

5. Literaturverzeichnis

- Agrawal, R. K., Heagle, A. B., Penczek, P., Grassucci, R. A., and Frank, J. (1999a). EF-G-dependent GTP hydrolysis induces translocation accompanied by large conformational changes in the 70S ribosome. *Nature Struct Biol* 6, 643-647.
- Agrawal, R. K., Penczek, P., Grassucci, R. A., Burkhardt, N., Nierhaus, K. H., and Frank, J. (1999b). Effect of buffer conditions on the position of tRNA on the 70S ribosome as visualized by cryo-electron microscopy. *J Biol Chem* 274, 8723-8729.
- Agrawal, R. K., Spahn, C. M. T., Penczek, P., Grassucci, R. A., Nierhaus, K. H., and Frank, J. (2000). Visualization of tRNA movements on the *Escherichia coli* 70S ribosome during the elongation cycle. *J Cell Biol* 150, 447-459.
- Allen, D. W., and Zamecnik, P. C. (1962). The effect of puromycin on rabbit reticulocyte ribosomes. *Biochim Biophys Acta* 55, 865-874.
- Asai, T., Zaporojets, D., Squires, C., and Squires, C. L. (1999). An *Escherichia coli* strain with all chromosomal rRNA operons inactivated: complete exchange of rRNA genes between bacteria. *Proc Natl Acad Sci U S A* 96, 1971-1976.
- Baierlein, R., and Infante, A. A. (1974). Pressure-induced dissociation of ribosomes. *Methods Enzymol* 30, 328-335.
- Bartetzko, A., and Nierhaus, K. H. (1988). A simple Mg^{2+}/NH_4^+ /polyamine system for poly(U) dependent poly(Phe) synthesis with near *in vivo* characteristics. *Methods Enzymol* 164, 650-658.
- Bashan, A., Agmon, I., Zarivach, R., Schluenzen, F., Harms, J., Berisio, R., Bartels, H., Franceschi, F., Auerbach, T., Hansen, H. A., et al. (2003). Structural basis of the ribosomal machinery for peptide bond formation, translocation, and nascent chain progression. *Mol Cell* 11, 91-102.
- Bashan, A., and Yonath, A. (2005). Ribosome crystallography: catalysis and evolution of peptide-bond formation, nascent chain elongation and its co-translational folding. *Biochem Soc Trans* 33, 488-492.
- Berg, O. G., and Kurland, C. G. (1997). Growth rate-optimised tRNA abundance and codon usage. *J Mol Biol* 270, 544-550.
- Bergemann, K., and Nierhaus, K. H. (1983). Spontaneous, elongation factor G independent translocation of *Escherichia coli* ribosomes. *J Biol Chem* 258, 15105-15113.

- Birnboim, H. C. (1983). A rapid alkaline extraction method for the isolation of plasmid DNA. *Meth Enzymol* 100, 243-255.
- Blaha, G., and Nierhaus, K. H. (2001). Features and functions of the ribosomal E site. *Cold Spring Harbor Symposia on Quantitative Biology* 65, 135-145.
- Blaha, G., Stelzl, U., Spahn, C. M. T., Agrawal, R. K., Frank, J., and Nierhaus, K. H. (2000). Preparation of functional ribosomal complexes and the effect of buffer conditions on tRNA positions observed by cryoelectron microscopy. *Methods Enzymol* 317, 292-309.
- Block, R., and Haseltine, W. (1975). Purification and properties of stringent factor. *J Biol Chem* 250, 1212-1217.
- Bommer, U., Burkhardt, N., Jünemann, R., Spahn, C. M. T., Triana-Alonso, F. J., and Nierhaus, K. H. (1996). Ribosomes and polysomes. In *Subcellular fractionation. A practical approach*, J. Graham, and D. Rickwoods, eds. (Oxford, IRL Press at Oxford University Press), pp. 271-301.
- Borovinskaya, M. A., Pai, R. D., Zhang, W., Schuwirth, B. S., Holton, J. M., Hirokawa, G., Kaji, H., Kaji, A., and Cate, J. H. (2007). Structural basis for aminoglycoside inhibition of bacterial ribosome recycling. *Nat Struct Mol Biol* 14, 727-732.
- Bouadloun, F., Donner, D., and Kurland, C. G. (1983). Codon-specific missense errors *in vivo*. *EMBO J* 2, 1351-1356.
- Brosius, J., Ullrich, A., Raker, M. A., Gray, A., Dull, T. J., Gutell, R. R., and Noller, H. F. (1981). Construction and fine mapping of recombinant plasmids containing the rrn B ribosomal RNA operon of *E. coli*. *Plasmid* 6, 112-118.
- Caskey, T., Scolnick, E., Tompkins, R., Goldstein, J., and Milman, G. (1969). Peptide chain termination, codon, protein factor, and ribosomal requirements. In *Cold Spring Harbor Symp. Quant. Biol.*, pp. 479-491.
- Cate, J. H., Yusupov, M. M., Yusupova, G. Z., Earnest, T. N., and Noller, H. F. (1999). X-ray crystal structures of 70S ribosome functional complexes. *Science* 285, 2095-2104.
- Christiansen, L., and Nierhaus, K. H. (1976). Ribosomal proteins of *Escherichia coli* stimulating stringent factor mediated pyrophosphoryl transfer *in vitro*. *Proc Natl Acad Sci USA* 73, 1839-1843.
- Cochran, J. W., and Byrne, R. W. (1974). Isolation and properties of a ribosome bound factor required for ppGpp and pppGpp synthesis in *Escherichia coli*. *J Biol Chem* 249, 353-360.

