REFENRENCE

1. Ahmed, M., L. Lyass, P.N. Markham, S.S. Taylor, N. Vazquez-Laslop, and A.A. Neyfakh. 1995. Two highly similar multidrug transporters of *Bacillus subtilis* whose expression is differentially regulated. *J Bacteriol JID - 2985120R* 177:3904-3910.

2. Aleixandre, V., G. Herrera, A. Urios, and M. Blanco. 1991. Effects of ciprofloxacin on plasmid DNA supercoiling of *Escherichia coli* topoisomerase I and gyrase mutants. *Antimicrob Agents Chemother JID - 0315061* 35:20-23.

3. Alekshun, M.N. and S.B. Levy. 1997. Regulation of chromosomally mediated multiple antibiotic resistance: the mar regulon. *Antimicrob Agents Chemother JID - 0315061* 41:2067-2075.

4. Andersen, J., N. Delihas, K. Ikenaka, P.J. Green, O. Pines, O. Ilercil, and M. Inouye. 1987. The isolation and characterization of RNA coded by the micF gene in *Escherichia coli. Nucleic Acids Res JID - 0411011* 15:2089-2101.

5. Aoyama, H., K. Sato, T. Kato, K. Hirai, and S. Mitsuhashi. 1987. Norfloxacin resistance in a clinical isolate of *Escherichia coli*. *Antimicrob Agents Chemother JID - 0315061* 31:1640-1641.

6. Aoyama, H., K. Sato, T. Fujii, K. Fujimaki, M. Inoue, and S. Mitsuhashi. 1988. Purification of *Citrobacter freundii* DNA gyrase and inhibition by quinolones. *Antimicrob Agents Chemother JID - 0315061* 32:104-109.

7. Ariza, R.R., S.P. Cohen, N. Bachhawat, S.B. Levy, and B. Demple. 1994. Repressor mutations in the *marRAB* operon that activate oxidative stress genes and multiple antibiotic resistance in *Escherichia coli*. *J Bacteriol JID - 2985120R* 176:143-148.

8. Barker, W.H.J. and E.J. Gangarosa. 1974. Food poisoning due to *Vibrio parahaemolyticus*. *Annu Rev Med JID - 2985151R* 25:75-81.

9. Barnard, F.M. and A. Maxwell. 2001. Interaction between DNA gyrase and quinolones: effects of alanine mutations at GyrA subunit residues Ser(83) and Asp(87). *Antimicrob Agents Chemother JID - 0315061* 45:1994-2000.

10. Barnard, F.M. and A. Maxwell. 2001. Interaction between DNA gyrase and quinolones: effects of alanine mutations at GyrA subunit residues Ser(83) and Asp(87). *Antimicrob Agents Chemother JID - 0315061* 45:1994-2000.

11. Barrett, T.J., P.A. Blake, G.K. Morris, N.D. Puhr, H.B. Bradford, and J.G. Wells. 1980. Use of Moore swabs for isolating *Vibrio cholerae* from sewage. *J Clin Microbiol JID - 7505564* 11:385-388.

12. Bates, A.D., M.H. O'Dea, and M. Gellert. 1996. Energy coupling in *Escherichia coli* DNA gyrase: the relationship between nucleotide binding, strand passage, and DNA supercoiling. *Biochemistry JID - 0370623* 35:1408-1416.

13. Baumann, P., and R.H.W. Schubert. 1984. Family II. *Vibrionaceae* Vernon 1965, 5245^{AL}. In *Bergey's manual of systematic bacteriology*, vol. 1.(N.R. Krieg and J.G. Holt Eds.), p. 516-517, The Wilkins Co., Baltimore.

14. Belland, R.J., S.G. Morrison, C. Ison, and W.M. Huang. 1994. *Neisseria gonorrhoeae* acquires mutations in analogous regions of *gyrA* and *parC* in fluoroquinolone-resistant isolates. *Mol Microbiol JID - 8712028* 14:371-380.

15. Blake, P.A., R.E. Weaver, and D.G. Hollis. 1980. Diseases of humans (other than cholera) caused by vibrios. *Annu Rev Microbiol JID - 0372370* 34:341-367.

16. Breines, D.M., S. Ouabdesselam, E.Y. Ng, J. Tankovic, S. Shah, C.J. Soussy, and D.C. Hooper. 1997. Quinolone resistance locus *nfxD* of *Escherichia coli* is

a mutant allele of the *parE* gene encoding a subunit of topoisomerase IV. *Antimicrob Agents Chemother JID - 0315061* 41:175-179.

17. Chowdhury, N.R., S. Chakraborty, T. Ramamurthy, M. Nishibuchi, S. Yamasaki, Y. Takeda, and G.B. Nair. 2000. Molecular evidence of clonal *Vibrio parahaemolyticus* pandemic strains. *Emerg Infect Dis JID - 9508155* 6:631-636.

18. Chou, J.H., J.L. Greenberg, B. Demple.1998. Postranscriptional repression of *Escherichia coli* OmpF protein in response to redox stress: possitive control of the *micF* antisense RNA by the *soxRS* locus. *J Bacteriol*; 175: 1026-1031.

