Another Brick in the Wall: the role of the actinobacterial cell wall in antibiotic resistance, phylogeny and development

Aart, L.T. van der

References

Ahmed, L., Jensen, P.R., Freel, K.C., Brown, R., Jones, A.L., Kim, B.Y., and Goodfellow, M. (2013) *Salinispora pacifica* sp. nov., an actinomycete from marine sediments. *Antonie Van Leeuwenhoek* **103**: 1069-1078.

Ainsa, J.A., Bird, N., Ryding, N.J., Findlay, K.C., and Chater, K.F. (2010) The complex *whiJ* locus mediates environmentally sensitive repression of development of *Streptomyces coelicolor* A3(2). *Antonie Van Leeuwenhoek* **98**: 225-236.

Ainsa, J.A., Parry, H.D., and Chater, K.F. (1999) A response regulator-like protein that functions at an intermediate stage of sporulation in *Streptomyces coelicolor* A3(2). *Mol Microbiol* **34**: 607-619.

Ainsa, J.A., Ryding, N.J., Hartley, N., Findlay, K.C., Bruton, C.J., and Chater, K.F. (2000) WhiA, a protein of unknown function conserved among gram-positive bacteria, is essential for sporulation in *Streptomyces coelicolor* A3(2). *J Bacteriol* **182**: 5470-5478.

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

Aráoz, R., Anhalt, E., René, L., Badet-Denisot, M.-A., Courvalin, P., and Badet, B. (2000) Mechanism-based inactivation of VanX, a D-alanyl-D-alanine dipeptidase necessary for vancomycin resistance. *Biochemistry* **39**: 15971-15979.

Arbeloa, A., Hugonnet, J.E., Sentilhes, A.C., Josseaume, N., Dubost, L., Monsempes, C., Blanot, D., Brouard, J.P., and Arthur, M. (2004) Synthesis of mosaic peptidoglycan cross-bridges by hybrid peptidoglycan assembly pathways in Gram-positive bacteria. *J Biol Chem* **279**: 41546-41556.

Arias, C.A., and Murray, B.E. (2009) Antibiotic-resistant bugs in the 21st century--a clinical super-challenge. *N Engl J Med* **360**: 439-443.

Arthur, M., Depardieu, F., Cabanie, L., Reynolds, P., and Courvalin, P. (1998) Requirement of the VanY and VanX D,D-peptidases for glycopeptide resistance in Enterococci. *Mol Microbiol* **30**: 819-830.

Arthur, M., Depardieu, F., Gerbaud, G., Galimand, M., Leclercq, R., and Courvalin, P. (1997) The VanS sensor negatively controls VanR-mediated transcriptional activation of glycopeptide resistance genes of Tn1546 and related elements in the absence of induction. *J Bacteriol* **179**: 97-106.

Arthur, M., Depardieu, F., Snaith, H.A., Reynolds, P.E., and Courvalin, P. (1994) Contribution of VanY D,D-carboxypeptidase to glycopeptide resistance in *Enterococcus faecalis* by hydrolysis of peptidoglycan precursors. *Antimicrob Agents Chemother* **38**: 1899-1903.

Aslangul, E., Baptista, M., Fantin, B., Depardieu, F., Arthur, M., Courvalin, P., and Carbon, C. (1997) Selection of glycopeptide-resistant mutants of VanB-type *Enterococcus faecalis* BM4281 in vitro and in experimental endocarditis. *J Infect Dis* **175**: 598-605.

Asojo, O.A., Nelson, S.K., Mootien, S., Lee, Y., Rezende, W.C., Hyman, D.A., Matsumoto, M.M., Reiling, S., Kelleher, A., Ledizet, M., Koski, R.A., and Anthony, K.G. (2014) Structural and biochemical analyses of alanine racemase from the multidrug-resistant *Clostridium difficile* strain 630. *Acta Crystallographica Section D: Biological Crystallography* **70**: 1922-1933.

Aziz, R.K., Bartels, D., Best, A.A., DeJongh, M., Disz, T., Edwards, R.A., Formsma, K., Gerdes, S., Glass, E.M., Kubal, M., Meyer, F., Olsen, G.J., Olson, R., Osterman, A.L., Overbeek, R.A., McNeil, L.K., Paarmann, D., Paczian, T., Parrello, B., Pusch, G.D., Reich, C., Stevens, R., Vassieva, O., Vonstein, V., Wilke, A., and Zagnitko, O. (2008) The RAST Server: rapid annotations using subsystems technology. *BMC genomics* **9**: 75.

Baldacci, E., Farina, G., and Locci, R. (1966) Emendation of Genus *Streptoverticillium Baldacci* (1958) and Revision of Some Species. *Giorn Microbiol* **14**: 153.

Baldacci, E., and Locci, R., (1974) Genus II. *Streptoverticillium* Baldacci 1958, 15, emed. mur. char. Baldacci, Farina and Locci 1966, 168. In: Bergey's Manual of Determinative Bacteriology. 8th Ed. R.E. Buchanan & N.E. Gibbons (eds). Baltimore: Williams & Wilkins, pp. 829-842.

Baranowski, C., Sham, L.-T., Eskandarian, H.A., Welsh, M.A., Lim, H.C., Kieser, K.J., Wagner, J.C., Walker, S., McKinney, J.D., Fantner, G.E., Ioerger, T.R., Bernhardt, T.G., Rubin, E.J., and Rego, E.H. (2018) Maturing Mycobacterial Peptidoglycan Requires Non-canonical Crosslinks to Maintain Shape. *bioRxiv*.

Barka, E.A., Vatsa, P., Sanchez, L., Gaveau-Vaillant, N., Jacquard, C., Klenk, H.-P., Clément, C., Ouhdouch, Y., and van Wezel, G.P. (2016) Taxonomy, Physiology, and Natural Products of Actinobacteria. *Microbiology and Molecular Biology Reviews* **80**: 1-43.

Bell, J.M., Paton, J.C., and Turnidge, J. (1998) Emergence of vancomycin-resistant Enterococci in Australia: phenotypic and genotypic characteristics of isolates. *J Clin Microbiol* **36**: 2187-2190.

Benedict, R.G., Dvonch, W., Shotwell, O.L., Pridham, T.G., and Lindenfelser, L.A. (1952) Cinnamycin, an antibiotic from *Streptomyces cinnamoneus* nov. sp. *Antibiot Chemother (Northfield)* **2**: 591-594.

Bentley, S.D., Chater, K.F., Cerdeno-Tarraga, A.M., Challis, G.L., Thomson, N.R., James, K.D., Harris, D.E., Quail, M.A., Kieser, H., Harper, D., Bateman, A., Brown, S., Chandra, G., Chen, C.W., Collins, M., Cronin, A., Fraser, A., Goble, A., Hidalgo, J., Hornsby, T., Howarth, S., Huang, C.H., Kieser, T., Larke, L., Murphy, L., Oliver, K., O'Neil, S., Rabbinowitsch, E., Rajandream, M.A., Rutherford, K., Rutter, S., Seeger, K., Saunders, D., Sharp, S., Squares, R., Squares, S., Taylor, K., Warren, T., Wietzorrek, A., Woodward, J., Barrell, B.G., Parkhill, J., and Hopwood, D.A. (2002) Complete genome sequence of the model actinomycete *Streptomyces coelicolor* A3(2). *Nature* **417**: 141-147.

Berdy, J. (2012) Thoughts and facts about antibiotics: where we are now and where we are heading. *J Antibiot (Tokyo)* **65**: 385-395.

Bérdy, J. (2005) Bioactive microbial metabolites. *J Antibiot (Tokyo)* **58**: 1-26.

Bhullar, K., Waglechner, N., Pawlowski, A., Koteva, K., Banks, E.D., Johnston, M.D., Barton, H.A., and Wright, G.D. (2012) Antibiotic resistance is prevalent in an isolated cave microbiome. *PLoS One* **7**: e34953.

Bisson-Filho, A.W., Hsu, Y.P., Squyres, G.R., Kuru, E., Wu, F., Jukes, C., Sun, Y., Dekker, C., Holden, S., VanNieuwenhze, M.S., Brun, Y.V., and Garner, E.C. (2017) Treadmilling by FtsZ filaments drives peptidoglycan synthesis and bacterial cell division. *Science* **355**: 739-743.

Blin, K., Wolf, T., Chevrette, M.G., Lu, X., Schwalen, C.J., Kautsar, S.A., Suarez Duran, H.G., de Los Santos, E.L.C., Kim, H.U., Nave, M., Dickschat, J.S., Mitchell, D.A., Shelest, E., Breitling, R., Takano, E., Lee, S.Y., Weber, T., and Medema, M.H. (2017) antiSMASH 4.0-improvements in chemistry prediction and gene cluster boundary identification. *Nucleic Acids Res*.

Bornikoel, J., Carrion, A., Fan, Q., Flores, E., Forchhammer, K., Mariscal, V., Mullineaux, C.W., Perez, R., Silber, N., Wolk, C.P., and Maldener, I. (2017) Role of Two Cell Wall Amidases in Septal Junction and Nanopore Formation in the Multicellular *Cyanobacterium Anabaena* sp. PCC 7120. *Front Cell Infect Microbiol* **7**: 386.

Boucher, H.W., Talbot, G.H., Bradley, J.S., Edwards, J.E., Gilbert, D., Rice, L.B., Scheld, M., Spellberg, B., and Bartlett, J. (2009) Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clin Infect Dis* **48**: 1-12.

Braun, V., Gotz, F., Schultz, J.E., and Wohlleben, W. (2015) The bacterial cell envelope: struc-

ture, function, and infection interface. *Int J Med Microbiol* **305**: 175-177.

Breukink, E., and de Kruijff, B. (2006) Lipid II as a target for antibiotics. *Nat Rev Drug Disc* **5**: 321-323.

Bugg, T.D., Braddick, D., Dowson, C.G., and Roper, D.I. (2011) Bacterial cell wall assembly: still an attractive antibacterial target. *Trends Biotechnol* **29**: 167-173.

Bugg, T.D., Dutka-Malen, S., Arthur, M., Courvalin, P., and Walsh, C.T. (1991a) Identification of vancomycin resistance protein VanA as a D-alanine:D-alanine ligase of altered substrate specificity. *Biochemistry* **30**: 2017-2021.

Bugg, T.D., Wright, G.D., Dutka-Malen, S., Arthur, M., Courvalin, P., and Walsh, C.T. (1991b) Molecular basis for vancomycin resistance in *Enterococcus faecium* BM4147: biosynthesis of a depsipeptide peptidoglycan precursor by vancomycin resistance proteins VanH and VanA. *Biochemistry* **30**: 10408-10415.

Bui, N.K., Eberhardt, A., Vollmer, D., Kern, T., Bougault, C., Tomasz, A., Simorre, J.P., and Vollmer, W. (2012) Isolation and analysis of cell wall components from *Streptococcus pneumoniae*. *Anal Biochem* **421**: 657-666.

Bui, N.K., Gray, J., Schwarz, H., Schumann, P., Blanot, D., and Vollmer, W. (2009) The peptidoglycan sacculus of *Myxococcus xanthus* has unusual structural features and is degraded during glycerol-induced myxospore development. *J Bacteriol* **191**: 494-505.

Bull, A.T., Asenjo, J.A., Goodfellow, M., and Gomez-Silva, B. (2016) The Atacama Desert: Technical Resources and the Growing Importance of Novel Microbial Diversity. *Annu Rev Microbiol* **70**: 215-234.

