

REFERENCES

Adekambi T, Colson P, Drancourt M. 2003. *rpoB* -Based Identification of Nonpigmented and Late-Pigmenting Rapidly Growing Mycobacteria. *J Clin Microbiol.* 41(12):5699–5708. doi:10.1128/JCM.41.12.5699.

Alhede Maria, Alhede Morten, Qvortrup K, Kragh KN, Jensen PØ, Stewart PS, Bjarnsholt T. 2020. The origin of extracellular DNA in bacterial biofilm infections in vivo. *Pathog Dis.* 78(2):ftaa018. doi:10.1093/femspd/ftaa018.

Allesen-Holm M, Barken KB, Yang L, Klausen M, Webb JS, Kjelleberg S, Molin S, Givskov M, Tim Tolker-Nielsen. 2006. A characterization of DNA release in *Pseudomonas aeruginosa* cultures and biofilms. *Mol Microbiol.* 59(4):1114–1128. doi:10.1111/j.1365-2958.2005.05008.x.

Almalki MA, Varghese R. 2020. Prevalence of catheter associated biofilm producing bacteria and their antibiotic sensitivity pattern. *J King Saud Univ - Sci.* 32(2):1427–1433. doi:10.1016/j.jksus.2019.11.037.

Amato SM, Fazen CH, Henry TC, Mok WWK, Orman MA, Sandvik EL, Volzing KG, Brynildsen MP. 2014. The role of metabolism in bacterial persistence. *Front Microbiol.* 5(3):1–9. doi:10.3389/fmicb.2014.00070.

Amato SM, Orman MA, Brynildsen MP. 2013. Metabolic Control of Persister Formation in *Escherichia coli*. *Mol Cell.* 50(4):475–487. doi:10.1016/j.molcel.2013.04.002. <http://dx.doi.org/10.1016/j.molcel.2013.04.002>.

Andersen SB, Ghoul M, Griffin AS, Petersen B, Johansen HK, Molin S. 2017. Diversity, prevalence, and longitudinal occurrence of type II toxin-antitoxin systems of *Pseudomonas aeruginosa* infecting cystic fibrosis lungs. *Front Microbiol.* 8(6):1180. doi:10.3389/FMICB.2017.01180/BIBTEX.

Asghari E, Kiel A, Kaltschmidt BP, Wortmann M, Schmidt N, Hüsken B, Hütten A, Knabbe C, Kaltschmidt C, Kaltschmidt B. 2021. Identification of microorganisms from several surfaces by maldi-tof ms: *P. aeruginosa* is leading in biofilm formation. *Microorganisms.* 9(5):1–18. doi:10.3390/microorganisms9050992.

Ashish A, Paterson S, Mowat E, Fothergill JL, Walshaw MJ, Winstanley C. 2013. Extensive diversification is a common feature of *Pseudomonas aeruginosa* populations during respiratory infections in cystic fibrosis. *J Cyst Fibros.* 12(6):790–793. doi:10.1016/j.jcf.2013.04.003.

- Baek MS, Chung ES, Jung DS, Ko KS. 2020. Effect of colistin-based antibiotic combinations on the eradication of persister cells in *Pseudomonas aeruginosa*. *J Antimicrob Chemother.* 75(4):917–924. doi:10.1093/jac/dkz552.
- Balaban NQ, Merrin J, Chait R, Kowalik L, Leibler S. 2004. Bacterial persistence as a phenotypic switch. *Science* (80-). 305(5690):1622–1625. doi:10.1126/science.1099390.
- Bankevich A, Nurk S, Antipov D, Gurevich AA, Dvorkin M, Kulikov AS, Lesin VM, Nikolenko SI, Pham S, Pribelski AD, et al. 2012. SPAdes: A new genome assembly algorithm and its applications to single-cell sequencing. *J Comput Biol.* 19(5):455–477. doi:10.1089/cmb.2012.0021.
- Bao K, Papadimitropoulos A, Akgül B, Belibasakis GN, Bostanci N. 2015. Establishment of an oral infection model resembling the periodontal pocket in a perfusion bioreactor system. *Virulence.* 6(3):265–273. doi:10.4161/21505594.2014.978721.
- Barrett TC, Mok WWK, Murawski AM, Brynildsen MP. 2019. Enhanced antibiotic resistance development from fluoroquinolone persisters after a single exposure to antibiotic. *Nat Commun.* 10(1):1–11. doi:10.1038/s41467-019-09058-4. <http://dx.doi.org/10.1038/s41467-019-09058-4>.
- Belibasakis GN, Thurnheer T, Bostanci N. 2014. *Porphyromonas gingivalis*: A heartfelt oral pathogen? *Virulence.* 5(4):463–464. doi:10.4161/viru.28930.
- Bergh B Van Den, Fauvart M, Michiels J. 2017. Formation , physiology , ecology , evolution and clinical importance of bacterial persisters. *FEMS Microbiol Lett.* 41(3):219–251. doi:10.1093/femsre/fux001.
- Bigger JW. 1944. Treatment of Staphylococcal Infections With Penicillin By Intermittent Sterilisation. *Lancet.* 244(6320):497–500. doi:10.1016/S0140-6736(00)74210-3.
- Bispo PJM, Haas W, Gilmore MS. 2015. Biofilms in infections of the eye. *Pathogens.* 4(1):111–136. doi:10.3390/pathogens4010111.
- Blomquist KC, Nix DE. 2021. A Critical Evaluation of Newer β -Lactam Antibiotics for Treatment of *Pseudomonas aeruginosa* Infections. *Ann Pharmacother.* 55(8):1010–1024. doi:10.1177/1060028020974003.
- Boles BR, Thoendel M, Singh PK. 2005. Rhamnolipids mediate detachment of *Pseudomonas aeruginosa* from biofilms. *Mol Microbiol.* 57(5):1210–1223. doi:10.1111/J.1365-

2958.2005.04743.X.

Bordi C, Lamy MC, Ventre I, Termine E, Hachani A, Fillet S, Roche B, Bleves S, Méjean V, Lazdunski A, et al. 2010. Regulatory RNAs and the HptB/RetS signalling pathways fine-tune *Pseudomonas aeruginosa* pathogenesis. *Mol Microbiol.* 76(6):1427–1443. doi:10.1111/j.1365-2958.2010.07146.x.

Borlee BR, Goldman AD, Murakami K, Samudrala R, Wozniak DJ, Parsek MR. 2010. *Pseudomonas aeruginosa* uses a cyclic-di-GMP-regulated adhesin to reinforce the biofilm extracellular matrix. *Mol Microbiol.* 75(4):827–842. doi:10.1111/j.1365-2958.2009.06991.x.

Borriello G, Werner E, Roe F, Kim AM, Ehrlich GD, Stewart PS. 2004. Oxygen limitation contributes to antibiotic tolerance of *Pseudomonas aeruginosa* in biofilms. *Antimicrob Agents Chemother.* 48(7):2659–2664. doi:10.1128/AAC.48.7.2659-2664.2004.

Bouza E, San Juan R, Muñoz P, Voss A, Kluytmans J. 2001. A European perspective on nosocomial urinary tract infections I. Report on the microbiology workload, etiology and antimicrobial susceptibility (ESGNI-003 study). *Clin Microbiol Infect.* 7(10):523–531. doi:10.1046/j.1198-743X.2001.00326.x.

Breidenstein EBM, de la Fuente-Núñez C, Hancock REW. 2011. *Pseudomonas aeruginosa*: All roads lead to resistance. *Trends Microbiol.* 19(8):419–426. doi:10.1016/j.tim.2011.04.005.

Bremer H, Dennis P. 2008. Feedback control of ribosome function in *Escherichia coli*. *Biochimie.* 90(3):493–499. doi:10.1016/j.biochi.2007.10.008.

Brencic A, McFarland KA, McManus HR, Castang S, Ilaria Mogno, Simon L. Dove and SL. 2009. The GacS/GacA signal transduction system of *Pseudomonas aeruginosa* acts exclusively through its control over the transcription of the RsmY and RsmZ regulatory small RNAs. *Mol Microbiol.* 73(3):434–445. doi:10.1111/j.1365-2958.2009.06782.x.The.

Brindhadevi K, Lewis Oscar F, Mylonakis E, Shanmugam S, Verma TN, Pugazhendhi A. 2020. Biofilm and Quorum sensing mediated pathogenicity in *Pseudomonas aeruginosa*. *Process Biochem.* 96:49–57. doi:10.1016/j.procbio.2020.06.001.

Brooun A, Liu S, Lewis K. 2000. A dose-response study of antibiotic resistance in *Pseudomonas aeruginosa* biofilms. *Antimicrob Agents Chemother.* 44(3):640–646. doi:10.1128/AAC.44.3.640-646.2000.

Buijs J, Dofferhoff ASM, Mouton JW, Wagenvoort JHT, Van Der Meer JWM. 2008.

Concentration-dependency of β -lactam-induced filament formation in Gram-negative bacteria. Clin Microbiol Infect. 14(4):344–349. doi:10.1111/j.1469-0691.2007.01940.x. <http://dx.doi.org/10.1111/j.1469-0691.2007.01940.x>.

Burrows LL. 2012. *Pseudomonas aeruginosa* twitching motility: Type IV pili in action. Annu Rev Microbiol. 66:493–520. doi:10.1146/annurev-micro-092611-150055.

Byrd MS, Pang B, Mishra M, Edwards W, Wozniak DJ. 2010. The *Pseudomonas aeruginosa* exopolysaccharide Psl facilitates surface adherence and NF- κ B activation in A549 cells. MBio. 1(3):3–6. doi:10.1128/mBio.00140-10.

Cameron DR, Shan Y, Zalis EA, Isabella V, Lewis K. 2018. A genetic determinant of persister cell formation in bacterial pathogens. J Bacteriol. 200(17):1–11. doi:10.1128/JB.00303-18.

Cao L, Srikumar R, Poole K. 2004. MexAB-OprM hyperexpression in NalC-type multidrug-resistant *Pseudomonas aeruginosa*: Identification and characterization of the nalC gene encoding a repressor of PA3720-PA3719. Mol Microbiol. 53(5):1423–1436. doi:10.1111/j.1365-2958.2004.04210.x.

Cendra M del M, Torrents E. 2021. *Pseudomonas aeruginosa* biofilms and their partners in crime. Biotechnol Adv. 49:107734. doi:10.1016/j.biotechadv.2021.107734.

Cesaretti M, Luppi E, Maccari F, Volpi N. 2003. A 96-well assay for uronic acid carbazole reaction. Carbohydr Polym. 54(1):59–61. doi:10.1016/S0144-8617(03)00144-9.

