The ecology and evolution of microbial warfare in streptomyces

Westhoff, S.

Author: Westhoff, S.
Title: The ecology and evolution of microbial warfare in streptomyces
Issue Date: 2021-01-23

R

References

Abrudan MI, Smakman F, Grimbergen AJ, Westhoff S, Miller EL, van Wezel GP, *et al.* (2015). Socially mediated induction and suppression of antibiosis during bacterial coexistence. *Proc Natl Acad Sci U S A* **112**: 11054–11059.

Adamek M, Alanjary M, Sales-Ortells H, Goodfellow M, Bull AT, Winkler A, *et al.* (2018). Comparative genomics reveals phylogenetic distribution patterns of secondary metabolites in *Amycolatopsis* species. *BMC Genomics* **19**: 1–15.

Adams J, Kinney T, Thompson S, Rubin L, Helling RB. (1979). Frequency-dependent selection for plasmid-containing cells of *Escheria coli*. *Genetics* **91**: 627–637.

Allen HK, Donato J, Wang HH, Cloud-Hansen KA, Davies J, Handelsman J. (2010). Call of the wild: antibiotic resistance genes in natural environments. *Nat Rev Microbiol* **8**: 251–259.

Allen HK, Moe LA, Rodbumrer J, Gaarder A, Handelsman J. (2009). Functional metagenomics reveals diverse beta-lactamases in a remote Alaskan soil. *ISME J* **3**: 243–251.

Amano S-I, Morota T, Kano Y-K, Narita H, Hashidzume T, Yamamoto S, *et al.* (2010). Promomycin, a polyether promoting antibiotic production in *Streptomyces* spp. *J Antibiot (Tokyo)* **63**: 486–491.

Aminov RI. (2009). The role of antibiotics and antibiotic resistance in nature. *Environ Microbiol* **11**: 2970–2988.

Andersson DI, Hughes D. (2014). Microbiological effects of sublethal levels of antibiotics. *Nat Rev Microbiol* **12**: 465–78.

Andersson DI, Hughes D. (2011). Persistence of antibiotic resistance in bacterial populations. *FEMS Microbiol Rev* **35**: 901–911.

Andersson DI, Levin BR. (1999). The biological cost of antibiotic resistance. *Curr Opin Microbiol* **2**: 489–493.

Andrews S. FastQC: a quality control tool for high throughput sequence data. http://www.bioinformatics.babraham.ac.uk/projects/fastqc/.

Aoki SK, Diner EJ, de Roodenbeke CT, Burgess BR, Poole SJ, Braaten BA, *et al.* (2010). A widespread family of polymorphic contact-dependent toxin delivery systems in bacteria. *Nature* **468**: 439–442.

Asfahl KL, Schuster M. (2016). Social interactions in bacterial cell–cell signaling. *FEMS Microbiol Rev* **41**: 92–107.

Avalos M, Garbeva P, Raaijmakers JM, van Wezel GP. (2020). Production of ammonia as a low-cost and long-distance antibiotic strategy by *Streptomyces* species. *ISME J* **14**: 569–583.

Avalos M, van Wezel GP, Raaijmakers JM, Garbeva P. (2018). Healthy scents: microbial volatiles as new frontier in antibiotic research? *Curr Opin Microbiol* **45**: 84–91.

Baltz RH. (2007). Antimicrobials from actinomycetes: Back to the future. *Microbe* **2**: 125–131.

Baltz RH. (2008). Renaissance in antibacterial discovery from actinomycetes. *Curr Opin Pharmacol* **8**: 557–563.

Baquero F. (2001). Low-level antibacterial resistance: a gateway to clinical resistance. *Drug Resist Updat* **4**: 93–105.

Baquero F, Alvarez-Ortega C, Martinez JL. (2009). Ecology and evolution of antibiotic resistance. *Environ Microbiol Rep* **1**: 469–76.

Baquero F, Negri M, Morosini M-I, Blazquez J. (1998). Antibiotic-Selective Environments. *Clin Infect Dis* **27**: 5–11.

Barka EA, Vatsa P, Sanchez L, Gaveau-Vaillant N, Jacquard C, Klenk H-P, *et al.* (2016). Taxonomy, Physiology, and Natural Products of *Actinobacteria*. *Microbiol Mol Biol Rev* **80**: 1–43.

Basler M, Ho BT, Mekalanos JJ. (2013). Tit-for-tat: Type VI secretion system counterattack during bacterial cell-cell interactions. *Cell* **152**: 884–894.

Basler M, Mekalanos JJ. (2012). Type 6 secretion dynamics within and between bacterial cells. *Science* **337**: 815.

Becher PG, Verschut V, Bibb MJ, Bush MJ, Molnár BP, Barane E, *et al.* (2020). Developmentally regulated volatiles geosmin and 2-methylisoborneol attract a soil arthropod to *Streptomyces* bacteria promoting spore dispersal. *Nat Microbiol* **5**: 821–829.

Bentley R, Meganathan R. (1981). Geosmin and methylisoborneol biosynthesis in Streptomycetes. *FEBS Lett* **125**: 220–222.

Bentley SD, Chater KF, Cerdeno-Tarraga A-M, Challis GL, Thomson NR, James KD, *et al.* (2002). Complete genome sequence of the model actinomycete *Streptomyces coelicolor* A3(2). *Nature* **3**: 141–147.

Bérdy J. (2005). Bioactive Microbial Metabolites. *J Antibiot (Tokyo)* **58**: 1–26.

Bérdy J. (2012). Thoughts and facts about antibiotics: Where we are now and where we are heading. *J Antibiot (Tokyo)* **65**: 441–441.

Bergeijk DA Van, Terlouw BR, Medema MH, Wezel GP Van. (2020). Ecology and genomics of Actinobacteria: new concepts for natural product discovery. *Nat Rev Microbiol* **18**: 546–558.

Bernier SP, Létoffé S, Delepierre M, Ghigo JM. (2011). Biogenic ammonia modifies antibiotic resistance at a distance in physically separated bacteria. *Mol Microbiol* **81**: 705–716.

Bertrand S, Bohni N, Schnee S, Schumpp O, Gindro K, Wolfender J-L. (2014). Metabolite induction via microorganism co-culture: A potential way to enhance chemical diversity for drug discovery. *Biotechnol Adv* **32**: 1180–1204.

Bibb MJ. (2005). Regulation of secondary metabolism in streptomycetes. *Curr Opin Microbiol* **8**: 208–215.

Bitas V, Kim H-S, Bennett JW, Kang S. (2013). Sniffing on microbes: diverse roles of microbial volatile organic compounds in plant health. *Mol Plant Microbe Interact* **26**: 835–43.