Caceres, N.E., Harris, N.B., Wellehan, J.F., Feng, Z., Kapur, V., and Barletta, R.G. (1997) Overexpression of the D-alanine racemase gene confers resistance to D-cycloserine in *Mycobacterium smegmatis*. *J Bacteriol* **179**: 5046-5055.

Cameron, T.A., Anderson-Furgeson, J., Zupan, J.R., Zik, J.J., and Zambryski, P.C. (2014) Peptidoglycan synthesis machinery in *Agrobacterium tumefaciens* during unipolar growth and cell division. *MBio* **5**: e01219-01214.

Cava, F., Lam, H., de Pedro, M.A., and Waldor, M.K. (2011) Emerging knowledge of regulatory roles of D-amino acids in bacteria. *Cell Mol Life Sci* **68**: 817-831.

Celler, K., Koning, R.I., Koster, A.J., and van Wezel, G.P. (2013) Multidimensional view of the bacterial cytoskeleton. *J Bacteriol* **195**: 1627-1636.

Celler, K., Koning, R.I., Willemse, J., Koster, A.J., and van Wezel, G.P. (2016) Cross-membranes orchestrate compartmentalization and morphogenesis in *Streptomyces*. *Nat Commun* **7**: ncomms11836.

Chang, Y.-P., Tseng, M.-J., and Chu, Y.-H. (2006) Using surface plasmon resonance to directly measure slow binding of low-molecular mass inhibitors to a VanX chip. *Anal Biochem* **359**: 63-71.

Chater, K.F. (1972) A morphological and genetic mapping study of white colony mutants of *Streptomyces coelicolor*. *J Gen Microbiol* **72**: 9-28.

Chater, K.F., Bruton, C.J., Plaskitt, K.A., Buttner, M.J., Mendez, C., and Helmann, J.D. (1989) The developmental fate of *S. coelicolor* hyphae depends upon a gene product homologous with the motility sigma factor of *B. subtilis*. *Cell* **59**: 133-143.

Chen, J.M., Uplekar, S., Gordon, S.V., and Cole, S.T. (2012) A point mutation in cycA partially contributes to the D-cycloserine resistance trait of *Mycobacterium bovis* BCG vaccine strains. *PLoS One* **7**: e43467.

Chun, J., and Rainey, F.A. (2014) Integrating genomics into the taxonomy and systematics of the Bacteria and Archaea. *Int J System Evol Microbiol* **64**: 316-324.

Claessen, D., Rozen, D.E., Kuipers, O.P., Sogaard-Andersen, L., and van Wezel, G.P. (2014) Bacterial solutions to multicellularity: a tale of biofilms, filaments and fruiting bodies.

Nat Rev Microbiol **12**: 115-124.

Collins, M.D., Goodfellow, M., Minnikin, D.E., and Alderson, G. (1985) Menaquinone Composition of Mycolic Acid-Containing Actinomycetes and Some Sporoactinomycetes. *J Appl Bacteriol* **58**: 77-86.

Colson, S., Stephan, J., Hertrich, T., Saito, A., van Wezel, G.P., Titgemeyer, F., and Rigali, S. (2007) Conserved cis-acting elements upstream of genes composing the chitinolytic system of streptomycetes are DasR-responsive elements. *J Mol Microbiol Biotechnol* **12**: 60-66.

Courvalin, P. (2006) Vancomycin resistance in Gram-positive cocci. *Clin Infect Dis* **42 Suppl 1**: S25-34.

Cummins, C.S. (1962) Chemical composition and antigenic structure of cell walls of *Corynebacterium*, *Mycobacterium*, *Nocardia,* Actinomyces and *Arthrobacter*. *J Gen Microbiol* **28**: 35-50.

Daniel, R.A., and Errington, J. (2003) Control of cell morphogenesis in bacteria: two distinct ways to make a rod-shaped cell. *Cell* **113**: 767-776.

Daniel, R.A., Harry, E.J., and Errington, J. (2000) Role of penicillin-binding protein PBP 2B in assembly and functioning of the division machinery of *Bacillus subtilis*. *Mol Microbiol* **35**: 299-311.

Decousser, J.W., Pina, P., Picot, F., Delalande, C., Pangon, B., Courvalin, P., Allouch, P., and Col, B.V.H.S.G. (2003) Frequency of isolation and antimicrobial susceptibility of bacterial pathogens isolated from patients with bloodstream infections: a French prospective national survey. *J Antimicrob Chemother* **51**: 1213-1222.

den Hengst, C.D., Tran, N.T., Bibb, M.J., Chandra, G., Leskiw, B.K., and Buttner, M.J. (2010) Genes essential for morphological development and antibiotic production in *Streptomyces coelicolor* are targets of BldD during vegetative growth. *Mol Microbiol* **78**: 361-379.

Desjardins, C.A., Cohen, K.A., Munsamy, V., Abeel, T., Maharaj, K., Walker, B.J., Shea, T.P., Almeida, D.V., Manson, A.L., Salazar, A., Padayatchi, N., O'Donnell, M.R., Mlisana, K.P., Wortman, J., Birren, B.W., Grosset, J., Earl, A.M., and Pym, A.S. (2016) Genomic and functional analyses of *Mycobacterium tuberculosis* strains implicate ald in D-cycloserine resistance. *Nat Genet* **48**: 544-551.

Edgar, R.C. (2004) MUSCLE: multiple sequence alignment with high accuracy and high throughput. *Nucleic Acids Res* **32**: 1792-1797.

Egan, A.J., Biboy, J., van't Veer, I., Breukink, E., and Vollmer, W. (2015) Activities and regulation of peptidoglycan synthases. *Philos Trans R Soc Lond B Biol Sci* **370**.

Egan, A.J., Cleverley, R.M., Peters, K., Lewis, R.J., and Vollmer, W. (2017) Regulation of bacterial cell wall growth. *FEBS J* **284**: 851-867.

Elliot, M.A., Bibb, M.J., Buttner, M.J., and Leskiw, B.K. (2001) BldD is a direct regulator of key developmental genes in *Streptomyces coelicolor* A3(2). *Mol Microbiol* **40**: 257-269.

Emami, K., Guyet, A., Kawai, Y., Devi, J., Wu, L.J., Allenby, N., Daniel, R.A., and Errington, J. (2017) RodA as the missing glycosyltransferase in *Bacillus subtilis* and antibiotic discovery for the peptidoglycan polymerase pathway. *Nat Microbiol* **2**: 16253.

Emsley, P., and Cowtan, K. (2004) Coot: model-building tools for molecular graphics. *Acta Crystallographica Section D* **60**: 2126-2132.

Engelberg-Kulka, H., Amitai, S., Kolodkin-Gal, I., and Hazan, R. (2006) Bacterial programmed cell death and multicellular behavior in bacteria. *PLoS Genet* **2**: e135.

Errington, J., Daniel, R.A., and Scheffers, D.J. (2003) Cytokinesis in bacteria. *Microbiol Mol Biol Rev* **67**: 52-65.

Evans, P.R., and Murshudov, G.N. (2013) How good are my data and what is the resolution?

Acta Crystallogr D Biol Crystallogr **69**: 1204-1214.

Fedoryshyn, M., Welle, E., Bechthold, A., and Luzhetskyy, A. (2008) Functional expression of the Cre recombinase in actinomycetes. *Appl Microbiol Biotechnol* **78**: 1065-1070.

Felsenstein, J. (1981) Evolutionary trees from DNA sequences: a maximum likelihood approach. *J Mol Evol* **17**: 368-376.

Felsenstein, J. (1985) Confidence Limits on Phylogenies: An Approach Using the Bootstrap. *Evolution* **39**: 783-791.

Feng, Z., and Barletta, R.G. (2003) Roles of *Mycobacterium smegmatis* D-alanine:D-alanine ligase and D-alanine racemase in the mechanisms of action of and resistance to the peptidoglycan inhibitor D-cycloserine. *Antimicrob Agents Chemother* **47**: 283-291.

Fenn, T.D., Stamper, G.F., Morollo, A.A., and Ringe, D. (2003) A Side Reaction of Alanine Racemase: Transamination of Cycloserine. *Biochemistry* **42**: 5775-5783.

Figueiredo, T.A., Sobral, R.G., Ludovice, A.M., Almeida, J.M., Bui, N.K., Vollmer, W., de Lencastre, H., and Tomasz, A. (2012) Identification of genetic determinants and enzymes involved with the amidation of glutamic acid residues in the peptidoglycan of *Staphylococcus aureus*. *PLoS Pathog* **8**: e1002508.

Fischer, M., Falke, D., and Sawers, R.G. (2013) A respiratory nitrate reductase active exclusively in resting spores of the obligate aerobe *Streptomyces coelicolor* A3(2). *Mol Microbiol* **89**: 1259-1273.

Fitch, W.M. (1971) Toward Defining Course of Evolution - Minimum Change for a Specific Tree Topology. *Syst Zool* **20**: 406-&.

Flärdh, K. (2010) Cell polarity and the control of apical growth in *Streptomyces*. *Curr Opin Microbiol* **13**: 758-765.

Flärdh, K., and Buttner, M.J. (2009) *Streptomyces* morphogenetics: dissecting differentiation in a filamentous bacterium. *Nat Rev Microbiol* **7**: 36-49.

Flärdh, K., Findlay, K.C., and Chater, K.F. (1999) Association of early sporulation genes with suggested developmental decision points in *Streptomyces coelicolor* A3(2). *Microbiology* **145**: 2229-2243.

Flärdh, K., Richards, D.M., Hempel, A.M., Howard, M., and Buttner, M.J. (2012) Regulation of apical growth and hyphal branching in *Streptomyces*. *Curr Opin Microbiol*.

Frieden, T.R., Sterling, T., Pablos-Mendez, A., Kilburn, J.O., Cauthen, G.M., and Dooley, S.W. (1993) The emergence of drug-resistant tuberculosis in New York City. *N Engl J Med* **328**: 521-526.

Gabadinho, J., Beteva, A., Guijarro, M., Rey-Bakaikoa, V., Spruce, D., Bowler, M.W., Brockhauser, S., Flot, D., Gordon, E.J., Hall, D.R., Lavault, B., McCarthy, A.A., McCarthy, J., Mitchell, E., Monaco, S., Mueller-Dieckmann, C., Nurizzo, D., Ravelli, R.B., Thibault, X., Walsh, M.A., Leonard, G.A., and McSweeney, S.M. (2010) MxCuBE: a synchrotron beamline control environment customized for macromolecular crystallography experiments. *J Synchrotron Radiat* **17**: 700-707.

Gao, C., Hindra, Mulder, D., Yin, C., and Elliot, M.A. (2012) Crp is a global regulator of antibiotic production in *Streptomyces*. *MBio* **3**: 00407-00412.

Girard, G., Traag, B.A., Sangal, V., Mascini, N., Hoskisson, P.A., Goodfellow, M., and van Wezel, G.P. (2013) A novel taxonomic marker that discriminates between morphologically complex actinomycetes. *Open Biol* **3**: 130073.

Girard, G., Willemse, J., Zhu, H., Claessen, D., Bukarasam, K., Goodfellow, M., and van Wezel, G.P. (2014) Analysis of novel kitasatosporae reveals significant evolutionary changes in conserved developmental genes between *Kitasatospora* and *Streptomyces*. *Antonie Van Leeuwenhoek* **106**: 365-380.

Glauner, B. (1988) Separation and quantification of muropeptides with high-performance liq-

uid chromatography. *Anal Biochem* **172**: 451-464.