- Colca, J. R., McDonald, W. G., Waldon, D. J., Thomasco, L. M., Gadwood, R. C., Lund, E. T., Cavey, G. S., Mathews, W. R., Adams, L. D., Cecil, E. T., *et al.* (2003). Crosslinking in the living cell locates the site of action of oxazolidinone antibiotics. *J Biol Chem* 278, 21972-21979.
- Dabrowski, M., Spahn, C. M. T., and Nierhaus, K. H. (1995). Interaction of tRNAs with the ribosome at the A and P sites. *EMBO J* 14, 4872-4882.
- Dabrowski, M., Spahn, C. M. T., Schäfer, M. A., Patzke, S., and Nierhaus, K. H. (1998). Contact patterns of tRNAs do not change during ribosomal translocation. *J Biol Chem* 273, 32793-32800.
- Dibb, N. J., and Wolfe, P. B. (1986). lep operon proximal gene is not required for growth or secretion by *Escherichia coli*. *J Bacteriol* 166, 83-87.
- Dinos, G., Kalpaxis, D. L., Wilson, D. N., and Nierhaus, K. H. (2005). Deacylated tRNA is released from the E site upon A site occupation but before GTP is hydrolyzed by EF-Tu. *Nucleic Acids Res* 33, 5291-5296.
- Dinos, G., Wilson, D. N., Teraoka, Y., Szaflarski, W., Fucini, P., Kalpaxis, D., and Nierhaus, K. H. (2004). Dissecting the ribosomal inhibition mechanisms of edeine and pactamycin: the universally conserved residues G693 and C795 regulate P-site tRNA binding. *Mol Cell* 13, 113-124.
- Dong, H. J., Nilsson, L., and Kurland, C. G. (1996). Co-variation of tRNA abundance and codon usage in *Escherichia coli* at different growth rates. *J Mol Biol* 260, 649-663.
- Dontsova, M., Frolova, L., Vassilieva, J., Piendl, W., Kisilev, L., and Garber, M. (2000). Translation termination factor aRF1 from the archaeon *Methanococcus jannaschii* is active with eukaryotic ribosomes. *FEBS Lett* 472, 213-216.
- Dorner, S., Brunelle, J. L., Sharma, D., and Green, R. (2006). The hybrid state of tRNA binding is an authentic translation elongation intermediate. *Nat Struct Mol Biol* 13, 234-241.
- Doudna, J. A., and Rath, V. L. (2002). Structure and function of the eukaryotic ribosome: the next frontier. *Cell* 109, 153-156.
- Erlacher, M. D., Lang, K., Shankaran, N., Wotzel, B., Huttenhofer, A., Micura, R., Mankin, A. S., and Polacek, N. (2005). Chemical engineering of the peptidyl transferase center reveals an important role of the 2'-hydroxyl group of A2451. *Nucleic Acids Res* 33, 1618-1627.

- Erlacher, M. D., Lang, K., Wotzel, B., Rieder, R., Micura, R., and Polacek, N. (2006). Efficient ribosomal peptidyl transfer critically relies on the presence of the ribose 2'-OH at A2451 of 23S rRNA. *J Am Chem Soc* **128**, 4453-4459.
- Frank, J. (2001). Cryo-electron microscopy as an investigative tool: the ribosome as an example. *Bioessays* **23**, 725-732.
- Frank, J. (2003). Electron microscopy of functional ribosome complexes. *Biopolymers* **68**, 223-233.
- Frank, J., and Agrawal, R. (2001). Ratchet-like movements between the two ribosomal subunits: their implications in elongation factor recognition and tRNA translocation. *Cold Spring Harb Symp Quant Biol* **66**, 67-75.
- Frank, J., Agrawal, R., and Verschoor, A. (1999). Ribosome structure and shape (Nature publishing Group).
- Frank, J., and Agrawal, R. K. (2000). A ratchet-like inter-subunit reorganization of the ribosome during translocation. *Nature* **406**, 318-322.
- Freistroffer, D. V., Pavlov, M. Y., MacDougall, J., Buckingham, R. H., and Ehrenberg, M. (1997). Release factor RF3 in *E. coli* accelerates the dissociation of release factors RF1 and RF2 from the ribosome in a GTP-dependent manner. *EMBO J* **16**, 4126-4133.
- Frolova, L., Le Goff, X., Rasmussen, H. H., Cheperegin, S., Drugeon, G., Kress, M., Arman, I., Haenni, A.-L., Celis, J. E., Philippe, M., *et al.* (1994). A highly conserved eukaryotic protein family possessing properties of polypeptide chain release factor. *Nature* **372**, 701-703.
- Frolova, L., Tsivkovskii, R., Sivolobova, G., Oparina, N., Serpinski, O., Blinov, V., Tatkov, S., and Kisilev, L. (1999). Mutations in the highly conserved GGQ motif of class 1 polypeptide release factors abolish the ability of human eRF1 to trigger peptidyl-tRNA hydrolysis. *RNA* **5**, 1014-1020.
- Gao, H., Sengupta, J., Valle, M., Korostelev, A., Eswar, N., Stagg, S. M., van Roey, P., Agrawal, R. K., Harvey, S. C., Sali, A., *et al.* (2003). Study of the structural dynamics of the *E. coli* 70S ribosome using real-space refinement. *Cell* **113**, 789–801.
- Gao, N., Zavialov, A. V., Li, W., Sengupta, J., Valle, M., Gursky, R. P., Ehrenberg, M., and Frank, J. (2005). Mechanism for the disassembly of the posttermination complex inferred from cryo-EM studies. *Mol Cell* **18**, 663-674.