19. Chowdhury, N.R., S. Chakraborty, B. Eampokalap, W. Chaicumpa, M. Chongsa-Nguan, P. Moolasart, R. Mitra, T. Ramamurthy, S.K. Bhattacharya, M. Nishibuchi, Y. Takeda, and G.B. Nair. 2000. Clonal dissemination of *Vibrio parahaemolyticus* displaying similar DNA fingerprint but belonging to two different serovars (O3:K6 and O4:K68) in Thailand and India. *Epidemiol Infect JID - 8703737* 125:17-25.

20. Chu, D.T., P.B. Fernandes, A.K. Claiborne, L. Shen, and A.G. Pernet. 1988. Structure-activity relationships in quinolone antibacterials: design,

synthesis and biological activities of novel isothiazoloquinolones. *Drugs Exp Clin Res JID - 7802135* 14:379-383.

21. Chu, D.T. and P.B. Fernandes. 1989. Structure-activity relationships of the fluoroquinolones. *Antimicrob Agents Chemother JID - 0315061* 33:131-135.

22. Cohen, S.P., L.M. McMurry, and S.B. Levy. 1988. marA locus causes decreased expression of OmpF porin in multiple-antibiotic-resistant (Mar) mutants of *Escherichia coli. J Bacteriol JID - 2985120R* 170:5416-5422.

23. Cohen, S.P., L.M. McMurry, D.C. Hooper, J.S. Wolfson, and S.B. Levy. 1989. Cross-resistance to fluoroquinolones in multiple-antibiotic-resistant (Mar) Escherichia coli selected by tetracycline or chloramphenicol: decreased drug accumulation associated with membrane changes in addition to OmpF reduction. *Antimicrob Agents Chemother JID - 0315061* 33:1318-1325.

24. De, S.P., M. Banerjee, B.C. Deb, P.G. Sengupta, J. Sil, B.K. Sircar, D. Sen, A. Ghosh, and S.C. Pal. 1977. Distribution of vibrios in Calcutta environment with particular reference to *V. parahaemolyticus. Indian J Med Res JID - 0374701* 65:21-28.

25. Deguchi, T., A. Fukuoka, M. Yasuda, M. Nakano, S. Ozeki, E. Kanematsu, Y. Nishino, S. Ishihara, Y. Ban, and Y. Kawada. 1997. Alterations in the

GyrA subunit of DNA gyrase and the ParC subunit of topoisomerase IV in quinolone-resistant clinical isolates of *Klebsiella pneumoniae*. *Antimicrob Agents Chemother JID - 0315061* 41:699-701.

26. Dessus-Babus, S., C.M. Bebear, A. Charron, C. Bebear, and B. de Barbeyrac. 1998. Sequencing of gyrase and topoisomerase IV quinolone-resistance-determining regions of *Chlamydia trachomatis* and characterization of quinolone-resistant mutants obtained In vitro. *Antimicrob Agents Chemother JID - 0315061* 42:2474-2481.

27. Doyle, M.P. 1990. Pathogenic *Escherichia coli*, *Yersinia enterocolitica*, and *Vibrio parahaemolyticus*. *Lancet JID - 2985213R* 336:1111-1115.

28. Farmer, J.J., III, E.W. Hickmann-Brenner, and M.T. Kelly. 1985. *Vibrio*, In *Manual of clinical microbiology*, 4th ed. (E.H. Lennette, A. Balows, W.J. Hausler, Jr., and H.J. Shadomy, Eds.), p. 282-301. American Society for Microbiology, Washington, D.C.

29. Ferrero, L., B. Cameron, B. Manse, D. Lagneaux, J. Crouzet, A. Famechon, and F. Blanche. 1994. Cloning and primary structure of *Staphylococcus aureus* DNA topoisomerase IV: a primary target of fluoroquinolones. *Mol Microbiol JID - 8712028* 13:641-653.

30. Fitzgibbon, J.E., J.F. John, J.L. Delucia, and D.T. Dubin. 1998. Topoisomerase mutations in trovafloxacin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother JID - 0315061* 42:2122-2124.

31. Fournier, B. and D.C. Hooper. 1998. Mutations in topoisomerase IV and DNA gyrase of *Staphylococcus aureus*: novel pleiotropic effects on quinolone and coumarin activity. *Antimicrob Agents Chemother JID - 0315061* 42:121-128.

32. George, A.M. and S.B. Levy. 1983. Gene in the major cotransduction gap of the *Escherichia coli* K-12 linkage map required for the expression of chromosomal resistance to tetracycline and other antibiotics. *J Bacteriol JID - 2985120R* 155:541-548.

33. George, A.M. and S.B. Levy. 1983. Amplifiable resistance to tetracycline, chloramphenicol, and other antibiotics in *Escherichia coli*: involvement of a non-plasmid-determined efflux of tetracycline. *J Bacteriol JID - 2985120R* 155:531-540.

34. George, A.M., R.M. Hall, and H.W. Stokes. 1995. Multidrug resistance in *Klebsiella pneumoniae*: a novel gene, ramA, confers a multidrug resistance phenotype in *Escherichia coli*. *Microbiology JID - 9430468* 141 (Pt 8):1909-1920.

35. Georgiou, M., R. Munoz, F. Roman, R. Canton, R. Gomez-Lus, J. Campos, and A.G. De La Campa. 1996. Ciprofloxacin-resistant *Haemophilus influenzae* strains possess mutations in analogous positions of GyrA and ParC. *Antimicrob Agents Chemother JID - 0315061* 40:1741-1744.