Blin K, Wolf T, Chevrette MG, Lu X, Schwalen CJ, Kautsar SA, *et al.* (2017). AntiSMASH 4.0 - improvements in chemistry prediction and gene cluster boundary identification. *Nucleic Acids Res* **45**: W36–W41.

Bobek J, Šmídová K, Čihák M. (2017). A waking review: Old and novel insights into the spore germination in *Streptomyces*. *Front Microbiol* **8**: 1–12.

Boyer F, Fichant G, Berthod J, Vandenbrouck Y, Attree I. (2009). Dissecting the bacterial type VI secretion system by a genome wide in silico analysis: what can be learned from available microbial genomic resources? *BMC Genomics* **10**: 104.

Caro-Astorga J, Frenzel E, Perkins JR, Álvarez-Mena A, de Vicente A, Ranea JAG, *et al.* (2020). Biofilm formation displays intrinsic offensive and defensive features of *Bacillus cereus*. *Biofilms and Microbiomes* **6**: 1–14.

Čepl J, Blahůšková A, Cvrčková F, Markoš A. (2014). Ammonia produced by bacterial colonies promotes growth of ampicillin-sensitive *Serratia* sp. by means of antibiotic inactivation. *FEMS Microbiol Lett* **354**: 126–132.

Challis GL, Hopwood DA. (2003). Synergy and contingency as driving forces for the evolution of multiple secondary metabolite production by *Streptomyces* species. *Proc Natl Acad Sci* **100**: 14555–14561.

Chao L, Levin BR. (1981). Structured habitats and the evolution of anticompetitor toxins in bacteria. *Proc Natl Acad Sci* **78**: 6324–6328.

Chater KF. (2016). Recent advances in understanding *Streptomyces*. *F1000Research* **5**: 1–16.

Chen Y, Gozzi K, Yan F, Chai Y. (2015). Acetic acid acts as a volatile signal to stimulate bacterial biofilm. *MBio* **6**: 1–13.

Chevrette MG, Carlos-Shanley C, Louie KB, Bowen BP, Northen TR, Currie CR. (2019). Taxonomic and Metabolic Incongruence in the Ancient Genus Streptomyces. *Front*

Microbiol **10**. e-pub ahead of print, doi: 10.3389/fmicb.2019.02170.

Chow L, Waldron L, Gillings MR. (2015). Potential impacts of aquatic pollutants: sub-clinical antibiotic concentrations induce genome changes and promote antibiotic resistance. *Front Microbiol* **6**: 1–10.

Cianfanelli FR, Monlezun L, Coulthurst SJ. (2016). Aim, Load, Fire: The Type VI Secretion System, a Bacterial Nanoweapon. *Trends Microbiol* **24**: 51–62.

Claessen D, Rink R, de Jong W, Siebring J, de Vreugd P, Boersma FGH, *et al.* (2003). A novel class of secreted hydrophobic proteins is involved in aerial hyphae formation in *Streptomyces coelicolor* by forming amyloid-like fibrils. *Genes Dev* **17**: 1714–26.

Claessen D, Rozen DE, Kuipers OP, Søgaard-Andersen L, van Wezel GP. (2014). Bacterial solutions to multicellularity: a tale of biofilms, filaments and fruiting bodies. *Nat Rev Microbiol* **12**: 115–24.

Claessen D, Wösten HAB, Keulen G van, Faber OG, Alves AMCR, Meijer WG, *et al.* (2002). Two novel homologous proteins of *Streptomyces coelicolor* and *Streptomyces lividans* are involved in the formation of the rodlet layer and mediate attachment to a hydrophobic surface. *Mol Microbiol* **44**: 1483–1492.

Cordovez V, Carrion VJ, Etalo DW, Mumm R, Zhu H, van Wezel GP, *et al.* (2015). Diversity and functions of volatile organic compounds produced by *Streptomyces* from a disease-suppressive soil. *Front Microbiol* **6**: 1–13.

Cornforth DM, Foster KR. (2013). Competition sensing: the social side of bacterial stress responses. *Nat Rev Microbiol* **11**: 285–93.

D'Costa VM, King CE, Kalan L, Morar M, Sung WWL, Schwarz C, *et al.* (2011). Antibiotic resistance is ancient. *Nature* **477**: 457–461.

D'Costa VM, McGrann KM, Hughes DW, Wright GD. (2006). Sampling the Antibiotic Resistome. *Science (80-)* **311**: 374–377.

Davies J. (2006). Are antibiotics naturally antibiotics? *J Ind Microbiol Biotechnol* **33**: 496–499.

Davies J, Davies D. (2010). Origins and evolution of antibiotic resistance. *Microbiol Mol Biol Rev* **74**: 417–433.

Davies J, Spiegelman GB, Yim G. (2006). The world of subinhibitory antibiotic concentrations. *Curr Opin Microbiol* **9**: 445–453.

Van Dessel W, Van Mellaert L, Geukens N, Lammertyn E, Anné J. (2004). Isolation of high quality RNA from *Streptomyces*. *J Microbiol Methods* **58**: 135–137.

Distler J, Mansouri K, Mayer G, Stockmann M, Piepersberg W. (1992). Streptomycin biosynthesis and its regulation in Streptomycetes. *Gene* **115**: 105–111.

Drlica K, Zhao X. (2007). Mutant Selection Window Hypothesis Updated. *Clin Infect Dis* **44**: 681–688.

Drusano GL. (2004). Antimicrobial pharmacodynamics: critical interactions of "bug and drug". *Nat Rev Microbiol* **2**: 289–300.

Elliot MA, Karoonuthaisiri N, Huang J, Bibb MJ, Cohen SN, Kao CM, *et al.* (2003). The chaplins: A family of hydrophobic cell-surface proteins involved in aerial mycelium formation in *Streptomyces coelicolor*. *Genes Dev* **17**: 1727–1740.

Fierer N, Lennon JT. (2011). The generation and maintenance of diversity in microbial communities. *Am J Bot* **98**: 439–448.

Fisher RA. (1992). Statistical Methods for Research Workers. In: Kotz S, Johnson NL (eds). *Breakthroughs in Statistics*. Springer, New York, NY, pp 66–70.

Flärdh K, Buttner MJ. (2009). *Streptomyces morphogenetics*: Dissecting differentiation in a filamentous bacterium. *Nat Rev Microbiol* **7**: 36–49.

Forsberg KJ, Reyes A, Wang B, Selleck EM, Sommer MOA, Dantas G. (2012). The shared antibiotic resistome of soil bacteria and human pathogens. *Science* **337**: 1107–11.