Chambers JR, Liao J, Schurr MJ, Sauer K. 2014. BrlR from *Pseudomonas aeruginosa* is a c-di-GMP-responsive transcription factor. Mol Microbiol. 92(3):471–487. doi:10.1007/978-3-540-29678-2_6069.

Chambers JR, Sauer K. 2013. The MerR-like regulator BrlR impairs *Pseudomonas aeruginosa* biofilm tolerance to colistin by repressing PhoPQ. J Bacteriol. 195(20):4678–4688. doi:10.1128/JB.00834-13.

Chiang WC, Nilsson M, Jensen PØ, Høiby N, Nielsen TE, Givskov M, Tolker-Nielsen T. 2013. Extracellular DNA shields against aminoglycosides in *Pseudomonas aeruginosa* biofilms. Antimicrob Agents Chemother. 57(5):2352–2361. doi:10.1128/AAC.00001-13.

Chowdhury N, Kwan BW, Wood TK. 2016. Persistence Increases in the Absence of the Alarmone Guanosine Tetraphosphate by Reducing Cell Growth. Sci Rep. 6:1–9. doi:10.1038/srep20519.

Christensen-Dalsgaard, Jørgensen MG, Kenn G. 2010. Molecular Microbiology - 2010 - Christensen-Dalsgaard - Three new RelE-homologous mRNA interferases of *Escherichia coli*.pdf. Mol Microbiol. 75(2):33–348.

Ciofu O, Tolker-Nielsen T. 2019. Tolerance and resistance of *Pseudomonas aeruginosa* biofilms to antimicrobial agents-how *P. aeruginosa* can escape antibiotics. Front Microbiol. 10:913. doi:10.3389/fmicb.2019.00913.

Ciszek-Lenda M, Strus M, Walczewska M, Majka G, Machul-Żwirbła A, Mikołajczyk D, Górska S, Gamian A, Chain B, Marcinkiewicz J. 2019. *Pseudomonas aeruginosa* biofilm is a potent inducer of phagocyte hyperinflammation. Inflamm Res. 68(5):397–413. doi:10.1007/S00011-019-01227-X.

Clark ST, Guttman DS, Hwang DM. 2018. Diversification of *Pseudomonas aeruginosa* within the cystic fibrosis lung and its effects on antibiotic resistance. FEMS Microbiol Lett. 365:fny026. doi:10.1093/FEMSLE/FNY026.

Cole SJ, Hall CL, Schniederberend M, Farrow JM, Goodson JR, Pesci EC, Kazmierczak BI, Lee VT. 2018. Host suppression of quorum sensing during catheter-associated urinary tract infections. Nat Commun. 9(1):1–8. doi:10.1038/s41467-018-06882-y.

Cole SJ, Records AR, Orr MW, Linden SB, Lee VT. 2014. Catheter-associated urinary tract infection by *Pseudomonas aeruginosa* is mediated by exopolysaccharide-independent biofilms. Infect Immun. 82(5):2048–2058. doi:10.1128/IAI.01652-14.

Colvin KM, Gordon VD, Murakami K, Borlee BR, Wozniak DJ, Wong GCL, Parsek MR. 2011. The *pel* polysaccharide can serve a structural and protective role in the biofilm matrix of *Pseudomonas aeruginosa*. PLoS Pathog. 7(1):e1001264. doi:10.1371/journal.ppat.1001264.

Comolli JC, Hauser AR, Waite L, Whitchurch CB, Mattick JS, Engel JN. 1999. *Pseudomonas aeruginosa* gene products PilT and PilU are required for cytotoxicity in vitro and virulence in a mouse model of acute pneumonia. Infect Immun. 67(7):3625–3630. doi:10.1128/iai.67.7.3625-3630.1999.

Corte L, Pierantoni DC, Tascini C, Roscini L, Cardinali G. 2019. Biofilm specific activity: A measure to quantify microbial biofilm. Microorganisms. 7(3):73. doi:10.3390/microorganisms7030073.

Coskun USS, Cicek AC, Kilinc C, Guckan R, Dagcioglu Y, Demir O, Sandallı C. 2018. Effect

of MazEF, HigBA and RelBE toxin-antitoxin systems on antibiotic resistance in *Pseudomonas aeruginosa* and *Staphylococcus* isolates. *Malawi Med J.* 30(2):67–72. doi:10.4314/mmj.v30i2.3.

Costerton JW, Stewart PS, Greenberg EP. 1999. Bacterial biofilms: A common cause of persistent infections. *Science* (80-). 284(5418):1318–1322. doi:10.1126/science.284.5418.1318.

Crespo A, Blanco-Cabra N, Torrents E. 2018. Aerobic vitamin B12 biosynthesis is essential for *Pseudomonas aeruginosa* Class II ribonucleotide reductase activity during planktonic and biofilm growth. *Front Microbiol.* 9:986. doi:10.3389/fmicb.2018.00986.

Dalebroux ZD, Swanson MS. 2012. PpGpp: Magic beyond RNA polymerase. *Nat Rev Microbiol.* 10(3):203–212. doi:10.1038/nrmicro2720. <http://dx.doi.org/10.1038/nrmicro2720>.

Daly JA, Boshard R, Matsen JM. 1984. Differential Primary Plating Medium for Enhancement of Pigment Production by *Pseudomonas aeruginosa*. 19(6):742–743.

Darzins A. 1993. The pilG gene product, required for *Pseudomonas aeruginosa* pilus production and twitching motility, is homologous to the enteric, single- domain response regulator CheY. *J Bacteriol.* 175(18):5934–5944. doi:10.1128/jb.175.18.5934-5944.1993.

Darzins A. 1994. Characterization of a *Pseudomonas aeruginosa* gene cluster involved in pilus biosynthesis and twitching motility: sequence similarity to the chemotaxis proteins of enterics and the gliding bacterium *Myxococcus xanthus*. *Mol Microbiol.* 11(1):137–153. doi:10.1111/j.1365-2958.1994.tb00296.x.

Darzins A. 1995. The *Pseudomonas aeruginosa* pilK gene encodes a chemotactic methyltransferase (CheR) homologue that is translationally regulated. *Mol Microbiol.* 15(4):703–717. doi:10.1111/j.1365-2958.1995.tb02379.x.

Das T, Manefield M. 2012. Pyocyanin Promotes Extracellular DNA Release in *Pseudomonas aeruginosa*. *PLoS One.* 7(10):e46718. doi:10.1371/journal.pone.0046718.

Das T, Sharma PK, Busscher HJ, Van Der Mei HC, Krom BP. 2010. Role of extracellular DNA in initial bacterial adhesion and surface aggregation. *Appl Environ Microbiol.* 76(10):3405–3408. doi:10.1128/AEM.03119-09.

Davey ME, Caiazza NC, O'Toole GA. 2003. Rhamnolipid surfactant production affects biofilm architecture in *Pseudomonas aeruginosa* PAO1. *J Bacteriol.* 185(3):1027–1036.

doi:10.1128/JB.185.3.1027-1036.2003.

Deng B, Ghatak S, Sarkar S, Singh K, Das Ghatak P, Mathew-Steiner SS, Roy S, Khanna S, Wozniak DJ, McComb DW, et al. 2020. Novel Bacterial Diversity and Fragmented eDNA Identified in Hyperbiofilm-Forming *Pseudomonas aeruginosa* Rugose Small Colony Variant. *iScience*. 23(2):100827. doi:10.1016/J.ISCI.2020.100827.

Desai S, Sanghrajka K, Gajjar D. 2019. High adhesion and increased cell death contribute to strong biofilm formation in *Klebsiella pneumoniae*. *Pathogens*. 8(4):277. doi:10.3390/pathogens8040277.

Deschaght P, Van daele S, De Baets F, Vaneechoutte M. 2011. PCR and the detection of *Pseudomonas aeruginosa* in respiratory samples of CF patients. A literature review. *J Cyst Fibros*. 10(5):293–297. doi:10.1016/j.jcf.2011.05.004.

Déziel E, Lépine F, Milot S, He J, Mindrinos MN, Tompkins RG, Rahme LG. 2004. Analysis of *Pseudomonas aeruginosa* 4-hydroxy-2-alkylquinolines (HAQs) reveals a role for 4-hydroxy-2-heptylquinoline in cell-to-cell communication. *Proc Natl Acad Sci U S A*. 101(5):1339–1344. doi:10.1073/pnas.0307694100.

Didelot X, Bowden R, Wilson DJ, Peto TEA, Derrick W. 2016. Europe PMC Funders Group Transforming clinical microbiology with bacterial genome sequencing. 13(9):601–612. doi:10.1038/nrg3226.

Diggle SP, Whiteley M. 2020. Microbe profile: *Pseudomonas aeruginosa*: Opportunistic pathogen and lab rat. *Microbiology*. 166(1):30–33. doi:10.1099/mic.0.000860.

Dingemans J, Al-Feghali RE, Lau GW, Sauer K. 2019. Controlling chronic *Pseudomonas aeruginosa* infections by strategically interfering with the sensory function of SagS. *Mol Microbiol*. 111(5):1211–1228. doi:10.1111/mmi.14215.

Dingemans J, Al-Feghali RE, Sondermann H, Karin Sauer. 2019. Signal Sensing and Transduction Are Conserved between the Periplasmic Sensory Domains of BifA and SagS. *mSphere*. 4(4):1–17. doi:10.1128/msphere.00442-19.

Dingemans J, Poudyal B, Sondermann H, Sauer K. 2018. The Yin and Yang of SagS: Distinct Residues in the HmsP Domain of SagS Independently Regulate Biofilm Formation and Biofilm Drug Tolerance. *mSphere*. 3(3):1–17. doi:10.1128/msphere.00192-18.

Divakar S, Lama M, Asad U. K. 2019. Antibiotics versus biofilm: an emerging battleground in

microbial communities | Enhanced Reader. *Antimicrob Resist Infect Control*. 8(76):1–10. doi:10.1186/s13756-019-0533-3.

Djordjevic Z, Folic MM, Zivic Z, Markovic V, Jankovic SM. 2013. Nosocomial urinary tract infections caused by *Pseudomonas aeruginosa* and *Acinetobacter* species: Sensitivity to antibiotics and risk factors. *Am J Infect Control*. 41(12):1182–1187. doi:10.1016/j.ajic.2013.02.018.

Donlan Rodney M. 2001. Biofilms and device-associated infections. *Emerg Infect Dis*. 7(2):277–281. doi:10.3201/eid0702.010226.