Gomez Casanova, N., Siller Ruiz, M., and Munoz Bellido, J.L. (2017) Mechanisms of resistance to daptomycin in *Staphylococcus aureus*. *Rev Esp Quimioter* **30**: 391-396.

Goodfellow, M., (2012) Phylum XXVI. Actinobacteria phyl. nov. In: Bergey's Manual of Systematic Bacteriology. M. Goodfellow, P. Kämpfer, H.-J. Busse, M.E. Trujillo, K.-I. Suzuki, W. Ludwig & W.B. Whitman (eds). New York: Springer, pp. 1-2083.

Goodfellow, M., Busarakam, K., Idris, H., Labeda, D.P., Nouioui, I., Brown, R., Kim, B.Y., Del Carmen Montero-Calasanz, M., Andrews, B.A., and Bull, A.T. (2017) *Streptomyces asenjonii* sp. nov., isolated from hyper-arid Atacama Desert soils and emended description of *Streptomyces viridosporus* Pridham et al. 1958. *Antonie Van Leeuwenhoek* **110**: 1133-1148.

Gray, D.I., Gooday, G.W., and Prosser, J.I. (1990) Apical hyphal extension in *Streptomyces coelicolor* A3(2). *J Gen Microbiol* **136**: 1077-1084.

Griffith, R.S. (1981) Introduction to vancomycin. *Rev Infect Dis* **3 suppl**: S200-204.

Gubbens, J., Wu, C., Zhu, H., Filippov, D.V., Florea, B.I., Rigali, S., Overkleeft, H.S., and van Wezel, G.P. (2017) Intertwined Precursor Supply during Biosynthesis of the Catecholate-Hydroxamate Siderophores Qinichelins in *Streptomyces* sp. MBT76. *ACS Chem Biol* **12**: 2756-2766.

Guindon, S., and Gascuel, O. (2003) A simple, fast, and accurate algorithm to estimate large phylogenies by maximum likelihood. *System Biol* **52**: 696-704.

Guiral, S., Mitchell, T.J., Martin, B., and Claverys, J.P. (2005) Competence-programmed predation of noncompetent cells in the human pathogen *Streptococcus pneumoniae*: genetic requirements. *Proc Natl Acad Sci U S A* **102**: 8710-8715.

Haiser, H.J., Yousef, M.R., and Elliot, M.A. (2009) Cell wall hydrolases affect germination, vegetative growth, and sporulation in *Streptomyces coelicolor*. *J Bacteriol* **191**: 6501-6512.

Hammes, W., Schleifer, K.H., and Kandler, O. (1973) Mode of action of glycine on the biosynthesis of peptidoglycan. *J Bacteriol* **116**: 1029-1053.

Hamoen, L.W., and Errington, J. (2003) Polar targeting of DivIVA in *Bacillus subtilis* is not directly dependent on FtsZ or PBP 2B. *J Bacteriol* **185**: 693-697.

Hasegawa, T., Takizawa, M., and Tanida, S. (1983) A Rapid Analysis for Chemical Grouping of Aerobic Actinomycetes. *J Gen Appl Microbiol* **29**: 319-322.

Hashimoto, A., Nishikawa, T., Oka, T., Takahashi, K., and Hayashi, T. (1992) Determination of free amino acid enantiomers in rat brain and serum by high-performance liquid chromatography after derivatization with N-tert.-butyloxycarbonyl-l-cysteine and o-phthaldialdehyde. *Journal of Chromatography B: Biomedical Sciences and Applications* **582**: 41-48.

Hatano, K., Nishii, T., and Kasai, H. (2003) Taxonomic re-evaluation of whorl-forming *Streptomyces* (formerly *Streptoverticillium*) species by using phenotypes, DNA-DNA hybridization and sequences of *gyrB*, and proposal of *Streptomyces luteireticuli* (ex Katoh and Arai 1957) corrig., sp. nov., nom. rev. *Int J Syst Evol Microbiol* **53**: 1519-1529.

Hayakawa, M., and Nomomura, H. (1989) A new method for the intensive isolation of actinomycetes from soil. *Actinomycetologica* **3**: 95-104.

Healy, V.L., Mullins, L.S., Li, X., Hall, S.E., Raushel, F.M., and Walsh, C.T. (2000) D-Ala-D-X ligases: evaluation of D-alanyl phosphate intermediate by MIX, PIX and rapid quench studies. *Chem Biol* **7**: 505-514.

Heidrich, C., Templin, M.F., Ursinus, A., Merdanovic, M., Berger, J., Schwarz, H., de Pedro, M.A., and Holtje, J.V. (2001) Involvement of N-acetylmuramyl-L-alanine amidases in cell separation and antibiotic-induced autolysis of *Escherichia coli*. *Mol Microbiol* **41**: 167-178.

Heidrich, C., Ursinus, A., Berger, J., Schwarz, H., and Holtje, J.V. (2002) Effects of multiple deletions of murein hydrolases on viability, septum cleavage, and sensitivity to large toxic molecules in *Escherichia coli*. *J Bacteriol* **184**: 6093-6099.

Hochman, A. (1997) Programmed cell death in prokaryotes. *Crit Rev Microbiol* **23**: 207-214.

Holmes, N.A., Walshaw, J., Leggett, R.M., Thibessard, A., Dalton, K.A., Gillespie, M.D., Hemmings, A.M., Gust, B., and Kelemen, G.H. (2013) Coiled-coil protein Scy is a key component of a multiprotein assembly controlling polarized growth in *Streptomyces*. *Proc Natl Acad Sci U S A* **110**: E397-406.

Höltje, J.-V., (1993) "Three for one" — a Simple Growth Mechanism that Guarantees a Precise Copy of the Thin, Rod-Shaped Murein Sacculus of *Escherichia coli*. In: Bacterial Growth and Lysis: Metabolism and Structure of the Bacterial Sacculus. M.A. de Pedro, J.V. Höltje & W. Löffelhardt (eds). Boston, MA: Springer US, pp. 419-426.

Homma, T., Nuxoll, A., Gandt, A.B., Ebner, P., Engels, I., Schneider, T., Gotz, F., Lewis, K., and Conlon, B.P. (2016) Dual Targeting of Cell Wall Precursors by Teixobactin Leads to Cell Lysis. *Antimicrob Agents Chemother* **60**: 6510-6517.

Hong, H.J., Hutchings, M.I., and Buttner, M.J. (2008) Vancomycin resistance VanS/VanR two-component systems. *Adv Exp Med Biol* **631**: 200-213.

Hong, H.J., Hutchings, M.I., Hill, L.M., and Buttner, M.J. (2005) The role of the novel Fem protein VanK in vancomycin resistance in *Streptomyces coelicolor*. *J Biol Chem* **280**: 13055-13061.

Hong, H.J., Hutchings, M.I., Neu, J.M., Wright, G.D., Paget, M.S., and Buttner, M.J. (2004) Characterization of an inducible vancomycin resistance system in *Streptomyces coelicolor* reveals a novel gene (vanK) required for drug resistance. *Mol Microbiol* **52**: 1107-1121.

Hong, W., Chen, L., and Xie, J. (2014) Molecular basis underlying *Mycobacterium tuberculosis* D-cycloserine resistance. Is there a role for ubiquinone and menaquinone metabolic pathways? *Expert Opin Ther Targets* **18**: 691-701.

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

Hopwood, D.A., Wright, H.M., Bibb, M.J., and Cohen, S.N. (1977) Genetic recombination through protoplast fusion in *Streptomyces*. *Nature* **268**: 171-174.

Howden, B.P., Davies, J.K., Johnson, P.D., Stinear, T.P., and Grayson, M.L. (2010) Reduced vancomycin susceptibility in *Staphylococcus aureus*, including vancomycin-intermediate and heterogeneous vancomycin-intermediate strains: resistance mechanisms, laboratory detection, and clinical implications. *Clin Microbiol Rev* **23**: 99-139.

Hugonnet, J.E., Haddache, N., Veckerle, C., Dubost, L., Marie, A., Shikura, N., Mainardi, J.L., Rice, L.B., and Arthur, M. (2014) Peptidoglycan cross-linking in glycopeptide-resistant *Actinomycetales*. *Antimicrob Agents Chemother* **58**: 1749-1756.

Hussain, S., Wivagg, C.N., Szwedziak, P., Wong, F., Schaefer, K., Izore, T., Renner, L.D., Holmes, M.J., Sun, Y., Bisson-Filho, A.W., Walker, S., Amir, A., Lowe, J., and Garner, E.C. (2018) MreB filaments align along greatest principal membrane curvature to orient cell wall synthesis. *Elife* **7**.

Hutchings, M.I., Hong, H.J., and Buttner, M.J. (2006) The vancomycin resistance VanRS two-component signal transduction system of *Streptomyces coelicolor*. *Mol Microbiol* **59**: 923-935.

Hwang, J.Y., Kim, S.H., Oh, H.R., Kwon, E., and Nam, D.H. (2015) Analysis of a draft genome sequence of *Kitasatospora cheerisanensis* KCTC 2395 producing bafilomycin antibiotics. *J Microbiol* **53**: 84-89.

Iannazzo, L., Soroka, D., Triboulet, S., Fonvielle, M., Compain, F., Dubée, V., Mainardi, J.L., Hugonnet, J.E., Braud, E., Arthur, M., and Etheve-Quelquejeu, M. (2016) Routes of

Synthesis of Carbapenems for Optimizing Both the Inactivation of L,D-Transpeptidase LdtMt1 of *Mycobacterium tuberculosis* and the Stability toward Hydrolysis by β-Lactamase BlaC. *J Med Chem* **59**: 3427-3438.

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

Inagaki, K., Tanizawa, K., Badet, B., Walsh, C., Tanaka, H., and Soda, K. (1986) Thermostable alanine racemase from *Bacillus stearothermophilus*: molecular cloning of the gene, enzyme purification, and characterization. *Biochemistry* **25**: 3268 - 3274.

Jakimowicz, D., and van Wezel, G.P. (2012) Cell division and DNA segregation in *Streptomyces*: how to build a septum in the middle of nowhere? *Mol Microbiol* **85**: 393-404.

Ju, J., Xu, S., Furukawa, Y., Zhang, Y., Misono, H., Minamino, T., Namba, K., Zhao, B., and Ohnishi, K. (2011) Correlation between catalytic activity and monomer-dimer equilibrium of bacterial alanine racemases. *J Biochem* **149**: 83 - 89.

Ju, J., Yokoigawa, K., Misono, H., and Ohnishi, K. (2005) Cloning of alanine racemase genes from *Pseudomonas fluorescens* strains and oligomerization states of gene products expressed in *Escherichia coli*. *Journal of Bioscience and Bioengineering* **100**: 409-417.

Jukes, T.H., and Cantor, C.R. (1969) Evolution of protein molecules. *Academic Pres, London* **3**: 21-132.

Kabsch, W. (2010) Integration, scaling, space-group assignment and post-refinement. *Acta Crystallogr D Biol Crystallogr* **66**: 125-132.

Kämpfer, P., (2012) Family 1. *Streptomycetaceae* Waksman and Henrici 1943, 339AL emend. Rainey, Ward-Rainey and Stackebrandt, 1997, 486 emend. Kim, Lonsdale, Seong and Goodfellow 2003b, 113 emend. Zhi, Li and Stackebrandt 2009, 600. In: Bergey's Manual of Systematic Bacteriology. M. Goodfellow, P. Kämpfer, H.-J. Busse, M.E. Trujillo, K.-I. Suzuki, W. Ludwig & W.B. Whitman (eds). New York: Springer, pp.