Foster KR, Bell T. (2012). Competition, not cooperation, dominates interactions among culturable microbial species. *Curr Biol* **22**: 1845–50.

Garbeva P, Hordijk C, Gerards S, De Boer W. (2014). Volatile-mediated interactions between phylogenetically different soil bacteria. *Front Microbiol* **5**: 1–9.

Garbeva P, Silby MW, Raaijmakers JM, Levy SB, Boer W De. (2011). Transcriptional and antagonistic responses of *Pseudomonas fluorescens* Pf0-1 to phylogenetically different bacterial competitors. *ISME J* **5**: 973–985.

Garcia EC, Anderson MS, Hagar JA, Cotter PA. (2013). *Burkholderia* BcpA mediates biofilm formation independently of interbacterial contact-dependent growth inhibition. *Mol Microbiol* **89**: 1213–1225.

Garcia EC, Perault AI, Marlatt SA, Cotter PA. (2016). Interbacterial signaling via *Burkholderia* contact-dependent growth inhibition system proteins. *Proc Natl Acad Sci* 201606323.

Gebbink MFBG, Claessen D, Bouma B, Dijkhuizen L, Wösten HAB. (2005). Amyloids - A functional coat for microorganisms. *Nat Rev Microbiol* **3**: 333–341.

Gerc AJ, Diepold A, Trunk K, Porter M, Rickman C, Armitage JP, *et al.* (2015). Visualization of the *Serratia* Type VI Secretion System Reveals Unprovoked Attacks and Dynamic Assembly. *Cell Rep* **12**: 2131–2142.

Ghoul M, Mitri S. (2016). The Ecology and Evolution of Microbial Competition. *Trends Microbiol* **24**: 833–845.

Gonzalez D, Sabnis A, Foster KR, Mavridou DAI. (2018). Costs and benefits of provocation in bacterial warfare. *Proc Natl Acad Sci U S A* **115**: 7593–7598.

Graff JR, Forschner-Dancause SR, Menden-Deuer S, Long RA, Rowley DC. (2013). *Vibrio cholerae* exploits sub-lethal concentrations of a competitor-produced antibiotic to avoid toxic interactions. *Front Microbiol* **4**: 1–11.

Granato ET, Foster KR. (2020). The Evolution of Mass Cell Suicide in Bacterial Warfare. *bio*Rxiv 2020.02.25.959577.

Granato ET, Meiller-Legrand TA, Foster KR. (2019). The Evolution and Ecology of Bacterial Warfare. *Curr Biol* **29**: R521–R537.

Greig D, Travisano M. (2008). Density-dependent effects on allelopathic interactions in yeast. *Evolution (N Y)* **62**: 521–527.

Groenhagen U, Baumgartner R, Bailly A, Gardiner A, Eberl L, Schulz S, *et al.* (2013). Production of Bioactive Volatiles by Different *Burkholderia ambifaria* Strains. *J Chem Ecol* **39**: 892–906.

Gubbens J, Janus M, Florea BI, Overkleeft HS, Wezel GP Van. (2012). Identification of glucose kinase-dependent and -independent pathways for carbon control of primary metabolism , development and antibiotic production in *Streptomyces coelicolor* by quantitative proteomics. *Mol Microbiol* **86**: 1490–1507.

Gullberg E, Albrecht LM, Karlsson C, Sandegren L, Andersson DI. (2014). Selection of a Multidrug Resistance Plasmid by Sublethal Levels of Antibiotics and Heavy Metals. *MBio* **5**: 19–23.

Gullberg E, Cao S, Berg OG, Ilbäck C, Sandegren L, Hughes D, *et al.* (2011). Selection of resistant bacteria at very low antibiotic concentrations. *PLoS Pathog* **7**: e1002158.

Guo YP, Zheng W, Rong XY, Huang Y. (2008). A multilocus phylogeny of the *Streptomyces griseus* 16S rRNA gene clade: Use of multilocus sequence analysis for streptomycete systematics. *Int J Syst Evol Microbiol* **58**: 149–159.

van der Heul HU, Bilyk BL, McDowall KJ, Seipke RF, van Wezel GP. (2018). Regulation of antibiotic production in Actinobacteria: New perspectives from the post-genomic era. *Nat Prod Rep* **35**: 575–604.

Hibbing ME, Fuqua C, Parsek MR, Peterson SB. (2010). Bacterial competition: surviving and thriving in the microbial jungle. *Nat Rev Microbiol* **8**: 15–25.

Ho BT, Basler M, Mekalanos JJ. (2013). Type 6 secretion system-mediated immunity to type 4 secretion system-mediated gene transfer. *Science* **342**: 250–3.

Hoffman LR, D'Argenio DA, MacCoss MJ, Zhang ZY, Jones RA, Miller SI. (2005). Aminoglycoside antibiotics induce bacterial biofilm formation. *Nature* **436**: 1171–1175.

Hopwood DA. (2007). *Streptomyces* in nature and medicine: the antibiotic makers. Oxford University Press: New York.

HORINOUCHI S. (2007). Mining and Polishing of the Treasure Trove in the Bacterial Genus Streptomyces. *Biosci Biotechnol Biochem* **71**: 283–299.

Hosaka T, Ohnishi-Kameyama M, Muramatsu H, Murakami K, Tsurumi Y, Kodani S, *et al.* (2009). Antibacterial discovery in actinomycetes strains with mutations in RNA polymerase or ribosomal protein S12. *Nat Biotechnol* **27**: 462–4.

Huang T-W, Chen CW. (2006). A *recA* Null Mutation May Be Generated in *Streptomyces coelicolor*. *J Bacteriol* **188**: 6771–6779.

Hughes D, Andersson DI. (2012). Selection of resistance at lethal and non-lethal antibiotic concentrations. *Curr Opin Microbiol* **15**: 555–60.

Ikeda H, Ishikawa J, Hanamoto A, Shinose M, Kikuchi H, Shiba T. (2003). Complete genome sequence and comparative analysis of the industrial microorganism *Streptomyces avermitilis*. *Nat Biotechnol* **21**: 526–531.

Imai Y, Sato S, Tanaka Y, Ochi K, Hosaka T. (2015). Lincomycin at Subinhibitory Concentrations Potentiates Secondary Metabolite Production by *Streptomyces* spp. Nojiri H (ed). *Appl Environ Microbiol* **81**: 3869–3879.

Jones C, Allsopp L, Horlick J, Kulasekara H, Filloux A. (2013). Subinhibitory concentration of kanamycin induces the *Pseudomonas aeruginosa* type VI secretion system. *PLoS One* **8**: 1–15.