Donlan R. M. 2001. Biofilm formation: A clinically relevant microbiological process. *Clin Infect Dis*. 33(8):1387–1392. doi:10.1086/322972.

Dötsch A, Eckweiler D, Schniederjans M, Zimmermann A, Jensen V, Scharfe M, Geffers R, Häussler S. 2012. The *pseudomonas aeruginosa* transcriptome in planktonic cultures and static biofilms using rna sequencing. *PLoS One*. 7(2):e31092. doi:10.1371/journal.pone.0031092.

Drescher SPM, Gallo SW, Ferreira PMA, Ferreira CAS, Oliveira SD de. 2019. *Salmonella enterica* persister cells form unstable small colony variants after in vitro exposure to ciprofloxacin. *Sci Rep*. 9(1):1–11. doi:10.1038/s41598-019-43631-7.

Elliott TSJ, Shelton A, Greenwood D. 1987. The response of *Escherichia coli* to ciprofloxacin and norfloxacin. *J Med Microbiol*. 23(1):83–88. doi:10.1099/00222615-23-1-83.

Essar DW, Eberly L, Hadero A, Crawford IP. 1990. Identification and characterization of genes for a second anthranilate synthase in *Pseudomonas aeruginosa*: Interchangeability of the two anthranilate synthase and evolutionary implications. *J Bacteriol*. 172(2):884–900. doi:10.1128/jb.172.2.884-900.1990.

Evans TJ. 2015. Small colony variants of *Pseudomonas aeruginosa* in chronic bacterial infection of the lung in cystic fibrosis. *Future Microbiol*. 10(2):231–239. doi:10.2217/fmb.14.107.

Fauvart M, de Groote VN, Michiels J. 2011. Role of persister cells in chronic infections: Clinical relevance and perspectives on anti-persister therapies. *J Med Microbiol*. 60(6):699–709. doi:10.1099/jmm.0.030932-0.

Feneley RCL, Hopley IB, Wells PNT. 2015. Urinary catheters: History, current status, adverse events and research agenda. *J Med Eng Technol*. 39(8):459–470.

doi:10.3109/03091902.2015.1085600.

Fernández L, Hancock REW. 2012. Adaptive and mutational resistance: Role of porins and efflux pumps in drug resistance. *Clin Microbiol Rev.* 25(4):661–681. doi:10.1128/CMR.00043-12.

Flemming HC, Wingender J. 2010. The biofilm matrix. *Nat Rev Microbiol.* 8(9):623–633. doi:10.1038/nrmicro2415. <http://dx.doi.org/10.1038/nrmicro2415>.

Fonseca K, MacDougall J, Pitt TL. 1986. Inhibition of *Pseudomonas aeruginosa* from cystic fibrosis by selective media. *J Clin Pathol.* 39(2):220–222. doi:10.1136/jcp.39.2.220.

Gallo SW, Donamore BK, Pagnussatti VE, Ferreira CAS, De Oliveira SD. 2017. Effects of meropenem exposure in persister cells of *Acinetobacter calcoaceticus-baumannii*. *Future Microbiol.* 12(2):131–140. doi:10.2217/FMB-2016-0118.

Gao R, Mack TR, Stock AM. 2007. Bacterial response regulators: versatile regulatory strategies from common domains. *Trends Biochem Sci.* 32(5):225–234. doi:10.1016/j.tibs.2007.03.002.

Ghafoor A, Hay ID, Rehm BHA. 2011. Role of exopolysaccharides in *Pseudomonas aeruginosa* biofilm formation and architecture. *Appl Environ Microbiol.* 77(15):5238–5246. doi:10.1128/AEM.00637-11.

Gloag ES, Turnbull L, Huang A, Vallotton P, Wang H, Nolan LM, Mililli L, Gee ML, Prabhakar R, Whitchurch CB. 2013. Self-organization of bacterial biofilms is facilitated by extracellular DNA. *PNAS.* 110(28):11541–11546. doi:10.1073/pnas.1218898110.

Golmoradi Zadeh R, Mirshekar M, Sadeghi Kalani B, Pourghader J, Barati M, Masjedian Jazi F. 2022. The expression of type II TA system genes following persister cell formation in *Pseudomonas aeruginosa* isolates in the exponential and stationary phases. *Arch Microbiol.* 204(8):451. doi:10.1007/S00203-022-03038-X.

Gómez-junyent J, Benavent E, Sierra Y, El C, Soldevila L, Torrejón B, Rigo-bonnin R, Tubau F, Ariza J, Murillo O. 2019. Efficacy of ceftolozane/tazobactam, alone and in combination with colistin, against multidrug-resistant *Pseudomonas aeruginosa* in an in vitro biofilm pharmacodynamic model. *Int J Antimicrob Agents.* 53(5):612–619. doi:10.1016/j.ijantimicag.2019.01.010.

Gomila A, Carratalà J, Eliakim-Raz N, Shaw E, Wiegand I, Vallejo-Torres L, Gorostiza A,

Vigo JM, Morris S, Stoddart M, et al. 2018. Risk factors and prognosis of complicated urinary tract infections caused by *Pseudomonas aeruginosa* in hospitalized patients: A retrospective multicenter cohort study. *Infect Drug Resist.* 11:2571–2581. doi:10.2147/IDR.S185753.

Goodman SD, Obergfell KP, Jurcisek JA, Novotny LA, Downey JS, Ayala EA, Tjokro N, Li B, Justice SS, Bakaletz LO. 2011. Biofilms can be dispersed by focusing the immune system on a common family of bacterial nucleoid-associated proteins. *Mucosal Immunol* 2011 46. 4(6):625–637. doi:10.1038/mi.2011.27.

Greenberg EP, Whiteley M, Bangera MG, Bumgarner RE, Parsek MR, Teitzel GM, Lory S. 2001. Gene expression in *Pseudomonas aeruginosa* biofilms. *Nature.* 413(6858):860–864. doi:10.1038/35101627.

De Groote VN, Verstraeten N, Fauvart M, Kint CI, Verbeeck AM, Beullens S, Cornelis P, Michiels J. 2009. Novel persistence genes in *Pseudomonas aeruginosa* identified by high-throughput screening. *FEMS Microbiol Lett.* 297(1):73–79. doi:10.1111/j.1574-6968.2009.01657.x.

Guasp C, Moore ERB, Lalucat J, Bennasar A. 2000. Utility of internally transcribed 16S – 23S rDNA spacer regions for the definition of *Pseudomonas stutzeri* genomovars and other *Pseudomonas* species. *Int J Syst Evol Microbiol.* 50:1629–1639. doi:10.1099/00207713-50-4-1629.

Guo Y, Sun C, Li Y, Tang K, Ni S, Wang X. 2019. Antitoxin HigA inhibits virulence gene *mvfR* expression in *Pseudomonas aeruginosa*. *Environ Microbiol.* 21(8):2707–2723. doi:10.1111/1462-2920.14595.

Gupta K, Liao J, Petrova OE, Cherny KE, Sauer K. 2014. Elevated levels of the second messenger c-di-GMP contribute to antimicrobial resistance of *Pseudomonas aeruginosa*. *Mol Microbiol.* 92(3):488–506. doi:10.1038/jid.2014.371.

Gupta K, Marques CNH, Petrova OE, Sauer K. 2013. Antimicrobial tolerance of *Pseudomonas aeruginosa* biofilms is activated during an early developmental stage and requires the two-component hybrid *sagS*. *J Bacteriol.* 195(21):4975–4987. doi:10.1128/JB.00732-13.

Gurevich A, Saveliev V, Vyahhi N, Tesler G. 2013. QUAST: Quality assessment tool for genome assemblies. *Bioinformatics.* 29(8):1072–1075. doi:10.1093/bioinformatics/btt086.

Guyard-Nicodème M, Bazire A, Hémery G, Meylheuc T, Mollé D, Orange N, Fito-Boncompagni

L, Feuilloley M, Haras D, Dufour A, et al. 2008. Outer membrane modifications of *Pseudomonas fluorescens* MF37 in response to hyperosmolarity. *J Proteome Res.* 7(3):1218–1225. doi:10.1021/pr070539x.

Haagensen J, Verotta D, Huang L, Engel J, Spormann AM, Yang K. 2017. Spatiotemporal pharmacodynamics of meropenem- and tobramycin-treated *Pseudomonas aeruginosa* biofilms. *J Antimicrob Chemother.* 72(12):3357–3365. doi:10.1093/JAC/DKX288.

Hall CW, Mah TF. 2017a. Molecular mechanisms of biofilm-based antibiotic resistance and tolerance in pathogenic bacteria. *FEMS Microbiol Rev.* 41(3):276–301. doi:10.1093/femsre/fux010.

Hall CW, Mah TF. 2017b. Molecular mechanisms of biofilm-based antibiotic resistance and tolerance in pathogenic bacteria. *FEMS Microbiol Rev.* 41(3):276–301. doi:10.1093/FEMSRE/FUX010.

Harms A, Maisonneuve E, Gerdes K. 2016. Mechanisms of bacterial persistence during stress and antibiotic exposure. *Science* (80-). 354(6318):aaf4268. doi:10.1126/science.aaf4268.

Harmsen M, Lappann M, Knöchel S, Molin S. 2010. Role of extracellular DNA during biofilm formation by *listeria monocytogenes*. *Appl Environ Microbiol.* 76(7):2271–2279. doi:10.1128/AEM.02361-09.

Hatch RA, Schiller NL. 1998. Alginate lyase promotes diffusion of aminoglycosides through the extracellular polysaccharide of mucoid *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother.* 42(4):974–977. doi:10.1128/aac.42.4.974.

Hazan R, Que YA, Maura D, Strobel B, Majcherczyk PA, Hopper LR, Wilbur DJ, Hreha TN, Barquera B, Rahme LG. 2016. Auto Poisoning of the Respiratory Chain by a Quorum-Sensing-Regulated Molecule Favors Biofilm Formation and Antibiotic Tolerance. *Curr Biol.* 26(2):195–206. doi:10.1016/J.CUB.2015.11.056.

Head NE, Yu H. 2004. Cross-Sectional Analysis of Clinical and Environmental Isolates of *Pseudomonas aeruginosa*: Biofilm Formation, Virulence, and Genome Diversity. *Infect Immun.* 72(1):133–144. doi:10.1128/IAI.72.1.133-144.2004.

Heidari H, Hadadi M, Sedigh Ebrahim-Saraie H, Mirzaei A, Taji A, Hosseini SR, Motamedifar M. 2018. Characterization of virulence factors, antimicrobial resistance patterns and biofilm formation of *Pseudomonas aeruginosa* and *Staphylococcus* spp. strains isolated from corneal

infection. *J Fr Ophtalmol*. 41(9):823–829. doi:10.1016/j.jfo.2018.01.012.