Karoui, M.E., and Errington, J. (2001) Isolation and characterization of topological specificity mutants of *minD* in *Bacillus subtilis*. *Mol Microbiol* **42**: 1211-1221.

Kato, S., Hemmi, H., and Yoshimura, T. (2012) Lysine racemase from a lactic acid bacterium, *Oenococcus oeni*: structural basis of substrate specificity. *J Biochem* **152**: 505-508.

Keep, N.H., Ward, J.M., Cohen-Gonsaud, M., and Henderson, B. (2006) Wake up! Peptidoglycan lysis and bacterial non-growth states. *Trends Microbiol* **14**: 271-276.

Keijser, B.J., Noens, E.E., Kraal, B., Koerten, H.K., and van Wezel, G.P. (2003) The *Streptomyces coelicolor ssgB* gene is required for early stages of sporulation. *FEMS Microbiol Lett* **225**: 59-67.

Kelley, L.A., Mezulis, S., Yates, C.M., Wass, M.N., and Sternberg, M.J. (2015) The Phyre2 web portal for protein modeling, prediction and analysis. *Nat Protoc* **10**: 845-858.

Kelly, K. (1964) Centroid notations for revised ISCC-NBS colour name blocks *J Res Nat Bur Stand USA*: 472.

Kieser, T., Bibb, M.J., Buttner, M.J., Chater, K.F., and Hopwood, D.A., (2000) *Practical Streptomyces genetics*. John Innes Foundation, Norwich, U.K.

Kim, B.J., Kim, C.J., Chun, J., Koh, Y.H., Lee, S.H., Hyun, J.W., Cha, C.Y., and Kook, Y.H. (2004) Phylogenetic analysis of the genera *Streptomyces* and *Kitasatospora* based on partial RNA polymerase beta-subunit gene (*rpoB*) sequences. *Int J Syst Evol Microbiol* **54**: 593-598.

Kimura, M. (1980) A simple method for estimating evolutionary rates of base substitutions through comparative studies of nucleotide sequences. *J Mol Evol* **16**: 111-120.

Knerr, P.J., and van der Donk, W.A. (2013) Chemical Synthesis of the lantibiotic lacticin 481

reveals the importance of lanthionine stereochemistry. *J Am Chem Soc* **135**: 7094-7097.

Koch, A.L. (1990) Additional Arguments for the Key Role of Smart Autolysins in the Enlargement of the Wall of Gram-Negative Bacteria. *Res Microbiol* **141**: 529-541.

Kolter, R., and van Wezel, G.P. (2016) Goodbye to brute force in antibiotic discovery? *Nat Microbiol* **1**: 15020.

Kühner, D., Stahl, M., Demircioglu, D.D., and Bertsche, U. (2014) From cells to muropeptide structures in 24 h: peptidoglycan mapping by UPLC-MS. *Sci Rep* **4**: 7494.

Kumar, S., Stecher, G., and Tamura, K. (2016) MEGA7: Molecular Evolutionary Genetics Analysis Version 7.0 for Bigger Datasets. *Mol Biol Evol* **33**: 1870-1874.

Kumar, Y., and Goodfellow, M. (2010) Reclassification of *Streptomyces hygroscopicus* strains as *Streptomyces aldersoniae* sp. nov., *Streptomyces angustmyceticus* sp. nov., comb. nov., *Streptomyces ascomycinicus* sp. nov., *Streptomyces decoyicus* sp. nov., comb. nov., *Streptomyces milbemycinicus* sp. nov. and *Streptomyces wellingtoniae* sp. nov. *Int J System Evol Microbiol* **60**: 769-775.

Kuru, E., Tekkam, S., Hall, E., Brun, Y.V., and Van Nieuwenhze, M.S. (2015) Synthesis of fluorescent D-amino acids and their use for probing peptidoglycan synthesis and bacterial growth in situ. *Nat Protoc* **10**: 33-52.

Kwun, M.J., Novotna, G., Hesketh, A.R., Hill, L., and Hong, H.J. (2013) *In vivo* studies suggest that induction of VanS-dependent vancomycin resistance requires binding of the drug to D-Ala-D-Ala termini in the peptidoglycan cell wall. *Antimicrob Agents Chemother* **57**: 4470-4480.

Kysela, D.T., Randich, A.M., Caccamo, P.D., and Brun, Y.V. (2016) Diversity Takes Shape: Understanding the Mechanistic and Adaptive Basis of Bacterial Morphology. *PLoS Biol* **14**: e1002565.

Labeda, D.P. (2011) Multilocus sequence analysis of phytopathogenic species of the genus *Streptomyces*. *Int J System Evol Microbiol* **61**: 2525-2531.

Labeda, D.P., Dunlap, C.A., Rong, X., Huang, Y., Doroghazi, J.R., Ju, K.S., and Metcalf, W.W. (2017) Phylogenetic relationships in the family *Streptomycetaceae* using multi-locus sequence analysis. *Antonie Van Leeuwenhoek* **110**: 563-583.

Labeda, D.P., Goodfellow, M., Brown, R., Ward, A.C., Lanoot, B., Vanncanneyt, M., Swings, J., Kim, S.B., Liu, Z., Chun, J., Tamura, T., Oguchi, A., Kikuchi, T., Kikuchi, H., Nishii, T., Tsuji, K., Yamaguchi, Y., Tase, A., Takahashi, M., Sakane, T., Suzuki, K.I., and Hatano, K. (2012) Phylogenetic study of the species within the family *Streptomycetaceae*. *Antonie Van Leeuwenhoek* **101**: 73-104.

Lam, H., Oh, D.C., Cava, F., Takacs, C.N., Clardy, J., de Pedro, M.A., and Waldor, M.K. (2009) D-amino acids govern stationary phase cell wall remodeling in bacteria. *Science* **325**: 1552-1555.

Lambert, M.P., and Neuhaus, F.C. (1972) Mechanism of D-cycloserine Action: Alanine Racemase from *Escherichia coli* W. *J Bacteriol* **110**: 978-987.

Larson, J.L., and Hershberger, C.L. (1986) The minimal replicon of a streptomycete plasmid produces an ultrahigh level of plasmid DNA. *Plasmid* **15**: 199-209.

Lavollay, M., Arthur, M., Fourgeaud, M., Dubost, L., Marie, A., Riegel, P., Gutmann, L., and Mainardi, J.L. (2009) The beta-lactam-sensitive D,D-carboxypeptidase activity of Pbp4 controls the L,D and D,D transpeptidation pathways in *Corynebacterium jeikeium*. *Mol Microbiol* **74**: 650-661.

Lavollay, M., Arthur, M., Fourgeaud, M., Dubost, L., Marie, A., Veziris, N., Blanot, D., Gutmann, L., and Mainardi, J.L. (2008) The peptidoglycan of stationary-phase *Mycobacterium tuberculosis* predominantly contains cross-links generated by L,D-transpeptidation. *J Bacteriol* **190**: 4360-4366.

Lavollay, M., Fourgeaud, M., Herrmann, J.L., Dubost, L., Marie, A., Gutmann, L., Arthur, M., and Mainardi, J.L. (2011) The peptidoglycan of *Mycobacterium abscessus* is predominantly cross-linked by L,D-transpeptidases. *J Bacteriol* **193**: 778-782.

Lawlor, E.J., Baylis, H.A., and Chater, K.F. (1987) Pleiotropic morphological and antibiotic deficiencies result from mutations in a gene encoding a tRNA-like product in *Streptomyces coelicolor* A3(2). *Genes Dev* **1**: 1305-1310.

Laxminarayan, R., Duse, A., Wattal, C., Zaidi, A.K., Wertheim, H.F., Sumpradit, N., Vlieghe, E., Hara, G.L., Gould, I.M., Goossens, H., Greko, C., So, A.D., Bigdeli, M., Tomson, G., Woodhouse, W., Ombaka, E., Peralta, A.Q., Qamar, F.N., Mir, F., Kariuki, S., Bhutta, Z.A., Coates, A., Bergstrom, R., Wright, G.D., Brown, E.D., and Cars, O. (2013) Antibiotic resistance-the need for global solutions. *Lancet Infect Dis* **13**: 1057-1098.

Lechevalier, H., and Lechevalier, M.P. (1965) Classification of aerobic actinomycetes based on their morphology and their chemical composition. *Ann Inst Pasteur (Paris)* **108**: 662-673.

Lechevalier, H.A., Lechevalier, M.P., and Gerber, N.N. (1971) Chemical composition as a criterion in the classification of actinomycetes. *Adv Appl Microbiol* **14**: 47-72.

Leclercq, R., Derlot, E., Duval, J., and Courvalin, P. (1988) Plasmid-mediated resistance to vancomycin and teicoplanin in *Enterococcus faecium*. *N Engl J Med* **319**: 157-161.

Leclercq, S., Derouaux, A., Olatunji, S., Fraipont, C., Egan, A.J., Vollmer, W., Breukink, E., and Terrak, M. (2017) Interplay between Penicillin-binding proteins and SEDS proteins promotes bacterial cell wall synthesis. *Sci Rep* **7**: 43306.

Leskiw, B.K., Bibb, M.J., and Chater, K.F. (1991) The use of a rare codon specifically during development? *Mol Microbiol* **5**: 2861-2867.

Lessard, I.A., Healy, V.L., Park, I.S., and Walsh, C.T. (1999) Determinants for differential effects on D-Ala-D-lactate vs D-Ala-D-Ala formation by the VanA ligase from vancomycin-resistant Enterococci. *Biochemistry* **38**: 14006-14022.

Lessard, I.A., and Walsh, C.T. (1999) VanX, a bacterial D-alanyl-D-alanine dipeptidase: resistance, immunity, or survival function? *Proc Natl Acad Sci U S A* **96**: 11028-11032.

Levefaudes, M., Patin, D., de Sousa-d'Auria, C., Chami, M., Blanot, D., Hervé, M., Arthur, M., Houssin, C., and Mengin-Lecreulx, D. (2015) Diaminopimelic Acid Amidation in *Corynebacteriales*: New insights into the role of LtsA in peptidoglycan modification. . *J Biol Chem* **290**: 13079-13094.

Ling, L.L., Schneider, T., Peoples, A.J., Spoering, A.L., Engels, I., Conlon, B.P., Mueller, A., Schaberle, T.F., Hughes, D.E., Epstein, S., Jones, M., Lazarides, L., Steadman, V.A., Cohen, D.R., Felix, C.R., Fetterman, K.A., Millett, W.P., Nitti, A.G., Zullo, A.M., Chen, C., and Lewis, K. (2015) A new antibiotic kills pathogens without detectable resistance. *Nature* **517**: 455-459.

Lutkenhaus, J. (2007) Assembly dynamics of the bacterial MinCDE system and spatial regulation of the Z ring. *Annu Rev Biochem* **76**: 539-562.

Lyons, N.A., and Kolter, R. (2015) On the evolution of bacterial multicellularity. *Curr Opin Microbiol* **24**: 21-28.

MacNeil, D.J., Gewain, K.M., Ruby, C.L., Dezeny, G., Gibbons, P.H., and MacNeil, T. (1992) Analysis of *Streptomyces avermitilis* genes required for avermectin biosynthesis utilizing a novel integration vector. *Gene* **111**: 61-68.

Mahr, K., van Wezel, G.P., Svensson, C., Krengel, U., Bibb, M.J., and Titgemeyer, F. (2000) Glucose kinase of *Streptomyces coelicolor* A3(2): large-scale purification and biochemical analysis. *Antonie Van Leeuwenhoek* **78**: 253-261.

