

7. Bibliography

- (1) Thomas, C. M. (2002) *The Horizontal Gene Pool*, (Harwood Academic Publishers, Amsterdam, 2000).
- (2) Hayes, F. *E. coli Plasmid Vectors: Methods and Applications*, A. Preston, N. Casali, Eds. (Humana, Totowa, NJ, 2003), pp. 1–17.
- (3) Read, T. D., Peterson, S. N., Tourasse, N., Baillie, L. W., Paulsen, I. T., Nelson, K. E., Tettelin, H., Fouts, D. E., Eisen, J. A., Gill, S. R., Holtapple, E. K., Okstad, O. A., Helgason, E., Rilstone, J., Wu, M., Kolonay, J. F., Beanan, M. J., Dodson, R. J., Brinkac, L. M., Gwinn, M., DeBoy, R. T., Madpu, R., Daugherty, S. C., Durkin, A. S., Haft, D. H., Nelson, W. C., Peterson, J. D., Pop, M., Khouri, H. M., Radune, D., Benton, J. L., Mahamoud, Y., Jiang, L., Hance, I. R., Weidman, J. F., Berry, K. J., Plaut, R. D., Wolf, A. M., Watkins, K. L., Nierman, W. C., Hazen, A., Cline, R., Redmond, C., Thwaite, J. E., White, O., Salzberg, S. L., Thomason, B., Friedlander, A. M., Koehler, T. M., Hanna, P. C., Kolsto, A. B., and Fraser, C. M. (2003) The genome sequence of *Bacillus anthracis Ames* and comparison to closely related bacteria. *Nature* 423, 81-6.
- (4) Fraser, C. M., Casjens, S., Huang, W. M., Sutton, G. G., Clayton, R., Lathigra, R., White, O., Ketchum, K. A., Dodson, R., Hickey, E. K., Gwinn, M., Dougherty, B., Tomb, J. F., Fleischmann, R. D., Richardson, D., Peterson, J., Kerlavage, A. R., Quackenbush, J., Salzberg, S., Hanson, M., van Vugt, R., Palmer, N., Adams, M. D., Gocayne, J., Weidman, J., Utterback, T., Watthey, L., McDonald, L., Artiach, P., Bowman, C., Garland, S., Fuji, C., Cotton, M. D., Horst, K., Roberts, K., Hatch, B., Smith, H. O., and Venter, J. C. (1997) Genomic sequence of a Lyme disease spirochaete, *Borrelia burgdorferi*. *Nature* 390, 580-6.
- (5) Carlson, C. R., and Kolsto, A. B. (1994) A small (2.4 Mb) *Bacillus cereus* chromosome corresponds to a conserved region of a larger (5.3 Mb) *Bacillus cereus* chromosome. *Mol Microbiol* 13, 161-9.
- (6) Nordstrom, K., and Austin, S. J. (1989) Mechanisms that contribute to the stable segregation of plasmids. *Annu Rev Genet* 23, 37-69.
- (7) Zielenkiewicz, U., and Ceglowski, P. (2001) Mechanisms of plasmid stable maintenance with special focus on plasmid addiction systems. *Acta Biochim Pol* 48, 1003-23.
- (8) Hayes, F. (2003) The function and organization of plasmids. *Methods Mol Biol* 235, 1-17.
- (9) Gerdes, K., Moller-Jensen, J., and Bugge Jensen, R. (2000) Plasmid and chromosome partitioning: surprises from phylogeny. *Mol Microbiol* 37, 455-66.
- (10) Moller-Jensen, J., Jensen, R. B., and Gerdes, K. (2000) Plasmid and chromosome segregation in prokaryotes. *Trends Microbiol* 8, 313-20.

- (11) Holliday, R. (1964) A mechanism for gene conversion in fungi. *Genetic Research* 5, 282.
- (12) Stahl, F. W. (1994) The Holliday junction on its thirtieth anniversary. *Genetics* 138, 241-6.
- (13) Ogawa, T., Yu, X., Shinohara, A., and Egelman, E. H. (1993) Similarity of the yeast RAD51 filament to the bacterial RecA filament. *Science* 259, 1896-9.
- (14) Shinohara, A., Ogawa, H., Matsuda, Y., Ushio, N., Ikeo, K., and Ogawa, T. (1993) Cloning of human, mouse and fission yeast recombination genes homologous to RAD51 and recA. *Nat Genet* 4, 239-43.
- (15) White, M. F., and Lilley, D. M. (1996) The structure-selectivity and sequence-preference of the junction-resolving enzyme CCE1 of *Saccharomyces cerevisiae*. *J Mol Biol* 257, 330-41.
- (16) Hyde, H., Davies, A. A., Benson, F. E., and West, S. C. (1994) Resolution of recombination intermediates by a mammalian activity functionally analogous to *Escherichia coli* RuvC resolvase. *J Biol Chem* 269, 5202-9.
- (17) Mizuuchi, K. (1997) Polynucleotidyl transfer reactions in site-specific DNA recombination. *Genes Cells* 2, 1-12.
- (18) Wyman, C., and Kanaar, R. (2004) Homologous recombination: down to the wire. *Curr Biol* 14, R629-31.
- (19) Hallet, B., and Sherratt, D. J. (1997) Transposition and site-specific recombination: adapting DNA cut-and-paste mechanisms to a variety of genetic rearrangements. *FEMS Microbiol Rev* 21, 157-78.
- (20) Nash, H. A. (1996) *The HU and IHF proteins: accessory factors for complex protein-DNA assemblies.*, 2nd ed., American Society for Microbiology, Washington, DC, pp. 2363–2376.
- (21) Grindley, N. D. F. (2002) *The movement of Tn3-like elements: transposition and resolution.*, In Craig,N., Craigie,R., Gellert,M. and Lambowitz,A. (eds), *Mobile DNA II*. ASM Press, Washington, DC, pp. 272–302.
- (22) Smith, M. C., and Thorpe, H. M. (2002) Diversity in the serine recombinases. *Mol Microbiol* 44, 299-307.
- (23) Alonso, J. C., Ayora, S., Canosa, I., Weise, F., and Rojo, F. (1996) Site-specific recombination in gram-positive theta-replicating plasmids. *FEMS Microbiol Lett* 142, 1-10.
- (24) Stark, W. M., Boocock, M. R., and Sherratt, D. J. (1992) Catalysis by site-specific recombinases. *Trends Genet* 8, 432-9.
- (25) Watson, M. A., Boocock, M. R., and Stark, W. M. (1996) Rate and selectively of synapsis of res recombination sites by Tn3 resolvase. *J Mol Biol* 257, 317-29.
- (26) Li, W., Kamtekar, S., Xiong, Y., Sarkis, G. J., Grindley, N. D., and Steitz, T. A. (2005) Structure of a synaptic gammadelta resolvase tetramer covalently linked to two cleaved DNAs. *Science* 309, 1210-5.