Hengge R. 2009. Principles of c-di-GMP signalling in bacteria. *Nat Rev Microbiol*. 7(4):263–273. doi:10.1038/nrmicro2109.

Hengzhuang W, Ciofu O, Yang L, Wu H, Song Z, Oliver A, Høiby N. 2013. High β -lactamase levels change the pharmacodynamics of β -lactam antibiotics in *Pseudomonas aeruginosa* biofilms. *Antimicrob Agents Chemother*. 57(1):196–204. doi:10.1128/AAC.01393-12.

Hengzhuang W, Wu H, Ciofu O, Song Z, Høiby N. 2011. Pharmacokinetics/pharmacodynamics of colistin and imipenem on mucoid and nonmucoid *Pseudomonas aeruginosa* biofilms. *Antimicrob Agents Chemother*. 55(9):4469–4474. doi:10.1128/AAC.00126-11.

Hobby L, Karl M, Eleanor C. 1942. Observations on the Mechanism of Action of Penicillin. *Proc Soc Exp Biol Med*. 50:281–285. doi:10.3181/00379727-50-13773.

Hoch JA. 2000. Two-component and phosphorelay signal transduction. *Curr Opin Microbiol*. 3(2):165–170. doi:10.1016/S1369-5274(00)00070-9.

Høiby N, Bjarnsholt T, Moser C, Bassi GL, Coenye T, Donelli G, Hall-Stoodley L, Holá V, Imbert C, Kirketerp-Møller K, et al. 2015. ESCMID* guideline for the diagnosis and treatment of biofilm infections 2014. *Clin Microbiol Infect*. 21:S1–S25. doi:10.1016/j.cmi.2014.10.024.

Horna G, Quezada K, Ramos S, Mosqueda N, Rubio M, Guerra H, Ruiz J. 2019. Specific type IV pili groups in clinical isolates of *Pseudomonas aeruginosa*. *Int Microbiol*. 22(1):131–141. doi:10.1007/s10123-018-00035-3.

Hossain M, Saha S, Rahman M, Singha J, Mamun A. 2013. Isolation, Identification and Antibiofilm Study of *Pseudomonas Aeruginosa* from Cattle in Bangladesh. *J Vet Adv*. 3(7):180–185. doi:10.5455/jva.20130717123841.

Hsu JL, Chen HC, Peng HL, Chang HY. 2008. Characterization of the histidine-containing phosphotransfer protein B-mediated multistep phosphorelay system in *Pseudomonas aeruginosa* PAO1. *J Biol Chem*. 283(15):9933–9944. doi:10.1074/jbc.M708836200.

Huang B, Whitchurch CB, Mattick JS. 2003. FimX, a Multidomain Protein Connecting Environmental Signals to Twitching Motility in *Pseudomonas aeruginosa*. *J Bacteriol*. 185(24):7068–7076. doi:10.1128/JB.185.24.7068-7076.2003.

- Inclan YF, Huseby MJ, Engel JN. 2011. FimL regulates cAMP synthesis in *Pseudomonas aeruginosa*. *PLoS One*. 6(1):e15867. doi:10.1371/journal.pone.0015867.
- Ironmonger D, Edeghere O, Bains A, Loy R, Woodford N, Hawkey PM. 2015. Surveillance of antibiotic susceptibility of urinary tract pathogens for a population of 5.6 million over 4 years. *J Antimicrob Chemother*. 70:1744–1750. doi:10.1093/jac/dkv043.
- J. William C, Cheng KJ, Greesy GG, Ladd TI, Nickel JC, Dasgupta M, Marrie TJ. 1987. Bacterial biofilms in nature and disease. *Ann Rev Microbiol*. 41:435–464. doi:10.1146/annurev.mi.41.100187.002251.
- Jangra V, Sharma N, Chhillar AK. 2022. Therapeutic approaches for combating *Pseudomonas aeruginosa* infections. *Microbes Infect*. 24(4):104950. doi:10.1016/j.micinf.2022.
- Jarvis WR, Martone WJ. 1992a. Predominant pathogens in hospital infections. *J Antimicrob Chemother*. 29:19–24. doi:10.1093/jac/29.suppl_a.19.
- Jarvis WR, Martone WJ. 1992b. Predominant pathogens in hospital infections. *J Antimicrob Chemother*. 29:19–24. doi:10.1093/jac/29.suppl_A.19.
- Jennings LK, Storek KM, Ledvina HE, Coulon C, Marmont LS, Sadovskaya I, Secor PR, Tseng BS, Scian M, Filloux A, et al. 2015. Pel is a cationic exopolysaccharide that cross-links extracellular DNA in the *Pseudomonas aeruginosa* biofilm matrix. *Proc Natl Acad Sci U S A*. 112(36):11353–11358. doi:10.1073/pnas.1503058112.
- Jordan RP, Malic S, Waters MG, Stickler DJ, Williams DW. 2015. Development of an antimicrobial urinary catheter to inhibit urinary catheter encrustation. *Microbiol Discov*. 3:1. doi:10.7243/2052-6180-3-1.
- Jurado-Martín I, Sainz-Mejías M, McClean S. 2021. *Pseudomonas aeruginosa*: An audacious pathogen with an adaptable arsenal of virulence factors. *Int J Mol Sci*. 22(6):1–37. doi:10.3390/ijms22063128.
- Kamali E, Jamali A, Izanloo A, Ardebili A. 2021. In vitro activities of cellulase and ceftazidime, alone and in combination against *Pseudomonas aeruginosa* biofilms. *BMC Microbiol*. 21(1):1–10. doi:10.1186/s12866-021-02411-y.
- Kaplan JB, Lovetri K, Cardona ST, Madhyastha S, Sadovskaya I, Jabbouri S, Izano EA. 2012. Recombinant human DNase I decreases biofilm and increases antimicrobial susceptibility in staphylococci. *J Antibiot (Tokyo)*. 65(2):73–77. doi:10.1038/ja.2011.113.

Karatan E, Watnick P. 2009. Signals, Regulatory Networks, and Materials That Build and Break Bacterial Biofilms. *Microbiol Mol Biol Rev.* 73(2):310–347. doi:10.1128/mmbr.00041-08.

Karballaei Mirzahosseini H, Hadadi-Fishani M, Morshedi K, Khaledi A. 2020. Meta-Analysis of Biofilm Formation, Antibiotic Resistance Pattern, and Biofilm-Related Genes in *Pseudomonas aeruginosa* Isolated from Clinical Samples. *Microb Drug Resist.* 26(7):815–824. doi:10.1089/mdr.2019.0274.

De Kievit TR, Parkins MD, Gillis RJ, Srikumar R, Ceri H, Poole K, Iglewski BH, Storey DG. 2001. Multidrug efflux pumps: Expression patterns and contribution to antibiotic resistance in *Pseudomonas aeruginosa* biofilms. *Antimicrob Agents Chemother.* 45(6):1761–1770. doi:10.1128/AAC.45.6.1761-1770.2001.

Kim JS, Yamasaki R, Song S, Zhang W, Wood TK. 2018. Single cell observations show persister cells wake based on ribosome content. *Environ Microbiol.* 20(6):2085–2098. doi:10.1111/1462-2920.14093.

Klausen M, Heydorn A, Ragas P, Lambertsen L, Aaes-Jørgensen A, Molin S, Tolker-Nielsen T. 2003. Biofilm formation by *Pseudomonas aeruginosa* wild type, flagella and type IV pili mutants. *Mol Microbiol.* 48(6):1511–1524. doi:10.1046/j.1365-2958.2003.03525.x.

Klevens RM, Edwards JR, Richards CL, Horan TC, Gaynes RP, Pollock DA, Cardo DM. 2007. Estimating health care-associated infections and deaths in U.S. Hospitals, 2002. *Public Health Rep.* 122(2):160–166. doi:10.1177/003335490712200205.

Knutson CA, Jeanes A. 1968. A new modification of the carbazole analysis: Application to heteropolysaccharides. *Anal Biochem.* 24(3):470–481. doi:10.1016/0003-2697(68)90154-1.

Koch MD, Black ME, Han E, Shaevitz JW, Zemer Gitai. 2022. *Pseudomonas aeruginosa* distinguishes surfaces by stiffness using retraction of type IV pili. *Proc Natl Acad Sci U S A.* 119(20). doi:10.1073/PNAS.2119434119.

Köhler T, Michea-Hamzehpour M, Epp SF, Pechere JC. 1999. Carbapenem activities against *Pseudomonas aeruginosa*: Respective contributions of OprD and efflux systems. *Antimicrob Agents Chemother.* 43(2):424–427. doi:10.1128/aac.43.2.424.

Köhler T, Michéa-Hamzehpour M, Henze U, Gotoh N, Curty LK, Pechère JC. 1997. Characterization of MexE-MexF-OprN, a positively regulated multidrug efflux system of

Pseudomonas aeruginosa. Mol Microbiol. 23(2):345–354. doi:10.1046/j.1365-2958.1997.2281594.x.

Kragh KN, Alhede M, Kvich L, Bjarnsholt T. 2019. Into the well—A close look at the complex structures of a microtiter biofilm and the crystal violet assay. Biofilm. 1:100006. doi:10.1016/j.bioflm.2019.100006.

Kumar A, Schweizer HP. 2005. Bacterial resistance to antibiotics: Active efflux and reduced uptake. Adv Drug Deliv Rev. 57(10):1486–1513. doi:10.1016/j.addr.2005.04.004.

kumari Minu, Khurana S, Bhardwaj N, Malhotra R, Purva M. 2019. Pathogen burden and associated antibiogram of *Pseudomonas* spp. in a tertiary care hospital of India. Indian J Med Res. 149(2):295–298. doi:10.4103/ijmr.IJMR_14_18.

Kwan BW, Valenta JA, Benedik MJ, Wood TK. 2013. Arrested protein synthesis increases persister-like cell formation. Antimicrob Agents Chemother. 57(3):1468–1473. doi:10.1128/AAC.02135-12.

Lamas Ferreira JL, Álvarez Otero J, González González L, Novoa Lamazares L, Arca Blanco A, Bermúdez Sanjurjo JR, Rodríguez Conde I, Fernández Soneira M, de la Fuente Aguado J. 2017. *Pseudomonas aeruginosa* urinary tract infections in hospitalized patients : Mortality and prognostic factors. PLoS One. 12(5):1–13. doi:10.1371/journal.pone.0178178.