36. Gootz, T.D. and B.A. Martin. 1991. Characterization of high-level quinolone resistance in *Campylobacter jejuni*. *Antimicrob Agents Chemother JID - 0315061* 35:840-845.

37. Gootz, T.D., R. Zaniewski, S. Haskell, B. Schmieder, J. Tankovic, D. Girard, P. Courvalin, and R.J. Polzer. 1996. Activity of the new fluoroquinolone trovafloxacin (CP-99,219) against DNA gyrase and topoisomerase IV mutants of *Streptococcus pneumoniae* selected in vitro. *Antimicrob Agents Chemother JID - 0315061* 40:2691-2697.

38. Hays, J.B. and S. Boehmer. 1978. Antagonists of DNA gyrase inhibit repair and recombination of UV-irradiated phage lambda. *Proc Natl Acad Sci U S A JID - 7505876* 75:4125-4129.

39. Heisig, P. 1996. Genetic evidence for a role of parC mutations in development of high-level fluoroquinolone resistance in *Escherichia coli*. *Antimicrob Agents Chemother JID - 0315061* 40:879-885.

40. Hiasa, H., D.O. Yousef, and K.J. Marians. 1996. DNA strand cleavage is required for replication fork arrest by a frozen topoisomerase-quinolone-DNA ternary complex. *J Biol Chem JID - 2985121R* 271:26424-26429.

41. Hirai, K., H. Aoyama, T. Irikura, S. Iyobe, and S. Mitsuhashi. 1986. Differences in susceptibility to quinolones of outer membrane mutants of *Salmonella typhimurium* and *Escherichia* coli. *Antimicrob Agents Chemother JID - 0315061* 29:535-538.

42. Hirai, K., S. Suzue, T. Irikura, S. Iyobe, and S. Mitsuhashi. 1987. Mutations producing resistance to norfloxacin in *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother JID - 0315061* 31:582-586.

43. Hollis, D.G., R.E. Weaver, C.N. Baker, and C. Thornsberry. 1976. Halophilic Vibrio species isolated from blood cultures. *J Clin Microbiol JID - 7505564* 3:425-431.

44. Honda, T., M.A. Abad-Lapuebla, Y.X. Ni, K. Yamamoto, and T. Miwatani. 1991. Characterization of a new thermostable direct haemolysin produced by a Kanagawa-phenomenon-negative clinical isolate of *Vibrio parahaemolyticus*. *J Gen Microbiol JID - 0375371* 137 (Pt 2):253-259.

45. Hooper, D.C., J.S. Wolfson, K.S. Souza, E.Y. Ng, G.L. McHugh, and M.N.

Swartz. 1989. Mechanisms of quinolone resistance in *Escherichia coli*: characterization of *nfxB* and *cfxB*, two mutant resistance loci decreasing norfloxacin accumulation. *Antimicrob Agents Chemother JID - 0315061* 33:283-290.

46. Hooper, D.C. and Wolfson, J.C.1993. Mechanism of bacteria resistance to quinolone. In *Quinolone Antimicrobial Agent,* 2nd ed (Hooper, D.C. and Wolfson, J.C., Eds.), pp. 97-119. American Society for Microbiology, Woshington, D.C.

47. Hooper, D.C. 1999. Mechanisms of fluoroquinolone resistance. *Drug Resist Updat* 2:38-55.

48. Horowitz, D.S. and J.C. Wang. 1987. Mapping the active site tyrosine of *Escherichia coli* DNA gyrase. *J Biol Chem JID - 2985121R* 262:5339-5344.

49. Hubschwerlen, C., P. Pflieger, J.L. Specklin, K. Gubernator, H. Gmunder, P. Angehrn, and I. Kompis. 1992. Pyrimido[1,6-a]benzimidazoles: a new class of DNA gyrase inhibitors. *J Med Chem JID - 9716531* 35:1385-1392.

50. Isberg, R.R. and M. Syvanen. 1982. DNA gyrase is a host factor required for transposition of Tn5. *Cell JID - 0413066* 30:9-18.

51. Isenberg, H.D. 1994. Clinical Microbiology Procedures Handbook. American society for Microbiology, Woshington, D.C.

52. Ishida, H., H. Fuziwara, Y. Kaibori, T. Horiuchi, K. Sato, and Y. Osada. 1995. Cloning of multidrug resistance gene pqrA from *Proteus vulgaris*. *Antimicrob Agents Chemother JID - 0315061* 39:453-457.

53. Janda, J.M., C. Powers, R.G. Bryant, and S.L. Abbott. 1988. Current perspectives on the epidemiology and pathogenesis of clinically significant *Vibrio spp.* *Clin Microbiol Rev JID - 8807282* 1:245-267.

54. Janoir, C., V. Zeller, M.D. Kitzis, N.J. Moreau, and L. Gutmann. 1996. High-level fluoroquinolone resistance in *Streptococcus pneumoniae* requires mutations in *parC* and *gyrA*. *Antimicrob Agents Chemother JID - 0315061* 40:2760-2764.

55. Joseph, S.W., R.R. Colwell, and J.B. Kaper. 1982. *Vibrio parahaemolyticus* and related halophilic Vibrios. *Crit Rev Microbiol JID - 8914274* 10:77-124.

