

## Curriculum vitae

<i>Name, Position</i>	Christian W Zwieb Professor of Molecular Biology
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<i>Citizenship</i>	German, US permanent residency
<b>Education/Professional Experience</b>	
<i>1979</i>	Ph.D. Free University, Berlin, Germany (Dr. R. Brimacombe, MPI, Berlin)
<i>1979-1981</i>	Post-doctoral Work at the Max-Planck Institute for Molecular Genetics, Berlin, Germany (Dr. R. Brimacombe)
<i>1982-84</i>	Post-doctoral Work at Brown University, Providence, RI (Prof. Dr. A. Dahlberg)
<i>1984-87</i>	Staff Member at the European Molecular Biology Laboratory, Heidelberg, Germany
<i>1987</i>	Lecturer and Habilitation at the Free University, Berlin, Germany
<i>1987-89</i>	Visiting Scientist at National Cancer Institute, NIH, Bethesda, MD (Dr. S. Adhya)
<i>1989-91</i>	Assistant Professor of Molecular Biology, The University of Texas Health Science Center at Tyler, TX
<i>1991-96</i>	Associate Professor of Molecular Biology, The University of Texas Health Science Center at Tyler, TX
<i>since 1996</i>	Professor of Molecular Biology, The University of Texas Health Science Center at Tyler, TX
<b>Professional Memberships</b>	
	American Association for the Advancement of Science The RNA Society
<b>Editorial Board Memberships</b>	
	Archaea (Assistant Editor) BMC Molecular Biology (Associate Editor)
<b>Funding (completed)</b>	
<i>1979-89</i>	Intramural resources of Max-Plank Institute, EMBL and NIH
<i>1991-95</i>	American Heart Association, Texas Affiliate,
<i>1996-98</i>	NIH-R01 GM 49034, Structure and Function of SRP RNA, P.I. \$578,422
<i>1998-2000</i>	NIH Supplement, High-Resolution structure of SRP54M, P.I. \$149,979
<i>1998-2003</i>	NIH-R01 GM 57506, Structure and Function of tmRNA, Co-P.I. with Dr. J. Wower (University of Auburn, Auburn, AL) Total award \$1,061,661
<i>1999-2001</i>	NIH Supplement, High-Resolution NMR structure of SRP19, P.I. \$125,994
<i>1999-2002</i>	NIH-R01 GM 49034, Structure and Function of SRP RNA, P.I. \$681,574
<i>2003-2004</i>	NIH 3R01GM058267-05S1 Structure and Function of tmRNA, Co-P.I. with Dr. J. Wower (University of Auburn, Auburn, AL) Total award \$80,801
<i>2003-2007</i>	NIH-R01 GM 49034, Structure and Function of SRP RNA, P.I. \$700,000

2005-2006	Wolf Benevolent Trust, Molecular Characterization of Zebrafish Telomerase, P.I. \$11,500
2006-2007	UTHSC Research Council, Synthesis of RNA-based hydrogels P.I. \$9,100
<b>Funding (pending)</b>	
07/01/09-06/30/14	NIH-R01 MGC, SRP-directed protein targeting in human cells, P.I. \$1,765,021, <i>scored</i>
02/01/09-01/31/11	American Heart Association, Texas Affiliate, Molecular basis of human signal peptide recognition, P.I. \$150,000, <i>under review</i>
<b>Teaching</b>	
since 1985	Advanced courses in Cell Biology. Habilitation (University level teaching certification) from the Free University Berlin, Germany in 1987
2005-present	Biotechnology Graduate Program at UTHSCT in collaboration with Stephen F. Austin State University, Nacogdoches, TX
2005-present	Critical Reading, Jointly with other faculty at UTHSCT
2005-present	Primary supervisor of four Biotechnology Graduate students, advisor of others

## Research Interests

My laboratory studies **translational ribonucleoprotein particles (RNPs)** and their effects on protein targeting. Methods for determining RNP structure and function include comparative sequence analyses (see <http://rnp.uthct.edu>), bioinformatics, cloning and purification of the constituents, reconstitution of recombinant RNPs, site-directed mutagenesis, crosslinking, molecular modeling, as well as collaborative biophysical approaches such as X-ray crystallography, NMR, and cryo EM.