- (27) Nollmann, M., He, J., Byron, O., and Stark, W. M. (2004) Solution structure of the Tn3 resolvase-crossover site synaptic complex. *Mol Cell* 16, 127-37.
- (28) Rowland, S. J., Stark, W. M., and Boocock, M. R. (2002) Sin recombinase from *Staphylococcus aureus*: synaptic complex architecture and transposon targeting. *Mol Microbiol* 44, 607-19.
- (29) Kanaar, R., and Cozzarelli, N. R. (1992) Roles of supercoiled DNA structure in DNA transactions. *Current Opinion in Structural Biology* 2, 369.
- (30) Deufel, A., Hermann, T., Kahmann, R., and Muskhelishvili, G. (1997) Stimulation of DNA inversion by FIS: evidence for enhancer-independent contacts with the Gin-gix complex. *Nucleic Acids Res* 25, 3832-9.
- (31) Merickel, S. K., Haykinson, M. J., and Johnson, R. C. (1998) Communication between Hin recombinase and Fis regulatory subunits during coordinate activation of Hin-catalyzed site-specific DNA inversion. *Genes Dev* 12, 2803-16.
- (32) Klippel, A., Cloppenborg, K., and Kahmann, R. (1988) Isolation and characterization of unusual gin mutants. *Embo J* 7, 3983-9.
- (33) Sarkis, G. J., Murley, L. L., Leschziner, A. E., Boocock, M. R., Stark, W. M., and Grindley, N. D. (2001) A model for the gamma delta resolvase synaptic complex. *Mol Cell* 8, 623-31.
- (34) Arnold, P. H., Blake, D. G., Grindley, N. D., Boocock, M. R., and Stark, W. M. (1999) Mutants of Tn3 resolvase which do not require accessory binding sites for recombination activity. *Embo J* 18, 1407-14.
- (35) Rojo, F., and Alonso, J. C. (1994) A novel site-specific recombinase encoded by the *Streptococcus pyogenes* plasmid pSM19035. *J Mol Biol* 238, 159-72.
- (36) Canosa, I., Lurz, R., Rojo, F., and Alonso, J. C. (1998) beta Recombinase catalyzes inversion and resolution between two inversely oriented six sites on a supercoiled DNA substrate and only inversion on relaxed or linear substrates. *J Biol Chem* 273, 13886-91.
- (37) Canosa, I., Lopez, G., Rojo, F., Boocock, M. R., and Alonso, J. C. (2003) Synapsis and strand exchange in the resolution and DNA inversion reactions catalysed by the beta recombinase. *Nucleic Acids Res* 31, 1038-44.
- (38) Alonso, J. C., Gutierrez, C., and Rojo, F. (1995) The role of chromatin-associated protein Hbsu in beta-mediated DNA recombination is to facilitate the joining of distant recombination sites. *Mol Microbiol* 18, 471-8.
- (39) Diaz, V., Rojo, F., Martinez, A. C., Alonso, J. C., and Bernad, A. (1999) The prokaryotic beta-recombinase catalyzes site-specific recombination in mammalian cells. *J Biol Chem* 274, 6634-40.
- (40) Diaz, V., Servert, P., Prieto, I., Gonzalez, M. A., Martinez, A. C., Alonso, J. C., and Bernad, A. (2001) New insights into host factor requirements for prokaryotic beta-recombinase-mediated reactions in mammalian cells. *J Biol Chem* 276, 16257-64.

- (41) Ceglowski, P., Lurz, R., and Alonso, J. C. (1993) Functional analysis of pSM19035-derived replicons in *Bacillus subtilis*. *FEMS Microbiol Lett* 109, 145-50.
- (42) Ceglowski, P., Boitsov, A., Karamyan, N., Chai, S., and Alonso, J. C. (1993) Characterization of the effectors required for stable inheritance of *Streptococcus pyogenes* pSM19035-derived plasmids in *Bacillus subtilis*. *Mol Gen Genet* 241, 579-85.
- (43) Ceglowski, P., Boitsov, A., Chai, S., and Alonso, J. C. (1993) Analysis of the stabilization system of pSM19035-derived plasmid pBT233 in *Bacillus subtilis*. *Gene* 136, 1-12.
- (44) Hughes, R. E., Rice, P. A., Steitz, T. A., and Grindley, N. D. (1993) Protein-protein interactions directing resolvase site-specific recombination: a structure-function analysis. *Embo J* 12, 1447-58.
- (45) Rice, P. A., and Steitz, T. A. (1994) Refinement of gamma delta resolvase reveals a strikingly flexible molecule. *Structure* 2, 371-84.
- (46) Yang, W., and Steitz, T. A. (1995) Crystal structure of the site-specific recombinase gamma delta resolvase complexed with a 34 bp cleavage site. *Cell* 82, 193-207.
- (47) Canosa, I., Ayora, S., Rojo, F., and Alonso, J. C. (1997) Mutational analysis of a site-specific recombinase: characterization of the catalytic and dimerization domains of the beta recombinase of pSM19035. *Mol Gen Genet* 255, 467-76.
- (48) Orth, P., Jekow, P., Alonso, J. C., and Hinrichs, W. (1999) Proteolytic cleavage of gram-positive beta recombinase is required for crystallization. *Protein Eng* 12, 371-3.
- (49) Pan, B., Deng, Z., Liu, D., Ghosh, S., and Mullen, G. P. (1997) Secondary and tertiary structural changes in gamma delta resolvase: comparison of the wild-type enzyme, the I110R mutant, and the C-terminal DNA binding domain in solution. *Protein Sci* 6, 1237-47.
- (50) Nollmann, M., Byron, O., and Stark, W. M. (2005) Behavior of Tn3 Resolvase in Solution and Its Interaction with res. *Biophys J* 89, 1920-31.
- (51) Burke, M. E., Arnold, P. H., He, J., Wenwieser, S. V., Rowland, S. J., Boocock, M. R., and Stark, W. M. (2004) Activating mutations of Tn3 resolvase marking interfaces important in recombination catalysis and its regulation. *Mol Microbiol* 51, 937-48.
- (52) Klippel, A., Mertens, G., Patschinsky, T., and Kahmann, R. (1988) The DNA invertase Gin of phage Mu: formation of a covalent complex with DNA via a phosphoserine at amino acid position 9. *Embo J* 7, 1229-37.
- (53) Sanders, E. R., and Johnson, R. C. (2004) Stepwise dissection of the Hin-catalyzed recombination reaction from synapsis to resolution. *J Mol Biol* 340, 753-66.
- (54) Gerdes, K. (2000) Toxin-antitoxin modules may regulate synthesis of macromolecules during nutritional stress. *J Bacteriol* 182, 561-72.