56. Kaatz, G.W. and S.M. Seo. 1995. Inducible NorA-mediated multidrug resistance in *Staphylococcus aureus*. *Antimicrob Agents Chemother JID - 0315061* 39:2650-2655.

57. Kaneko, T. and R.R. Colwell. 1973. Ecology of *Vibrio parahaemolyticus* in Chesapeake Bay. *J Bacteriol JID - 2985120R* 113:24-32.

58. Kaneko, T. and R.R. Colwell. 1975. Adsorption of *Vibrio parahaemolyticus* onto chitin and copepods. *Appl Microbiol JID - 7605802* 29:269-274.

59. Kanematsu, E., T. Deguchi, M. Yasuda, T. Kawamura, Y. Nishino, and Y. Kawada. 1998. Alterations in the GyrA subunit of DNA gyrase and the ParC subunit of DNA topoisomerase IV associated with quinolone resistance in *Enterococcus faecalis*. *Antimicrob Agents Chemother JID - 0315061* 42:433-435.

60. Karunasagar, I., M.N. Venugopal, and K. Segar. 1986. Evaluation of methods for enumeration of *Vibrio parahaemolyticus* from seafood. *Appl Environ Microbiol JID - 7605801* 52:583-585.

61. Kato, J., Y. Nishimura, R. Imamura, H. Niki, S. Hiraga, and H. Suzuki. 1990. New topoisomerase essential for chromosome segregation in *E. coli*. *Cell JID - 0413066* 63:393-404.

62. Kato, J., H. Suzuki, and H. Ikeda. 1992. Purification and characterization of DNA topoisomerase IV in *Escherichia coli*. *J Biol Chem JID - 2985121R* 267:25676-25684.

63. Kelly, M.T., E.W. Hickmann-Brenner, and J.J. Farmer III. 1995. *Vibrio*, In In

Manual of clinical microbiology, 6th ed. (E.H. Lennette, A. Balows, W.J. Hausler, Jr., and H.J. Shadomy, Eds.), p. 282-301. American Society for Microbiology, Washington, D.C.

64. Korten, V., W.M. Huang, and B.E. Murray. 1994. Analysis by PCR and direct DNA sequencing of *gyrA* mutations associated with fluoroquinolone resistance in *Enterococcus faecalis*. *Antimicrob Agents Chemother JID - 0315061* 38:2091-2094.

65. Kumagai, Y., J.I. Kato, K. Hoshino, T. Akasaka, K. Sato, and H. Ikeda. 1996. Quinolone-resistant mutants of *Escherichia coli* DNA topoisomerase IV *parC* gene. *Antimicrob Agents Chemother JID - 0315061* 40:710-714.

66. Lee, S. and Y. Lee.1998. Laboratory developed fluoroquinolone resistant *Escherichia coli* has a new missense mutation in QRDR of *parC*. *J. Microbiol* ;36:106-110.

67. Lockshon, D. and D.R. Morris. 1983. Positively supercoiled plasmid DNA is produced by treatment of *Escherichia coli* with DNA gyrase inhibitors. *Nucleic Acids Res JID - 0411011* 11:2999-3017.

68. Markham, P.N. and A.A. Neyfakh. 1996. Inhibition of the multidrug transporter NorA prevents emergence of norfloxacin resistance in *Staphylococcus aureus*. *Antimicrob Agents Chemother JID - 0315061* 40:2673-2674.

69. Markham, P.N., M. Ahmed, and A.A. Neyfakh. 1996. The drug-binding activity of the multidrug-responding transcriptional regulator BmrR resides in its C-terminal domain. *J Bacteriol JID - 2985120R* 178:1473-1475.

70. Martinez, J.L., A. Alonso, J.M. Gomez-Gomez, and F. Baquero. 1998. Quinolone resistance by mutations in chromosomal gyrase genes. Just the tip of the iceberg? *J Antimicrob Chemother JID - 7513617* 42:683-688.

71. Masecar, B.L. and N.J. Robillard. 1991. Spontaneous quinolone resistance in *Serratia marcescens* due to a mutation in gyrA. *Antimicrob Agents Chemother JID - 0315061* 35:898-902.

72. Miller, P.F., L.F. Gambino, M.C. Sulavik, and S.J. Gracheck. 1994. Genetic relationship between *soxRS* and mar loci in promoting multiple antibiotic resistance in *Escherichia coli*. *Antimicrob Agents Chemother JID - 0315061* 38:1773-1779.

73. Miyamoto, Y., T. Kato, Y. Obara, S. Akiyama, K. Takizawa, and S. Yamai. 1969. In vitro hemolytic characteristic of *Vibrio parahaemolyticus*: its close correlation with human pathogenicity. *J Bacteriol JID - 2985120R* 100:1147-1149.

74. Morrison, A. and N.R. Cozzarelli. 1979. Site-specific cleavage of DNA *by E. coli* DNA gyrase. *Cell JID - 0413066* 17:175-184.

75. Munoz, R. and A.G. De La Campa. 1996. ParC subunit of DNA topoisomerase IV of *Streptococcus pneumoniae* is a primary target of fluoroquinolones and cooperates with DNA gyrase A subunit in forming resistance phenotype. *Antimicrob Agents Chemother JID - 0315061* 40:2252-2257.