The **signal recognition particle (SRP)** plays an critical role in the membrane-targeting and secretion of proteins including those essential for human health. SRP binds to the signals of secretory proteins as they emerge from the large ribosomal subunit and delays translation until the ribosome reaches the SRP receptor in the membrane. An SRP RNA molecule and six SRP proteins are indispensable components of the human SRP and contain features of functional importance. The purpose of the research is to better understand the contribution of these features to the assembly, structure, and function of the SRP. Two major topics are currently under investigation: (1) the role of proteins SRP72 and SRP68 in SRP assembly, structure, and function, and (2) the structural and functional basis of the transient nature of signal peptide recognition.

The bacterial **transfer-messenger RNP (tmRNP)** recycles ribosomes that are trapped on broken mRNAs lacking stop codons and tags the partially-translated proteins for degradation. Components of the tmRNP are the tmRNA, small protein B (SmpB), and ribosomal protein S1. The investigations focus on (1) identifying the varied features of the tmRNAs across the phylogenetic spectrum, (2) resolving the structures of the free, protein-, and ribosome bound *E. coli* tmRNP, and (3) identify regions which are important for tmRNP structure and function. A better understanding of this process is essential for counteracting the survival strategies of harmful bacteria and the development of new antibiotic targets.

**Combinatorial RNA-based sensors and drug delivery.** We exploit the vast potential of RNA molecules to interact with a wide variety of targets. Unlike conventional protein- and DNA-based detection systems, RNA reagents are quicker and more affordable to manufacture and fulfill the urgent need for materials that instantaneously detect targets in technologically modest environments but then are degraded in a controlled fashion. We synthesize long RNA chains designed to form an RNA network or gel. The RNAs can be combined to achieve a multitude of

detection needs. We foresee broad application of the proposed technology in field kits for the rapid identification of numerous targets and nanotechnological drug delivery.

### List of Publications

1. Möller, K., Zwieb, C., and Brimacombe, R. (1978). Identification of the oligonucleotide and oligopeptide involved in an RNA-Protein cross-link by ultraviolet irradiation of *Escherichia coli* 30S ribosomal subunits. *J. Mol. Biol.* **126**, 489-506.
2. Zwieb, C., and Brimacombe, R. (1978). RNA-Protein cross-linking in *Escherichia coli* ribosomal subunits: a method for the direct analysis of the RNA-region involved in the cross-link. *Nucleic Acids Res.* **5**, 1189-1203.
3. Zwieb, C., Ross, A., Rinke, J., Meinke, M., and Brimacombe, R. (1978). Evidence for RNA-RNA cross-link formation in *Escherichia coli* ribosomes. *Nucleic Acids Res.* **5**, 2705-2720.
4. Zwieb, C., and Brimacombe, R. (1979). RNA-Protein cross-linking in *Escherichia coli* ribosomal subunits: precise location of the nucleotide in 16S RNA which is coupled to protein S7 by ultraviolet irradiation. *Nucleic Acids Res.* **6**, 1775-1790.
5. Maly, P., Rinke, J., Ulmer, E., Zwieb, C., and Brimacombe, R. (1980). Precise location of the site of cross-linking between protein L4 and 23S ribonucleic acid induced by mild ultraviolet irradiation of *Escherichia coli* 50S ribosomal subunits. *Biochem.* **19**, 4179-4188.
6. Zwieb, C., and Brimacombe, R. (1980). Location of series of intra-RNA cross-links in 16S RNA, induced by ultraviolet irradiation of *Escherichia coli* 30 S ribosomal subunits. *Nucleic Acids Res.* **8**, 2397-2411.
7. Glotz, C., Zwieb, C., Brimacombe, R., Edwards, K., and Kössel, H. (1981). Secondary structure of the large subunit ribosomal RNA from *Escherichia coli*, *Zea mays* chloroplast, and human and mouse mitochondrial ribosomes. *Nucleic Acids Res.* **9**, 3287-3306.
8. Zwieb, C., Glotz, C., and Brimacombe, R. (1981). Secondary structure comparisons between small subunit ribosomal RNA-molecules from six different species. *Nucleic Acids Res.* **9**, 3621-3640.
9. Stiege, W., Zwieb, C., and Brimacombe, R. (1982). Precise location of three intra RNA cross-links in 23S RNA, and one in 5S RNA, induced by treatment of *Escherichia coli* 50S ribosomal subunits with bis-(2-chloroethyl)-methylamine. *Nucleic Acids Res.* **10**, 7211-7229.
10. Brimacombe, R., Maly, P., and Zwieb, C. (1983). The structure of the ribosomal RNA and its organization relative to ribosomal protein. *Prog. Nucl. Acid Res. Mol. Biol.* **28**, 1-48.
11. Göringer, H., Wagner, R., Jacob, W., Dahlberg, A. E., and Zwieb, C. (1984). Oligonucleotide directed mutagenesis of *Escherichia coli* 5S ribosomal RNA: construction of mutant and structural analysis. *Nucleic Acids Res.* **12**, 6935-6950.
12. Stark, M., Gregory, R., Gource, R., Thurlow, D., Zwieb, C., Zimmerman, R., and Dahlberg, A. (1984). Effects of site-directed mutations in the central domain of 16S ribosomal RNA upon ribosomal protein binding, RNA processing and 30S subunit assembly. *J. Mol. Biol.* **178**, 303-322.
13. Zwieb, C., and Dahlberg, A. E. (1984). Point mutations in the middle of 16S ribosomal RNA of *Escherichia coli* produced by deletion loop mutagenesis. *Nucleic Acids Res.* **12**, 4361-4375.