- Gavrilova, L. P., Kostiashkina, O. E., Koteliansky, V. E., Rutkevitch, N. M., and Spirin, A. S. (1976). Factor-free(non-enzymic and factor-dependent systems of translation of polyU by *E coli* ribosomes. *J Mol Biol* *101*, 537-552.
- Gavrilova, L. P., Perminova, I. N., and Spirin, A. S. (1981). Elongation factor Tu can reduce translation errors in poly(U)-directed cell-free systems. *J Mol Biol* *149*, 69-78.
- Gilbert, R., Fucini, P., Connell, S., Fuller, S., Nierhaus, K., Robinson, C., Dobson, C., and Stuart, D. (2004). Three-dimensional structures of translating ribosomes by cryo-EM. *Mol Cell* *14*, 57-66.
- Gnirke, A., Geigenmüller, U., Rheinberger, H.-J., and Nierhaus, K. H. (1989). The allosteric three-site model for the ribosomal elongation cycle. *J Biol Chem* *264*, 7291-7301.
- Gnirke, A., and Nierhaus, K. H. (1986). tRNA binding sites on the subunits of *Escherichia coli* ribosomes. *J Biol Chem* *261*, 14506-14514.
- Gourse, R. L., Gaal, T., Bartlett, M. S., Appleman, J. A., and Ross, W. (1996). rRNA transcription and growth rate-dependent regulation of ribosome synthesis in *Escherichia coli*. *Annu Rev Microbiol* *50*, 645-677.
- Grajevskaia, R. A., Ivanov, Y. V., and Saminsky, E. M. (1982). 70-S ribosomes of *Escherichia coli* have an additional site for deacylated tRNA binding. *Eur J Biochem* *128*, 47-52.
- Gualerzi, C., Brandi, L., Caserta, E., La teana, A., Spurio, R., Tomsic, J., and Pon, C. (2000). Translation initiation in bacteria. In *The ribosome. structure, function, antibiotics, and cellular interactions*, R. A. Garrett, S. R. Douthwaite, A. Liljas, A. T. Matheson, P. B. Moore, and H. F. Noller, eds. (Washington D.C., ASM Press), pp. 477-494.
- Haenni, A., and Chapeville, F. (1966). The behaviour of acetylphenylalanyl soluble ribonucleic acid in polyphenylalanine synthesis. *Biochim Biophys Acta* *114*, 135-148.
- Halic, M., Becker, T., Pool, M., Spahn, C., Grassucci, R., Frank, J., and Beckmann, R. (2004). Structure of the signal recognition particle interacting with the elongation-arrested ribosome. *Nature* *427*, 808-814.
- Hapke, B., and Noll, H. (1976). Structural dynamics of bacterial ribosomes: IV. Classification of ribosomes by subunit interaction. *J Mol Biol* *105*, 97-109.
- Hartz, D., McPheevers, D. S., and Gold, L. (1989). Selection of the initiator tRNA by *Escherichia coli* initiation factors. *Genes Dev* *3*, 1899-1912.
- Hartz, D., McPheevers, D. S., Traut, R., and Gold, L. (1988). Extension inhibition analysis of translation initiation complexes. *Methods Enzymol* *164*, 419-425.

- Hausner, T. P., Geigenmüller, U., and Nierhaus, K. H. (1988). The allosteric three site model for the ribosomal elongation cycle. New insights into the inhibition mechanisms of aminoglycosides, thiostrepton, and viomycin. *J Biol Chem* 263, 13103-13111.
- Hill, W., Weller, J., Gluick, T. C., Merryman, C., Marconi, R., Tassanakajohn, A., and Tapprich, W. (1990). Probing ribosome structure and function by using short complementary DNA oligomers. In *The Ribosome: Structure, Function, & Evolution* W. E. Hill, A. E. Dahlberg, R. A. Garrett, P. B. Moore, D. Schlessinger, and J. R. Warner, eds. (Washington, D.C, American Society for Microbiology), pp. 253-261.
- Hill, W. E., Camp, D. G., Tapprich, W. E., and Tassanakajohn, A. (1988). Probing ribosome structure and function using short oligodeoxyribonucleotides. *Methods Enzymol* 164, 401-419.
- Hill, W. E., Tapprich, W. E., and Tassanakajohn, A. (1985). Probing ribosomal structure and function. *Struct, Funct, Genet Ribosomes, ["Ribosome Conf"]*, Meeting Date.
- Hill, W. E., and Tassanakajohn, A. (1987). Probing ribosome structure using short oligodeoxyribonucleotides: the question of resolution. *Biochimie* 69, 1071-1080.
- Hirashima, A., and Kaji, A. (1972a). Factor-dependent release of ribosomes from mRNA. Requirement for 2 heat-stable factors. *J Mol Biol* 65, 43-58.
- Hirashima, A., and Kaji, A. (1972b). Purification and properties of ribosome-releasing factor. *Biochemistry* 11, 4037-4044.
- Hirashima, A., and Kaji, A. (1973). Role of elongation factor G and a protein factor on the release of ribosomes from messenger ribonucleic acid. *J Biol Chem* 248, 7580-7587.
- Hirokawa, G., Demeshkina, N., Iwakura, N., Kaji, H., and Kaji, A. (2006). The ribosome-recycling step: consensus or controversy? *Trends Biochem Sci* 31, 143-149.
- Hirokawa, G., Kiel, M. C., Muto, A., Selmer, M., Raj, V. S., Liljas, A., Igarashi, K., Kaji, H., and Kaji, A. (2002). Post-termination complex disassembly by ribosome recycling factor, a functional tRNA mimic. *EMBO J* 21, 2272-2281.
- Hirokawa, G., Nijman, R., Raj, V., Kaji, H., Igarashi, K., and Kaji, A. (2005). The role of ribosome recycling factor in dissociation of 70S ribosomes into subunits. *RNA* 11, 1317-1128.
- Inge-Vechtomov, S., Zhouravleva, G., and Philippe, M. (2003). Eukaryotic release factors (eRFs) history. *Biol Cell* 95, 195-209.
- Ito, K., Uno, M., and Nakamura, Y. (1998). Single amino acid substitution in prokaryote polypeptide release factor 2 permits it to terminate translation at all three stop codons. *Proc Natl Acad Sci USA* 95, 8165-8169.