- (55) Galvani, C., Terry, J., and Ishiguro, E. E. (2001) Purification of the RelB and RelE proteins of *Escherichia coli*: RelE binds to RelB and to ribosomes. *J Bacteriol* 183, 2700-3.
- (56) Gotfredsen, M., and Gerdes, K. (1998) The *Escherichia coli* relBE genes belong to a new toxin-antitoxin gene family. *Mol Microbiol* 29, 1065-76.
- (57) Christensen, S. K., Mikkelsen, M., Pedersen, K., and Gerdes, K. (2001) RelE, a global inhibitor of translation, is activated during nutritional stress. *Proc Natl Acad Sci U S A* 98, 14328-33.
- (58) Hayes, F. (2003) Toxins-antitoxins: plasmid maintenance, programmed cell death, and cell cycle arrest. *Science* 301, 1496-9.
- (59) Jaffe, A., Ogura, T., and Hiraga, S. (1985) Effects of the ccd function of the F plasmid on bacterial growth. *J Bacteriol* 163, 841-9.
- (60) Gerdes, K., Rasmussen, P. B., and Molin, S. (1986) Unique type of plasmid maintenance function: postsegregational killing of plasmid-free cells. *Proc Natl Acad Sci U S A* 83, 3116-20.
- (61) Gerdes, K., Moller-Jensen, J., Ebersbach, G., Kruse, T., and Nordstrom, K. (2004) Bacterial mitotic machineries. *Cell* 116, 359-66.
- (62) Gerdes, K., Christensen, S. K., and Lobner-Olesen, A. (2005) Prokaryotic toxin-antitoxin stress response loci. *Nat Rev Microbiol* 3, 371-82.
- (63) Ogura, T., and Hiraga, S. (1983) Mini-F plasmid genes that couple host cell division to plasmid proliferation. *Proc Natl Acad Sci U S A* 80, 4784-8.
- (64) Greenfield, T. J., Ehli, E., Kirshenmann, T., Franch, T., Gerdes, K., and Weaver, K. E. (2000) The antisense RNA of the par locus of pAD1 regulates the expression of a 33-amino-acid toxic peptide by an unusual mechanism. *Mol Microbiol* 37, 652-60.
- (65) Koyama, A. H., Wada, C., Nagata, T., and Yura, T. (1975) Indirect selection for plasmid mutants: isolation of ColVBtrp mutants defective in self-maintenance in *Escherichia coli*. *J Bacteriol* 122, 73-9.
- (66) Engelberg-Kulka, H., and Glaser, G. (1999) Addiction modules and programmed cell death and antideath in bacterial cultures. *Annu Rev Microbiol* 53, 43-70.
- (67) Hargreaves, D., Santos-Sierra, S., Giraldo, R., Sabariegos-Jareno, R., de la Cueva-Mendez, G., Boelens, R., Diaz-Orejas, R., and Rafferty, J. B. (2002) Structural and functional analysis of the kid toxin protein from *E. coli* plasmid R1. *Structure (Camb)* 10, 1425-33.
- (68) Grady, R., and Hayes, F. (2003) Axe-Txe, a broad-spectrum proteic toxin-antitoxin system specified by a multidrug-resistant, clinical isolate of *Enterococcus faecium*. *Mol Microbiol* 47, 1419-32.
- (69) Meinhart, A., Alonso, J. C., Strater, N., and Saenger, W. (2003) Crystal structure of the plasmid maintenance system epsilon/zeta: functional mechanism of toxin zeta and inactivation by epsilon 2 zeta 2 complex formation. *Proc Natl Acad Sci U S A* 100, 1661-6.
- (70) Kobayashi, I. (2001) Behavior of restriction-modification systems as selfish mobile elements and their impact on genome evolution. *Nucleic Acids Res* 29, 3742-56.