Langendonk RF, Neill DR, Fothergill JL. 2021. The Building Blocks of Antimicrobial Resistance in *Pseudomonas aeruginosa*: Implications for Current Resistance-Breaking Therapies. Front Cell Infect Microbiol. 11:665759. doi:10.3389/fcimb.2021.665759.

Laub MT, Goulian M. 2007. Specificity in two-component signal transduction pathways. Annu Rev Genet. 41:121–145. doi:10.1146/annurev.genet.41.042007.170548.

Lee B, Haagensen JAJ, Ciofu O, Andersen JB, Høiby N, Molin S, Al LEEET. 2005. Heterogeneity of Biofilms Formed by Nonmucoid *Pseudomonas aeruginosa* Isolates from Patients with Cystic Fibrosis. J Clin Microbiol. 43(10):5247–5255. doi:10.1128/JCM.43.10.5247.

Lee KH, Park SJ, Choi SJ, Uh Y, Park JY, Han KH. 2017. The influence of urinary catheter materials on forming biofilms of microorganisms. J Bacteriol Virol. 47(1):32–40. doi:10.4167/jbv.2017.47.1.32.

Leighton TL, Buensuceso RNC, Howell PL, Burrows LL. 2015. Biogenesis of *Pseudomonas aeruginosa* type IV pili and regulation of their function. Environ Microbiol. 17(11):4148–4163.

doi:10.1111/1462-2920.12849.

Levin-Reisman I, Ronin I, Gefen O, Braniss I, Shores N, Balaban NQ. 2017. Antibiotic tolerance facilitates the evolution of resistance. *Science* (80-). 355(6327):826–830. doi:10.1126/science.aaj2191.

Lewis K. 2007. Persister cells, dormancy and infectious disease. *Nat Rev Microbiol.* 5(1):48–56. doi:10.1038/nrmicro1557.

Lewis K, Shan Y. 2017. Why tolerance invites resistance: Bacteria that encounter antibiotics first become tolerant and then resistant to them. *Science* (80-). 355(6327):796. doi:10.1126/science.aam7926.

Li G, Shen M, Lu S, Le S, Tan Y, Wang J, Zhao X, Shen W, Guo K, Yang Y, et al. 2016. Identification and characterization of the HicAB toxin-antitoxin system in the opportunistic pathogen *Pseudomonas aeruginosa*. *Toxins (Basel).* 8(4):1–12. doi:10.3390/toxins8040113.

Li M, Long Y, Liu Ying, Liu Yang, Chen R, Shi J, Zhang L, Jin Y, Yang L, Bai F, et al. 2016. HigB of *Pseudomonas aeruginosa* enhances killing of phagocytes by up-regulating the type III secretion system in ciprofloxacin induced persister cells. *Front Cell Infect Microbiol.* 6:125. doi:10.3389/fcimb.2016.00125.

Liao J, Sauer K. 2012. The MerR-like transcriptional regulator BrlR contributes to *Pseudomonas aeruginosa* biofilm tolerance. *J Bacteriol.* 194(18):4823–4836. doi:10.1128/JB.00765-12.

Liao J, Schurr MJ, Sauera K. 2013. The merR-like regulator brlR confers biofilm tolerance by activating multidrug efflux pumps in *Pseudomonas aeruginosa* biofilms. *J Bacteriol.* 195(15):3352–3363. doi:10.1128/JB.00318-13.

Liebens V, Defraigne V, Van der Leyden A, De Groote VN, Fierro C, Beullens S, Verstraeten N, Kint C, Jans A, Frangipani E, et al. 2014. A putative de-N-acetylase of the PIG-L superfamily affects fluoroquinolone tolerance in *Pseudomonas aeruginosa*. *Pathog Dis.* 71(1):39–54. doi:10.1111/2049-632X.12174.

Lilly HA, Lowbury EJ. 1972. Cefrimide-nalidixic acid agar as a selective medium for *Pseudomonas aeruginosa*. *J Med Microbiol.* 5(1):151–153. doi:10.1099/00222615-5-1-151.

Lister PD, Wolter DJ, Hanson ND. 2009. Antibacterial-resistant *Pseudomonas aeruginosa*: Clinical impact and complex regulation of chromosomally encoded resistance mechanisms.

Clin Microbiol Rev. 22(4):582–610. doi:10.1128/CMR.00040-09.

Liu J, Gefen O, Ronin I, Bar-Meir M, Balaban NQ. 2020. Effect of tolerance on the evolution of antibiotic resistance under drug combinations. *Science* (80-). 367(6474):200–204. doi:10.1126/science.aay3041.

Llanes C, Hocquet D, Vogne C, Benali-Baitich D, Neuwirth C, Plésiat P. 2004. Clinical Strains of *Pseudomonas aeruginosa* Overproducing MexAB-OprM and MexXY Efflux Pumps Simultaneously. *Antimicrob Agents Chemother.* 48(5):1797–1802. doi:10.1128/AAC.48.5.1797-1802.2004.

Lopez D, Vlamakis H, Kolter R. 2010. Biofilms. 7:a000398. doi:10.1101/cshperspect.a000398.

Luther MK, Parente DM, Caffrey AR, Daffinee KE, Lopes V V, Martin ET, Laplante KL. 2018. Clinical and Genetic Risk Factors for Biofilm-Forming *Staphylococcus aureus*. *Antimicrob Agents Chemother.* 62(5):e02252-17. doi:10.1128/aac.02252-17.

Ma L, Conover M, Lu H, Parsek MR, Bayles K, Wozniak DJ. 2009. Assembly and Development of the *Pseudomonas aeruginosa* Biofilm Matrix. *PLoS Pathog.* 5(3):e1000354. doi:10.1371/journal.ppat.1000354.

Ma L, Jackson KD, Landry RM, Parsek MR, Wozniak DJ. 2006. Analysis of *Pseudomonas aeruginosa* conditional psl variants reveals roles for the psl polysaccharide in adhesion and maintaining biofilm structure postattachment. *J Bacteriol.* 188(23):8213–8221. doi:10.1128/JB.01202-06.

Macià MD, Rojo-Molinero E, Oliver A. 2014. Antimicrobial susceptibility testing in biofilm-growing bacteria. *Clin Microbiol Infect.* 20(10):981–990. doi:10.1111/1469-0691.12651.

Madsen JS, Lin YC, Squyres GR, Price-Whelan A, Torio A de S, Song A, Cornell WC, Sørensen SJ, Xavier JB, Dietrich LEP. 2015. Facultative control of matrix production optimizes competitive fitness in *Pseudomonas aeruginosa* PA14 biofilm models. *Appl Environ Microbiol.* 81(24):8414–8426. doi:10.1128/AEM.02628-15.

Mah TF, Pitts B, Pellock B, Walker GC, Stewart PS, O'Toole GA. 2003. A genetic basis for *Pseudomonas aeruginosa* biofilm antibiotic resistance. *Nat* 2003. 426(6964):306–310. doi:10.1038/nature02122.

Marr AK, Overhage J, Bains M, Hancock REW. 2007. The Lon protease of *Pseudomonas aeruginosa* is induced by aminoglycosides and is involved in biofilm formation and motility.

Microbiology. 153(2):474–482. doi:10.1099/mic.0.2006/002519-0.

Maseda H, Yoneyama H, Nakae T. 2000. Assignment of the substrate-selective subunits of the MexEF-OprN multidrug efflux pump of *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother*. 44(3):658–664. doi:10.1128/AAC.44.3.658-664.2000.

Maunder E, Welch M. 2017. Matrix exopolysaccharides; the sticky side of biofilm formation. *FEMS Microbiol Lett*. 364(13):fnx120. doi:10.1093/femsle/fnx120.

Mitrophanov AY, Groisman EA. 2008. Signal integration in bacterial two-component regulatory systems. *Genes Dev*. 22(19):2601–2611. doi:10.1101/gad.1700308.

Monds RD, O'Toole GA. 2009. The developmental model of microbial biofilms: ten years of a paradigm up for review. *Trends Microbiol*. 17(2):73–87. doi:10.1016/j.tim.2008.11.001.

Moradali MF, Ghods S, Rehm BHA. 2017. *Pseudomonas aeruginosa* Lifestyle : A Paradigm for Adaptation , Survival , and Persistence. *Front Cell Infect Microbiol*. 7:39. doi:10.3389/fcimb.2017.00039.

Morita Y, Cao L, Gould VC, Avison MB, Poole K. 2006. nalD encodes a second repressor of the mexAB-oprM multidrug efflux operon of *Pseudomonas aeruginosa*. *J Bacteriol*. 188(24):8649–8654. doi:10.1128/JB.01342-06.

Mulcahy H, Charron-Mazenod L, Lewenza S. 2008. Extracellular DNA Chelates Cations and Induces Antibiotic Resistance in *Pseudomonas aeruginosa* Biofilms. *PLOS Pathog*. 4(11):e1000213. doi:10.1371/JOURNAL.PPAT.1000213.

Mulcahy LR, Burns JL, Lory S, Lewis K. 2010. Emergence of *Pseudomonas aeruginosa* strains producing high levels of persister cells in patients with cystic fibrosis. *J Bacteriol*. 192(23):6191–6199. doi:10.1128/JB.01651-09.

Mulcahy LR, Isabella VM, Lewis K. 2014. *Pseudomonas aeruginosa* Biofilms in Disease. *Microb Ecol*. 68(1):1–12. doi:10.1007/s00248-013-0297-x.

Murakami K, Ono T, Viducic D, Kayama S, Mori M, Hirota K, Nemoto K, Miyake Y. 2005. Role for rpoS gene of *Pseudomonas aeruginosa* in antibiotic tolerance. *FEMS Microbiol Lett*. 242(1):161–167. doi:10.1016/j.femsle.2004.11.005.

Muthuramalingam M, White JC, Murphy T, Ames JR, Bourne CR. 2019. The toxin from a ParDE toxin-antitoxin system found in *Pseudomonas aeruginosa* offers protection to cells

challenged with anti-gyrase antibiotics. *Mol Microbiol.* 111(2):441–454. doi:10.1111/mmi.14165.

Mysorekar IU, Hultgren SJ. 2006. Mechanisms of uropathogenic *Escherichia coli* persistence and eradication from the urinary tract. *Proc Natl Acad Sci U S A.* 103(38):14170–14175. doi:10.1073/pnas.0602136103.