- Ito, K., Uno, M., and Nakamura, Y. (2000). A tripeptide 'anticodon' deciphers stop codons in messenger RNA. *Nature* *403*, 680-684.
- Jelenc, P. C. (1980). Rapid purification of highly active ribosomes from *Escherichia coli*. *Anal Biochem* *105*, 369-374.
- Jenni, S., and Ban, N. (2003). The chemistry of protein synthesis and voyage through the ribosomal tunnel. *Curr Opin Struct Biol* *13*, 212-219.
- Joseph, S., and Noller, H. F. (1998). EF-G-catalyzed translocation of anticodon stem-loop analogs of transfer RNA in the ribosome. *EMBO J* *17*, 3478-3483.
- Kaempfer, R. (1972). Initiation factor IF-3: a specific inhibitor of ribosomal subunit association. *J Mol Biol* *71*, 583-598.
- Karimi, R., Pavlov, M., Buckingham, R., and Ehrenberg, M. (1999). Novel roles for classical factors at the interface between translation termination and initiation. *Mol Cell* *3*, 601-609.
- Kennel, D., and Riezman, H. (1977). Transcription Initiation Frequencies of the *Escherichia coli* lac Operon. *J Mol Biol* *114*, 4-21.
- Kiel, M., Raj, V., Kaji, H., and Kaji, A. (2003). Release of ribosome-bound ribosome recycling factor by elongation factor G. *J Biol Chem* *278*, 48041-48050.
- Kisselev, L., Ehrenberg, M., and Frolova, L. (2003). Termination of translation: interplay of mRNA, rRNAs and release factors? *EMBO J* *22*, 175-182.
- Kjeldgaard, N. O., and Gausing, K. (1974). Regulation of biosynthesis of ribosomes. In Ribosomes, A. T. M. Nomura, P. Lengyel, ed. (Cold Spring Harbor, Cold Spring Harbor Laboratory), pp. 369-392.
- Klaholz, B. P., Pape, T., Zavialov, A. V., Myasnikov, A. G., Orlova, E. V., Vestergaard, B., Ehrenberg, M., and Van Heel, M. (2003). Structure of the *Escherichia coli* ribosomal termination complex with release factor 2. *Nature* *421*, 90-94.
- Konevega, A. L., Fischer, N., Semenkov, Y. P., Stark, H., Wintermeyer, W., and Rodnina, M. V. (2007). Spontaneous reverse movement of mRNA-bound tRNA through the ribosome. *Nat Struct Mol Biol* *14*, 318-324.
- Krayevsky, A. A., and Kukhanova, M. K. (1979). The peptidyltransferase centre of ribosomes. *Prog Nucl Acid Res Mol Biol* *23*, 1-51.
- Kurland, C. G. (1982). Translational accuracy in vitro. *Cell* *28*, 201-202.
- Laemmli, U. K. (1970). Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* *227*, 680-685.

- Lancaster, L., Kiel, M. C., Kaji, A., and Noller, H. F. (2002). Orientation of ribosome recycling factor from directed hydroxyl radical probing. *Cell* 111, 129-140.
- Lim, V. I., and Curran, J. F. (2001). Analysis of codon:anticodon interactions within the ribosome provides new insights into codon reading and the genetic code structure. *RNA* 7, 942-957.
- Lu, J., and Deutsch, C. (2005). Folding zones inside the ribosomal exit tunnel. *Nat Struct Mol Biol* 12, 1123-1129.
- Mankin, A. S., Skripkin, E. A., Chichkova, N. V., Kopylov, A. M., and Bogdanov, A. A. (1981). An enzymatic approach for localization of oligodeoxyribonucleotide binding sites on RNA. Application to studying rRNA topography. *FEBS Lett* 131, 253-256.
- Márquez, V. (2002) Switching off the mechanism for maintaining the ribosomal reading frame: Translational regulation of release factor 2, Free University Berlin, Berlin.
- Márquez, V., Wilson, D. N., and Nierhaus, K. N. (2002). Functions and interplay of the tRNA-binding sites of the ribosome. *Biochemical Society Transactions* 30, 133-140.
- Marquez, V., Wilson, D. N., Tate, W. P., Triana-Alonso, F., and Nierhaus, K. H. (2004). Maintaining the ribosomal reading frame: The influence of the E site during translational regulation of release factor 2. *Cell* 118, 45-55.
- Martemyanov, K. A., and Gudkov, A. T. (1999). Domain IV of elongation factor G from *Thermus thermophilus* is strictly required for translocation. *FEBS Lett* 452, 155-159.
- Martemyanov, K. A., Yarunin, A. S., Liljas, A., and Gudkov, A. T. (1998). An intact conformation at the tip of elongation factor G domain IV is functionally important. *FEBS Lett* 434, 205-208.
- 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, 15699-15704.
- Moazed, D., and Noller, H. F. (1986). Transfer RNA shields specific nucleotides in 16S ribosomal RNA from attack by chemical probes. *Cell* 47, 985-994.
- Moazed, D., and Noller, H. F. (1989a). Interaction of tRNA with 23S rRNA in the ribosomal A, P, and E sites. *Cell* 57, 585-597.
- Moazed, D., and Noller, H. F. (1989b). Intermediate states in the movement of transfer RNA in the ribosome. *Nature* 342, 142-148.
- Moazed, D., and Noller, H. F. (1991). Sites of interaction of the CCA end of peptidyl-tRNA with 23S rRNA. *Proc Natl Acad Sci USA* 88, 3725-3728.