- (71) Rawlings, D. E. (1999) Proteic toxin-antitoxin, bacterial plasmid addiction systems and their evolution with special reference to the pas system of pTF-FC2. *FEMS Microbiol Lett* 176, 269-77.
- (72) Pandey, D. P., and Gerdes, K. (2005) Toxin-antitoxin loci are highly abundant in free-living but lost from host-associated prokaryotes. *Nucleic Acids Res* 33, 966-76.
- (73) Jensen, R. B., Grohmann, E., Schwab, H., Diaz-Orejas, R., and Gerdes, K. (1995) Comparison of ccd of F, parDE of RP4, and parD of R1 using a novel conditional replication control system of plasmid R1. *Mol Microbiol* 17, 211-20.
- (74) Boe, L., Gerdes, K., and Molin, S. (1987) Effects of genes exerting growth inhibition and plasmid stability on plasmid maintenance. *J Bacteriol* 169, 4646-50.
- (75) Miki, T., Yoshioka, K., and Horiuchi, T. (1984) Control of cell division by sex factor F in Escherichia coli. I. The 42.84-43.6 F segment couples cell division of the host bacteria with replication of plasmid DNA. *J Mol Biol* 174, 605-25.
- (76) Allen, G. C., Jr., and Kornberg, A. (1991) Fine balance in the regulation of DnaB helicase by DnaC protein in replication in Escherichia coli. *J Biol Chem* 266, 22096-101.
- (77) Hiraga, S., Jaffe, A., Ogura, T., Mori, H., and Takahashi, H. (1986) F plasmid ccd mechanism in Escherichia coli. *J Bacteriol* 166, 100-4.
- (78) Pedersen, K., Christensen, S. K., and Gerdes, K. (2002) Rapid induction and reversal of a bacteriostatic condition by controlled expression of toxins and antitoxins. *Mol Microbiol* 45, 501-10.
- (79) Gronlund, H., and Gerdes, K. (1999) Toxin-antitoxin systems homologous with relBE of Escherichia coli plasmid P307 are ubiquitous in prokaryotes. *J Mol Biol* 285, 1401-15.
- (80) Smith, A. S., and Rawlings, D. E. (1997) The poison-antidote stability system of the broad-host-range *Thiobacillus ferrooxidans* plasmid pTF-FC2. *Mol Microbiol* 26, 961-70.
- (81) Tian, Q. B., Ohnishi, M., Tabuchi, A., and Terawaki, Y. (1996) A new plasmid-encoded proteic killer gene system: cloning, sequencing, and analyzing hig locus of plasmid Rts1. *Biochem Biophys Res Commun* 220, 280-4.
- (82) Tian, Q. B., Ohnishi, M., Murata, T., Nakayama, K., Terawaki, Y., and Hayashi, T. (2001) Specific protein-DNA and protein-protein interaction in the hig gene system, a plasmid-borne proteic killer gene system of plasmid Rts1. *Plasmid* 45, 63-74.
- (83) Roberts, R. C., and Helinski, D. R. (1992) Definition of a minimal plasmid stabilization system from the broad-host-range plasmid RK2. *J Bacteriol* 174, 8119-32.
- (84) Gerlitz, M., Hrabak, O., and Schwab, H. (1990) Partitioning of broad-host-range plasmid RP4 is a complex system involving site-specific recombination. *J Bacteriol* 172, 6194-203.

- (85) Sobecky, P. A., Easter, C. L., Bear, P. D., and Helinski, D. R. (1996) Characterization of the stable maintenance properties of the par region of broad-host-range plasmid RK2. *J Bacteriol* 178, 2086-93.
- (86) Roberts, R. C., Strom, A. R., and Helinski, D. R. (1994) The parDE operon of the broad-host-range plasmid RK2 specifies growth inhibition associated with plasmid loss. *J Mol Biol* 237, 35-51.
- (87) Haigermoser, C., Chen, G. Q., Grohmann, E., Hrabak, O., and Schwab, H. (1993) Stability of r-microbes: stabilization of plasmid vectors by the partitioning function of broad-host-range plasmid RP4. *J Biotechnol* 28, 291-9.
- (88) Sia, E. A., Roberts, R. C., Easter, C., Helinski, D. R., and Figurski, D. H. (1995) Different relative importances of the par operons and the effect of conjugal transfer on the maintenance of intact promiscuous plasmid RK2. *J Bacteriol* 177, 2789-97.
- (89) Ruiz-Echevarria, M. J., de la Torre, M. A., and Diaz-Orejas, R. (1995) A mutation that decreases the efficiency of plasmid R1 replication leads to the activation of parD, a killer stability system of the plasmid. *FEMS Microbiol Lett* 130, 129-35.
- (90) Tsuchimoto, S., Ohtsubo, H., and Ohtsubo, E. (1988) Two genes, pemK and pemI, responsible for stable maintenance of resistance plasmid R100. *J Bacteriol* 170, 1461-6.
- (91) Bravo, A., de Torrontegui, G., and Diaz, R. (1987) Identification of components of a new stability system of plasmid R1, ParD, that is close to the origin of replication of this plasmid. *Mol Gen Genet* 210, 101-10.
- (92) Masuda, Y., and Ohtsubo, E. (1994) Mapping and disruption of the chpB locus in *Escherichia coli*. *J Bacteriol* 176, 5861-3.
- (93) Masuda, Y., Miyakawa, K., Nishimura, Y., and Ohtsubo, E. (1993) chpA and chpB, *Escherichia coli* chromosomal homologs of the pem locus responsible for stable maintenance of plasmid R100. *J Bacteriol* 175, 6850-6.
- (94) Metzger, S., Dror, I. B., Aizenman, E., Schreiber, G., Toone, M., Friesen, J. D., Cashel, M., and Glaser, G. (1988) The nucleotide sequence and characterization of the relA gene of *Escherichia coli*. *J Biol Chem* 263, 15699-704.
- (95) Lehnher, H., Maguin, E., Jafri, S., and Yarmolinsky, M. B. (1993) Plasmid addiction genes of bacteriophage P1: doc, which causes cell death on curing of prophage, and phd, which prevents host death when prophage is retained. *J Mol Biol* 233, 414-28.
- (96) Lehnher, H., and Yarmolinsky, M. B. (1995) Addiction protein Phd of plasmid prophage P1 is a substrate of the ClpXP serine protease of *Escherichia coli*. *Proc Natl Acad Sci U S A* 92, 3274-7.
- (97) Gazit, E., and Sauer, R. T. (1999) The Doc toxin and Phd antidote proteins of the bacteriophage P1 plasmid addiction system form a heterotrimeric complex. *J Biol Chem* 274, 16813-8.

