakesh, Lee, R. E., et al. (2018). Exposure of Methicillin-Resistant Staphylococcus aureus to Low Levels of the Antibacterial THAM-3ΦG Generates a Small Colony Drug-Resistant Phenotype. *Sci Rep* 8, 9850. doi: 10.1038/s41598-018-28283-3.
- Wiltshire, M. D., and Foster, S. J. (2001). Identification and analysis of Staphylococcus aureus components expressed by a model system of growth in serum. *Infect Immun* 69, 5198–5202. doi: 10.1128/IAI.69.8.5198-5202.2001.
- Windham, I. H., Chaudhari, S. S., Bose, J. L., Thomas, V. C., and Bayles, K. W. (2016). SrrAB Modulates Staphylococcus aureus Cell Death through Regulation of *cidABC* Transcription. *J Bacteriol* 198, 1114–1122. doi: 10.1128/JB.00954-15.
- Wolz, C., Pohlmann-Dietze, P., Steinhuber, A., Chien, Y.-T., Manna, A., van Wamel, W., et al. (2000). Agr-independent regulation of fibronectin-binding protein(s) by the regulatory locus sar in Staphylococcus aureus. *Mol Microbiol* 36, 230–243. doi: 10.1046/j.1365-2958.2000.01853.x.
- Wozniak, D. J., Tiwari, K. B., Soufan, R., and Jayaswal, R. K. (2012). The mcsB gene of the clpC operon is required for stress tolerance and virulence in Staphylococcus aureus. *Microbiology (Reading)* 158, 2568–2576. doi: 10.1099/mic.0.060749-0.
- Xiong, A., and Jayaswal, R. K. (1998). Molecular characterization of a

- chromosomal determinant conferring resistance to zinc and cobalt ions in Staphylococcus aureus. *J Bacteriol* 180, 4024–4029. doi: 10.1128/JB.180.16.4024-4029.1998.
- Xue, T., You, Y., Hong, D., Sun, H., and Sun, B. (2011). The Staphylococcus aureus KdpDE Two-Component System Couples Extracellular K + Sensing and Agr Signaling to Infection Programming. *Infect Immun* 79, 2154–2167. doi: 10.1128/IAI.01180-10.
- Yang, S.-J., Rice, K. C., Brown, R. J., Patton, T. G., Liou, L. E., Park, Y. H., et al. (2005). A LysR-type regulator, CidR, is required for induction of the Staphylococcus aureus cidABC operon. *J Bacteriol* 187, 5893–5900. doi: 10.1128/JB.187.17.5893-5900.2005.
- Yao, X., and Lu, C.-D. (2014). Functional Characterization of the potRABCD Operon for Spermine and Spermidine Uptake and Regulation in Staphylococcus aureus. *Curr Microbiol* 69, 75–81. doi: 10.1007/s00284-014-0556-1.
- Yarwood, J. M., McCormick, J. K., and Schlievert, P. M. (2001). Identification of a Novel Two-Component Regulatory System That Acts in Global Regulation of Virulence Factors of *Staphylococcus aureus*. *J Bacteriol* 183, 1113–1123. doi: 10.1128/JB.183.4.1113-1123.2001.
- Yoshida, Y., Matsuo, M., Oogai, Y., Kato, F., Nakamura, N., Sugai, M., et al. (2011). Bacitracin sensing and resistance in Staphylococcus aureus. *FEMS Microbiol Lett* 320, 33–39. doi: 10.1111/j.1574-6968.2011.02291.x.
- You, Y., Xue, T., Cao, L., Zhao, L., Sun, H., and Sun, B. (2014). Staphylococcus aureus glucose-induced biofilm accessory proteins, GbaAB, influence biofilm formation in a PIA-dependent manner. *Int J Med Microbiol* 304, 603–612. doi: 10.1016/j.ijmm.2014.04.003.
- Zhou, C., Bhinderwala, F., Lehman, M. K., Thomas, V. C., Chaudhari, S. S., Yamada, K. J., et al. (2019). Urease is an essential component of the acid response network of Staphylococcus aureus and is required for a persistent murine kidney infection. *PLoS Pathog* 15, e1007538. doi: 10.1371/journal.ppat.1007538.