Nguyen D, Joshi-Datar A, Lepine F, Bauerle E, Olakanmi O, Beer K, McKay G, Siehnel R, Schafhauser J, Wang Y, et al. 2011. Active starvation responses mediate antibiotic tolerance in biofilms and nutrient-limited bacteria. *Science* (80-). 334(6058):982–986. doi:10.1126/science.1211037.

Nicolle LE, Evans G, Laverdieu M, Phillips P, Quan C, Rotstein C. 2005. Complicated urinary tract infection in adults. *Can J Infect Dis Med Microbiol.* 16(6):349–360. doi:10.1155/2005/385768.

Nolan LM, McCaughey LC, Merjane J, Turnbull L, Whitchurch CB. 2020. ChpC controls twitching motility-mediated expansion of *Pseudomonas aeruginosa* biofilms in response to serum albumin, mucin and oligopeptides. *Microbiol (United Kingdom).* 166(7):669–678. doi:10.1099/mic.0.000911.

Novotny LA, Amer AO, Brockson ME, Goodman SD, Bakaletz LO. 2013. Structural Stability of *Burkholderia cenocepacia* Biofilms Is Reliant on eDNA Structure and Presence of a Bacterial Nucleic Acid Binding Protein. *PLoS One.* 8(6):e67629. doi:10.1371/JOURNAL.PONE.0067629.

O'Toole GA. 2010. Microtiter dish Biofilm formation assay. *J Vis Exp.*(47):2437. doi:10.3791/2437.

O'Toole GA, Kolter R. 1998. Flagellar and twitching motility are necessary for *Pseudomonas aeruginosa* biofilm development. *Mol Microbiol.* 30(2):295–304. doi:10.1046/j.1365-2958.1998.01062.x.

Orman MA, Brynildsen MP. 2013. Dormancy is not necessary or sufficient for bacterial persistence. *Antimicrob Agents Chemother.* 57(7):3230–3239. doi:10.1128/AAC.00243-13.

Orman MA, Henry TC, Decoste CJ, Brynildsen MP, Engineering B. 2016. Analyzing persister physiology with fluorescence activated cell sorting. *Bact Persistence.* 1333:83–100. doi:10.1007/978-1-4939-2854-5_8.

Page R, Peti W. 2016. Toxin-antitoxin systems in bacterial growth arrest and persistence. *Nat Chem Biol.* 12(4):208–214. doi:10.1038/nchembio.2044.

Pamp SJ, Tolker-Nielsen T. 2007. Multiple roles of biosurfactants in structural biofilm development by *Pseudomonas aeruginosa*. *J Bacteriol.* 189(6):2531–2539. doi:10.1128/JB.01515-06.

Park AJ, Murphy K, Krieger JR, Brewer D, Taylor P, Habash M, Khursigara CM. 2014. A temporal examination of the planktonic and biofilm proteome of whole cell *pseudomonas aeruginosa* pao1 using quantitative mass spectrometry. *Mol Cell Proteomics.* 13(4):1095–1105. doi:10.1074/mcp.M113.033985.

Park S, Dingemans J, Gowett M, Sauer K. 2021. Glucose-6-Phosphate Acts as an Extracellular Signal of SagS To Modulate *Pseudomonas aeruginosa* c-di-GMP Levels, Attachment, and Biofilm Formation . *mSphere.* 6(1):1–17. doi:10.1128/msphere.01231-20.

Park S, Sauer K. 2021. SagS and its unorthodox contributions to *Pseudomonas aeruginosa* biofilm development. *Biofilm.* 3:100059. doi:10.1016/j.bioflm.2021.100059.

Patel H, Gajjar D. 2022. Cell adhesion and twitching motility influence strong biofilm formation in *Pseudomonas aeruginosa*. *Biofouling.* 38(3):235–249. doi:10.1080/08927014.2022.2054703.

Percival SL, Hill KE, Williams DW, Hooper SJ, Thomas DW, Costerton JW. 2012. A review of the scientific evidence for biofilms in wounds. *Wound Repair Regen.* 20(5):647–657. doi:10.1111/j.1524-475X.2012.00836.x.

Percival SL, Suleman L, Vuotto C, Donelli G. 2015. Healthcare-Associated infections, medical devices and biofilms: Risk, tolerance and control. *J Med Microbiol.* 64(4):323–334. doi:10.1099/jmm.0.000032.

Petrova OE, Gupta K, Liao J, Goodwine JS, Sauer K. 2017. Divide and conquer: The *Pseudomonas aeruginosa* two- component hybrid SagS enables biofilm formation and recalcitrance of biofilm cells to antimicrobial agents via distinct regulatory circuits. *Environ Microbiol.* 19(5):2005–2024. doi:10.1111/1462-2920.13719.Divide.

Petrova OE, Sauer K. 2009. A novel signaling network essential for regulating *Pseudomonas aeruginosa* biofilm development. *PLoS Pathog.* 5(11):e1000668. doi:10.1371/journal.ppat.1000668.

- Petrova OE, Sauer K. 2010. The novel two-component regulatory system BfiSR regulates biofilm development by controlling the small RNA rsmZ through CafA. *J Bacteriol.* 192(20):5275–5288. doi:10.1128/JB.00387-10.
- Petrova OE, Sauer K. 2011. SagS contributes to the motile-sessile switch and acts in concert with BfiSR to enable *Pseudomonas aeruginosa* biofilm formation. *J Bacteriol.* 193(23):6614–6628. doi:10.1128/JB.00305-11.
- Pinzon NM, Ju L. 2009. Analysis of rhamnolipid biosurfactants by methylene blue complexation. *Appl Microb Biotechnol.* 82:975–981. doi:10.1007/s00253-009-1896-9.
- Poole K. 2005. Aminoglycoside Resistance in *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother.* 49(2):479–487. doi:10.1186/s12864-019-6378-6.
- Potrykus K, Cashel M. 2008. (p)ppGpp: Still magical? *Annu Rev Microbiol.* 62:35–51. doi:10.1146/annurev.micro.62.081307.162903.
- Poudyal B, Sauer K. 2018a. The ABC of biofilm drug tolerance: the MerR-like regulator brlr is an activator of ABC transport systems, with PA1874-77 contributing to the tolerance of *Pseudomonas aeruginosa* biofilms to tobramycin. *Antimicrob Agents Chemother.* 62(2):e01981-17. doi:10.1128/AAC.01981-17.
- Poudyal B, Sauer K. 2018b. The PA3177 Gene Encodes an Active Diguanilate Cyclase That Formation by *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother.* 62(10):e01049-18. doi:10.1128/AAC.01049-18.
- Qi Q, Kamruzzaman M, Iredell JR. 2021. The higBA- Type Toxin-Antitoxin System in IncC Plasmids Is a Mobilizable Ciprofloxacin-Inducible System. *mSphere.* 6(3):e0042421. doi:10.1128/mSphere.00424-21.
- Raghavan V, Groisman EA. 2010. Orphan and hybrid two-component system proteins in health and disease. *Curr Opin Microbiol.* 13(2):226–231. doi:10.1016/j.mib.2009.12.010.
- Rahbari M, Rahlfs S, Jortzik E, Bogeski I, Becker K. 2017. H₂O₂ dynamics in the malaria parasite *Plasmodium falciparum*. *PLoS One.* 12(4):e0174837. doi:10.1371/journal.pone.0174837.
- Ramakrishnan Srikumar CJP, Poole Keith. 2000. Influence of Mutations in the mexR Repressor Gene on Expression of the MexA-MexB-OprM Multidrug Efflux System of *Pseudomonas aeruginosa*. *J Bacteriol.* 182(5):1410–1414. doi:10.1093/jac/46.6.885.

Reichhardt C, Jacobs HM, Matwichuk M, Wong C, Wozniak DJ, Parsek MR. 2020. The Versatile *Pseudomonas aeruginosa* Biofilm Matrix Protein CdrA Promotes Aggregation through Different Extracellular Exopolysaccharide Interactions. *J Bacteriol.* 202(19):1–9. doi:10.1128/JB.00216-20.

Reichhardt C, Wong C, da Silva DP, Wozniak DJ, Parsek MR. 2018. CDRA interactions within the *pseudomonas aeruginosa* biofilm matrix safeguard it from proteolysis and promote cellular packing. *MBio.* 9(5):1–12. doi:10.1128/mBio.01376-18.

Resch A, Rosenstein R, Nerz C, Götz F. 2005. Differential gene expression profiling of *Staphylococcus aureus* cultivated under biofilm and planktonic conditions. *Appl Environ Microbiol.* 71(5):2663–2676. doi:10.1128/AEM.71.5.2663-2676.2005.

Reyes EAP, Bale MJ, Cannon WH, Matsen JM. 1981. Identification of *Pseudomonas aeruginosa* by pyocyanin production on Tech agar. *J Clin Microbiol.* 13(3):456–458. doi:10.1128/jcm.13.3.456-458.1981.

Rocha AJ, De Oliveira Barsottini MR, Rocha RR, Laurindo MV, De Moraes FLL, Da Rocha SL. 2019. *Pseudomonas aeruginosa*: Virulence factors and antibiotic resistance Genes. *Brazilian Arch Biol Technol.* 62:e19180503. doi:10.1590/1678-4324-2019180503.

Rodrigue A, Quentin Y, Lazdunski A, Méjean V, Foglino M. 2000. Two-component systems in *Pseudomonas aeruginosa*: Why so many? *Trends Microbiol.* 8(11):498–504. doi:10.1016/S0966-842X(00)01833-3.

Rojo-Molinero E, Macià MD, Rubio R, Moyà B, Cabot G, López-Causapé C, Pérez JL, Cantón R, Oliver A. 2016. Sequential treatment of biofilms with aztreonam and tobramycin is a novel strategy for combating *Pseudomonas aeruginosa* chronic respiratory infections. *Antimicrob Agents Chemother.* 60(5):2912–2922. doi:10.1128/AAC.00196-16.

Römling U, Balsalobre C. 2012. Biofilm infections, their resilience to therapy and innovative treatment strategies. *J Intern Med.* 272(6):541–561. doi:10.1111/joim.12004.

Römling U, Galperin MY, Gomelsky M. 2013. Cyclic di-GMP: the First 25 Years of a Universal Bacterial Second Messenger. *Microbiol Mol Biol Rev.* 77(1):1–52. doi:10.1128/mmbr.00043-12.

Rossi E, La Rosa R, Bartell JA, Marvig RL, Haagensen JAJ, Sommer LM, Molin S, Johansen HK. 2021. *Pseudomonas aeruginosa* adaptation and evolution in patients with cystic fibrosis.

Nat Rev Microbiol. 19(5):331–342. doi:10.1038/s41579-020-00477-5.