- (98) Cherny, I., and Gazit, E. (2004) The YefM antitoxin defines a family of natively unfolded proteins: implications as a novel antibacterial target. *J Biol Chem* 279, 8252-61.
- (99) Pomerantsev, A. P., Golovliov, I. R., Ohara, Y., Mokrievich, A. N., Obuchi, M., Norqvist, A., Kuoppa, K., and Pavlov, V. M. (2001) Genetic organization of the *Francisella* plasmid pFNL10. *Plasmid* 46, 210-22.
- (100) Hazan, R., Sat, B., Reches, M., and Engelberg-Kulka, H. (2001) Postsegregational killing mediated by the P1 phage "addiction module" phd-doc requires the *Escherichia coli* programmed cell death system mazEF. *J Bacteriol* 183, 2046-50.
- (101) Pullinger, G. D., and Lax, A. J. (1992) A *Salmonella dublin* virulence plasmid locus that affects bacterial growth under nutrient-limited conditions. *Mol Microbiol* 6, 1631-43.
- (102) de la Hoz, A. B., Ayora, S., Sitkiewicz, I., Fernandez, S., Pankiewicz, R., Alonso, J. C., and Ceglowski, P. (2000) Plasmid copy-number control and better-than-random segregation genes of pSM19035 share a common regulator. *Proc Natl Acad Sci U S A* 97, 728-33.
- (103) Camacho, A. G., Misselwitz, R., Behlke, J., Ayora, S., Welfle, K., Meinhart, A., Lara, B., Saenger, W., Welfle, H., and Alonso, J. C. (2002) In vitro and in vivo stability of the epsilon2zeta2 protein complex of the broad host-range *Streptococcus pyogenes* pSM19035 addiction system. *Biol Chem* 383, 1701-13.
- (104) Christensen, S. K., and Gerdes, K. (2003) RelE toxins from bacteria and Archaea cleave mRNAs on translating ribosomes, which are rescued by tmRNA. *Mol Microbiol* 48, 1389-400.
- (105) Pedersen, K., Zavialov, A. V., Pavlov, M. Y., Elf, J., Gerdes, K., and Ehrenberg, M. (2003) The bacterial toxin RelE displays codon-specific cleavage of mRNAs in the ribosomal A site. *Cell* 112, 131-40.
- (106) Zavialov, A. V., Mora, L., Buckingham, R. H., and Ehrenberg, M. (2002) Release of peptide promoted by the GGQ motif of class 1 release factors regulates the GTPase activity of RF3. *Mol Cell* 10, 789-98.
- (107) Christensen, S. K., Maenhaut-Michel, G., Mine, N., Gottesman, S., Gerdes, K., and Van Melderen, L. (2004) Overproduction of the Lon protease triggers inhibition of translation in *Escherichia coli*: involvement of the yefM-yoeB toxin-antitoxin system. *Mol Microbiol* 51, 1705-17.
- (108) Takagi, H., Kakuta, Y., Okada, T., Yao, M., Tanaka, I., and Kimura, M. (2005) Crystal structure of archaeal toxin-antitoxin RelE-RelB complex with implications for toxin activity and antitoxin effects. *Nat Struct Mol Biol* 12, 327-31.
- (109) Kamada, K., Hanaoka, F., and Burley, S. K. (2003) Crystal structure of the MazE/MazF complex: molecular bases of antidote-toxin recognition. *Mol Cell* 11, 875-84.
- (110) Wilson, D. N., and Nierhaus, K. H. (2005) RelBE or not to be. *Nat Struct Mol Biol* 12, 282-4.

- (111) Mirny, L., and Shakhnovich, E. (2001) Protein folding theory: from lattice to all-atom models. *Annu Rev Biophys Biomol Struct* 30, 361-96.
- (112) Epstein CJ, G. R., Anfinsen CB. (1963) The genetic control of tertiary protein structure: Studies with model systems. *Cold Spring Harbor Symp. Quant. Biol.* 27, 439-449.
- (113) Stryer L (1995) *Biochemistry*, 4th ed., W.H. Freeman and company, New York.
- (114) Anfinsen, C. B. (1973) Principles that govern the folding of protein chains. *Science* 181, 223-30.
- (115) Anfinsen, C. B., and Haber, E. (1961) Studies on the reduction and reformation of protein disulfide bonds. *J Biol Chem* 236, 1361-3.
- (116) Anfinsen, C. B., Haber, E., Sela, M., and White, F. H., Jr. (1961) The kinetics of formation of native ribonuclease during oxidation of the reduced polypeptide chain. *Proc Natl Acad Sci U S A* 47, 1309-14.
- (117) Dill, K. A., and Chan, H. S. (1997) From Levinthal to pathways to funnels. *Nat Struct Biol* 4, 10-9.
- (118) Levinthal, C. (1968) Are there pathways for protein folding? *J. Chim. Phys.* 65, 44-45.
- (119) Baldwin, R. L. R., G.D. (1999) Is protein folding hierachic? I. Local structure and peptide folding. *Trends Biochem Sci*. 24, 26-33.
- (120) Baldwin, R. L. R., G.D. (1999) Is protein folding hierachic? II. Folding intermediates and transition states. *Trends Biochem Sci*. 24, 77-83.
- (121) Chan, H. S., Bromberg, S., and Dill, K. A. (1995) Models of cooperativity in protein folding. *Philos Trans R Soc Lond B Biol Sci* 348, 61-70.
- (122) Dill, K. A., Bromberg, S., Yue, K., Fiebig, K. M., Yee, D. P., Thomas, P. D., and Chan, H. S. (1995) Principles of protein folding--a perspective from simple exact models. *Protein Sci* 4, 561-602.
- (123) Pace, C. N., Shirley, B. A., McNutt, M., and Gajiwala, K. (1996) Forces contributing to the conformational stability of proteins. *Faseb J* 10, 75-83.
- (124) Eftink, M. R., and Shastry, M. C. (1997) Fluorescence methods for studying kinetics of protein-folding reactions. *Methods Enzymol* 278, 258-86.
- (125) Vivian, J. T., and Callis, P. R. (2001) Mechanisms of tryptophan fluorescence shifts in proteins. *Biophys J* 80, 2093-109.
- (126) Woody, R. W. (1995) Circular dichroism. *Methods Enzymol* 246, 34-71.
- (127) Callis, P. R. (1997) 1La and 1Lb transitions of tryptophan: applications of theory and experimental observations to fluorescence of proteins. *Methods Enzymol* 278, 113-50.
- (128) Callis, P. R., and Burgess, B. K. (1997) Tryptophan Fluorescence Shifts in Proteins from Hybrid Simulations: An Electrostatic Approach. *J. Phys. Chem. B* 101, 9429-9432.
- (129) Chen, Y., and Barkley, M. D. (1998) Toward understanding tryptophan fluorescence in proteins. *Biochemistry* 37, 9976-82.
- (130) Chen, Y., Liu, B., Yu, H. T., and Barkley, M. D. (1996) The Peptide Bond Quenches Indole Fluorescence. *J. Am. Chem. Soc.* 118, 9271-9278.

