

Milton H. Werner, Ph.D.
VP, Discovery Research
Celtaxsys, Inc.
ATDC Biosciences Center, #0390
311 Ferst Drive
Atlanta, GA 30332

(917) 494-0831 (cell)

(404) 920-0708 (private office)

m Werner@celtaxsys.com

Profile

Former Associate Professor and Head of Laboratory at the Rockefeller University with a national reputation as an expert in the underlying causes of human cancers of the blood and bone. Developed new therapeutic leads for solid tumors targeting tumor necrosis factor (TNF) death receptors. Extensive experience in pathway analysis inside and outside of both prokaryotic and eukaryotic cells, with emphasis on bio-analytical and structural biology techniques and protein biochemistry. Developed two industrial processes for nucleic acid synthesis and production of biologics. Holder of technology patent in nucleic acid synthesis. Developer of new anti-microbial therapy and holder of a broad patent in transcription-based anti-microbial therapeutics; pending patent applications for anti-tumor therapeutics targeting TNF death receptors. Extensive track record in cellular, molecular and structural biochemistry and integration of these methods to build a pre-clinical research pipeline. Operated at executive level in management of a complex research laboratory, developing budgets and supervising scientists both pre- and postdoctoral.

Management Expertise

Vice President, Discovery Research
Celtaxsys, Inc.

May 2007 – present

Director of Research for biotechnology company focused on modulating cell migration for a therapeutic purpose. Built interdisciplinary team of cell biologists and biochemists to develop high throughput screening approach to immune cell migration.

Department Head, Laboratory of Molecular Biophysics

September 1996 – May 2007

The Rockefeller University, New York, NY

Principal Investigator managing a 7000 sq. ft. laboratory employing cellular, molecular and structural biochemistry approaches to understanding human disease mechanisms in the blood and bone. Supervised vertically integrated team of pre- and postdoctoral students to achieve stated research goals. Operated at executive level with VP of Finance, Executive VP and President of the University at the equivalent of the Department Chairperson level.

Key accomplishments:

- Supervised 10-25 people in cell, molecular and structural biology research
- Oversaw research progression in multiple scientific areas simultaneously; excellent at multi-tasking projects with diverse or competing objectives
- Managed university budgets in excess of \$1M annually
- Built, staffed and managed university bio-analytical core facilities and developed core facility budgets and strategic plans for facility improvements
- Raised more than \$3M in external grant support from private foundations and federal government
- Designed and oversaw construction of 16,000 sq. ft. of laboratory space
- Founding member of the New York Structural Biology Center, a multi-disciplinary technology Center in Manhattan dedicated to understanding the molecular basis of human diseases

Educational Administration

- Admissions committee Cornell/Memorial Sloan-Kettering/Rockefeller University Medical Scientist Training Program 1997-2002
- Curriculum Committee, Cornell/ Memorial Sloan-Kettering/Rockefeller University Medical Scientist Training Program 1997-2005
- Curriculum Committee, Cornell/Rockefeller Training Program in Chemical Biology 1998-2000
- Steering Committee, Cornell/Rockefeller Training Program in Chemical Biology 1998-2002
- Development Committee, New York Structural Biology Center 1998-2000
- Steering Committee, New York Structural Biology Center 2001-2006
- Operations Committee, New York Structural Biology Center 2001-2006

Scientific Expertise

Associate Professor/Head of Laboratory

April 2003-May 2007

The Rockefeller University, New York, NY

Integrated cellular biologists, molecular biologists and physical chemists into focused research teams in human cancer research. Nationally known structural biochemist and bio-analytical scientist.

Key accomplishments

- Defined new paradigm for programmed cell death (apoptosis) and its role in autoimmune and lymphoproliferation diseases. Developed new theory of signal transduction for the tumor necrosis factor (TNF) receptor family. Developed novel strategy for targeting human solid tumors employing the TRAIL receptors.
- Structural biology of transmembrane proteins and their intracellular complexes in signal transduction.
- Employed protein engineering and computer aided design to develop mimetics of biological function inside and outside of mammalian cells.
- Extensive experience in mammalian cell culture and biology, microscopy and proteomics.
- Built vertically-integrated team of post-doctoral scientists to solve complex disease origins in the immune system.

Assistant Professor/Head of Laboratory

September 1996-April 2003

The Rockefeller University, New York, NY

Principal investigator in mechanisms of gene regulation and relationship to acute human leukemia.