Rumbaugh KP, Diggle SP, Watters CM, Ross-Gillespie A, Griffin AS, West SA. 2009. Quorum Sensing and the Social Evolution of Bacterial Virulence. Elsevier Ltd.

Ryder C, Byrd M, Wozniak DJ. 2007. Role of polysaccharides in *Pseudomonas aeruginosa* biofilm development. Curr Opin Microbiol. 10(6):644–648. doi:10.1016/j.mib.2007.09.010.

S. Andrews. 2010. FASTQC. A quality control tool for high throughput sequence data | BibSonomy.

Sabbuba N, Hughes G, Stickler DJ. 2002. The migration of *Proteus mirabilis* and other urinary tract pathogens over Foley catheters. BJU Int. 89(1):55–60. doi:10.1046/J.1464-410X.2002.02560.X.

Saito K, Yoneyama H, Nakae T. 1999. nalB-type mutations causing the overexpression of the MexAB-OprM efflux pump are located in the mexR gene of the *Pseudomonas aeruginosa* chromosome. FEMS Microbiol Lett. 179(1):67–72. doi:10.1016/S0378-1097(99)00394-8.

Sarkar S. 2020. Release mechanisms and molecular interactions of *Pseudomonas aeruginosa* extracellular DNA. Appl Microbiol Biotechnol. 104(15):6549–6564. doi:10.1007/s00253-020-10687-9.

Sauer K, Camper AK, Ehrlich GD, Costerton JW, Davies DG. 2002. *Pseudomonas aeruginosa* displays multiple phenotypes during development as a biofilm. J Bacteriol. 184(4):1140–1154. doi:10.1128/jb.184.4.1140-1154.2002.

Saxena S, Banerjee G, Garg R, Singh M. 2014. Comparative study of biofilm formation in *pseudomonas aeruginosa* isolates from patients of lower respiratory tract infection. J Clin Diagnostic Res. 8(5):9–11. doi:10.7860/JCDR/2014/7808.4330.

Schaik EJ Van, Giltner CL, Audette GF, Keizer DW, Bautista DL, Slupsky CM, Sykes BD, Irvin RT. 2005. DNA binding: A novel function of *Pseudomonas aeruginosa* type IV pili. J Bacteriol. 187(4):1455–1464. doi:10.1128/JB.187.4.1455-1464.2005.

Seemann T. 2014. Prokka: Rapid prokaryotic genome annotation. Bioinformatics. 30(14):2068–2069. doi:10.1093/bioinformatics/btu153.

Senthil R, Angel KJ, Malathi R, Venkatesan D. 2011. Isolation, identification and computational studies on *Pseudomonas aeruginosa* sp. strain MPC1 in tannery effluent.

Bioinformation. 6(5):187–190. doi:10.6026/97320630006187.

Shigemura K, Arakawa S, Sakai Y, Kinoshita S, Tanaka K, Fujisawa M. 2006. Complicated urinary tract infection caused by *Pseudomonas aeruginosa* in a single institution (1999-2003). *Int J Urol*. 13(5):538–542. doi:10.1111/j.1442-2042.2006.01359.x.

Sinha M, Ghosh N, Wijesinghe DS, Mathew-Steiner SS, Das A, Singh K, Masry M El, Khanna S, Inoue H, Yamazaki K, et al. 2021. *Pseudomonas Aeruginosa* Theft Biofilm Require Host Lipids of Cutaneous Wound. *Ann Surg*.:10.1097/SLA.000000000000525. doi:10.1097/sla.0000000000005252.

Soares A, Alexandre K, Etienne M. 2020. Tolerance and Persistence of *Pseudomonas aeruginosa* in Biofilms Exposed to Antibiotics: Molecular Mechanisms, Antibiotic Strategies and Therapeutic Perspectives. *Front Microbiol*. 11:2057. doi:10.3389/fmicb.2020.02057.

Soares A, Roussel V, Pestel-Caron M, Barreau M, Caron F, Bouffartigues E, Chevalier S, Etienne M. 2019. Understanding Ciprofloxacin Failure in *Pseudomonas aeruginosa* Biofilm: Persister Cells Survive Matrix Disruption. *Front Microbiol*. 10:2603. doi:10.3389/fmicb.2019.02603.

Song Y, Luo G, Zhu Y, Li T, Li C, He L, Zhao N, Zhao C, Yang J, Huang Q, et al. 2020. *Pseudomonas aeruginosa* antitoxin HigA functions as a diverse regulatory factor by recognizing specific pseudopalindromic DNA motifs. *Environ Microbiol*. 60(2):192–206. doi:10.1111/1462-2920.15365.

Southey-Pillig CJ, Davies DG, Sauer K. 2005. Characterization of temporal protein production in *Pseudomonas aeruginosa* biofilms. *J Bacteriol*. 187(23):8114–8126. doi:10.1128/JB.187.23.8114-8126.2005.

Spilker T, Coenye T, Vandamme P, Lipuma JJ. 2004. PCR-Based Assay for Differentiation of *Pseudomonas aeruginosa* from Other *Pseudomonas* Species Recovered from Cystic Fibrosis Patients. *J Clin Microbiol*. 42(5):2074–2079. doi:10.1128/JCM.42.5.2074.

Spoering AMYL, Lewis KIM. 2001. Biofilms and Planktonic Cells of *Pseudomonas aeruginosa* Have Similar Resistance to Killing by Antimicrobials. *J Bacteriol*. 183(23):6746–6751. doi:10.1128/JB.183.23.6746.

Stepanović S, Ćirković I, Ranin L, Švabić-Vlahović M. 2004. Biofilm formation by *Salmonella* spp. and *Listeria monocytogenes* on plastic surface. *Lett Appl Microbiol*. 38(5):428–432.

doi:10.1111/j.1472-765X.2004.01513.x.

Stewart PS, Costerton JW. 2001. Antibiotic resistance of bacteria in biofilms. *Lancet*. 358:135–138. doi:10.1016/S0140-6736(01)05321-1.

Stewart PS, Franklin MJ. 2008. Physiological heterogeneity in biofilms. *Nat Rev Microbiol*. 6(3):199–210. doi:10.1038/nrmicro1838.

Stickler DJ. 2008. Bacterial biofilms in patients with indwelling urinary catheters. *Nat Clin Pract Urol* 2008 511. 5(11):598–608. doi:10.1038/ncpuro1231.

Subedi D, Vijay AK, Kohli GS, Rice SA, Willcox M. 2018. Comparative genomics of clinical strains of *Pseudomonas aeruginosa* strains isolated from different geographic sites. *Sci Rep*. 8(1):1–14. doi:10.1038/s41598-018-34020-7.

Sulaiman JE, Lam H. 2020. Proteomic Study of the Survival and Resuscitation Mechanisms of Filamentous Persisters in an Evolved *Escherichia coli* Population from Cyclic Ampicillin Treatment. *mSystems*. 5(4):1–21. doi:10.1128/msystems.00462-20.

Suriyanarayanan T, Qingsong L, Kwang LT, Mun LY, Seneviratne CJ. 2018. Quantitative proteomics of strong and weak biofilm formers of *enterococcus faecalis* reveals novel regulators of biofilm formation. *Mol Cell Proteomics*. 17(4):643–654. doi:10.1074/mcp.RA117.000461.

Sweere JM, Van Bellegheem JD, Ishak H, Bach MS, Popescu M, Sunkari V, Kaber G, Manasherob R, Suh GA, Cao X, et al. 2019. Bacteriophage trigger antiviral immunity and prevent clearance of bacterial infection. *Science*. 363(6434):eaat9691. doi:10.1126/science.aat9691.

Tacconelli E. 2017. WHO (2017) Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics.

Tahrioui A, Duchesne R, Bouffartigues E, Rodrigues S, Maillot O, Tortuel D, Hardouin J, Taupin L, Groleau M, Dufour A, et al. 2019. Extracellular DNA release, quorum sensing, and PrrF1 / F2 small RNAs are key players in *Pseudomonas aeruginosa* tobramycin-enhanced biofilm formation. *npj Biofilms Microbiomes*. 5(1):15. doi:10.1038/s41522-019-0088-3.

Tarafder AK, von K  gelgen A, Mellul AJ, Schulze U, Aarts DGAL, Bharat TAM. 2020. Phage liquid crystalline droplets form occlusive sheaths that encapsulate and protect infectious rod-shaped bacteria. *Proc Natl Acad Sci U S A*. 117(9):4724–4731. doi:10.1073/pnas.1917726117.

- Tellis RC, Mososabba MS, Roche RA. 2017. Correlation Between Biofilm Formation and Antibiotic Resistance in Uropathogenic *Pseudomonas Aeruginosa* Causing Catheter Associated Urinary Tract Infections. *Eur J Pharm Med Res.* 4(10):248–252.
- Tetz G V., Artemenko NK, Tetz V V. 2009. Effect of DNase and antibiotics on biofilm characteristics. *Antimicrob Agents Chemother.* 53(3):1204–1209. doi:10.1128/AAC.00471-08.
- Thi MTT, Wibowo D, Rehm BHA. 2020. *Pseudomonas aeruginosa* biofilms. *Int J Mol Sci.* 21(22):1–25. doi:10.3390/ijms21228671.
- Thibeaux R, Kainiu M, Goarant C. 2020. Biofilm Formation and Quantification Using the 96-Microtiter Plate. In: *Leptospira spp.* Springer. p. 207–214.
- Toole GO, Kaplan HB, Kolter R. 2000. Biofilm formation as microbial development. In: *Ann. Rev. Microbiol.* Vol. 54. p. 49–79.
- Tseng BS, Reichhardt C, Merrihew GE, Araujo-Hernandez SA, Harrison JJ, MacCoss MJ, Matthew R. Parsek. 2018. A biofilm matrix-associated protease inhibitor protects *Pseudomonas aeruginosa* from proteolytic attack. *MBio.* 9(2):e00543-18. doi:10.1128/mBio.00543-18.
- Valentini M, Filloux A. 2016. Biofilms and Cyclic di-GMP (c-di-GMP) signaling: Lessons from *Pseudomonas aeruginosa* and other bacteria. *J Biol Chem.* 291(24):12547–12555. doi:10.1074/jbc.R115.711507.
- Valentini M, Laventie BJ, Moscoso J, Jenal U, Filloux A. 2016. The Diguanylate Cyclase HsbD Intersects with the HptB Regulatory Cascade to Control *Pseudomonas aeruginosa* Biofilm and Motility. *PLoS Genet.* 12(10):1–30. doi:10.1371/journal.pgen.1006354.
- Vasseur P, Vallet-Gely I, Soscia C, Genin S, Filloux A. 2005. The *pel* genes of the *Pseudomonas aeruginosa* PAK strain are involved at early and late stages of biofilm formation. *Microbiology.* 151(3):985–997. doi:10.1099/mic.0.27410-0.
- Ventre I, Goodman AL, Vallet-Gely I, Vasseur P, Soscia C, Molin S, Bleves S, Lazdunski A, Lory S, Filloux A. 2006. Multiple sensors control reciprocal expression of *Pseudomonas aeruginosa* regulatory RNA and virulence genes. *Proc Natl Acad Sci U S A.* 103(1):171–176. doi:10.1073/pnas.0507407103.
- Vicente L, Da F, Filho S, Levi JE, Oda CN, Regina S, Da T, Ramos S, Rozov T. 1999. PCR

identification of *Pseudomonas aeruginosa* and direct detection in clinical samples from cystic fibrosis patients. *J Med Microbiol.* 48(4):357–361. doi:10.1099/00222615-48-4-357.