- (131) Meagher, J. L., Beechem, J. M., Olson, S. T., and Gettins, P. G. (1998) Deconvolution of the fluorescence emission spectrum of human antithrombin and identification of the tryptophan residues that are responsive to heparin binding. *J Biol Chem* 273, 23283-9.
- (132) Beechem, J. M., and Brand, L. (1985) Time-resolved fluorescence of proteins. *Annu Rev Biochem* 54, 43-71.
- (133) Eftink, M. R. (1991) Fluorescence techniques for studying protein structure. *Methods Biochem Anal* 35, 127-205.
- (134) Lakowicz, J. R. (1983) *Principles of fluorescence spectroscopy*, Plenum Press, New York.
- (135) Lakowicz, J. R. (1999) *Principles of fluorescence spectroscopy*, 2nd ed., Kluwer Academic/Plenum Publishers, New York.
- (136) Harpaz, Y., Gerstein, M., and Chothia, C. (1994) Volume changes on protein folding. *Structure* 2, 641-9.
- (137) Lesser, G. J., and Rose, G. D. (1990) Hydrophobicity of amino acid subgroups in proteins. *Proteins* 8, 6-13.
- (138) Fauchere, J. L., and Pliska, V.E. (1983) Hydrophobic parameters of amino-acid side-chains from the partitioning of N-acetyl-amino-acid amides. *Eur J Med Chem* 18, 369-375.
- (139) Schmid, F. X. (1997) Optical spectroscopy to characterize protein conformation and conformational changes. In *Protein Structure: A practical approach*, (ed. T.E. Creighton) ed., pp. 261-297, Oxford university press, Oxford.
- (140) Ross, J. B., Szabo, A.G., and Hogue, C.W., 1997. Enhancement of protein spectra with tryptophan analogs: fluorescence spectroscopy of protein-protein and protein-nucleic acid interactions. *Methods Enzymol*, Vol. 278, 151-190.
- (141) Konev, S. V. (1967) *Fluorescence and phosphorescence of proteins and nucleic acids*, Plenum Press, New York.
- (142) Reshetnyak, Y. K., and Burstein, E. A. (2001) Decomposition of protein tryptophan fluorescence spectra into log-normal components. II. The statistical proof of discreteness of tryptophan classes in proteins. *Biophys J* 81, 1710-34.
- (143) Burstein, E. A., Abornev, S. M., and Reshetnyak, Y. K. (2001) Decomposition of protein tryptophan fluorescence spectra into log-normal components. I. Decomposition algorithms. *Biophys J* 81, 1699-709.
- (144) Burstein, E. A., Vedenkina, N. S., and Ivkova, M. N. (1973) Fluorescence and the location of tryptophan residues in protein molecules. *Photochem Photobiol* 18, 263-79.
- (145) Reshetnyak, Y. K., Koshevnik, Y., and Burstein, E. A. (2001) Decomposition of protein tryptophan fluorescence spectra into log-normal components. III. Correlation between fluorescence and microenvironment parameters of individual tryptophan residues. *Biophys J* 81, 1735-58.
- (146) Engelborghs, Y. (2003) Correlating protein structure and protein fluorescence. *J Fluoresc* 13, 9-16.