Mainardi, J.L., Fourgeaud, M., Hugonnet, J.E., Dubost, L., Brouard, J.P., Ouazzani, J., Rice, L.B., Gutmann, L., and Arthur, M. (2005) A novel peptidoglycan cross-linking enzyme for a beta-lactam-resistant transpeptidation pathway. *J Biol Chem* **280**: 38146-38152.

Mainardi, J.L., Morel, V., Fourgeaud, M., Cremniter, J., Blanot, D., Legrand, R., Frehel, C., Arthur, M., Van Heijenoort, J., and Gutmann, L. (2002) Balance between two transpeptidation mechanisms determines the expression of beta-lactam resistance in *Enterococcus faecium*. *J Biol Chem* **277**: 35801-35807.

Mainardi, J.L., Villet, R., Bugg, T.D., Mayer, C., and Arthur, M. (2008) Evolution of peptidoglycan biosynthesis under the selective pressure of antibiotics in Gram-positive bacteria. *FEMS Microbiol Rev* **32**: 386-408.

Maldonado, L.A., Fenical, W., Jensen, P.R., Kauffman, C.A., Mincer, T.J., Ward, A.C., Bull, A.T., and Goodfellow, M. (2005) *Salinispora arenicola* gen. nov., sp. nov. and *Salinispora tropica* sp. nov., obligate marine actinomycetes belonging to the family *Micromonosporaceae*. *Int J Syst Evol Microbiol* **55**: 1759-1766.

Manteca, A., Alvarez, R., Salazar, N., Yague, P., and Sanchez, J. (2008) Mycelium differentiation and antibiotic production in submerged cultures of *Streptomyces coelicolor*. *Appl Environ Microbiol* **74**: 3877-3886.

Manteca, A., Fernandez, M., and Sanchez, J. (2005) Mycelium development in *Streptomyces antibioticus* ATCC11891 occurs in an orderly pattern which determines multiphase growth curves. *BMC Microbiol* **5**: 51.

Manteca, A., Mader, U., Connolly, B.A., and Sanchez, J. (2006) A proteomic analysis of *Streptomyces coelicolor* programmed cell death. *Proteomics* **6**: 6008-6022.

Margolin, W. (2005) FtsZ and the division of prokaryotic cells and organelles. *Nat Rev Mol Cell Biol* **6**: 862-871.

Marshall, C.G., Broadhead, G., Leskiw, B.K., and Wright, G.D. (1997) D-Ala-D-Ala ligases from glycopeptide antibiotic-producing organisms are highly homologous to the enterococcal vancomycin-resistance ligases VanA and VanB. *Proc Natl Acad Sci U S A* **94**: 6480-6483.

Marshall, C.G., Lessard, I.A., Park, I., and Wright, G.D. (1998) Glycopeptide antibiotic resistance genes in glycopeptide-producing organisms. *Antimicrob Agents Chemother* **42**: 2215-2220.

Matsuo, H., Kumagai, T., Mori, K., and Sugiyama, M. (2003) Molecular cloning of a D-cycloserine resistance gene from D-cycloserine-producing *Streptomyces garyphalus*. *J Antibiot (Tokyo)* **56**: 762-767.

Mazza, P., Noens, E.E., Schirner, K., Grantcharova, N., Mommaas, A.M., Koerten, H.K., Muth, G., Flardh, K., van Wezel, G.P., and Wohlleben, W. (2006) MreB of *Streptomyces coelicolor* is not essential for vegetative growth but is required for the integrity of aerial hyphae and spores. *Mol Microbiol* **60**: 838-852.

McCormick, J.R. (2009) Cell division is dispensable but not irrelevant in *Streptomyces*. *Curr Opin Microbiol* **12**: 689-698.

McCormick, J.R., Su, E.P., Driks, A., and Losick, R. (1994) Growth and viability of *Streptomyces coelicolor* mutant for the cell division gene *ftsZ*. *Mol Microbiol* **14**: 243-254.

McHenney, M.A., Hosted, T.J., Dehoff, B.S., Rosteck, P.R., Jr., and Baltz, R.H. (1998) Molecular cloning and physical mapping of the daptomycin gene cluster from *Streptomyces roseosporus*. *J Bacteriol* **180**: 143-151.

Meeske, A.J., Riley, E.P., Robins, W.P., Uehara, T., Mekalanos, J.J., Kahne, D., Walker, S., Kruse, A.C., Bernhardt, T.G., and Rudner, D.Z. (2016) SEDS proteins are a widespread family of bacterial cell wall polymerases. *Nature* **537**: 634-638.

Meeske, A.J., Sham, L.T., Kimsey, H., Koo, B.M., Gross, C.A., Bernhardt, T.G., and Rudner, D.Z. (2015) MurJ and a novel lipid II flippase are required for cell wall biogenesis in *Bacillus subtilis*. *Proc Natl Acad Sci U S A* **112**: 6437-6442.

Meier-Kolthoff, J.P., Auch, A.F., Klenk, H.P., and Göker, M. (2013) Genome sequence-based species delimitation with confidence intervals and improved distance functions. *BMC*

Bioinformatics **14**: 60.

Merrick, M.J. (1976) A morphological and genetic mapping study of bald colony mutants of *Streptomyces coelicolor*. *J Gen Microbiol* **96**: 299-315.

Meyrand, M., Boughammoura, A., Courtin, P., Mezange, C., Guillot, A., and Chapot-Chartier, M.P. (2007) Peptidoglycan N-acetylglucosamine deacetylation decreases autolysis in *Lactococcus lactis*. *Microbiology* **153**: 3275-3285.

Miguelez, E.M., Hardisson, C., and Manzanal, M.B. (1999) Hyphal death during colony development in *Streptomyces antibioticus*: morphological evidence for the existence of a process of cell deletion in a multicellular prokaryote. *J Cell Biol* **145**: 515-525.

Miguelez, E.M., Hardisson, C., and Manzanal, M.B. (2000) Streptomycetes: a new model to study cell death. *Int Microbiol* **3**: 153-158.

Mohammadi, T., Sijbrandi, R., Lutters, M., Verheul, J., Martin, N.I., den Blaauwen, T., de Kruijff, B., and Breukink, E. (2014) Specificity of the transport of lipid II by FtsW in *Escherichia coli*. *J Biol Chem* **289**: 14707-14718.

Mohammadi, T., van Dam, V., Sijbrandi, R., Vernet, T., Zapun, A., Bouhss, A., Diepeveen-de Bruin, M., Nguyen-Disteche, M., de Kruijff, B., and Breukink, E. (2011) Identification of FtsW as a transporter of lipid-linked cell wall precursors across the membrane. *Embo J* **30**: 1425-1432.

Molle, V., Palframan, W.J., Findlay, K.C., and Buttner, M.J. (2000) WhiD and WhiB, homologous proteins required for different stages of sporulation in *Streptomyces coelicolor* A3(2). *J Bacteriol* **182**: 1286-1295.

Morales Angeles, D., Liu, Y., Hartman, A.M., Borisova, M., de Sousa Borges, A., de Kok, N., Beilharz, K., Veening, J.W., Mayer, C., Hirsch, A.K., and Scheffers, D.J. (2017) Pentapeptide-rich peptidoglycan at the *Bacillus subtilis* cell-division site. *Mol Microbiol* **104**: 319-333.

Morollo, A., Petsko, G., and Ringe, D. (1999) Structure of a Michaelis complex analogue: propionate binds in the substrate carboxylate site of alanine racemase. *Biochemistry* **38**: 3293 - 3301.

Mukamolova, G.V., Murzin, A.G., Salina, E.G., Demina, G.R., Kell, D.B., Kaprelyants, A.S., and Young, M. (2006) Muralytic activity of *Micrococcus luteus* Rpf and its relationship to physiological activity in promoting bacterial growth and resuscitation. *Mol Microbiol* **59**: 84-98.

Mukamolova, G.V., Turapov, O.A., Kazarian, K., Telkov, M., Kaprelyants, A.S., Kell, D.B., and Young, M. (2002) The rpf gene of *Micrococcus luteus* encodes an essential secreted growth factor. *Mol Microbiol* **46**: 611-621.

Murray, B.E. (2000) Vancomycin-resistant enterococcal infections. *N Engl J Med* **342**: 710-721.

Murray, P., Barron, E., Phaller, M., Ternover, J., and Yolkken, R. (1999) Manual of Clinical Microbiology. *Mycopathologia* **146**: 107-108.

Murshudov, G.N., Skubak, P., Lebedev, A.A., Pannu, N.S., Steiner, R.A., Nicholls, R.A., Winn, M.D., Long, F., and Vagin, A.A. (2011) REFMAC5 for the refinement of macromolecular crystal structures. *Acta Crystallogr D Biol Crystallogr* **67**: 355-367.

Muthyala, R., Rastogi, N., Shin, W.S., Peterson, M.L., and Sham, Y.Y. (2014) Cell permeable VanX inhibitors as vancomycin re-sensitizing agents. *Bioorg Med Chem Lett* **24**: 2535-2538.

Nagatsu, J., and Suzuki, S. (1963) Studies on an Antitumor Antibiotic, Cervicarcin. Iii. Taxonomic Studies on the Cervicarcin-Producing Organism, *Streptomyces Ogaensis* Nov. Sp. *J Antibiot (Tokyo)* **16**: 203-206.

Nei, M., and Kumar, S. (2000) Molecular evolution and phylogenetics. *Oxford University Press, New York*.

Nikitushkin, V.D., Demina, G.R., Shleeva, M.O., and Kaprelyants, A.S. (2013) Peptidoglycan fragments stimulate resuscitation of “non-culturable” Mycobacteria. *Antonie Van Leeuwenhoek* **103**: 37-46.

Ning, S.B., Guo, H.L., Wang, L., and Song, Y.C. (2002) Salt stress induces programmed cell death in prokaryotic organism *Anabaena*. *J Appl Microbiol* **93**: 15-28.

Noda, M., Kawahara, Y., Ichikawa, A., Matoba, Y., Matsuo, H., Lee, D.G., Kumagai, T., and Sugiyama, M. (2004a) Self-protection mechanism in D-cycloserine-producing *Streptomyces lavendulae*. Gene cloning, characterization, and kinetics of its alanine racemase and D-alanyl-D-alanine ligase, which are target enzymes of D-cycloserine. *J Biol Chem* **279**: 46143-46152.

Noda, M., Matoba, Y., Kumagai, T., and Sugiyama, M. (2004b) Structural evidence that alanine racemase from a D-cycloserine-producing microorganism exhibits resistance to its own product. *J Biol Chem* **279**: 46153-46161.

Noda, M., Matoba, Y., Kumagai, T., and Sugiyama, M. (2005) A novel assay method for an amino acid racemase reaction based on circular dichroism. *Biochem J* **389**: 491 - 496.

Noens, E.E., (2007) Control of sporulation-specific cell division in *Streptomyces coelicolor*. In: PhD Thesis. Leiden: Leiden University, pp.

Noens, E.E., Mersinias, V., Traag, B.A., Smith, C.P., Koerten, H.K., and van Wezel, G.P. (2005) SsgA-like proteins determine the fate of peptidoglycan during sporulation of *Streptomyces coelicolor*. *Mol Microbiol* **58**: 929-944.

Noens, E.E., Mersinias, V., Willemse, J., Traag, B.A., Laing, E., Chater, K.F., Smith, C.P., Koerten, H.K., and van Wezel, G.P. (2007) Loss of the controlled localization of growth stage-specific cell-wall synthesis pleiotropically affects developmental gene expression in an *ssgA* mutant of *Streptomyces coelicolor*. *Mol Microbiol* **64**: 1244-1259.