76. Nakamura, S., M. Nakamura, T. Kojima, and H. Yoshida. 1989. *gyrA* and *gyrB* mutations in quinolone-resistant strains of *Escherichia coli*. *Antimicrob Agents Chemother JID - 0315061* 33:254-255.

77. Nakanishi, N., S. Yoshida, H. Wakebe, M. Inoue, and S. Mitsuhashi. 1991. Mechanisms of clinical resistance to fluoroquinolones in *Enterococcus faecalis*. *Antimicrob Agents Chemother JID - 0315061* 35:1053-1059.

78. Nakano, M., T. Deguchi, T. Kawamura, M. Yasuda, M. Kimura, Y. Okano, and Y. Kawada. 1997. Mutations in the *gyrA* and *parC* genes in fluoroquinolone-resistant clinical isolates of *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother JID - 0315061* 41:2289-2291.

79. National committee on Clinical Laboratory Standards. 1997. Methods for

Dilution antimicrobial susceptibility tests for bacteria which grow aerobically-Forth edition: Approved Standard. National Committee on Clinical Laboratory Standards, Villanova, P.A.

80. Neyfakh, A.A. 1992. The multidrug efflux transporter of *Bacillus subtilis* is a structural and functional homolog of the Staphylococcus NorA protein. *Antimicrob Agents Chemother JID - 0315061* 36:484-485.

81. Neyfakh, A.A., C.M. Borsch, and G.W. Kaatz. 1993. Fluoroquinolone resistance protein NorA of *Staphylococcus aureus* is a multidrug efflux transporter. *Antimicrob Agents Chemother JID - 0315061* 37:128-129.

82. Ng, E.Y., M. Trucksis, and D.C. Hooper. 1996. Quinolone resistance mutations in topoisomerase IV: relationship to the *flqA* locus and genetic evidence that topoisomerase IV is the primary target and DNA gyrase is the secondary target of fluoroquinolones in *Staphylococcus aureus*. *Antimicrob Agents Chemother JID - 0315061* 40:1881-1888.

83. Ng, E.Y., G. L. McHugh, J.S. Wolfson, and D.C. Hooper.1992. Other genetic loci involved in quinolone resistance in *Escherichia coli*, abstr.1546. *Program Abstr. 32nd Intersci. Conf. Antimicrob. Agents Chemother.*

84. Nikaido, H. and D.G. Thanassi. 1993. Penetration of lipophilic agents with

multiple protonation sites into bacterial cells: tetracyclines and fluoroquinolones as examples. *Antimicrob Agents Chemother JID - 0315061* 37:1393-1399.

85. Nishibuchi, M., A. Fasano, R.G. Russell, and J.B. Kaper. 1992.

Enterotoxigenicity of *Vibrio parahaemolyticus* with and without genes encoding thermostable direct hemolysin. *Infect Immun JID - 0246127* 60:3539-3545.

86. Nishino, Y., T. Deguchi, M. Yasuda, T. Kawamura, M. Nakano, E. Kanematsu,

S. Ozeki, and Y. Kawada. 1997. Mutations in the *gyrA* and *parC* genes associated with fluoroquinolone resistance in clinical isolates of *Citrobacter freundii. FEMS Microbiol Lett JID - 7705721* 154:409-414.

87. Oethinger, M., I. Podglajen, W.V. Kern, and S.B. Levy. 1998. Overexpression of

the *marA* or *soxS* regulatory gene in clinical topoisomerase mutants of *Escherichia coli. Antimicrob Agents Chemother JID - 0315061* 42:2089-2094.

88. Ohashi, M., H. Murakami, Y. Kudo, and S. Sakai.1978. Manual for the

Laboratory diagnostic of bacteria food poisoning and the assesment of sanitary quality of food. Southeast Asian Medical Information Center. Institute of Basic medical Science, The University of Tsukuba.

89. Okuda, J., S. Okamoto, M. Takahata, and T. Nishino. 1991. Inhibitory effects of ciprofloxacin and sparfloxacin on DNA gyrase purified from fluoroquinolone-resistant strains of methicillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother JID - 0315061* 35:2288-2293.

90. Okuda, J., E. Hayakawa, M. Nishibuchi, and T. Nishino. 1999. Sequence analysis of the *gyrA* and *parC* homologues of a wild-type strain of *Vibrio parahaemolyticus* and its fluoroquinolone-resistant mutants. *Antimicrob Agents Chemother JID - 0315061* 43:1156-1162.

91. Palasuntheram, C., and S. Selvarajah. 1980. Vibrio parahaemolyticus in colombo environment. *Indian J. Med Res.*; 73: 13-17.

92. Pan, X.S. and L.M. Fisher. 1996. Cloning and characterization of the *parC* and *parE* genes of *Streptococcus pneumoniae* encoding DNA topoisomerase IV: role in fluoroquinolone resistance. *J Bacteriol JID - 2985120R* 178:4060-4069.

93. Pan, X.S. and L.M. Fisher. 1997. Targeting of DNA gyrase in *Streptococcus pneumoniae* by sparfloxacin: selective targeting of gyrase or topoisomerase IV by quinolones. *Antimicrob Agents Chemother JID - 0315061* 41:471-474.