- (147) Aronsson, G., Brorsson, A. C., Sahlman, L., and Jonsson, B. H. (1997) Remarkably slow folding of a small protein. *FEBS Lett* 411, 359-64.
- (148) Nicholson, E. M., and Scholtz, J. M. (1996) Conformational stability of the *Escherichia coli* HPr protein: test of the linear extrapolation method and a thermodynamic characterization of cold denaturation. *Biochemistry* 35, 11369-78.
- (149) Scholtz, J. M. (1995) Conformational stability of HPr: the histidine-containing phosphocarrier protein from *Bacillus subtilis*. *Protein Sci* 4, 35-43.
- (150) Taddei, N., Chiti, F., Paoli, P., Fiaschi, T., Bucciantini, M., Stefani, M., Dobson, C. M., and Ramponi, G. (1999) Thermodynamics and kinetics of folding of common-type acylphosphatase: comparison to the highly homologous muscle isoenzyme. *Biochemistry* 38, 2135-42.
- (151) Van Nuland, N. A., Meijberg, W., Warner, J., Forge, V., Scheek, R. M., Robillard, G. T., and Dobson, C. M. (1998) Slow cooperative folding of a small globular protein HPr. *Biochemistry* 37, 622-37.
- (152) Greene, R. F., Jr., and Pace, C. N. (1974) Urea and guanidine hydrochloride denaturation of ribonuclease, lysozyme, alpha-chymotrypsin, and beta-lactoglobulin. *J Biol Chem* 249, 5388-93.
- (153) Santoro, M. M., and Bolen, D. W. (1988) Unfolding free energy changes determined by the linear extrapolation method. 1. Unfolding of phenylmethanesulfonyl alpha-chymotrypsin using different denaturants. *Biochemistry* 27, 8063-8.
- (154) Pace, C. N., and Laurents, D. V. (1989) A new method for determining the heat capacity change for protein folding. *Biochemistry* 28, 2520-5.
- (155) Freire, E. (1995) Differential scanning calorimetry. *Methods Mol Biol* 40, 191-218.
- (156) Freire, E. (1995) Thermal denaturation methods in the study of protein folding. *Methods Enzymol* 259, 144-68.
- (157) Ceglowski, P., and Alonso, J. C. (1994) Gene organization of the *Streptococcus pyogenes* plasmid pDB101: sequence analysis of the orf eta-copS region. *Gene* 145, 33-9.
- (158) Studier, F. W., and Moffatt, B. A. (1986) Use of bacteriophage T7 RNA polymerase to direct selective high-level expression of cloned genes. *J Mol Biol* 189, 113-30.
- (159) Rojo, F., Weise, F., and Alonso, J. C. (1993) Purification of the beta product encoded by the *Streptococcus pyogenes* plasmid pSM19035. A putative DNA recombinase required to resolve plasmid oligomers. *FEBS Lett* 328, 169-73.
- (160) Bech, F. W., Jorgensen, S. T., Diderichsen, B., and Karlstrom, O. H. (1985) Sequence of the relB transcription unit from *Escherichia coli* and identification of the relB gene. *Embo J* 4, 1059-66.
- (161) Blattner, F. R., Plunkett, G., 3rd, Bloch, C. A., Perna, N. T., Burland, V., Riley, M., Collado-Vides, J., Glasner, J. D., Rode, C. K., Mayhew, G. F., Gregor, J., Davis, N. W., Kirkpatrick, H. A., Goeden, M. A., Rose, D. J.,

- Mau, B., and Shao, Y. (1997) The complete genome sequence of *Escherichia coli* K-12. *Science* 277, 1453-74.
- (162) Aiba, H., Baba, T., Hayashi, K., Inada, T., Isono, K., Itoh, T., Kasai, H., Kashimoto, K., Kimura, S., Kitakawa, M., Kitagawa, M., Makino, K., Miki, T., Mizobuchi, K., Mori, H., Mori, T., Motomura, K., Nakade, S., Nakamura, Y., Nashimoto, H., Nishio, Y., Oshima, T., Saito, N., Sampei, G., Horiuchi, T., and et al. (1996) A 570-kb DNA sequence of the *Escherichia coli* K-12 genome corresponding to the 28.0-40.1 min region on the linkage map. *DNA Res* 3, 363-77.
- (163) Cantor, E. J., and Chong, S. (2001) Intein-mediated rapid purification of Cre recombinase. *Protein Expr Purif* 22, 135-40.
- (164) Bult, C. J., White, O., Olsen, G. J., Zhou, L., Fleischmann, R. D., Sutton, G. G., Blake, J. A., FitzGerald, L. M., Clayton, R. A., Gocayne, J. D., Kerlavage, A. R., Dougherty, B. A., Tomb, J. F., Adams, M. D., Reich, C. I., Overbeek, R., Kirkness, E. F., Weinstock, K. G., Merrick, J. M., Glodek, A., Scott, J. L., Geoghegan, N. S., and Venter, J. C. (1996) Complete genome sequence of the methanogenic archaeon, *Methanococcus jannaschii*. *Science* 273, 1058-73.
- (165) Gomori, G. (1955) Preparation of buffers for use in enzyme studies. *Methods Enzymol.*, Vol. 1: 138-146.
- (166) Kawahara, K., and Tanford, C. (1966) Viscosity and density of aqueous solutions of urea and guanidine hydrochloride. *J Biol Chem* 241, 3228-32.
- (167) Warren, J. R., Gordon, J.A. (1966) On the refractive indices of aqueous solutions of urea. *J Phys Chem* 70, 297-300.
- (168) Hagel, P., Gerding, J. J., Fiegen, W., and Bloemendaal, H. (1971) Cyanate formation in solutions of urea. I. Calculation of cyanate concentrations at different temperature and pH. *Biochim Biophys Acta* 243, 366-73.
- (169) Nozaki, Y. (1972) The preparation of guanidine hydrochloride. *Methods Enzymol* 26 PtC, 43-50.
- (170) Harlow, E., Lane, D. (1988) *Antibodies: A laboratory manual.*, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York.
- (171) Laemmli, U. K. (1970) Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* 227, 680-5.
- (172) Manavalan, P., and Johnson, W. C., Jr. (1987) Variable selection method improves the prediction of protein secondary structure from circular dichroism spectra. *Anal Biochem* 167, 76-85.
- (173) Andrade, M. A., Chacon, P., Merelo, J. J., and Moran, F. (1993) Evaluation of secondary structure of proteins from UV circular dichroism spectra using an unsupervised learning neural network. *Protein Eng* 6, 383-90.
- (174) Hedwig G.R., Lilley T.H., and Linsdell H. (1991) Calorimetric and volumetric studies of the interactions of some amides in water and in 6 mol dm⁻³ aqueous guanidinium chloride. *Journal of the Chemical Society, Faraday Transactions* 87, 2975 - 2982.