Nothaft, H., Rigali, S., Boomsma, B., Swiatek, M., McDowall, K.J., van Wezel, G.P., and Titgemeyer, F. (2010) The permease gene *nagE2* is the key to N-acetylglucosamine sensing and utilization in *Streptomyces coelicolor* and is subject to multi-level control. *Mol Microbiol* **75**: 1133-1144.

Novotna, G., Hill, C., Vincent, K., Liu, C., and Hong, H.J. (2012) A novel membrane protein, VanJ, conferring resistance to teicoplanin. *Antimicrob Agents Chemother* **56**: 1784-1796.

Ogawara, H., Kawamura, N., Kudo, T., Suzuki, K.I., and Nakase, T. (1999) Distribution of beta-lactamases in actinomycetes. *Antimicrob Agents Chemother* **43**: 3014-3017.

Okanishi, M., Suzuki, K., and Umezawa, H. (1974) Formation and reversion of *Streptomycete* protoplasts: cultural condition and morphological study. *J Gen Microbiol* **80**: 389-400.

Okoro, C.K., Brown, R., Jones, A.L., Andrews, B.A., Asenjo, J.A., Goodfellow, M., and Bull, A.T. (2009) Diversity of culturable actinomycetes in hyper-arid soils of the Atacama Desert, Chile. *Antonie Van Leeuwenhoek* **95**: 121-133.

Park, J.T., and Strominger, J.L. (1957) Mode of action of penicillin. *Science* **125**: 99-101.

Parker, C.T., Tindall, B.J., and Garrity, G.M. (2015) International Code of Nomenclature of Prokaryotes. *Int J System Evol Microbiol*: 10.1099/ijsem.1090.000778.

Patrick, W., Weisner, J., and Blackburn, J. (2002) Site-directed mutagenesis of Tyr354 in *Geobacillus stearothermophilus* alanine racemase identifies a role in controlling substrate specificity and a possible role in the evolution of antibiotic resistance. *Chembiochem* **3**: 789 - 792.

Perry, J.A., and Wright, G.D. (2013) The antibiotic resistance “mobilome”: searching for the link between environment and clinic. *Front Microbiol* **4**: 138.

Peters, K., Kannan, S., Rao, V.A., Biboy, J., Vollmer, D., Erickson, S.W., Lewis, R.J., Young, K.D., and Vollmer, W. (2016) The Redundancy of Peptidoglycan Carboxypeptidases

Ensures Robust Cell Shape Maintenance in *Escherichia coli*. *MBio* **7**.

Piette, A., Derouaux, A., Gerkens, P., Noens, E.E., Mazzucchelli, G., Vion, S., Koerten, H.K., Titgemeyer, F., De Pauw, E., Leprince, P., van Wezel, G.P., Galleni, M., and Rigali, S. (2005) From dormant to germinating spores of *Streptomyces coelicolor* A3(2): new perspectives from the crp null mutant. *J Proteome Res* **4**: 1699-1708.

Pisabarro, A.G., de Pedro, M.A., and Vazquez, D. (1985) Structural modifications in the peptidoglycan of *Escherichia coli* associated with changes in the state of growth of the culture. *J Bacteriol* **161**: 238-242.

Pluskal, T., Castillo, S., Villar-Briones, A., and Oresic, M. (2010) MZmine 2: modular framework for processing, visualizing, and analyzing mass spectrometry-based molecular profile data. *BMC Bioinformatics* **11**: 395.

Pope, M.K., Green, B., and Westpheling, J. (1998) The *bldB* gene encodes a small protein required for morphogenesis, antibiotic production, and catabolite control in *Streptomyces coelicolor*. *J Bacteriol* **180**: 1556-1562.

Pope, M.K., Green, B.D., and Westpheling, J. (1996) The *bld* mutants of *Streptomyces coelicolor* are defective in the regulation of carbon utilization, morphogenesis and cell--cell signalling. *Mol Microbiol* **19**: 747-756.

Popham, D.L. (2002) Specialized peptidoglycan of the bacterial endospore: the inner wall of the lockbox. *Cell Mol Life Sci* **59**: 426-433.

Popham, D.L., Helin, J., Costello, C.E., and Setlow, P. (1996) Analysis of the peptidoglycan structure of *Bacillus subtilis* endospores. *J Bacteriol* **178**: 6451-6458.

Priyadarshi, A., Lee, E., Sung, M., Nam, K., Lee, W., Kim, E., and Hwang, K. (2009) Structural insights into the alanine racemase from *Enterococcus faecalis*. *Biochim Biophys Acta* **1794**: 1030 - 1040.

Radkov, A.D., and Moe, L.A. (2014) Bacterial synthesis of D-amino acids. *Appl Microbiol Biotechnol* **98**: 5363-5374.

Ramijan, K., Ultee, E., Willemse, J., Wondergem, J., Heinrich, D., Briegel, A., van Wezel, G., and Claessen, D. (2018) Stress-induced formation of cell wall-deficient cells in filamentous actinomycetes. *bioRxiv*.

Ramijan, K., van Wezel, G.P., and Claessen, D. (2017) Genome Sequence of the Filamentous Actinomycete *Kitasatospora viridifaciens*. *Genome Announc* **5**.

Reading, C., and Cole, M. (1977) Clavulanic acid: a beta-lactamase-inhibiting beta-lactam from *Streptomyces clavuligerus*. *Antimicrob Agents Chemother* **11**: 852-857.

Reynolds, P.E. (1989) Structure, biochemistry and mechanism of action of glycopeptide antibiotics. *European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology* **8**: 943-950.

Reynolds, P.E., Depardieu, F., Dutka-Malen, S., Arthur, M., and Courvalin, P. (1994) Glycopeptide resistance mediated by enterococcal transposon Tn1546 requires production of VanX for hydrolysis of D-alanyl-D-alanine. *Mol Microbiol* **13**: 1065-1070.

Rice, K.C., and Bayles, K.W. (2003) Death's toolbox: examining the molecular components of bacterial programmed cell death. *Mol Microbiol* **50**: 729-738.

Rice, L.B. (2001) Emergence of vancomycin-resistant Enterococci. *Emerg Infect Dis* **7**: 183.

Richter, M., and Rossello-Mora, R. (2009) Shifting the genomic gold standard for the prokaryotic species definition. *Proc Natl Acad Sci U S A* **106**: 19126-19131.

Rigali, S., Titgemeyer, F., Barends, S., Mulder, S., Thomae, A.W., Hopwood, D.A., and van Wezel, G.P. (2008) Feast or famine: the global regulator DasR links nutrient stress to antibiotic production by *Streptomyces*. *EMBO Rep* **9**: 670-675.

Rioseras, B., Yague, P., Lopez-Garcia, M.T., Gonzalez-Quinonez, N., Binda, E., Marinelli, F., and Manteca, A. (2016) Characterization of SCO4439, a D-alanyl-D-alanine car-

boxypeptidase involved in spore cell wall maturation, resistance, and germination in *Streptomyces coelicolor*. *Sci Rep* **6**: 21659.

Rocaboy, M., Herman, R., Sauvage, E., Remaut, H., Moonens, K., Terrak, M., Charlier, P., and Kerff, F. (2013) The crystal structure of the cell division amidase AmiC reveals the fold of the AMIN domain, a new peptidoglycan binding domain. *Mol Microbiol* **90**: 267-277.

Rong, X., and Huang, Y. (2012) Taxonomic evaluation of the *Streptomyces hygroscopicus* clade using multilocus sequence analysis and DNA-DNA hybridization, validating the MLSA scheme for systematics of the whole genus. *Systematic and applied microbiology* **35**: 7-18.

Rong, X., and Huang, Y. (2014) Multi-locus sequence analysis: taking prokaryotic systematics to the next level. *Methods Microbiol* **41**: 221–251.

Roper, D.I., Huyton, T., Vagin, A., and Dodson, G. (2000) The molecular basis of vancomycin resistance in clinically relevant Enterococci: crystal structure of D-alanyl-D-lactate ligase (VanA). *Proc Natl Acad Sci U S A* **97**: 8921-8925.

Rutledge, P.J., and Challis, G.L. (2015) Discovery of microbial natural products by activation of silent biosynthetic gene clusters. *Nat Rev Microbiol* **13**: 509-523.

Sacco, E., Hugonnet, J.E., Josseaume, N., Cremniter, J., Dubost, L., Marie, A., Patin, D., Blanot, D., Rice, L.B., Mainardi, J.L., and Arthur, M. (2010) Activation of the L,D-transpeptidation peptidoglycan cross-linking pathway by a metallo-D,D-carboxypeptidase in *Enterococcus faecium*. *Mol Microbiol* **75**: 874-885.

Saitou, N., and Nei, M. (1987) The neighbor-joining method: a new method for reconstructing phylogenetic trees. *Mol Biol Evol* **4**: 406-425.

Sambrook, J., Fritsch, E.F., and Maniatis, T., (1989) *Molecular cloning: a laboratory manual*. Cold Spring Harbor laboratory press, Cold Spring harbor, N.Y.

Sanders, A.N., Wright, L.F., and Pavelka, M.S., Jr. (2014) Genetic characterization of mycobacterial L,D-transpeptidases. *Microbiology* **160**: 1795-1806.

Sasser, M. (1990) Identification of bacteria by gas chromatography of cellular fatty acids *MIDI Inc. Technical Notes* **101**: 1.

Schaberle, T.F., Vollmer, W., Frasch, H.J., Huttel, S., Kulik, A., Rottgen, M., von Thaler, A.K., Wohlleben, W., and Stegmann, E. (2011) Self-resistance and cell wall composition in the glycopeptide producer *Amycolatopsis balhimycina*. *Antimicrobial agents and chemotherapy* **55**: 4283-4289.

Scheffers, D.J., and Tol, M.B. (2015) LipidII: Just Another Brick in the Wall? *PLoS Pathog* **11**: e1005213.

Schleifer, K.H., and Kandler, O. (1972) Peptidoglycan types of bacterial cell walls and their taxonomic implications. *Bacteriol Rev* **36**: 407-477.

Schneider, T., and Sahl, H.G. (2010) An oldie but a goodie - cell wall biosynthesis as antibiotic target pathway. *Int J Med Microbiol* **300**: 161-169.

Sexton, D.L., St-Onge, R.J., Haiser, H.J., Yousef, M.R., Brady, L., Gao, C., Leonard, J., and Elliot, M.A. (2015) Resuscitation-promoting factors are cell wall-lytic enzymes with important roles in the germination and growth of *Streptomyces coelicolor*. *J Bacteriol* **197**: 848-860.

Sham, L.T., Butler, E.K., Lebar, M.D., Kahne, D., Bernhardt, T.G., and Ruiz, N. (2014) MurJ is the flippase of lipid-linked precursors for peptidoglycan biogenesis. *Science* **345**: 220-222.

Shapiro, J.A. (1988) Bacteria as multicellular organisms. *Sci Am* **256**: 82-89.

Shaw, J.P., Petsko, G.A., and Ringe, D. (1997) Determination of the Structure of Alanine Racemase from *Bacillus stearothermophilus* at 1.9-Å Resolution. *Biochemistry* **36**:

1329-1342.

Shinobu, R. (1955) On *Streptomyces hiroshimensis* nov. sp. *Seibutsugakkaishi* **6**: 43-46.

Shirling, E., and Gottlieb, D. (1966) Methods for characterization of *Streptomyces* species. *Int J Syst Evol Microbiol* **16:313-340**.