94. Pan, X.S. and L.M. Fisher. 1998. DNA gyrase and topoisomerase IV are dual

targets of clinafloxacin action in *Streptococcus pneumoniae*. *Antimicrob Agents Chemother JID - 0315061* 42:2810-2816.

95. Pavia, A.t., J.A. Bryan, K.L. Maher, T.R. Hester, Jr., and J.J. Farmer. 1989. *Vibrio carchariae* infection after a shark bite. *Ann. Intern. Med* ; 111:85-86.

96. Peng, H. and K.J. Marians. 1993. *Escherichia coli* topoisomerase IV. Purification, characterization, subunit structure, and subunit interactions. *J Biol Chem JID - 2985121R* 268:24481-24490.

97. Perichon, B., J. Tankovic, and P. Courvalin. 1997. Characterization of a mutation in the *parE* gene that confers fluoroquinolone resistance in *Streptococcus pneumoniae*. *Antimicrob Agents Chemother JID - 0315061* 41:1166-1167.

98. Piddock, L.J. and R. Wise. 1986. The effect of altered porin expression in *Escherichia coli* upon susceptibility to 4-quinolones. *J Antimicrob Chemother JID - 7513617* 18:547-549.

99. Piddock, L.J. 1999. Mechanisms of fluoroquinolone resistance: an update 1994-1998. *Drugs JID - 7600076* 58 Suppi 2:11-18.

100. Rahman, M., G. Mauff, J. Levy, M. Couturier, G. Pulverer, N. Glasdorff, and J.P. Butzler. 1994. Detection of 4-quinolone resistance mutation in *gyrA* gene

of *Shigella dysenteriae* type 1 by PCR. *Antimicrob Agents Chemother JID - 0315061* 38:2488-2491.

101. Reyna, F., M. Huesca, V. Gonzalez, and L.Y. Fuchs. 1995. *Salmonella typhimurium gyrA* mutations associated with fluoroquinolone resistance. *Antimicrob Agents Chemother JID - 0315061* 39:1621-1623.

102. Robillard, N.J. and A.L. Scarpa. 1988. Genetic and physiological characterization of ciprofloxacin resistance in *Pseudomonas aeruginosa* PAO. *Antimicrob Agents Chemother JID - 0315061* 32:535-539.

103. Ross, D.L., and C.M. Riley. 1990. Aqueous solubilities of some variously substituted quinolone antimicrobials. *Int. J. Pharm* ;63: 237-250.

104. Sakazaki, R., K. Tamura, T. Kato, Y. Obara, and S. Yamai. 1968. Studies on the enteropathogenic, facultatively halophilic bacterium, *Vibrio parahaemolyticus*. 3. Enteropathogenicity. *Jpn J Med Sci Biol JID - 0243706* 21:325-331.

105. Sakurai, J., A. Matsuzaki, and T. Miwatani. 1973. Purification and characterization of thermostable direct hemolysin of *Vibrio parahaemolyticus*. *Infect Immun JID - 0246127* 8:775-780.

106. Sato, K., Y. Inoue, T. Fujii, H. Aoyama, M. Inoue, and S. Mitsuhashi. 1986. Purification and properties of DNA gyrase from a fluoroquinolone-

resistant strain of *Escherichia coli*. *Antimicrob Agents Chemother JID - 0315061* 30:777-780.

107. Schmitz, F.J., B. Hofmann, B. Hansen, S. Scheuring, M. Luckefahr, M. Klootwijk, J. Verhoef, A. Fluit, H.P. Heinz, K. Kohrer, and M.E. Jones. 1998. Relationship between ciprofloxacin, ofloxacin, levofloxacin, sparfloxacin and moxifloxacin (BAY 12-8039) MICs and mutations in *grlA*, *grlB*, *gyrA* and *gyrB* in 116 unrelated clinical isolates of *Staphylococcus aureus*. *J Antimicrob Chemother JID - 7513617* 41:481-484.

108. Setlow, J.K., E. Cabrera-Juarez, W.L. Albritton, D. Spikes, and A. Mutschler. 1985. Mutations affecting gyrase in *Haemophilus influenzae*. *J Bacteriol JID - 2985120R* 164:525-534.

109. Shen, L.L. and A.G. Pernet. 1985. Mechanism of inhibition of DNA gyrase by analogues of nalidixic acid: the target of the drugs is DNA. *Proc Natl Acad Sci U S A JID - 7505876* 82:307-311.

110. Shen, L.L., L.A. Mitscher, P.N. Sharma, T.J. O'Donnell, D.W. Chu, C.S. Cooper, T. Rosen, and A.G. Pernet. 1989. Mechanism of inhibition of DNA gyrase by quinolone antibacterials: a cooperative drug--DNA binding model. *Biochemistry JID - 0370623* 28:3886-3894.

111. Spira, W.M. and Q.S. Ahmed. 1981. Gauze filtration and enrichment procedures for recovery of *Vibrio cholerae* from contaminated waters. *Appl Environ Microbiol JID - 7605801* 42:730-733.

112. Sugino, A., N.P. Higgins, P.O. Brown, C.L. Peebles, and N.R. Cozzarelli. 1978. Energy coupling in DNA gyrase and the mechanism of action of novobiocin. *Proc Natl Acad Sci U S A JID - 7505876* 75:4838-4842.