Jones SE, Ho L, Rees CA, Hill JE, Nodwell JR, Elliot MA. (2017). *Streptomyces* exploration is triggered by fungal interactions and volatile signals. *Elife* **6**: 1–21.

Jorgensen KM, Wassermann T, Jensen PO, Hengzuang W, Molin S, Hoiby N, *et al.* (2013). Sublethal Ciprofloxacin Treatment Leads to Rapid Development of High-Level Ciprofloxacin Resistance during Long-Term Experimental Evolution of *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother* **57**: 4215–4221.

Kahlmeter G, Brown DFJ, Goldstein FW, MacGowan AP, Mouton JW, Osterlund A, *et al.* (2003). European harmonization of MIC breakpoints for antimicrobial susceptibility testing of bacteria. *J Antimicrob Chemother* **52**: 145–8.

Keijser BJF, Noens EEE, Kraal B, Koerten HK, Van Wezel GP. (2003). The *Streptomyces* *coelicolor ssgB* gene is required for early stages of sporulation. *FEMS Microbiol Lett* **225**: 59–67.

Kelemen GH, Brian P, Flärdh K, Chamberlin L, Chater KF, Buttner MJ. (1998). Developmental regulation of transcription of *whiE*, a locus specifying the polyketide spore pigment in *Streptomyces coelicolor* A3(2). *J Bacteriol* **180**: 2515–2521.

Kelsic ED, Zhao J, Vetsigian K, Kishony R. (2015). Counteraction of antibiotic production and degradation stabilizes microbial communities. *Nature* **521**: 516–519.

Kerr B, Riley MA, Feldman MW, Bohannan BJM. (2002). Local dispersal promotes biodiversity in a real-life game of rock-paper-scissors. *Nature* **418**: 171–174.

Kim D, Langmead B, Salzberg1 SL. (2015). HISAT: a fast spliced aligner with low memory requirements Daehwan HHS Public Access. *Nat Methods* **12**: 357–360.

Kim K, Lee S, Ryu C-M. (2013). Interspecific bacterial sensing through airborne signals modulates locomotion and drug resistance. *Nat Commun* **4**: 1809.

Kinkel LL, Schlatter DC, Xiao K, Baines AD. (2014). Sympatric inhibition and niche differentiation suggest alternative coevolutionary trajectories among *Streptomycetes*. *ISME J* **8**: 249–56.

Kirkup BC, Riley MA. (2004). Antibiotic-meidated antagonism leads to a bacterial game of rock-paper-scissors in vivo. *Nature* **428**: 694–696.

Kodani S, Hudson ME, Durrant MC, Buttner MJ, Nodwell JR, Willey JM. (2004). The SapB morphogen is a lantibiotic-like peptide derived from the product of the developmental gene *ramS* in *Streptomyces coelicolor*. *Proc Natl Acad Sci U S A* **101**: 11448–11453.

Korgaonkar AK, Whiteley M. (2011a). Pseudomonas aeruginosa enhances production of an antimicrobial in response to N-acetylglucosamine and peptidoglycan. *J Bacteriol* **193**: 909–917.

Korgaonkar AK, Whiteley M. (2011b). *Pseudomonas aeruginosa* enhances production of an antimicrobial in response to N-acetylglucosamine and peptidoglycan. *J Bacteriol* **193**: 909–917.

Kurland CG. (1992). Translational accuracy and the fitness of bacteria. *Annu Rev Genet* **26**: 29–50.

Labeda DP, Goodfellow M, Brown R, Ward AC, Lanoot B, Vanncanneyt M, *et al.* (2012). Phylogenetic study of the species within the family *Streptomycetaceae*. In: Vol. 101. *Antonie van Leeuwenhoek, International Journal of General and Molecular Microbiology*. pp 73–104.

Lambert S, Traxler MF, Craig M, Maciejewska M, Ongena M, Van Wezel GP, *et al.* (2014).

Altered desferrioxamine-mediated iron utilization is a common trait of bald mutants of *Streptomyces coelicolor*. *Metallomics* **6**: 1390–1399.

Laskaris P, Gaze WH, Wellington EMH. (2011). Environmental reservoirs of resistance genes in antibiotic-producing bacteria and their possible impact on the evolution of antibiotic resistance. In: Keen PL, Montforts MHMM (eds). *Antimicrobial Resistance in the Environment*. John Wiley & Sons, Inc., pp 73–92.

Laskaris P, Tolba S, Calvo-Bado L, Wellington L. (2010). Coevolution of antibiotic production and counter-resistance in soil bacteria. *Environ Microbiol* **12**: 783–796.

Lee HH, Molla MN, Cantor CR, Collins JJ. (2010). Bacterial charity work leads to population-wide resistance. *Nature* **467**: 82–5.

Lee N, Kim W, Chung J, Lee Y, Cho S, Jang K-S, *et al.* (2020). Iron competition triggers antibiotic biosynthesis in Streptomyces coelicolor during coculture with Myxococcus xanthus. *ISME J* **14**: 1111–1124.

Lenski R, Rose M, Simpson S, Tadler S. (1991). Long-term experimental evolution in *Escherichia coli*. I. Adaptation and divergence during 2,000 generations. *Am Nat*.

LeRoux M, Kirkpatrick RL, Montauti EI, Tran BQ, Brook Peterson S, Harding BN, *et al.* (2015). Kin cell lysis is a danger signal that activates antibacterial pathways of *Pseudomonas aeruginosa*. *Elife* **2015**: 1–65.

LeRoux M, De Leon JA, Kuwanda NJ, Russell AB, Pinto-Santini D, Hood RD, *et al.* (2012). Quantitative single-cell characterization of bacterial interactions. *Proc Natl Acad Sci U S A* **109**: 19804–19809.

Leroux M, Peterson SB, Mougous JD. (2015). Bacterial danger sensing. *J Mol Biol* **427**: 3744–3753.

Létoffé S, Audrain B, Bernier SP, Delepierre M, Ghigo JM. (2014). Aerial exposure to the bacterial volatile compound trimethylamine modifies antibiotic resistance of physically separated bacteria by raising culture medium pH. *MBio* **5**: 1–12.

Li H, Handsaker B, Wysoker A, Fennell T, Ruan J, Homer N, *et al.* (2009). The Sequence Alignment/Map format and SAMtools. *Bioinformatics* **25**: 2078–2079.

Liao Y, Smyth GK, Shi W. (2014). FeatureCounts: An efficient general purpose program for assigning sequence reads to genomic features. *Bioinformatics* **30**: 923–930.