- Moll, I., Hirokawa, G., Kiel, M. C., Kaji, A., and Blasi, U. (2004). Translation initiation with 70S ribosomes: an alternative pathway for leaderless mRNAs. *Nucleic Acids Res* 32, 3354-3363.
- Moll, I., Leitsch, D., Steinhauser, T., and Blasi, U. (2003). RNA chaperone activity of the Sm-like Hfq protein. *EMBO Rep* 4, 284-289.
- Mora, L., Heurgue-Hamard, V., Champ, S., Ehrenberg, M., Kisseelev, L. L., and Buckingham, R. H. (2003). The essential role of the invariant GGQ motif in the function and stability in vivo of bacterial release factors RF1 and RF2. *Mol Microbiol* 47, 267-275.
- Munro, J. B., Altman, R. B., O'Connor, N., and Blanchard, S. C. (2007). Identification of two distinct hybrid state intermediates on the ribosome. *Mol Cell* 25, 505-517.
- Nakamura, Y., Ito, K., and Ehrenberg, M. (2000). Mimicry grasps reality in translation termination. *Cell* 101, 349-352.
- Nakano, H., Yoshida, T., Uchiyama, S., Kawachi, M., Matsuo, H., Kato, T., Ohshima, A., Yamaichi, Y., Honda, T., Kato, H., *et al.* (2003). Structure and binding mode of a ribosome recycling factor (RRF) from mesophilic bacterium. *J Biol Chem* 278, 3427-3436.
- Nakatogawa, H., Murakami, A., and Ito, K. (2004). Control of SecA and SecM translation by protein secretion. *Curr Opin Microbiol* 7, 145-150.
- Neidhardt, F. C. (1987). Chemical composition of *Escherichia coli*. In *Escherichia coli* and *Salmonella typhimurium*: cellular and molecular biology, F. C. Neidhardt, J. L. Ingraham, K. B. Low, B. Magasanik, M. Schaester, and H. E. Umbarger, eds. (Washington, D.C., American Society for Microbiology), pp. 3-6.
- Nierhaus, K. H. (1990). The allosteric three-site model for the ribosomal elongation cycle: features and future. *Biochemistry* 29, 4997-5008.
- Nierhaus, K. H. (1996). Protein synthesis - An elongation factor turn-on. *Nature* 379, 491-492.
- Nierhaus, K. H. (2006a). Decoding errors and the involvement of the E-site. *Biochimie*.
- Nierhaus, K. H. (2006b). Gene expression: Decoding and accuracy of translation. In Encyclopedia of Life Sciences (Chichester <http://www.els.net/>, John Wiley & Sons, Ltd), pp. [doi:10.1038/npg.els.0003950] in press.
- Nierhaus, K. H., Schulze, H., and Cooperman, B. S. (1980). Molecular mechanisms of the ribosomal peptidyltransferase center. *Biochem Int* 1, 185-192.
- Nierhaus, K. H., Spahn, C. M. T., Burkhardt, N., Dabrowski, M., Diedrich, G., Einfeldt, E., Kamp, D., Marquez, V., Patzke, S., Schäfer, M. A., *et al.* (2000). Ribosomal

- elongation cycle. In The ribosome. structure, function, antibiotics, and cellular interactions, R. A. Garrett, S. R. Douthwaite, A. Liljas, A. T. Matheson, P. B. Moore, and H. F. Noller, eds. (Washington D.C., ASM Press), pp. 319-335.
- Nierhaus, K. H., and Wilson, D. N., eds. (2004). Protein Synthesis and Ribosome Structure: Translating the Genome (Weinheim, WILEY-VCH Verlag GmbH&Co.).
- Ninio, J. (1986). Fine tuning of ribosomal accuracy. In Febs Lett, pp. 1-4.
- Nissen, P., Kjeldgaard, M., and Nyborg, J. (2000). Macromolecular mimicry. EMBO J 19, 489-495.
- Ogawa, K., and Kaji, A. (1975a). Requirement for ribosome-releasing factor for the release of ribosomes at the termination codon. Eur J Biochem 58, 411-419.
- Ogawa, K., and Kaji, A. (1975b). Ribosome run through of the termination codon in the absence of the ribosome releasing factor. Biochim Biophys Acta 402, 288-296.
- Ogden, R. C., and Adams, D. A. (1987). Electrophoresis in agarose and acrylamide gels. Methods Enzymol 152, 61-87.
- Ogle, J., Carter, A., and Ramakrishnan, V. (2003). Insights into the decoding mechanism from recent ribosome structures. TIBS 28, 259-266.
- Ogle, J. M., Brodersen, D. E., Clemons Jr, W. M., Tarry, M. J., Carter, A. P., and Ramakrishnan, V. (2001). Recognition of cognate transfer RNA by the 30S ribosomal subunit. Science 292, 897-902.
- Pan, D., Kirillov, S. V., and Cooperman, B. S. (2007). Kinetically competent intermediates in the translocation step of protein synthesis. Mol Cell 25, 519-529.
- Pavlov, M. Y., Freistroffer, D. V., Heurgue-Hamard, V., Buckingham, R. H., and Ehrenberg, M. (1997a). Release factor RF3 abolishes competition between release factor RF1 and ribosome recycling factor (RRF) for a ribosome binding site. J Mol Biol 273, 389-401.
- Pavlov, M. Y., Freistroffer, D. V., MacDougall, J., Buckingham, R. H., and Ehrenberg, M. (1997b). Fast recycling of *Escherichia coli* ribosomes requires both ribosome recycling factor (RRF) and release factor RF3. EMBO J 16, 4134-4141.
- Pedersen, F. S., and Kjeldgaard, N. O. (1977). Analysis of the relA gene product of *Escherichia coli*. Eur J Biochem 76, 91-97.
- Pel, H., Moffat, J., Ito, K., Nakamura, Y., and Tate, W. (1998). *Escherichia coli* relaease fator 3: Resolving the paradox of a typical G protein structure and atypical function with guanine nucleotides. RNA 4, 47-54.
- Peske, F., Rodnina, M., and Wintermeyer, W. (2005). Sequence of steps in ribosome recycling as defined by kinetic analysis. Mol Cell 18, 403-412.