Silver, L.L. (2013) Viable screening targets related to the bacterial cell wall. *Ann N Y Acad Sci* **1277**: 29-53.

Smith, C.A. (2006) Structure, function and dynamics in the mur family of bacterial cell wall ligases. *J Mol Biol* **362**: 640-655.

Smith, T.L., Pearson, M.L., Wilcox, K.R., Cruz, C., Lancaster, M.V., Robinson-Dunn, B., Tenover, F.C., Zervos, M.J., Band, J.D., and White, E. (1999) Emergence of vancomycin resistance in *Staphylococcus aureus*. *N Engl J Med* **340**: 493-501.

Sogaard-Andersen, L., and Yang, Z. (2008) Programmed cell death: role for MazF and MrpC in *Myxococcus* multicellular development. *Curr Biol* **18**: R337-339.

Steen, A., Palumbo, E., Deghorain, M., Cocconcelli, P.S., Delcour, J., Kuipers, O.P., Kok, J., Buist, G., and Hols, P. (2005) Autolysis of *Lactococcus lactis* is increased upon D-alanine depletion of peptidoglycan and lipoteichoic acids. *J Bacteriol* **187**: 114-124.

Strych, U., Davlieva, M., Longtin, J.P., Murphy, E.L., Im, H., Benedik, M.J., and Krause, K.L. (2007) Purification and preliminary crystallization of alanine racemase from *Streptococcus pneumoniae*. *BMC Microbiol* **7**: 40.

Susstrunk, U., Pidoux, J., Taubert, S., Ullmann, A., and Thompson, C.J. (1998) Pleiotropic effects of cAMP on germination, antibiotic biosynthesis and morphological development in *Streptomyces coelicolor*. *Mol Microbiol* **30**: 33-46.

Swiatek, M.A., Tenconi, E., Rigali, S., and van Wezel, G.P. (2012) Functional analysis of the N-acetylglucosamine metabolic genes of *Streptomyces coelicolor* and role in the control of development and antibiotic production. *J Bacteriol* **194**: 1136-1144.

Sycuro, L.K., Wyckoff, T.J., Biboy, J., Born, P., Pincus, Z., Vollmer, W., and Salama, N.R. (2012) Multiple peptidoglycan modification networks modulate *Helicobacter pylori*'s cell shape, motility, and colonization potential. *PLoS Pathog* **8**: e1002603.

Takacs, C.N., Hocking, J., Cabeen, M.T., Bui, N.K., Poggio, S., Vollmer, W., and Jacobs-Wagner, C. (2013) Growth medium-dependent glycine incorporation into the peptidoglycan of *Caulobacter crescentus*. *PLoS One* **8**: e57579.

Takahashi, Y. (2017) Genus *Kitasatospora*, taxonomic features and diversity of secondary metabolites. *J Antibiot (Tokyo)* **70**: 506-513.

Takahashi, Y., Seino, A., Iwai, Y., and Omura, S. (1999) Taxonomic study and morphological differentiation of an actinomycete genus, *Kitasatospora*. *Zentralbl Bakteriol* **289**: 265-284.

Tamura, K., Peterson, D., Peterson, N., Stecher, G., Nei, M., and Kumar, S. (2011) MEGA5: molecular evolutionary genetics analysis using maximum likelihood, evolutionary distance, and maximum parsimony methods. *Mol Biol Evol* **28**: 2731-2739.

Tan, A.L., Loke, P., and Sim, T.S. (2002) Molecular cloning and functional characterisation of VanX, a D-alanyl-D-alanine dipeptidase from *Streptomyces coelicolor* A3(2). *Res Microbiol* **153**: 27-32.

Tassoni, R., van der Aart, L.T., Ubbink, M., van Wezel, G.P., and Pannu, N.S. (2017) Structural and functional characterization of the alanine racemase from *Streptomyces coelicolor* A3(2). *Biochem Biophys Res Commun* **483**: 122-128.

Taylor, S.D., and Palmer, M. (2016) The action mechanism of daptomycin. *Bioorg Med Chem* **24**: 6253-6268.

Tenconi, E., Traxler, M.F., Hoebreck, C., van Wezel, G.P., and Rigali, S. (2018) Production of prodiginines Is part of a programmed cell death process in *Streptomyces coelicolor*.

Frontiers Microbiol: in press.

Thaker, M.N., Kalan, L., Waglechner, N., Eshaghi, A., Patel, S.N., Poutanen, S., Willey, B., Coburn, B., McGeer, A., Low, D.E., and Wright, G.D. (2015) Vancomycin-variable enterococci can give rise to constitutive resistance during antibiotic therapy. *Antimicrob Agents Chemother* **59**: 1405-1410.

Thompson, J.D., Higgins, D.G., and Gibson, T.J. (1994) CLUSTAL W: improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position-specific gap penalties and weight matrix choice. *Nucleic Acids Res* **22**: 4673-4680.

Traag, B.A., and van Wezel, G.P. (2008) The SsgA-like proteins in actinomycetes: small proteins up to a big task. *Antonie Van Leeuwenhoek* **94**: 85-97.

Uehara, T., Parzych, K.R., Dinh, T., and Bernhardt, T.G. (2010) Daughter cell separation is controlled by cytokinetic ring-activated cell wall hydrolysis. *Embo J* **29**: 1412-1422.

Urem, M., Swiatek-Polatynska, M.A., Rigali, S., and van Wezel, G.P. (2016) Intertwining nutrient-sensory networks and the control of antibiotic production in *Streptomyces*. *Mol Microbiol* **102**: 183-195.

Vagin, A., and Teplyakov, A. (1997) MOLREP: an Automated Program for Molecular Replacement. *Journal of Applied Crystallography* **30**: 1022-1025.

van der Aart, L.T., Spijksma, G.K., Harms, A., Vollmer, W., Hankemeier, T., and van Wezel, G.P. (2018) High-resolution analysis of the peptidoglycan composition in *Streptomyces coelicolor*. *J Bacteriol*.

van der Heul, H.U., Bilyk, B.L., McDowall, K.J., Seipke, R.F., and van Wezel, G.P. (2018) Regulation of antibiotic production in Actinobacteria: new perspectives from the post-genomic era. *Nat Prod Rep* **35**: 575-604.

van der Meij, A., Worsley, S.F., Hutchings, M.I., and van Wezel, G.P. (2017) Chemical ecology of antibiotic production by actinomycetes. *FEMS Microbiol Rev* **41**: 392-416.

van Dissel, D., Claessen, D., and Van Wezel, G.P. (2014) Morphogenesis of *Streptomyces* in submerged cultures. *Adv Appl Microbiol* **89**: 1-45.

van Wageningen, A.M., Kirkpatrick, P.N., Williams, D.H., Harris, B.R., Kershaw, J.K., Lennard, N.J., Jones, M., Jones, S.J., and Solenberg, P.J. (1998) Sequencing and analysis of genes involved in the biosynthesis of a vancomycin group antibiotic. *Chem Biol* **5**: 155-162.

van Wezel, G.P., Krabben, P., Traag, B.A., Keijser, B.J., Kerste, R., Vijgenboom, E., Heijnen, J.J., and Kraal, B. (2006) Unlocking *Streptomyces* spp. for use as sustainable industrial production platforms by morphological engineering. *Appl Environ Microbiol* **72**: 5283-5288.

van Wezel, G.P., Mahr, K., Konig, M., Traag, B.A., Pimentel-Schmitt, E.F., Willimek, A., and Titgemeyer, F. (2005) GlcP constitutes the major glucose uptake system of *Streptomyces coelicolor* A3(2). *Mol Microbiol* **55**: 624-636.

van Wezel, G.P., and McDowall, K.J. (2011) The regulation of the secondary metabolism of *Streptomyces*: new links and experimental advances. *Nat Prod Rep* **28**: 1311-1333.

van Wezel, G.P., van der Meulen, J., Kawamoto, S., Luiten, R.G., Koerten, H.K., and Kraal, B. (2000a) *ssgA* is essential for sporulation of *Streptomyces coelicolor* A3(2) and affects hyphal development by stimulating septum formation. *J Bacteriol* **182**: 5653-5662.

van Wezel, G.P., White, J., Hoogvliet, G., and Bibb, M.J. (2000b) Application of *redD*, the transcriptional activator gene of the undecylprodigiosin biosynthetic pathway, as a reporter for transcriptional activity in *Streptomyces coelicolor* A3(2) and *Streptomyces lividans*. *J Mol Microbiol Biotechnol* **2**: 551-556.

Vara, J., Lewandowska-Skarbek, M., Wang, Y.G., Donadio, S., and Hutchinson, C.R. (1989)

Cloning of genes governing the deoxysugar portion of the erythromycin biosynthesis pathway in *Saccharopolyspora erythraea* (*Streptomyces erythreus*). *J Bacteriol* **171**: 5872-5881.

Verkade, P. (2008) Moving EM: the Rapid Transfer System as a new tool for correlative light and electron microscopy and high throughput for high-pressure freezing. *Journal of microscopy* **230**: 317-328.

Vollmer, W. (2008) Structural variation in the glycan strands of bacterial peptidoglycan. *FEMS Microbiol Rev* **32**: 287-306.

Vollmer, W., Blanot, D., and de Pedro, M.A. (2008a) Peptidoglycan structure and architecture. *FEMS Microbiol Rev* **32**: 149-167.

Vollmer, W., Joris, B., Charlier, P., and Foster, S. (2008b) Bacterial peptidoglycan (murein) hydrolases. *FEMS Microbiol Rev* **32**: 259-286.

Waksman, S.A., and Henrici, A.T. (1943) The Nomenclature and Classification of the Actinomycetes. *J Bacteriol* **46**: 337-341.

Walsh, C.T. (1989) Enzymes in the D-alanine branch of bacterial cell wall peptidoglycan assembly. *J Biol Chem* **264**: 2393-2396.

Walsh, C.T., Fisher, S.L., Park, I.S., Prahalad, M., and Wu, Z. (1996) Bacterial resistance to vancomycin: five genes and one missing hydrogen bond tell the story. *Chem Biol* **3**: 21-28.

Wang, Z.M., Li, X., Cocklin, R.R., Wang, M., Fukase, K., Inamura, S., Kusumoto, S., Gupta, D., and Dziarski, R. (2003) Human peptidoglycan recognition protein-L is an N-acetylmuramoyl-L-alanine amidase. *J Biol Chem* **278**: 49044-49052.

Wayne, L.G., Brenner, D.J., Colwell, R.R., Grimont, P.A.D., Kandler, O., Krichevsky, M.I., Moore, L.H., Moore, W.E.C., Murray, R.G.E., Stackebrandt, E., Starr, M.P., and Truper, H.G. (1987) Report of the Ad-Hoc-Committee on Reconciliation of Approaches to Bacterial Systematics. *Int J Syst Bacteriol* **37**: 463-464.

WHO, (2014) *Antimicrobial Resistance: Global Report on Surveillance*. Geneva, Switserland.

Wiener, P., Egan, S., and Wellington, E. (1998) Evidence for transfer of antibiotic resistance genes in soil populations of streptomycetes. *Mol Ecol* **7**: 1205-1216.

Willemse, J., Borst, J.W., de Waal, E., Bisseling, T., and van Wezel, G.P. (2011) Positive control of cell division: FtsZ is recruited by SsgB during sporulation of *Streptomyces*. *Genes Dev* **25**: 89-99.

Willemse, J., and van Wezel, G.P. (2009) Imaging of *Streptomyces coelicolor* A3(2) with Reduced Autofluorescence Reveals a Novel Stage of FtsZ Localization. *PLoS ONE* **4**: e4242.