14. Zwieb, C., and Dahlberg, A. E. (1984). Structural and functional analysis of Escherichia coli ribosomes containing small deletions around position 1760 in the 23S ribosomal RNA. *Nucleic Acids Res.* **12**, 7135-7152.
15. Jemiolo, D. K., Zwieb, C., and Dahlberg, A. E. (1985). Point mutations in the 3' minor domain of 16S rRNA of E. coli. *Nucleic Acids Res.* **13**, 8631-8643.
16. Zwieb, C. (1985). The secondary structure of the 7SL RNA in the signal recognition particle: functional implications. *Nucleic Acids Res.* **13**, 6105-6124.
17. Dahlberg, A., Jacob, W., Santer, M., Zwieb, C., and Jemiolo, D. (1986). Mutagenesis of ribosomal RNA as a method to investigate interactions between rRNA, mRNA and tRNA. *Structure and Dynamics of RNA ed.: van Knippenberg P.H. and Hilbers C.W.NATO ASI series A*, **110**, 265-271.
18. Zwieb, C. (1986). The dynamics of 7SL RNA: A model for the action of signal recognition particle. *Endocyt. C. Res.* **3**, 167-177.
19. Zwieb, C. (1986). Is the 6S RNA of prokaryotes an equivalent to the 7SL RNA of eukaryotes? *Endocyt. C. Res.* **3**, 41-51.
20. Zwieb, C., Jemiolo, D. K., Jacob, W. F., Wagner, R., and Dahlberg, A. E. (1986). Characterization of a collection of deletion mutants at the 3'-end of 16S ribosomal RNA of Escherichia coli. *Mol. Gen. Genet.* **203**, 256-264.
21. Zwieb, C., and Ullu, E. (1986). Identification of dynamic sequences in the central domain of 7SL RNA. *Nucleic Acids Res.* **14**, 4639-4657.
22. Marshallsay, C., and Zwieb, C. (1987). Ribonucleic Acid: properties of a primordial structure in molecular evolution. *Endocyt. C. Res.* **4**, 1-12.
23. Prehn, S., Wiedmann, M., Rapoport, T. A., and Zwieb, C. (1987). Protein translocation across wheat germ microsomal membranes requires an SRP-like component. *EMBO J.*, **6**, 2093-2097.
24. Zwieb, C. (1987). 3D-modeling of the 7SL RNA of the signal recognition particle. *Mol. Biol. Reports* **12**, 221-222.
25. Gentz, R., Kuys, Y., Zwieb, C., Taatjes, D., Bannwarth, W., Stüber, D., and Ibrahim, I. (1988). The degradation of three chimeric polypeptides in Escherichia coli is associated with their secretion. *J. Bact.* **170**, 2212-2220.
26. Lingelbach, K., Zwieb, C., Webb, J. R., Marshallsay, C., Hoben, P. J., Walter, P., and Dobberstein, B. (1988). Isolation and characterization of a cDNA clone encoding the 19 kDa protein of signal recognition particle (SRP): expression and binding to 7SL RNA. *Nucleic Acids Res.* **16**, 9431-9442.
27. Zwieb, C. (1988). Possible interactions between signal recognition particle and the ribosome: a model for protein translocation. *Mol. Cell. Biol. (Life Sci. Adv.)* **7**, 159-163.
28. Zwieb, C. (1988). 3D-modeling of the 7SL RNA of the signal recognition particle. *J. Cell. Biochem*, Supplement 12D, 27.
29. Zwieb, C. (1988). 4.5S RNA of E. coli and the conserved central domain of signal recognition particle RNA are homologous. *Endocyt. C. Res.* **5**, 327-336.
30. Campos, N., Palau, J., and Zwieb, C. (1989). Diversity of 7SL RNA from the signal recognition particle of maize endosperm. *Nucleic Acids Res.* **17**, 1573-1588.
31. Kim, J., Zwieb, C., Wu, C., and Adhya, S. (1989). Bending of DNA by gene regulatory protein: construction and use of a DNA bending vector. *Gene* **85**, 15-23.