- Pestova, T. V., and Hellen, C. U. T. (2000). The structure and function of initiation factors in eukaryotic protein synthesis. *Cellular & Molecular Life Sciences* *57*, 651-674.
- Pestova, T. V., Kolupaeva, V. G., Lomakin, I. B., Pilipenko, E. V., Shatsky, I. N., Agol, V. I., and Hellen, C. U. T. (2001). Molecular mechanisms of translation initiation in eukaryotes. *Proc Natl Acad Sci USA* *98*, 7029-7036.
- Polacek, N., Gomez, M. J., Ito, K., Xiong, L., Nakamura, Y., and Mankin, A. (2003). The critical role of the universally conserved A2602 of 23S ribosomal RNA in the release of the nascent peptide during translation termination. *Mol Cell* *11*, 103-112.
- Polacek, N., Patzke, S., Nierhaus, K. H., and Barta, A. (2000). Periodic conformational changes in rRNA: Monitoring the dynamics of translating ribosomes. *Mol Cell* *6*, 159-171.
- Powers, T., and Noller, H. F. (1990). Dominant Lethal Mutations in a Conserved Loop in 16S Ribosomal-RNA. *Proceedings Of The National Academy Of Sciences* *87*, 1042-1046.
- Qin, Y. (2006). The highly conserved LepA is a ribosomal elongation factor that back-translocates the ribosome and is essential for viability at high ionic strength (Berlin, Dissertation at the Freie Universität Berlin).
- Qin, Y., Polacek, N., Vesper, O., Staub, E., Einfeldt, E., Wilson, D. N., and Nierhaus, K. H. (2006). The highly conserved LepA is a ribosomal elongation factor that back-translocates the ribosome. *Cell* *127*, 721-733.
- Ramakrishnan, V., and Moore, P. B. (2001). Atomic structures at last: the ribosome in 2000. *Curr Opin Struct Biol* *11*, 144-154.
- Rawat, U. B., Zavialov, A. V., Sengupta, J., Valle, M., Grassucci, R. A., Linde, J., Vestergaard, B., Ehrenberg, M., and Frank, J. (2003). A cryo-electron microscopic study of ribosome-bound termination factor RF2. *Nature* *421*, 87-90.
- Remme, J., Margus, T., Villems, R., and Nierhaus, K. H. (1989). The third ribosomal tRNA-binding site, the E site, is occupied in native polysomes. *Eur J Biochem* *183*, 281-284.
- Rheinberger, H.-J., Geigenmüller, U., Gnirke, A., Hausner, T. P., Remme, J., Saruyam, H., and Nierhaus, K. H. (1990). Allosteric three-site model for the ribosomal elongation cycle. In *The Ribosome: Structure, Function, & Evolution*, W. E. Hill, A. E. Dahlberg, R. A. Garrett, P. B. Moore, D. Schlessinger, and J. R. Warner, eds. (Washington, D.C, American Society for Microbiology), pp. 318-330.
- Rheinberger, H.-J., Geigenmüller, U., Wedde, M., and Nierhaus, K. H. (1988). Parameters for the preparation of *Escherichia coli* ribosomes and ribosomal subunits active in tRNA binding. *Methods Enzymol* *164*, 658-670.

- Rheinberger, H.-J., and Nierhaus, K. H. (1980). Simultaneous binding of the 3 tRNA molecules by the ribosome of *E coli*. *Biochem Internat* 1, 297-303.
- Rheinberger, H.-J., and Nierhaus, K. H. (1983). Testing an alternative model for the ribosomal peptide elongation cycle. *Proc Natl Acad Sci USA* 80, 4213-4217.
- Rheinberger, H.-J., and Nierhaus, K. H. (1986). Adjacent codon-anticodon interactions of both tRNAs present at the ribosomal A and P or P and E sites. *FEBS Lett* 204, 97-99.
- Rheinberger, H.-J., Sternbach, H., and Nierhaus, K. H. (1981). Three tRNA binding sites on *Escherichia coli* ribosomes. *Proc Natl Acad Sci USA* 78, 5310-5314.
- Rheinberger, H. J. (1991). The function of the translating ribosome: allosteric three-site model of elongation. *Biochimie* 73, 1067-1088.
- Rheinberger, H. J., and Nierhaus, K. H. (1987). The ribosomal E site at low magnesium: coordinate inactivation of ribosomal functions at magnesium concentrations below 10 mM and its prevention by polyamines. *J Biomol Struct Dyn* 5, 435-446.
- Rodnina, M. V., Daviter, T., Gromadski, K., and Wintermeyer, W. (2002). Structural dynamics of ribosomal RNA during decoding on the ribosome. *Biochimie* 84, 745-754.
- Rodnina, M. V., Savelsbergh, A., Katunin, V. I., and Wintermeyer, W. (1997). Hydrolysis of GTP by elongation factor G drives tRNA movement on the ribosome. *Nature* 385, 37-41.
- Ryabova, L. A., Vinokurov, L. M., Shekhovtsova, E. A., Alakhov, Y. B., and Spirin, A. S. (1995). Acetyl phosphate as an energy source for bacterial cell-free translation systems. *Anal Biochem* 226, 184-186.
- Sambrook, J., Fritsch, E. F., and Maniatis, T. (1989). Molecular Cloning, a laboratory manual: 2nd edition (Cold Spring Harbour, NY, Cold Spring Harbour Laboratory Press).
- Savelsbergh, A., Katunin, V. I., Mohr, D., Peske, F., Rodnina, M. V., and Wintermeyer, W. (2003). An elongation factor G-induced ribosome rearrangement precedes tRNA-mRNA translocation. *Mol Cell* 11, 1517-1523.
- Schäfer, M. A., Tastan, A. O., Patzke, S., Blaha, G., Spahn, C. M., Wilson, D. N., and Nierhaus, K. H. (2002). Codon-anticodon interaction at the P Site is a prerequisite for tRNA interaction with the small ribosomal subunit. *J Biol Chem* 277, 19095-19105.
- Schilling-Bartetzko, S., Bartetzko, A., and Nierhaus, K. H. (1992a). Kinetic and thermodynamic parameters for transfer RNA binding to the ribosome and for the translocation reaction. *J Biol Chem* 267, 4703-4712.