Williams, S.T., Goodfellow, M., Alderson, G., Wellington, E.M., Sneath, P.H., and Sackin, M.J. (1983) Numerical classification of *Streptomyces* and related genera. *J Gen Microbiol* **129**: 1743-1813.

Winn, M.D., Ballard, C.C., Cowtan, K.D., Dodson, E.J., Emsley, P., Evans, P.R., Keegan, R.M., Krissinel, E.B., Leslie, A.G.W., McCoy, A., McNicholas, S.J., Murshudov, G.N., Pannu, N.S., Potterton, E.A., Powell, H.R., Read, R.J., Vagin, A., and Wilson, K.S. (2011) Overview of the CCP4 suite and current developments. *Acta Crystallographica Section D: Biological Crystallography* **67**: 235-242.

Witt, D., and Stackebrandt, E. (1990) Unification of the Genera *Streptoverticillum* and *Streptomyces*, and Amendation of *Streptomyces*-Waksman and Henrici-1943, 339al. *Syst Appl Microbiol* **13**: 361-371.

Wolanski, M., Wali, R., Tilley, E., Jakimowicz, D., Zakrzewska-Czerwinska, J., and Herron, P. (2011) Replisome trafficking in growing vegetative hyphae of *Streptomyces coelicolor* A3(2). *J Bacteriol* **193**: 1273-1275.

Wright, G.D., and Walsh, C.T. (1992) D-Alanyl-D-Alanine Ligases and the Molecular Mechanism of Vancomycin Resistance. *Accounts Chem Res* **25**: 468-473.

Wu, C., Du, C., Ichinose, K., Choi, Y.H., and van Wezel, G.P. (2017a) Discovery of C-Glycosylpyranonaphthoquinones in *Streptomyces* sp. MBT76 by a Combined NMR-Based Metabolomics and Bioinformatics Workflow. *J Nat Prod* **80**: 269-277.

Wu, C., Ichinose, K., Choi, Y.H., and van Wezel, G.P. (2017b) Aromatic polyketide GTRI-02 is a previously unidentified product of the *act* gene cluster in *Streptomyces coelicolor* A3(2). *Chembiochem* **18**: 1428-1434.

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

Wu, C., Zhu, H., van Wezel, G.P., and Choi, Y.H. (2016) Metabolomics-guided analysis of isocoumarin production by *Streptomyces* species MBT76 and biotransformation of flavonoids and phenylpropanoids. *Metabolomics* **12**: 90.

Wu, D., Hu, T., Zhang, L., Chen, J., Du, J., Ding, J., Jiang, H., and Shen, X. (2008) Residues Asp164 and Glu165 at the substrate entryway function potently in substrate orientation of alanine racemase from E. coli: Enzymatic characterization with crystal structure analysis. *Protein Sci* **17**: 1066 - 1076.

Wu, L.J., and Errington, J. (2011) Nucleoid occlusion and bacterial cell division. *Nat Rev Microbiol* **10**: 8-12.

Wu, Z., Wright, G.D., and Walsh, C.T. (1995) Overexpression, purification, and characterization of VanX, a D-, D-dipeptidase which is essential for vancomycin resistance in *Enterococcus faecium* BM4147. *Biochemistry* **34**: 2455-2463.

Xia, J., Sinelnikov, I.V., Han, B., and Wishart, D.S. (2015) MetaboAnalyst 3.0--making metabolomics more meaningful. *Nucleic Acids Res* **43**: W251-257.

Xie, J., Pierce, J.G., James, R.C., Okano, A., and Boger, D.L. (2011) A redesigned vancomycin engineered for dual D-Ala-D-ala And D-Ala-D-Lac binding exhibits potent antimicrobial activity against vancomycin-resistant bacteria. *J Am Chem Soc* **133**: 13946-13949.

Yague, P., Lopez-Garcia, M.T., Rioseras, B., Sanchez, J., and Manteca, A. (2013) Pre-sporulation stages of *Streptomyces* differentiation: state-of-the-art and future perspectives. *FEMS Microbiol Lett* **342**: 79-88.

Yague, P., Manteca, A., Simon, A., Diaz-Garcia, M.E., and Sanchez, J. (2010) New method for monitoring programmed cell death and differentiation in submerged *Streptomyces* cultures. *Appl Environ Microbiol* **76**: 3401-3404.

Yague, P., Willemse, J., Koning, R.I., Rioseras, B., Lopez-Garcia, M.T., Gonzalez-Quinonez, N., Lopez-Iglesias, C., Shliaha, P.V., Rogowska-Wrzesinska, A., Koster, A.J., Jensen, O.N., van Wezel, G.P., and Manteca, A. (2016) Subcompartmentalization by cross-membranes during early growth of *Streptomyces* hyphae. *Nat Commun* **7**: 12467.

Yamasaki, M., Miyashita, K., Cullum, J., and Kinashi, H. (2000) A complex insertion sequence cluster at a point of interaction between the linear plasmid SCP1 and the linear chromosome of *Streptomyces coelicolor* A3 (2). *J Bacteriol* **182**: 3104-3110.

Yang, D.C., Peters, N.T., Parzych, K.R., Uehara, T., Markovski, M., and Bernhardt, T.G. (2011a) An ATP-binding cassette transporter-like complex governs cell-wall hydrolysis at the bacterial cytokinetic ring. *Proc Natl Acad Sci U S A* **108**: E1052-1060.

Yang, K.-W., Cheng, X., Zhao, C., Liu, C.-C., Jia, C., Feng, L., Xiao, J.-M., Zhou, L.-S., Gao, H.-Z., and Yang, X. (2011b) Synthesis and activity study of phosphonamidate dipeptides as potential inhibitors of VanX. *Bioorg Med Chem Lett* **21**: 7224-7227.

Yoon, S.H., Ha, S.M., Kwon, S., Lim, J., Kim, Y., Seo, H., and Chun, J. (2017a) Introducing

EzBioCloud: a taxonomically united database of 16S rRNA gene sequences and whole-genome assemblies. *Int J System Evol Microbiol* **67**: 1613-1617.

Yoon, S.H., Ha, S.M., Lim, J., Kwon, S., and Chun, J. (2017b) A large-scale evaluation of algorithms to calculate average nucleotide identity. *Antonie Van Leeuwenhoek* **110**: 1281-1286.

Zarlenga, L.J., Gilmore, M.S., and Sahm, D.F. (1992) Effects of amino acids on expression of enterococcal vancomycin resistance. *Antimicrob Agents Chemother* **36**: 902-905.

Zhang, L., Willemse, J., Claessen, D., and van Wezel, G.P. (2016a) SepG coordinates sporulation-specific cell division and nucleoid organization in *Streptomyces coelicolor*. *Open Biol* **6**: 150164.

Zhang, Z., Claessen, D., and Rozen, D.E. (2016b) Understanding Microbial Divisions of Labor. *Front Microbiol* **7**: 2070.

Zhang, Z., Wang, Y., and Ruan, J. (1997) A proposal to revive the genus *Kitasatospora* (Omura, Takahashi, Iwai, and Tanaka 1982). *Int J Syst Bacteriol* **47**: 1048-1054.

Zhu, H., Sandiford, S.K., and van Wezel, G.P. (2014a) Triggers and cues that activate antibiotic production by actinomycetes. *J Ind Microbiol Biotechnol* **41**: 371-386.

Zhu, H., Swierstra, J., Wu, C., Girard, G., Choi, Y.H., van Wamel, W., Sandiford, S.K., and van Wezel, G.P. (2014b) Eliciting antibiotics active against the ESKAPE pathogens in a collection of actinomycetes isolated from mountain soils. *Microbiology* **160**: 1714-1725.

Ziemert, N., Lechner, A., Wietz, M., Millan-Aguinaga, N., Chavarria, K.L., and Jensen, P.R. (2014) Diversity and evolution of secondary metabolism in the marine actinomycete genus *Salinispora*. *Proc Natl Acad Sci U S A* **111**: E1130-1139.

Curriculum vitae

Lizah Tanja van der Aart was born on the 7th of August 1991 in Haarlem, the Netherlands. In 2009, she graduated with a Nature and Health profile from the Kennemer Lyceum in Overveen. That same year, she started her Bachelor's programme at the Institute of Biology, Leiden University. She finished her Bachelor's studies in 2012 with a research internship p on the topic of Streptomyces L-forms in the group of Dr. Dennis Claessen. Lizah then followed a Masters programme in Molecular Biotechnology and Health at the Leiden University where she did a research project on Streptomyces development in the lab of Prof. Gilles van Wezel. In the summer of 2014 she joined a Top Sector competition hosted by the NWO with the team "Pulp Fraction" and worked on the reduction of orange peel waste using Natural Deep Eutectic Solvents (NADES) under the supervision of Prof.Dr. Geert-Jan Witkamp and Dr. Young Choi at the Plant Sciences and Natural Products lab at the Leiden University. She obtained her Master degree, cum laude, in 2014. That same year, Lizah began as a PhD student under the supervision of Prof. Gilles van Wezel and Prof. Thomas Hankemeier; the results of this work are presented in this thesis. During her work as a PhD student, she has spent 3 weeks in Prof. Waldemar Vollmer's lab to learn about peptidoglycan isolation and analysis. She received an EMBO short-term fellowship to spend two months in the Lab of Prof. Michael Goodfellow to perform taxonomy on Streptomyces roseifaciens. She participated at several conferences, among which the ISBA17 in Turkey, The Great Wall Symposium 2017 in Portugal, and the GRC Cell Surface Conference at Mount Snow, USA, 2018. After her PhD, she will join the lab of Prof. Jeff Errington at the Centre for Bacterial Cell Biology in Newcastle upon Tyne (United Kingdom).

List of publications:

Lizah T. van der Aart, Imen Nouioui, Alexander Kloosterman, Joost Willemse, Hua Zhu, Michael Goodfellow, Gilles P. van Wezel. (2019) Classification of *Streptomyces roseifaciens* sp. nov. as a novel verticillate strain with high potential for specialized metabolite production. *IJSEM*, Jan 9.

Lizah T. van der Aart, Gerwin K. Spijksma, Amy Harms, Waldemar Vollmer, Thomas Hankemeier, Gilles P. van Wezel. (2018) High-resolution analysis of the peptidoglycan composition in *Streptomyces coelicolor*. J Bacteriol 200:e00290-18. (with Cover image)

Raffaella Tassoni, Lizah T. van der Aart, Marcellus Ubbink, Gilles P.van Wezel, Navraj S.Pannu. (2017) Structural and functional characterization of the alanine racemase from *Streptomyces coelicolor* A3(2) Biochemical and Biophysical Research Communications Vol. 483, Issue 1, 29 January 2017, Pages 122-128

Lizah T. van der Aart, Nicole Lemmens, Willem J van Wamel, Gilles P. van Wezel. (2016) Substrate inhibition of VanA by D-alanine reduces vancomycin resistance in a VanX-dependent manner. Antimicrob. Agents Chemother. vol. 60 no. 8 4930-4939

Patent application:

Lizah T. van der Aart, Nicole Lemmens, Willem J van Wamel, Gilles P. van Wezel. (2016) Composition and method for treating infections caused by vancomycin-resistant infectious agents in a subject. European Patent Application PCT/NL2016/050919

Popular Scientific blog posts (Dutch):

Lizah van der Aart and Anne van der Meij write about microbiology for Wetenschap.nu
https://wetenschap.nu/auteur/lizah-van-der-aart-en-anne-van-der-meij/