Liu G, Chater KF, Chandra G, Niu G, Tan H. (2013). Molecular Regulation of Antibiotic Biosynthesis in *Streptomyces*. *Microbiol Mol Biol Rev* **77**: 112–143.

Locey KJ, Lennon JT. (2016). Scaling laws predict global microbial diversity. *Proc Natl Acad Sci*

113: 5970–5975.

Love MI, Huber W, Anders S. (2014). Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. *Genome Biol* **15**: 1–21.

Ma LS, Hachani A, Lin JS, Filloux A, Lai EM. (2014). *Agrobacterium tumefaciens* deploys a superfamily of type VI secretion DNase effectors as weapons for interbacterial competition in planta. *Cell Host Microbe* **16**: 94–104.

Majeed H, Gillor O, Kerr B, Riley MA. (2011). Competitive interactions in *Escherichia coli* populations: The role of bacteriocins. *ISME J* **5**: 71–81.

Majeed H, Lampert A, Ghazaryan L, Gillor O. (2013). The Weak Shall Inherit: Bacteriocin-Mediated Interactions in Bacterial Populations. *PLoS One* **8**. e-pub ahead of print, doi: 10.1371/journal.pone.0063837.

Mak S, Xu Y, Nodwell JR. (2014). The expression of antibiotic resistance genes in antibiotic-producing bacteria. *Mol Microbiol* **93**: 391–402.

Martín-Sánchez L, Singh KS, Avalos M, Van Wezel GP, Dickschat JS, Garbeva P. (2019). Phylogenomic analyses and distribution of terpene synthases among *Streptomyces*. *Beilstein J Org Chem* **15**: 1181–1193.

Martínez JL. (2008). Antibiotics and Antibiotic Resistance. *Science (80-)* **321**: 365–367.

Mavridou DAI, Gonzalez D, Kim W, West SA, Foster KR. (2018). Bacteria Use Collective Behavior to Generate Diverse Combat Strategies. *Curr Biol* **28**: 345-355.e4.

Melnyk AH, Wong A, Kassen R. (2014). The fitness costs of antibiotic resistance mutations. *Evol Appl* **8**: n/a-n/a.

Mendez C, Chater KF. (1987). Cloning of *whiG*, a gene critical for sporulation of *Streptomyces coelicolor* A3(2). *J Bacteriol* **169**: 5715–5720.

Miller EL, Kjos M, Abrudan MI, Roberts IS, Veening JW, Rozen DE. (2018). Eavesdropping and crosstalk between secreted quorum sensing peptide signals that regulate bacteriocin production in *Streptococcus pneumoniae*. *ISME J* **12**: 2363–2375.

Mitri S, Foster KR. (2013). The genotypic view of social interactions in microbial communities. *Annu Rev Genet* **47**: 247–73.

Molina-Santiago C, Daddaoua A, Fillet S, Duque E, Ramos J-L. (2014). Interspecies signalling: *Pseudomonas putida* efflux pump TtgGHI is activated by indole to increase antibiotic resistance. *Environ Microbiol* **16**: 1267–81.

Murdoch SL, Trunk K, English G, Fritsch MJ, Pourkarimi E, Coulthurst SJ. (2011). The opportunistic pathogen *Serratia marcescens* utilizes type VI secretion to target bacterial competitors. *J Bacteriol* **193**: 6057–6069.

Navarro-Muñoz JC, Selem-Mojica N, Mullowney MW, Kautsar SA, Tryon JH, Parkinson EI, *et al.* (2020). A computational framework to explore large-scale biosynthetic diversity. *Nat Chem Biol* **16**: 60–68.

Negri MC, Lipsitch M, Blázquez J, Levin BR, Baquero F. (2000). Concentration-dependent selection of small phenotypic differences in TEM beta-lactamase-mediated antibiotic resistance. *Antimicrob Agents Chemother* **44**: 2485–91.

Nett M, Ikeda H, Moore BS. (2009). Genomic basis for natural product biosynthetic diversity in the actinomycetes. *Nat Prod Rep* **26**: 1362–1384.

Nijland R, Burgess JG. (2010). Bacterial olfaction. *Biotechnol J* **5**: 974–977.

Nishimura K, Hosaka T, Tokuyama S, Okamoto S, Ochi K. (2007a). Mutations in rsmG, encoding a 16S rRNA methyltransferase, result in low-level streptomycin resistance and antibiotic overproduction in Streptomyces coelicolor A3(2). *J Bacteriol* **189**: 3876–3883.

Nishimura K, Hosaka T, Tokuyama S, Okamoto S, Ochi K. (2007b). Mutations in *rsmG*, encoding a 16S rRNA methyltransferase, result in low-level streptomycin resistance and antibiotic overproduction in *Streptomyces coelicolor* A3(2). *J Bacteriol* **189**: 3876–3883.

Nishimura K, Johansen SK, Inaoka T, Hosaka T, Tokuyama S, Tahara Y, *et al.* (2007c). Identification of the RsmG methyltransferase target as 16S rRNA nucleotide G527 and characterization of Bacillus subtilis rsmG mutants. *J Bacteriol* **189**: 6068–6073.

Nodwell JR. (2014). Are you talking to me? A possible role for γ-butyrolactones in interspecies signalling. *Mol Microbiol* **94**: 483–485.

Nodwell JR, McGovern K, Losick R. (1996). An oligopeptide permease responsible for the import of an extracellular signal governing aerial mycelium formation in *Streptomyces coelicolor*. *Mol Microbiol* **22**: 881–893.

Ohnishi Y, Ishikawa J, Hara H, Suzuki H, Ikenoya M, Ikeda H, *et al.* (2008). Genome Sequence of the Streptomycin-Producing Microorganism *Streptomyces griseus* IFO 13350. *J Bacteriol* **190**: 4050–4060.

Ohnishi Y, Kameyama S, Onaka H, Horinouchi S. (1999). The A-factor regulatory cascade leading to streptomycin biosynthesis in *Streptomyces griseus*: Identification of a target gene of the A-factor receptor. *Mol Microbiol* **34**: 102–111.

Okonechnikov K, Conesa A, García-Alcalde F. (2016). Qualimap 2: Advanced multi-sample quality control for high-throughput sequencing data. *Bioinformatics* **32**: 292–294.

van Overbeek LS, Wellington EMH, Egan S, Smalla K, Heuer H, Collard JM, *et al.* (2002).

Prevalence of streptomycin-resistance genes in bacterial populations in European habitats. (Special issue: The contribution of mobile genetic elements in bacterial adaptability and diversity.). *FEMS Microbiol Ecol* **42**: 277-288. 53 ref.