- Schilling-Bartetzko, S., Franceschi, F., Sternbach, H., and Nierhaus, K. H. (1992b). Apparent Association Constants of Transfer RNAs for the Ribosomal A-Site, P-Site, and E-Site. *J Biol Chem* 267, 4693-4702.
- Schlünzen, F., Zarivach, R., Harms, J., Bashan, A., Tocilj, A., Albrecht, R., Yonath, A., and Franceschi, F. (2001). Structural basis for the interaction of antibiotics with the peptidyl transferase centre in eubacteria. *Nature* 413, 814-821.
- Schmeing, T. M., Huang, K. S., Kitchen, D. E., Strobel, S. A., and Steitz, T. A. (2005a). Structural insights into the roles of water and the 2' hydroxyl of the P site tRNA in the peptidyl transferase reaction. *Mol Cell* 20, 437-448.
- Schmeing, T. M., Huang, K. S., Strobel, S. A., and Steitz, T. A. (2005b). An induced-fit mechanism to promote peptide bond formation and exclude hydrolysis of peptidyl-tRNA. *Nature* 438, 520-524.
- Schuwirth, B., Borovinskaya, M., Hau, C., Zhang, W., Vila-Sanjurjo, A., Holton, J., and Cate, J. (2005). Structures of the bacterial ribosome at 3.5 Å resolution. *Science* 310, 827-834.
- Scolnick, E., Tompkins, R., Caskey, T., and Nirenberg, M. (1968). Release factors differing in specificity for terminator codons. *Proc Natl Acad Sci USA* 61, 768-774.
- Selmer, M., Al-Karadaghi, S., Hirakawa, G., Kaji, A., and Liljas, A. (1999). Crystal structure of *Thermotoga maritima* ribosome recycling factor: A tRNA mimic. *Science* 286, 2349-2352.
- Semenkov, Y. P., Rodnina, M. V., and Wintermeyer, W. (1996). The "allosteric three-site model" of elongation cannot be confirmed in a well-defined ribosome system from *Escherichia coli*. *Proc Natl Acad Sci U S A* 93, 12183-12188.
- Seo, H., Abedin, S., Kamp, D., Wilson, D., Nierhaus, K., and Cooperman, B. (2006). EF-G-dependent GTPase on the ribosome. Conformational change and fusidic acid inhibition. *Biochemistry* 45, 2504-2514.
- Sergiev, P., Lesnyak, D., Kiparisov, S., Burakovskiy, D., Leonov, A., Bogdanov, A., Brimacombe, R., and Dontsova, O. (2005). Function of the ribosomal E-site: a mutagenesis study. *Nucleic Acids Res* 33, 6048-6056.
- Sharma, D., Southworth, D. R., and Green, R. (2004). EF-G-independent reactivity of a pre-translocation-state ribosome complex with the aminoacyl tRNA substrate puromycin supports an intermediate (hybrid) state of tRNA binding. *RNA* 10, 102-113.
- Shoji, S., Walker, S. E., and Fredrick, K. (2006). Reverse translocation of tRNA in the ribosome. *Mol Cell* 24, 931-942.

- Shuman, S. (1991). Recombination mediated by vaccinia virus DNA topoisomerase I in *Escherichia coli* is sequence specific. *Proc Natl Acad Sci U S A* *88*, 10104-10108.
- Sievers, A., Beringer, M., Rodnina, M. V., and Wolfenden, R. (2004). The ribosome as an entropy trap. *Proc Natl Acad Sci U S A* *101*, 7897-7901.
- Singh, N., Das, G., Seshadri, A., Sangeetha, R., and Varshney, U. (2005). Evidence for a role of initiation factor 3 in recycling of ribosomal complexes stalled on mRNAs in *Escherichia coli*. *Nucleic Acids Res* *33*, 5591-5601.
- Spahn, C. M. T., and Nierhaus, K. H. (1998). Models of the elongation cycle: An evaluation. *Biol Chem* *379*, 753-772.
- Spirin, A. (1987). Structural dynamic aspects of protein synthesis on ribosomes. *Biochimie* *69*, 949-956.
- Stark, H., Rodnina, M. V., Wieden, H. J., van Heel, M., and Wintermeyer, W. (2000). Large-scale movement of elongation factor G and extensive conformational change of the ribosome during translocation. *Cell* *100*, 301-309.
- Tabor, C. W., and Tabor, H. (1985). Polyamines in microorganisms. *Microbiol Rev* *49*, 81-99.
- Thompson, J., Cundliffe, E., and Dahlberg, A. E. (1988). Site-directed mutagenesis of *Escherichia coli* 23 S ribosomal RNA at position 1067 within the GTP hydrolysis center. *J Mol Biol* *203*, 457-465.
- Traub, P., and Nomura, M. (1968). Reconstitution of functionally active 30S ribosomal particles from RNA and proteins. *Proc Natl Acad Sci USA* *59*, 777-784.
- Traut, R. R., and Monro, R. E. (1964). The puromycin reaction and its relation to protein synthesis. *J Mol Biol* *10*, 63-72.
- Trobro, S., and Aqvist, J. (2005). Mechanism of peptide bond synthesis on the ribosome. *Proc Natl Acad Sci U S A* *102*, 12395-12400.
- Tu, D., Blaha, G., Moore, P., and Steitz, T. (2005). Structures of MLSBK antibiotics bound to mutated large ribosomal subunits provide a structural explanation for resistance. *Cell* *121*, 257-270.
- Umekage, S., and Ueda, T. (2006). Spermidine inhibits transient and stable ribosome subunit dissociation. *FEBS Lett* *580*, 1222-1226.
- Valle, M., Zavialov, A., Sengupta, J., Rawat, U., Ehrenberg, M., and Frank, J. (2003). Locking and unlocking of ribosomal motions. *Cell* *114*, 123-134.
- Vanatalu, K., Paalme, T., Vilu, R., Burkhardt, N., Junemann, R., May, R., Ruhl, M., Wadzack, J., and Nierhaus, K. H. (1993). Large-Scale Preparation of Fully Deuterated

Cell Components - Ribosomes from Escherichia-coli with High Biological Activity.
Eur J Biochem 216, 315-321.

Vesper, O. (2003). Aufbau eines *in vitro* - Terminationssystems zur Funktionsanalyse von RRF (Berlin, Diplomarbeit at the Freie Universität Berlin).

Vesper, O., and Wilson, D. N. (2006). Ribosome recycling revisited. Mol Biol (Mosk) 40, 742-750.