32. Marshallsay, C., Prehn, S., and Zwieb, C. (1989). cDNA cloning of the wheat germ SRP 7S RNAs. *Nucleic Acids Res.* **17**, 1771.
33. Orban, L., Sullivan, J. V., Zwieb, C., and Chrambach, A. (1989). A thin layer multislabs polyacrylamide gel electrophoresis apparatus for Ferguson plot analysis at the sub-microgram load level. *Electrophoresis* **10**, 726-729.
34. Zwieb, C. (1989). Structure and function of signal recognition particle RNA. *Prog. Nucl. Acid Res. Mol. Biol.* **37**, 207-234.
35. Zwieb, C., Kim, J., and Adhya, S. (1989). DNA bending by negative regulatory proteins: Gal and Lac repressors. *Genes and Development* **3**, 606-611.
36. Zwieb, C., and Schüler, D. (1989). Low resolution three-dimensional models of the 7SL RNA of the signal recognition particle, based on an intramolecular cross-link introduced by mild irradiation with ultraviolet light. *Biochem. and Cell Biol.* **67**, 434-442.
37. Zwieb, C., and Brown, R. S. (1990). Absence of substantial bending in the *Xenopus laevis* transcription factor IIIA-DNA complex. *Nucleic Acids Res.* **18**, 583-587.
38. Larsen, N., and Zwieb, C. (1991). SRP-RNA sequence alignment and secondary structure. *Nucleic Acids Res.* **19**, 209-215.
39. Orban, L., Chrambach, A., Zwieb, C., and Adhya, S. (1991). Detection of conformational and net charge differences in DNA-protein complexes by quantitative electrophoresis on polyacrylamide-agarose copolymer gels. *Electrophoresis* **12**, 391-396.
40. Zwieb, C. (1991). Interaction of protein SRP19 with signal recognition particle RNA lacking individual RNA helices. *Nucleic Acids Res.* **19**, 2955-2960.
41. Zwieb, C. (1991). A basic region neighboring the lysine-rich C-terminus of protein SRP19 is required for binding to signal recognition particle RNA. *Biochem. and Cell Biol.* **69**, 649-654.
42. Zwieb, C., Kim, J., and Adhya, S. (1991). Detection of bending of a DNA by gel electrophoresis: use of plasmid vectors in: A laboratory guide to in vitro studies of protein-DNA interactions J. P. Jost and H.P. Saluz (eds.). *BioMethods Series (Birkhäuser Verlag)*, **5**, 245-257.
43. Idell, S., Zwieb, C., Boggaram, J., Holiday, D., Johnson, R., and Raghu, G. (1992). Mechanisms of fibrin formation and lysis by human lung fibroblasts: influence of TGF- $\beta$  and TNF- $\alpha$ . *American J. Physiol.* **263**, L487-L494.
44. Idell, S., Zwieb, C., Kumar, A., Koenig, K., and Johnson, A. (1992). Pathways of fibrin turnover of human pleural mesothelial cells in vitro. *Am. J. Resp. Cell Mol. Biol.* **7**, 414-426.
45. Zwieb, C. (1992). Conformity of RNAs that interact with tetranucleotide loop binding proteins. *Nucleic Acids Res.* **20**, 4397-4400.
46. Zwieb, C. (1992). Recognition of a tetranucleotide loop of signal recognition particle RNA by protein SRP19. *J. Biol. Chem.*, **267**, 15650-15656.
47. Zwieb, C., and Larsen, N. (1992). The signal recognition particle (SRP) database. *Nucleic Acids Res.* **20**, Supplement, 2207.
48. Larsen, N., and Zwieb, C. (1993). The signal recognition particle database (SRPDB). *Nucleic Acids Res.* **21**, 3019-3020.
49. Chittenden, K., Black, S., and Zwieb, C. (1994). Systematic site-directed mutagenesis of protein SRP19: identification of the residues essential for binding to signal recognition particle RNA. *J. Biol. Chem.*, **269**, 20497-20502.