Pfuetze KH, Pyle MM, Hinshaw HC, Feldman WH. (1955). The first clinical trial of streptomycin in human tuberculosis. *Am Rev Tuberc* **71**: 752–4.

Ponomarova O, Patil KR. (2015). Metabolic interactions in microbial communities: Untangling the Gordian knot. *Curr Opin Microbiol* **27**: 37–44.

Probandt D, Eickhorst T, Ellrott A, Amann R, Knittel K. (2018). Microbial life on a sand grain: From bulk sediment to single grains. *ISME J* **12**: 623–633.

Que YA, Hazan R, Strobel B, Maura D, He J, Kesarwani M, *et al.* (2013). A quorum sensing small volatile molecule promotes antibiotic tolerance in bacteria. *PLoS One* **8**: 1–9.

Raaijmakers JM, Mazzola M. (2012). Diversity and Natural Functions of Antibiotics Produced by Beneficial and Plant Pathogenic Bacteria. *Annu Rev Phytopathol* **50**: 403–424.

Raynaud X, Nunan N. (2014). Spatial Ecology of Bacteria at the Microscale in Soil Pappalardo F (ed). *PLoS One* **9**: e87217.

Rigali S, Titgemeyer F, Barends S, Mulder S, Thomae AW, Hopwood DA, *et al.* (2008). Feast or famine: the global regulator DasR links nutrient stress to antibiotic production by *Streptomyces*. *EMBO Rep* **9**: 670–675.

Riley MA, Gordon DM. (1999). The ecological role of bacteriocins in bacterial competition. 129–133.

Roesch LFW, Fulthorpe RR, Riva A, Casella G, Hadwin AKM, Kent AD, *et al.* (2007). Pyrosequencing enumerates and contrasts soil microbial diversity. *ISME J* **1**: 283–290.

Ruhe ZC, Low DA, Hayes CS. (2013). Bacterial contact-dependent growth inhibition. *Trends Microbiol* **21**: 230–237.

Ruhe ZC, Townsley L, Wallace AB, King A, Van der Woude MW, Low DA, *et al.* (2015). CdiA promotes receptor-independent intercellular adhesion. *Mol Microbiol* **98**: 175–192.

Rumbaugh KP, Diggle SP, Watters CM, Ross-Gillespie A, Griffin AS, West SA. (2009). Quorum Sensing and the Social Evolution of Bacterial Virulence. *Curr Biol* **19**: 341–345.

Russel J, Røder HL, Madsen JS, Burmølle M, Sørensen SJ. (2017). Antagonism correlates with metabolic similarity in diverse bacteria. *Proc Natl Acad Sci* 201706016.

Rutledge PJ, Challis GL. (2015). Discovery of microbial natural products by activation of silent biosynthetic gene clusters. *Nat Rev Microbiol* **13**: 509–523.

Ruusala T, Andersson D, Ehrenberg M, Kurland CG. (1984). Hyper-accurate ribosomes inhibit growth. *EMBO J* **3**: 2575–80.

Salerno P, Persson J, Bucca G, Laing E, Ausmees N, Smith CP, *et al.* (2013). Identification of new developmentally regulated genes involved in *Streptomyces coelicolor* sporulation. *BMC Microbiol* **13**: 1–18.

Sandegren L, Andersson DI. (2009). Bacterial gene amplification: implications for the evolution of antibiotic resistance. *Nat Rev Microbiol* **7**: 578–588.

Sanz a B, García R, Rodríguez-Peña JM, Díez-Muñiz S, Nombela C, Peterson CL, *et al.* (2012). Chromatin remodeling by the SWI/SNF complex is essential for transcription mediated by the yeast cell wall integrity MAPK pathway. *Mol Biol Cell* **23**: 2805–17.

Schäberle TF, Orland A, König GM. (2014). Enhanced production of undecylprodigiosin in *Streptomyces coelicolor* by co-cultivation with the corallopyronin A-producing myxobacterium, *Corallococcus coralloides* . *Biotechnol Lett* **36**: 641–648.

Schatz A, Bugie E, Waksman SA. (1944). Streptomycin, a Substance Exhibiting Antibiotic Activity against Gram-Positive and Gram-Negative Bacteria. *Proc Soc Exp Biol Med* **55**: 66–69.

Schlatter D, Fubuh A, Xiao K, Hernandez D, Hobbie S, Kinkel L. (2009). Resource amendments influence density and competitive phenotypes of *Streptomyces* in soil. *Microb Ecol* **57**: 413–20.

Schmidt R, Cordovez V, de Boer W, Raaijmakers J, Garbeva P. (2015). Volatile affairs in microbial interactions. *ISME J* **9**: 1–7.

Schöller CEG, Gürtler H, Pedersen R, Molin S, Wilkins K. (2002). Volatile metabolites from actinomycetes. *J Agric Food Chem* **50**: 2615–2621.

Schulz-Bohm K, Martín-Sánchez L, Garbeva P. (2017). Microbial volatiles: Small molecules with an important role in intra- and inter-kingdom interactions. *Front Microbiol* **8**: 1–10.

Schulz S, Dickschat JS. (2007). Bacterial volatiles: the smell of small organisms. *Nat Prod Rep* **24**: 814–842.

Schulz S, Dickschat JS, Kunze B, Wagner-Dobler I, Diestel R, Sasse F. (2010). Biological activity of volatiles from marine and terrestrial bacteria. *Mar Drugs* **8**: 2976–2987.

Shima J, Hesketh A, Okamoto S, Kawamoto S, Ochi K. (1996). Induction of Actinorhodin Production by *rpsL* (Encoding Ribosomal Protein S12) Mutations That Confer Streptomycin Resistance in *Streptomyces lividans* and *Streptomyces coelicolor* A3 (2). *J Bacteriol* **178**: 7276–7284.

Stubbendieck RM, Straight PD. (2016). Multifaceted interfaces of bacterial competition. *J*

Bacteriol **198**: 2145–2155.

Takano E. (2006). γ-Butyrolactones: *Streptomyces* signalling molecules regulating antibiotic production and differentiation. *Curr Opin Microbiol* **9**: 287–294.

Takano E, Kinoshita H, Mersinias V, Bucca G, Hotchkiss G, Nihira T, *et al.* (2005). A bacterial hormone (the SCB1) directly controls the expression of a pathway-specific regulatory gene in the cryptic type I polyketide biosynthetic gene cluster of *Streptomyces coelicolor*. *Mol Microbiol* **56**: 465–479.