Wagner, E. G., Jelenc, P. C., Ehrenberg, M., and Kurland, C. G. (1982). Rate of elongation of polyphenylalanine *in vitro*. Eur J Biochem 122, 193-197.

Watanabe, S. (1972). Interaction of siomycin with the acceptor site of Escherichia coli ribosomes. J Mol Biol 67, 443-457.

Watanabe, S., and Tanaka, K. (1973). Studies on the release of N-Ac(Phe-Ala)-tRNA from its ribosomal complex: effect of size of polyU. Biochim Biophys Acta 319, 383-387.

Watson, J. D. (1964). The synthesis of proteins upon ribosomes. Bull Soc Chim Biol 46, 1399-1425.

Weijland, A., and Parmeggiani, A. (1993). Toward a model for the interaction between elongation factor Tu and the ribosome. Science 259, 1311-1314.

Welch, M., Chastang, J., and Yarus, M. (1995). An inhibitor of ribosomal peptidyl transferase using transition-state analogy. Biochemistry 34, 385-390.

Wendrich, T. M., Blaha, G., Wilson, D. N., Marahiel, M. A., and Nierhaus, K. H. (2002). Dissection of the mechanism for the stringent factor RelA. Mol Cell 10, 779-788.

Wilden, B., Savelbergh, A., Rodnina, M. V., and Wintermeyer, W. (2006). Role and timing of GTP binding and hydrolysis during EF-G-dependent tRNA translocation on the ribosome. Proc Natl Acad Sci U S A 103, 13670-13675.

Wilson, D. (2004). Antibiotics and the inhibition of ribosome function. In Protein Synthesis and Ribosome Structure, K. Nierhaus, and D. Wilson, eds. (Weinheim, Wiley-VCH), pp. 449-527.

Wilson, D. N., Blaha, G., Connell, S. R., Ivanov, P. V., Jenke, H., Stelzl, U., Teraoka, Y., and Nierhaus, K. H. (2002). Protein synthesis at atomic resolution: mechanistics of translation in the light of highly resolved structures for the ribosome. Curr Protein Pept Sci 3, 1-53.

Wilson, D. N., Dalphin, M. E., Pel, H. J., Major, L. L., Mansell, J. B., and Tate, W. P. (2000). Factor-mediated termination of protein synthesis: a welcome return to the mainstream of translation. In The ribosome. structure, function, antibiotics, and cellular

- interactions, R. A. Garrett, S. R. Douthwaite, A. Liljas, A. T. Matheson, P. B. Moore, and H. F. Noller, eds. (Washington, DC, ASM press), pp. 495-508.
- Wilson, D. N., and Nierhaus, K. H. (2003). The ribosome through the looking glass. *Angew Chem Int Ed Engl* 42, 3464-3486.
- Wilson, D. N., Schlunzen, F., Harms, J. M., Yoshida, T., Ohkubo, T., Albrecht, R., Buerger, J., Kobayashi, Y., and Fucini, P. (2005). X-ray crystallography study on ribosome recycling: the mechanism of binding and action of RRF on the 50S ribosomal subunit. *EMBO J* 24, 251-260.
- Wilson, K. S., and Noller, H. F. (1998). Molecular movement inside the translational engine. *Cell* 92, 337-349.
- Wintermeyer, W., Lill, R., and Robertson, J. M. (1990). Role of the tRNA exit site in ribosomal translocation. In *The ribosome: Structure, function and evolution*, W. Hill, A. Dahlberg, R. A. Garrett, P. B. Moore, D. Schlessinger, and J. R. Warner, eds. (Washington, American Society for Microbiology), pp. 348-357.
- Youngman, E. M., Brunelle, J. L., Kochaniak, A. B., and Green, R. (2004). The active site of the ribosome is composed of two layers of conserved nucleotides with distinct roles in peptide bond formation and peptide release. *Cell* 117, 589-599.
- Yusupov, M. M., Yusupova, G. Z., Baucom, A., Lieberman, K., Earnest, T. N., Cate, J. H., and Noller, H. F. (2001). Crystal structure of the ribosome at 5.5 Å resolution. *Science* 292, 883-896.
- Zaniewski, R., Petkaites, E., and Deutscher, M. P. (1984). A multiple mutant of *Escherichia coli* lacking the exoribonucleases RNase II, RNase D, and RNase BN. *J Biol Chem* 259, 11651-11653.
- Zavialov, A. V., Buckingham, R. H., and Ehrenberg, M. (2001). A posttermination ribosomal complex is the guanine nucleotide exchange factor for peptide release factor RF3. *Cell* 107, 115-124.
- Zavialov, A. V., and Ehrenberg, M. (2003). Peptidyl-tRNA regulates the GTPase activity of translational factors. *Cell* 114, 113-122.
- Zavialov, A. V., Hauryliuk, V. V., and Ehrenberg, M. (2005). Guanine-nucleotide exchange on ribosome-bound elongation factor G initiates the translocation of tRNAs. *J Biol* 4, 9.
- 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, 789-798.

Zimmermann, R. A., Garvin, R. T., and Gorini, L. (1971). Alteration of a 30S ribosomal protein accompanying the ram mutation in *Escherichia coli*. Proc Natl Acad Sci U S A 68, 2263-2267.

Zuker, M. (2003). Mfold web server for nucleic acid folding and hybridization prediction. Nucleic Acids Res 31, 3406-3415.

6. Verzeichnis eigener Publikationen

Vesper, O. and Nierhaus, K. H. (2004) Translation Elongation in Bacteria. Encyclopedia of Biological Chemistry 4, 214-223

Qin, Y., Polacek, N., Vesper, O., Staub, E., Einfeldt, E., Wilson, D. N., and Nierhaus, K. H. (2006). The highly conserved LepA is a ribosomal elongation factor that back-translocates the ribosome. *Cell* 127, 721-733.

Vesper, O., and Wilson, D. N. (2006). Ribosome recycling revisited. *Mol Biol (Mosk)* 40, 742-750.

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