- (175) Dunbar, J., Yennawar, H. P., Banerjee, S., Luo, J., and Farber, G. K. (1997) The effect of denaturants on protein structure. *Protein Sci* 6, 1727-33.
- (176) Pace, C. N. (1986) Determination and analysis of urea and guanidine hydrochloride denaturation curves. *Methods Enzymol* 131, 266-80.
- (177) Privalov, P. L., and Potekhin, S. A. (1986) Scanning microcalorimetry in studying temperature-induced changes in proteins. *Methods Enzymol* 131, 4-51.
- (178) Sturtevant, J. M. (1987) Biochemical applications of differential scanning calorimetry. *Annu. Rev. Phys. Chem.* 38, 463-488.
- (179) Leharne, S. A., and Chowdry, B. Z. (1998) Thermodynamic background to differential scanning calorimetry. In *Biocalorimetry: Applications in the Biological Sciences*, John Wiley, Chichester, UK, 157-182.
- (180) Behlke, J., and Ristau, O. (2003) Sedimentation equilibrium: a valuable tool to study homologous and heterogeneous interactions of proteins or proteins and nucleic acids. *Eur Biophys J* 32, 427-31.
- (181) Bonvin, A. M., Vis, H., Breg, J. N., Burgering, M. J., Boelens, R., and Kaptein, R. (1994) Nuclear magnetic resonance solution structure of the Arc repressor using relaxation matrix calculations. *J Mol Biol* 236, 328-41.
- (182) Lawson, C. L., Zhang, R. G., Schevitz, R. W., Otwinowski, Z., Joachimiak, A., and Sigler, P. B. (1988) Flexibility of the DNA-binding domains of trp repressor. *Proteins* 3, 18-31.
- (183) Ohlendorf, D. H., Tronrud, D. E., and Matthews, B. W. (1998) Refined structure of Cro repressor protein from bacteriophage lambda suggests both flexibility and plasticity. *J Mol Biol* 280, 129-36.
- (184) Dhar, G., Sanders, E. R., and Johnson, R. C. (2004) Architecture of the hin synaptic complex during recombination: the recombinase subunits translocate with the DNA strands. *Cell* 119, 33-45.
- (185) Krasnow, M. A., and Cozzarelli, N. R. (1983) Site-specific relaxation and recombination by the Tn3 resolvase: recognition of the DNA path between oriented res sites. *Cell* 32, 1313-24.
- (186) Baldwin, T. O., Ziegler, M. M., Chaffotte, A. F., and Goldberg, M. E. (1993) Contribution of folding steps involving the individual subunits of bacterial luciferase to the assembly of the active heterodimeric enzyme. *J Biol Chem* 268, 10766-72.
- (187) Blackburn, M. N., and Noltmann, E. A. (1981) Evidence for an intermediate in the denaturation and assembly of phosphoglucose isomerase. *Arch Biochem Biophys* 212, 162-9.
- (188) Doyle, S. M., Braswell, E. H., and Teschke, C. M. (2000) SecA folds via a dimeric intermediate. *Biochemistry* 39, 11667-76.
- (189) Jaenicke, R., and Lilie, H. (2000) Folding and association of oligomeric and multimeric proteins. *Adv Protein Chem* 53, 329-401.
- (190) Louzada, P. R., Sebollela, A., Scaramello, M. E., and Ferreira, S. T. (2003) Predissociated dimers and molten globule monomers in the

- equilibrium unfolding of yeast glutathione reductase. *Biophys J* 85, 3255-61.
- (191) Morjana, N. A., McKeone, B. J., and Gilbert, H. F. (1993) Guanidine hydrochloride stabilization of a partially unfolded intermediate during the reversible denaturation of protein disulfide isomerase. *Proc Natl Acad Sci U S A* 90, 2107-11.
- (192) Shortle, D., and Ackerman, M. S. (2001) Persistence of native-like topology in a denatured protein in 8 M urea. *Science* 293, 487-9.
- (193) Welfle, K., Pratto, F., Misselwitz, R., Behlke, J., Alonso, J. C., and Welfle, H. (2005) Role of the N-terminal region and of beta-sheet residue Thr29 on the activity of the omega(2) global regulator from the broad-host range *Streptococcus pyogenes* plasmid pSM19035. *Biol Chem* 386, 881-94.
- (194) Robinson, C. R., Rentzepis, D., Silva, J. L., and Sauer, R. T. (1997) Formation of a denatured dimer limits the thermal stability of Arc repressor. *J Mol Biol* 273, 692-700.
- (195) Oberer, M., Lindner, H., Glatter, O., Kratky, C., and Keller, W. (1999) Thermodynamic properties and DNA binding of the ParD protein from the broad host-range plasmid RK2/RP4 killing system. *Biol Chem* 380, 1413-20.
- (196) Bowie, J. U., and Sauer, R. T. (1989) Equilibrium dissociation and unfolding of the Arc repressor dimer. *Biochemistry* 28, 7139-43.
- (197) Neet, K. E., and Timm, D. E. (1994) Conformational stability of dimeric proteins: quantitative studies by equilibrium denaturation. *Protein Sci* 3, 2167-74.
- (198) Jana, R., Hazbun, T. R., Mollah, A. K., and Mossing, M. C. (1997) A folded monomeric intermediate in the formation of lambda Cro dimer-DNA complexes. *J Mol Biol* 273, 402-16.
- (199) De Francesco, R., Pastore, A., Vecchio, G., and Cortese, R. (1991) Circular dichroism study on the conformational stability of the dimerization domain of transcription factor LFB1. *Biochemistry* 30, 143-7.
- (200) Lah, J., Marianovsky, I., Glaser, G., Engelberg-Kulka, H., Kinne, J., Wyns, L., and Loris, R. (2003) Recognition of the intrinsically flexible addiction antidote MazE by a dromedary single domain antibody fragment. Structure, thermodynamics of binding, stability, and influence on interactions with DNA. *J Biol Chem* 278, 14101-11.
- (201) Martin, M. C., Alonso, J. C., Suarez, J. E., and Alvarez, M. A. (2000) Generation of food-grade recombinant lactic acid bacterium strains by site-specific recombination. *Appl Environ Microbiol* 66, 2599-604.
- (202) Engelberg-Kulka, H., Sat, B., Reches, M., Amitai, S., and Hazan, R. (2004) Bacterial programmed cell death systems as targets for antibiotics. *Trends Microbiol* 12, 66-71.
- (203) Bolen, D. W., and Santoro, M. M. (1988) Unfolding free energy changes determined by the linear extrapolation method. 2. Incorporation of ΔG°_{N-U} values in a thermodynamic cycle. *Biochemistry* 27, 8069-74.