Tanaka Y, Komatsu M, Okamoto S, Tokuyama S, Kaji A, Ikeda H, *et al.* (2009a). Antibiotic overproduction by rpsL and rsmG mutants of various actinomycetes. *Appl Environ Microbiol* **75**: 4919–4922.

Tanaka Y, Komatsu M, Okamoto S, Tokuyama S, Kaji A, Ikeda H, *et al.* (2009b). Antibiotic overproduction by *rpsL* and *rsmG* mutants of various actinomycetes. *Appl Environ Microbiol* **75**: 4919–4922.

Thiele-Bruhn S. (2003). Pharmaceutical antibiotic compounds in soils - A review. *J Plant Nutr Soil Sci* **166**: 145–167.

Thomas PD, Campbell MJ, Kejariwal A, Mi H, Karlak B, Daverman R, *et al.* (2003). PANTHER: A library of protein families and subfamilies indexed by function. *Genome Res* **13**: 2129–2141.

Tolba S, Egan S, Kallifidas D, Wellington EMH. (2002). Distribution of streptomycin resistance and biosynthesis genes in streptomycetes recovered from different soil sites. *FEMS Microbiol Ecol* **42**: 269–276.

Torsvik V, Goksoyr J, Daae FL. (1990). High diversity in DNA of soil bacteria. *Appl Environ Microbiol* **56**: 782–787.

Travisano M, Lenski RE. (1996). Long-term experimental evolution in *Escherichia coli*. IV. Targets of selection and the specificity of adaptation. *Genetics* **143**: 15–26.

Traxler MF, Seyedsayamdost MR, Clardy J, Kolter R. (2012). Interspecies modulation of bacterial development through iron competition and siderophore piracy. *Mol Microbiol* **86**: 628–644.

Traxler MF, Watrous JD, Alexandrov T, Dorrestein PC, Kolter R. (2013). Interspecies interactions stimulate diversification of the *Streptomyces coelicolor* secreted metabolome. *MBio* **4**: 1–12.

Tyc, O, Song C, Dickschat JS, Vos M, Garbeva P. (2016). The Ecological Role of Volatile and Soluble Secondary Metabolites Produced by Soil Bacteria. *Trends Microbiol* **xx**: 1–13.

Tyc O, van den Berg M, Gerards S, van Veen JA, Raaijmakers JM, de Boer W, *et al.* (2014). Impact of interspecific interactions on antimicrobial activity among soil bacteria. *Front Microbiol* **5**: 1–10.

Tyc O, Zweers H, de Boer W, Garbeva P. (2015). Volatiles in inter-specific bacterial interactions. *Front Microbiol* **6**: 1–15.

Ueda K, Kawai S, Ogawa HO, Kiyama A, Kubota T, Kawanobe H, *et al.* (2000). Wide distribution of interspecific stimulatory events on antibiotic production and sporulation among *Streptomyces* species. *J Antibiot (Tokyo)* **53**: 979–982.

Vaz Jauri P, Kinkel LL. (2014). Nutrient overlap, genetic relatedness and spatial origin influence interaction-mediated shifts in inhibitory phenotype among *Streptomyces* spp. *FEMS Microbiol Ecol* **90**: 264–275.

Venkataraman A, Rosenbaum MA, Werner JJ, Winans SC, Angenent LT. (2014). Metabolite transfer with the fermentation product 2,3-butanediol enhances virulence by *Pseudomonas aeruginosa*. *ISME J* **8**: 1210–20.

Vetsigian K, Jajoo R, Kishony R. (2011). Structure and evolution of *Streptomyces* interaction networks in soil and in silico. *PLoS Biol* **9**: e1001184.

Vicente C, Thibessard A, Lorenzi J-N, Benhadj M, Hôtel L, Gacemi-Kirane D, *et al.* (2018). Comparative Genomics among Closely Related *Streptomyces* Strains Revealed Specialized Metabolite Biosynthetic Gene Cluster Diversity. *Antibiotics* **7**: 86.

Virtanen P, Gommers R, Oliphant TE, Haberland M, Reddy T, Cournapeau D, *et al.* (2020). SciPy 1.0: fundamental algorithms for scientific computing in Python. *Nat Methods* **17**: 261–272.

Vos M, Wolf AB, Jennings SJ, Kowalchuk GA. (2013). Micro-scale determinants of bacterial diversity in soil. *FEMS Microbiol Rev* **37**: 936–954.

Waksman G, Orlova E V. (2014). Structural organisation of the type IV secretion systems. *Curr Opin Microbiol* **17**: 24–31.

Wang W, Ji J, Li X, Wang J, Li S, Pan G, *et al.* (2014). Angucyclines as signals modulate the behaviors of *Streptomyces coelicolor*. *Proc Natl Acad Sci U S A* **111**: 5688–93.

West SA, Diggle SP, Buckling A, Gardner A, Griffin AS. (2007). The Social Lives of Microbes. *Annu Rev Ecol Evol Syst* **38**: 53–77.

West SA, Griffin AS, Gardner A, Diggle SP. (2006). Social evolution theory for microorganisms. *Nat Rev Microbiol* **4**: 597–607.

Westhoff S, van Leeuwe TM, Qachach O, Zhang Z, van Wezel GP, Rozen DE. (2017). The evolution of no-cost resistance at sub-MIC concentrations of streptomycin in *Streptomyces coelicolor*. *ISME J* **11**: 1168–1178.

Westhoff S, Otto SB, Swinkels A, Bode B, van Wezel GP, Rozen DE. (2020). Spatial structure increases the benefits of antibiotic production in *Streptomyces*. *Evolution (N Y)* **74**: 179–187.

van Wezel GP, McDowall KJ. (2011). The regulation of the secondary metabolism of *Streptomyces*: new links and experimental advances. *Nat Prod Rep* **28**: 1311.

Van Wezel GP, Van der Meulen J, Kawamoto S, Luiten RGM, Koerten HK, Kraal B. (2000). *ssgA* is essential for sporulation of *Streptomyces coelicolor* A3(2) and affects hyphal development by stimulating septum formation. *J Bacteriol* **182**: 5653–5662.

Wiener P. (2000). Antibiotic production in a spatially structured environment. *Ecol Lett* **3**: 122–130.

Wiener P. (1996). Experimental studies on the ecological role of antibiotic production in bacteria. *Evol Ecol* **10**: 405–421.

Willett JLE, Ruhe ZC, Goulding CW, Low DA, Hayes CS. (2015). Contact-Dependent Growth Inhibition (CDI) and CdiB/CdiA Two-Partner Secretion Proteins. *J Mol Biol* **427**: 3754–3765.