113. Sulavik, M.C., M. Dazer, and P.F. Miller. 1997. The *Salmonella typhimurium* mar locus: molecular and genetic analyses and assessment of its role in virulence. *J Bacteriol JID - 2985120R* 179:1857-1866.

114. Takenouchi, T., C. Ishii, M. Sugawara, Y. Tokue, and S. Ohya. 1995. Incidence of various *gyrA* mutants in 451 *Staphylococcus aureus* strains isolated in Japan and their susceptibilities to 10 fluoroquinolones. *Antimicrob Agents Chemother JID - 0315061* 39:1414-1418.

115. Takiff, H.E., L. Salazar, C. Guerrero, W. Philipp, W.M. Huang, B. Kreiswirth, S.T. Cole, W.R.J. Jacobs, and A. Telenti. 1994. Cloning and nucleotide sequence of *Mycobacterium tuberculosis gyrA* and *gyrB* genes and detection of quinolone resistance mutations. *Antimicrob Agents Chemother JID - 0315061* 38:773-780.

116. Tang, G.Q., T. Iida, K. Yamamoto, and T. Honda. 1994. A mutant toxin of *Vibrio parahaemolyticus* thermostable direct hemolysin which has lost

hemolytic activity but retains ability to bind to erythrocytes. *Infect Immun JID - 0246127* 62:3299-3304.

117. Tankovic, J., F. Mahjoubi, P. Courvalin, J. Duval, and R. Leclerco. 1996. Development of fluoroquinolone resistance in *Enterococcus faecalis* and role of mutations in the DNA gyrase *gyrA* gene. *Antimicrob Agents Chemother JID - 0315061* 40:2558-2561.

118. Tankovic, J., B. Perichon, J. Duval, and P. Courvalin. 1996. Contribution of mutations in *gyrA* and *parC* genes to fluoroquinolone resistance of mutants of *Streptococcus pneumoniae* obtained in vivo and in vitro. *Antimicrob Agents Chemother JID - 0315061* 40:2505-2510.

119. Tison, D.L. and M.T. Kelly. 1984. Vibrio species of medical importance. *Diagn Microbiol Infect Dis JID - 8305899* 2:263-276.

120. Trees, D.L., A.L. Sandul, W.L. Whittington, and J.S. Knapp. 1998. Identification of novel mutation patterns in the *parC* gene of ciprofloxacin-resistant isolates of *Neisseria gonorrhoeae*. *Antimicrob Agents Chemother JID - 0315061* 42:2103-2105.

121. Vila, J., J. Ruiz, P. Goni, and M.T. De Anta. 1996. Detection of mutations in *parC* in quinolone-resistant clinical isolates of *Escherichia coli*. *Antimicrob Agents Chemother JID - 0315061* 40:491-493.

122. von Wright, A. and B.A. Bridges. 1981. Effect of *gyrB*-mediated changes in chromosome structure on killing of *Escherichia coli* by ultraviolet light: experiments with strains differing in deoxyribonucleic acid repair capacity. *J Bacteriol JID - 2985120R* 146:18-23.

123. Wang, T., M. Tanaka, and K. Sato. 1998. Detection of *grlA* and *gyrA* mutations in 344 *Staphylococcus aureus* strains. *Antimicrob Agents Chemother JID - 0315061* 42:236-240.

122. Wentland, M.P. 1990. Structure-activity relationships of fluoroquinolone. . In *The New generation of Quinolone* (C. Siporin, C.L. Heifetz, and J.M. Domagala, Eds.) p. 1-43.Marcel Dekker, Inc., New York.

123. West, P.A., and R.R. Cowell. 1984. Vibrios in the environment. John Wiley & Sons Inc., New York, N.Y.

124. Willmott, C.J. and A. Maxwell. 1993. A single point mutation in the DNA gyrase A protein greatly reduces binding of fluoroquinolones to the gyrase-DNA complex. *Antimicrob Agents Chemother JID - 0315061* 37:126-127.

125. Wolfson, J.S. and D.C. Hooper. 1985. The fluoroquinolones: structures, mechanisms of action and resistance, and spectra of activity in vitro. *Antimicrob Agents Chemother JID - 0315061* 28:581-586.

126. World Health Organization Scientific Working Group.1980. Cholera and other vibrio-associated diarrhoeas. Bull. W.H.O.; 58:353-374.

127. World Health Organization, Emerging and other communicable Diseases, Surveillance and Control. Use of Quinolone in Food animals and potential Impact on Human heath. Report of WHO Meeting, geneva, Switzerland 2-5 June 1998. http://www.who.int/emc.

128. Woolridge, D.P., N. Vazquez-Laslop, P.N. Markham, M.S. Chevalier, E.W. Gerner, and A.A. Neyfakh. 1997. Efflux of the natural polyamine spermidine facilitated by the Bacillus subtilis multidrug transporter Blt. *J Biol Chem JID - 2985121R* 272:8864-8866.

129. Yoshida, H., T. Kojima, J. Yamagishi, and S. Nakamura. 1988. Quinolone-resistant mutations of the *gyrA* gene of *Escherichia coli*. *Mol Gen Genet JID - 0125036* 211:1-7.