50. Zwieb, C., and Adhya, S. (1994) Improved plasmid vectors for the analysis of protein-induced DNA bending. *Methods Mol. Biol.* **30**, 281-294 (1994)
51. Idell, S., Kumar, A., Zwieb, C., Holiday, D., Koenig, K., and Johnson, R. (1994). Effects of TGF- $\beta$  and TNF- $\alpha$  on procoagulant and fibrinolytic pathways of human tracheal epithelial cells. *American J. Physiol.* **267**, L693-L703.
52. Zwieb, C. (1994). Site-directed mutagenesis of signal recognition particle RNA: identification of the nucleotides in helix 8 required for interaction with protein SRP19. *Eur. J. Biochem.* **222**, 885-890.
53. Zwieb, C., and Adhya, S. (1994) Improved plasmid vectors for the analysis of protein-induced DNA bending. In G. G. Kneale (Eds.), DNA-protein Interactions: principles and protocols (pp. 281-294). Totowa, NJ: Humana Press Inc.
54. Zwieb, C., and Larsen, N. (1994). The signal recognition particle database (SRPDB). *Nucleic Acids Res.* **22**, 3483-3487.
55. Walker, P., Black, S., and Zwieb, C. (1995). Cooperative assembly of signal recognition particle RNA with protein SRP19. *Biochemistry* **34**, 11989-11997.
56. Sakakibara, Y., Takami, Y., Zwieb, C., Nakayama, T., Suiko, M., Nakajima, H., and Liu, M.-C. (1995). Purification, characterization and molecular cloning of a novel rat liver Dopa/Tyrosine Sulfotransferase. *J. Biol. Chem.*, **270**, 30470-30478.
57. Zwieb, C. (1996). The uRNA database. *Nucleic Acids Res.* **24**, 76-79.
58. Larsen, N., and Zwieb, C. (1996). The signal recognition particle database (SRPDB). *Nucleic Acids Res.* **24**, 80-81.
59. Zwieb, C., Müller, F., and Larsen, N. (1996). Comparative analysis of tertiary structure elements in signal recognition particle RNA. *Folding & Design* **1**, 315-324.
60. Henry, K., Zwieb, C., and Fried, H. (1997). Purification and Biochemical Characterization of the 19-kDa Signal Recognition Particle RNA-binding protein expressed as a Hexahistidine-tagged Polypeptide in *Escherichia coli*. *Protein Expression and Purification* **9**, 15-26.
61. Zwieb, C. (1997). The uRNA database. *Nucleic Acids Res.* **25**, 102-103.
62. Zwieb, C., and Larsen, N. (1997). The signal recognition particle database (SRPDB). *Nucleic Acids Res.* **25**, 107-108.
63. Gowda, K., Chittenden, K., and Zwieb, C. (1997) Binding site of the M-domain of human protein SRP 54 determined by systematic site directed mutagenesis of signal recognition particle RNA. *Nucleic Acids Res.* **25**, 388-394.
64. Black, S.D., Gowda, K., Chittenden, K., Walker III K. P., and Zwieb, C. (1997) Identification of an RNA binding-region in the N-domain of signal recognition particle protein SRP19. *Eur. J. Biochem.* **245**, 564-572.
65. Chittenden, K., Gowda, K., Black, S.D., and Zwieb, C. (1997) Interaction of rice and human SRP19 polypeptides with signal recognition particle RNA. *Plant Mol. Biol.* **34**, 507-515.
66. Gowda, K., and Zwieb, C. (1997) Determinants of a protein-induced RNA switch in the large domain of signal recognition particle identified by systematic site-directed mutagenesis. *Nucleic Acids Res.* **25**, 2835-2840.
67. Zwieb, C., and Müller, F. (1997) Three-dimensional comparative modeling of RNA. *Nucleic Acids Symposium Series*, No. **36**, 69-71.

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93. Yang, C.H, and Zwieb, C. (2001) Swapping of functional domains using a chimeric monster deletion mutagenesis strategy. *BioTechniques* **31**, 724-728.
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96. Wower, J., Knudsen, B., Gorodkin, J., and Zwieb, C., (2001) tmRDB. *Nucleic Acids Res.* Database Issue.
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98. Pakhomova, O.P., Deep, S., Huang, Q., Zwieb, C., and Hinck, A.P. (2002) Solution Structure of Protein SRP19 of *Archaeoglobus fulgidus* Signal Recognition Particle. *J. Mol. Biol.* **317**, 145-158.
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