Willey J, Santamaria R, Guijarro J, Geistlich M, Losick R. (1991). Extracellular complementation of a developmental mutation implicates a small sporulation protein in aerial mycelium formation by *S. coelicolor*. *Cell* **65**: 641–650.

Wright ES, Vetsigian KH. (2016). Inhibitory interactions promote frequent bistability among competing bacteria. *Nat Commun* **7**: 11274.

Wu C, Du C, Gubbens J, Choi YH, van Wezel GP. (2015a). Metabolomics-Driven Discovery of a Prenylated Isatin Antibiotic Produced by *Streptomyces* Species MBT28. *J Nat Prod* **78**: 2355–2363.

Wu C, Kim HK, Van Wezel GP, Choi YH. (2015b). Metabolomics in the natural products field - A gateway to novel antibiotics. *Drug Discov Today Technol* **13**: 11–17.

Wu C, Zacchetti B, Ram AFJ, van Wezel GP, Claessen D, Hae Choi Y. (2015c). Expanding the chemical space for natural products by *Aspergillus-Streptomyces* co-cultivation and biotransformation. *Sci Rep* **5**: 10868.

Xu G, Wang J, Wang L, Tian X, Yang H, Fan K, *et al.* (2010). "Pseudo" γ-butyrolactone receptors respond to antibiotic signals to coordinate antibiotic biosynthesis. *J Biol Chem* **285**: 27440–27448.

Xu Y, Vetsigian K. (2017). Phenotypic variability and community interactions of germinating

R

Streptomyces spores. *Sci Rep* **7**: 1–13.

Yamanaka K, Oikawa H, Ogawa HO, Hosono K, Shinmachi F, Takano H, *et al.* (2005). Desferrioxamine E produced by *Streptomyces griseus* stimulates growth and development of *Streptomyces tanashiensis*. *Microbiology* **151**: 2899–2905.

Yeo KJ, Kim EH, Hwang E, Han Y-H, Eo Y, Kim HJ, *et al.* (2013). pH-dependent structural change of the extracellular sensor domain of the DraK histidine kinase from *Streptomyces coelicolor*. *Biochem Biophys Res Commun* **431**: 554–559.

Yim G, Wang HH, Davies J. (2007). Antibiotics as signalling molecules. *Philos Trans R Soc Lond B Biol Sci* **362**: 1195–200.

Yim G, Wang HH, Davies J. (2006). The truth about antibiotics. *Int J Med Microbiol* **296**: 163–170.

Yu Z, Zhu H, Dang F, Zhang W, Qin Z, Yang S, *et al.* (2012). Differential regulation of antibiotic biosynthesis by DraR-K, a novel two-component system in *Streptomyces coelicolor*. *Mol Microbiol* **85**: 535–556.

Zhang Z, Du C, de Barsy F, Liem M, Liakopoulos A, van Wezel GP, *et al.* (2020). Antibiotic production in *Streptomyces* is organized by a division of labor through terminal genomic differentiation. *Sci Adv* **6**: 1–10.

Zhu H, Swierstra J, Wu C, Girard G, Choi YH, van Wamel W, *et al.* (2014). Eliciting antibiotics active against the ESKAPE pathogens in a collection of actinomycetes isolated from mountain soils. *Microbiology* **160**: 1714–1725.

Zhu J, Sun D, Liu W, Chen Z, Li J, Wen Y. (2016). AvaR2, a pseudo γ-butyrolactone receptor homologue from *Streptomyces avermitilis*, is a pleiotropic repressor of avermectin and avenolide biosynthesis and cell growth. *Mol Microbiol* **102**: 562–578.

Zou Z, Du D, Zhang Y, Zhang J, Niu G, Tan H. (2014). A γ-butyrolactone-sensing activator/repressor, JadR3, controls a regulatory mini-network for jadomycin biosynthesis. *Mol Microbiol* **94**: 490–505.

Curriculum Vitae

Sanne Westhoff was born on the 3rd of May 1991 in Woerden, The Netherlands. In 2009 she graduated from Het Minkema College in Woerden. That same year she started her Bachelor programme in Biology at Leiden University in Leiden. As part of her Bachelor she completed a BSc research project at the Leiden University Medical Center (LUMC) on the effect of adipocyte derived extracts on human T cell proliferation. She graduated cum laude for her Bachelor in 2012 and started that same year with her MSc programme in Biology. During her MSc research projects she worked on signalling pathways in filamentous fungi, studying *Aspergillus fumigatus* at Leiden University and *Schizophyllum commune* at Utrecht University. She graduated cum laude for her MSc in 2014. She decided to pursue a PhD in the field of ecology and evolution studying antibiotic production and resistance in the bacterial genus *Streptomyces*. The results of this work are published in this thesis and in several international peer reviewed journals. During her PhD studies she presented her work at national and international conferences. She will now continue her work on antibiotic resistance by studying the mechanisms of antibiotic interactions in the lab of Prof. dr. Andersson at the University of Uppsala, Sweden.

List of publications

- **Westhoff S**, Kloosterman A, van Hoesel SFA, van Wezel GP, Rozen DE. (2020). Competition sensing changes antibiotic production in *Streptomyces*. *mBio* (under revision).
- **Westhoff S**, Otto SB, Swinkels A, Bode B, van Wezel GP, Rozen DE. (2020). Spatial structure increases the benefits of antibiotic production in *Streptomyces*. *Evolution* **74**: 179–187.
- **Westhoff S**, van Leeuwe TM, Qachach O, Zhang Z, van Wezel GP, Rozen DE. (2017). The evolution of no-cost resistance at sub-MIC concentrations of streptomycin in *Streptomyces coelicolor*. *The ISME Journal* **11**: 1168–1178.
- **Westhoff S**, van Wezel GP, Rozen DE. (2017). Distance-dependent danger responses in bacteria. *Current Opinion in Microbiology* **36**: 95–101.
- Abrudan MI, Smakman F, Grimbergen AJ, **Westhoff S**, Miller EL, van Wezel GP, Rozen, DE. (2015). Socially mediated induction and suppression of antibiosis during bacterial coexistence. *Proc Natl Acad Sci U S A* **112**: 11054–11059.
- Ioan-Facsinay A, Kwekkeboom JC, **Westhoff S**, Giera M, Rombouts Y, van Harmelen V, Huizinga TWJ, Deelder A, Kloppenburg M and Toes REM. (2013). Adipocyte-derived lipids modulate CD4+ T-cell function. *European Journal of Immunology* **43**: 1578–1587.