130. Yoshida, H., M. Bogaki, M. Nakamura, and S. Nakamura. 1990. Quinolone resistance-determining region in the DNA gyrase *gyrA* gene of *Escherichia coli*. *Antimicrob Agents Chemother JID - 0315061* 34:1271-1272.

131. Yoshida, H., M. Bogaki, M. Nakamura, L.M. Yamanaka, and S. Nakamura. 1991. Quinolone resistance-determining region in the DNA gyrase *gyrB*

gene of Escherichia coli. *Antimicrob Agents Chemother JID - 0315061* 35:1647-1650.

132. Zechiedrich, E.L. and N.R. Cozzarelli. 1995. Roles of topoisomerase IV and DNA gyrase in DNA unlinking during replication in *Escherichia coli*. *Genes Dev JID - 8711660* 9:2859-2869.

APPENDICES

APPENDIX I

REAGENTS AND EQUIPMENT

1) Media and reagents

α- Naphthol	Merck, Germany
p-Dimethylaminobenzaldehyde	Merck, Germany
Absolute ethanol	Merck, Germany
Agarose (ultrapure)	GibcoBRL, USA
Arabinose	Sigma, USA
Bacteriological peptone	Oxoid, USA
Boric acid	Sigma, USA
Bromthymol blue	Fluka, Germany
Decarboxylase medium base	Difco, USA
EDTA	Amresco, USA
Ethidium bromide	Amresco, USA
Glacial acetic acid	Merck, Germany
Glucose	Difco, USA
Horse serum	GibcoBRL, USA
Hydrochloric acid	Merck, Germany
Inositol	Sigma, USA
Iso amyl alcohol	Merck, Germany
L- Arginine hyhdrochloride	Sigma, USA

Lactose	Oxoid, USA
L-Lysine monohydrochlorided	Sigma, USA
L-ornithine monohydrochloride	Sigma, USA
Manitol	Difco, USA
Mannose	Sigma, USA
Methyl red	Riedel-deHaen, Germany
Motility test medium	BBL, USA
N,N,N'.N'-tetramethyl-p Phenylenediamine dihydrochloride	Sigma, USA
Potassium dihydrogen phosphate	Merck, Germany
Potassium hydroxide	Merck, Germany
Rhamnose	Pfanstiehl, USA
Simmon citrate	BBL, USA
Sodium acetate	Merck, Germany
Sodium chloride	Merck, Germany
Sucrose	Hermann, Germany
TCBS	Nissui, Japan
Thymol blue	Harleco, USA
Triple sugar iron agar	BIOTEC, UK
Tris base	Sigma, USA
Trypticase soy agar	Oxoid, USA
Trypticase soy broth	Oxoid, USA

2) Equipments

Spectophotometer	BIORAD, USA
PCR machine	Perkin Elmer, USA
Gelmate 2000 electrophoresis	Toyobo, Japan
ABI prism 310 automated sequencer	Perkin Elmer, USA
Chemi Doc	BIORAD, USA

APPENDIX II

REAGENTS PREPARATION

1) Oxidase test reagent

Prepare a fresh solution of tetramethyl-*p*-phenylenediamine dihydrochloride each time of use by adding a loopful of it to about 3 ml of sterile distilled water or saline. Do not use if it becomes blue. Autoxidation of the reagent occurs rapidly and although this can be related by the addtion of 1% ascobic acid. It is not sufficiently stable in aqueous solution for storage.

2) Kovac's reagent

p-Dimethylaminobenzaldehyde	5 g
Iso amyl alcohol	75 ml
Conc. HCl	25 ml

Dissolve the aldehyde in the alcohol by gently warming in a water bath (about 50-55^{0}C). Cool and add the acid with care. Protect from light and store at 4^{0}C.

3) Methyl red solution

Methyl red	0.04 g
Absolute ethanol	40 ml

Dissolve the methyl red in the ethanol and dilute to volume 100 ml with distilled water.

4) VP reagent

Solution 1

α- Naphthol	5 g
Absolute ethanol	100 ml

Dissolve α- Naphthol in ethanol then mix well and store at 4^0C.

Solution 2

Potassium hydroxide	40 g
Distilled water	100 ml

Dissolve Potassium hydroxide in distilled water then mix well and store at 4^0C.

5) 0.5 M EDTA, pH 8.0

Disodium ethylene diamine tetraacetate.$2H_2O$	186.1 g
Distilled water	800 ml

Adjust pH to 8.0 with sodium hydroxide pellet then adjust volume to 1,000 ml.

6) 50x Tris-acetate buffer (TAE)

Tris base	242 g
Glacial acetic acid	57.1 ml
0.5M EDTA, pH 8.0	100 ml

Adjust volume to 1,000 ml with distilled water and sterilize by autoclaving

7) 10x Tris-borate buffer (TBE)

Tris base	108 g
Boric acid	55 g
0.5M EDTA, pH 8.0	40 ml

Adjust volume to 1,000 ml with H_2O then sterilize by autoclaving

8) 1.5% Agarose gel

Agarose powder	0.3 g
TAE or TBE buffer	20 ml

BIOGRAPHY

Miss Supawadee Na-pompet was born on February 1, 1977 in Bangkok, Thailand. She graduated with a Bachelor of Science in Microbiology from Kasetsart University in 1997.