Viducic D, Murakami K, Amoh T, Ono T, Miyake Y. 2017. RpoN promotes *pseudomonas aeruginosa* survival in the presence of tobramycin. *Front Microbiol.* 8:839. doi:10.3389/fmicb.2017.00839.

Viducic D, Ono T, Murakami K, Susilowati H, Kayama S, Hirota K, Miyake Y. 2006. Functional Analysis of *spoT*, *relA* and *dksA* Genes on Quinolone Tolerance in *Pseudomonas aeruginosa* under Nongrowing Condition. *Microbiol Immunol.* 50(4):349–357. doi:10.1111/j.1348-0421.2006.tb03793.x.

Vipin C, Mujeeburahiman M, Arun AB, Ashwini P, Mangesh S V., Rekha PD. 2019. Adaptation and diversification in virulence factors among urinary catheter-associated *Pseudomonas aeruginosa* isolates. *J Appl Microbiol.* 126(2):641–650. doi:10.1111/jam.14143.

Völzing KG, Brynildsen MP. 2015. Stationary-phase persisters to ofloxacin sustain DNA damage and require repair systems only during recovery. *MBio.* 6(5):e00731-15. doi:10.1128/mBio.00731-15.

Vos D De, Chial M De, Cochez C, Jansen S. 2001. Study of pyoverdine type and production by *Pseudomonas aeruginosa* isolated from cystic fibrosis patients: prevalence of type II pyoverdine isolates and accumulation of pyoverdine-negative mutations. *Arch Microbiol.* 175(5):384–388. doi:10.1007/s002030100278.

Waite RD, Papakonstantinou A, Littler E, Curtis M a. 2005. Transcriptome Analysis of *Pseudomonas aeruginosa* growth. *Society.* 187(18):6571–6576. doi:10.1128/JB.187.18.6571.

Walters III MC, Roe F, Bugnicourt A, Franklin MJ, Stewart PS. 2003. Contributions of Antibiotic Penetration, Oxygen Limitation, and Low Metabolic Activity to Tolerance of *Pseudomonas aeruginosa* Biofilms to Ciprofloxacin and Tobramycin. *Antimicrob Agents Chemother.* 47(1):317–323. doi:10.1128/AAC.47.1.317.

Wang F, He Q, Yin J, Xu S, Hu W, Gu L. 2018. BrlR from *Pseudomonas aeruginosa* is a receptor for both cyclic di-GMP and pyocyanin. *Nat Commun.* 9(1):2563. doi:10.1038/s41467-018-05004-y.

Wang H, Wu H, Ciofu O, Song Z, Høiby Niels. 2012. In Vivo pharmacokinetics/pharmacodynamics of colistin and imipenem in *Pseudomonas aeruginosa*

biofilm infection. *Antimicrob Agents Chemother.* 56(5):2683–2690. doi:10.1128/AAC.06486-11.

Webb JS, Thompson LS, James S, Charlton T, Tolker-Nielsen T, Koch B, Givskov M, Kjelleberg S. 2003. Cell death in *Pseudomonas aeruginosa* biofilm development. *J Bacteriol.* 185(15):4585–4592. doi:10.1128/JB.185.15.4585-4592.2003.

Webster SS, Lee CK, Schmidt WC, Wong GCL, O'Toole GA. 2021. Interaction between the type 4 pili machinery and a diguanylate cyclase fine-tune c-di-GMP levels during early biofilm formation. *Proc Natl Acad Sci U S A.* 118(26):1–9. doi:10.1073/pnas.2105566118.

Weiser R, Donoghue D, Weightman A, Mahenthiralingam E. 2014. Evaluation of five selective media for the detection of *Pseudomonas aeruginosa* using a strain panel from clinical, environmental and industrial sources. *J Microbiol Methods.* 99(1):8–14. doi:10.1016/j.mimet.2014.01.010.

Wen Y, Behiels E, Devreese B. 2014. Toxin-Antitoxin systems: Their role in persistence, biofilm formation, and pathogenicity. *Pathog Dis.* 70(3):240–249. doi:10.1111/2049-632X.12145.

Whitchurch CB. 2006. Biogenesis and function of type IV pili in *pseudomonas* species. In: *Pseudomonas*. Vol. 4. p. 139–188.

Whitchurch CB, Beatson SA, Comolli JC, Jakobsen T, Sargent JL, Bertrand JJ, West J, Klausen M, Waite LL, Kang PJ, et al. 2005. *Pseudomonas aeruginosa* fimL regulates multiple virulence functions by intersecting with Vfr-modulated pathways. *Mol Microbiol.* 55(5):1357–1378. doi:10.1111/j.1365-2958.2005.04479.x.

Whitchurch CB, Tolker-Nielsen T, Ragas PC, Mattick JS. 2002. Extracellular DNA required for bacterial biofilm formation. *Science* (80-). 295(5559):1487. doi:10.1126/science.295.5559.1487.

Wiegand I, Hilpert K, Hancock REW. 2008. Agar and broth dilution methods to determine the minimal inhibitory concentration (MIC) of antimicrobial substances. *Nat Protoc.* 3(2):163–175. doi:10.1038/nprot.2007.521.

Williams JJ, Halvorsen EM, Dwyer EM, Difazio RM, Hergenrother PJ. 2011. Toxin–antitoxin (TA) systems are prevalent and transcribed in clinical isolates of *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*. *FEMS Microbiol Lett.* 322(1):41–50.

doi:10.1111/J.1574-6968.2011.02330.X.

Wood TL, Wood TK. 2016. The HigB/HigA toxin/antitoxin system of *Pseudomonas aeruginosa* influences the virulence factors pyochelin, pyocyanin, and biofilm formation. *Microbiologyopen*. 5(3):499–511. doi:10.1002/mbo3.346.

Wu H, Moser C, Wang HZ, Høiby N, Song ZJ. 2015. Strategies for combating bacterial biofilm infections. *Int J Oral Sci*. 7(1):1–7. doi:10.1038/ijos.2014.65.

Wu J, Xi C. 2009. Evaluation of Different Methods for Extracting Extracellular DNA from the Biofilm Matrix. *Appl Environ Microbiol*. 75(16):5390–5395. doi:10.1128/AEM.00400-09.

Xu J, Chiang HC, Bjursell MK, Gordon JI. 2004. Message from a human gut symbiont: sensitivity is a prerequisite for sharing. *12(1):21–28*. doi:10.1016/j.tim.2003.11.007.

Xu ZG, Gao Y, He JG, Xu WF, Jiang M, Jin HS. 2015. Effects of azithromycin on *Pseudomonas aeruginosa* isolates from catheter-associated urinary tract infection. *Exp Ther Med*. 9(2):569–572. doi:10.3892/etm.2014.2120.

Yang L, Barken KB, Skindersoe ME, Christensen AB, Givskov M, Tolker-Nielsen T. 2007. Effects of iron on DNA release and biofilm development by *Pseudomonas aeruginosa*. *Microbiology*. 153(5):1318–1328. doi:10.1099/mic.0.2006/004911-0.

Yang L, Hu Y, Liu Y, Zhang J, Ulstrup J, Molin S. 2011. Distinct roles of extracellular polymeric substances in *Pseudomonas aeruginosa* biofilm development. *Environ Microbiol*. 13(7):1705–1717. doi:10.1111/j.1462-2920.2011.02503.x.

Yayan J, Ghebremedhin B, Rasche K. 2015. Antibiotic resistance of *pseudomonas aeruginosa* in pneumonia at a single university hospital center in Germany over a 10-Year Period. *PLoS One*. 10(10):e0139836. doi:10.1371/journal.pone.0139836.

Zhang L, Fritsch M, Hammond L, Landreville R, Slatculescu C, Colavita A, Mah TF. 2013. Identification of Genes Involved in *Pseudomonas aeruginosa* Biofilm-Specific Resistance to Antibiotics. *PLoS One*. 8(4):e61625. doi:10.1371/journal.pone.0061625.

Zhang L, Mah TF. 2008. Involvement of a novel efflux system in biofilm-specific resistance to antibiotics. *J Bacteriol*. 190(13):4447–4452. doi:10.1128/JB.01655-07.

Zhang W, Sun J, Ding W, Lin J, Tian R, Lu L, Liu X, Shen X, Qian PY. 2015. Extracellular matrix-associated proteins form an integral and dynamic system during *Pseudomonas*

aeruginosa biofilm development. *Front Cell Infect Microbiol.* 5:40. doi:10.3389/fcimb.2015.00040.

Zhang Y, Xia B, Li M, Shi J, Long Y, Jin Y, Bai F, Cheng Z, Jin S, Wu W. 2018. HlgB reciprocally controls biofilm formation and the expression of type III secretion system genes through influencing the intracellular c-di-GMP level in *Pseudomonas aeruginosa*. *Toxins (Basel)*. 10(11):1–12. doi:10.3390/toxins10110424.

Zhao K, Tseng BS, Beckerman B, Jin F, Gibiansky ML, Harrison JJ, Luijten E, Parsek MR, Wong GCL. 2013. Psl trails guide exploration and microcolony formation in *Pseudomonas aeruginosa* biofilms. *Nature*. 497(7449):388–391. doi:10.1038/nature12155.

Zheng S, Bawazir M, Dhall A, Kim HE, He L, Heo J, Hwang G. 2021. Implication of Surface Properties, Bacterial Motility, and Hydrodynamic Conditions on Bacterial Surface Sensing and Their Initial Adhesion. *Front Bioeng Biotechnol.* 9:643722. doi:10.3389/fbioe.2021.643722.