Key accomplishments

- Elucidated underlying mechanism of RUNX-related (AML-related) acute human leukemias resulting from spontaneous chromosomal translocation. Discovered co-regulator exchange mechanism underlying loss of transcriptional control in leukemic cells.
- Invented new synthetic route to large nucleic acids of defined sequence (Patent #6,194,179 (issued Feb 27, 2001): Methods for preparing polynucleotide sequences and uses thereof. A novel method for preparation of long oligonucleotides (20-2000 bp) on the milligram scale).
- Identified novel mode of gene regulation utilized by pathogens of bacteria and developed scheme to mimic this mechanism in human anti-microbial therapy (Patent #6,994,985 (issued Feb 7, 2006) Development of anti-sigma factor agents. A novel antimicrobial strategy based on the model of viral transcription factors which remodel bacterial RNA polymerase).
- Extensive experience in bacterial cell culture, protein expression, purification and process scale production of proteins using fermentation.
- Developed and employed industrial scale production of biologics based on adaptive control fermentation.

IRTA Fellow

December 1991-August 1996

National Institutes of Health, Bethesda, MD

Intramural research fellow at the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK)

Key accomplishments

- Developed new methods for the analysis of protein/nucleic interactions in solution using NMR spectroscopy
- Determined underlying cause of human 46(X,Y) sex reversal; solved the molecular structure of the human testis determining factor SRY bound to its target site in DNA
- Developed new methods for purifying protein/nucleic acid complexes

Technical Expertise

Protein Biochemistry/Proteomics

- Protein expression/production in bacteria, yeast, insect and mammalian cells. Developed novel bacterial fermentation strategy based on adaptive control
- Protein purification using FPLC and HPLC on preparative scale (reverse-phase, ion exchange, affinity and size exclusion)
- Protein characterization by fluorescence, spectrophotometry, calorimetry (ITC and DSC), kinetics, light scattering, centrifugation, electrophoresis, Western blot
- Proteomic methods: 1D and 2D gel electrophoresis, phage display, two-hybrid (bacterial, yeast, mammalian), TAP tagging, MALDI-TOF, ESI MS, LC/MS

Molecular Biology

- Mammalian cell culture and maintenance, development of stable cell lines and viral transduction
- RNA interference (RNAi) for conditional protein knockout
- Bacterial cell culture and gene cloning
- Microarray analysis
- Quantitative PCR (qPCR)

Structural Biology

- Solution of three-dimensional protein and nucleic acid structures by multi-nuclear NMR spectroscopy
- Protein and nucleic acid modeling (homology modeling with Modeller and threading)
- Computer-aided design (DOCK, HADDOCK)
- Biological computing (UNIX, LINUX, Windows and Mac OS)

Scientific Honors

2006-2008	Research Chair of the Brain Tumor Society (\$200,000 prize)
2006-2009	Investigator, American Heart Association (\$180,000 prize)
2000-2005	W. M. Keck Foundation Distinguished Young Scholar (\$1M prize)
1999	Naito Memorial Foundation International Lectureship (\$50,000 prize)
1999-2000	New York Community Trust Scholar (\$180,000 prize)
1999-2003	Irma T. Hirschl Trust Scholar (\$120,000 prize)
1998-2001	Alexander and Alexandrine Sinsheimer Scholar (\$100,000 prize)
1997-1999	Kimmel Cancer Foundation Scholar (\$200,000 prize)

Education

University of California, Berkeley

September 1985-December 1991

Ph.D. Physical Chemistry and Structural Biology

- Magna Cum Laude (GPA 3.88)
- Graduate Student Research Assistantship from Lawrence Berkeley Laboratory (DOE National Lab)

University of Southern California

September 1984-August 1985

M.A. Candidate Chemistry

- Enzyme kinetics research at USC Medical School

B. S. Biological Sciences

- Suma Cum Laude (GPA 3.91)
- Phi Beta Kappa
- Phi Kappa Phi
- Sigma XI

Extracurricular Activities

- Interned high school juniors in my research lab to help young people start on the career path in research. High school students have been authors on laboratory publications
- Active participant in professional organizations: Leukemia/Lymphoma Society, American Cancer Society, American Association for the Advancement of Science, Brain Tumor Society, Protein Society, American Association for Cancer Research
- Sat on national and international review boards for research grants and programs.
- Promoted science and education programs City-wide through development of seminar programs in structural biochemistry and molecular biology.

Publications

- Natarajan, R, Werner, M. H., Fife, T. (1987) Effect of the Leaving Group in the Hydrolysis of N-Acylimidazoles. The Hydroxide Ion, Water and General Base Catalyzed Hydrolysis of N-Acyl-4(5)-nitroimidazoles. **J. Org. Chem.** **52**, 740-746.
- Werner, M. H. & Wemmer, D. E. (1991) ¹H Assignments and Secondary Structure Determination of Soybean Trypsin/Chymotrypsin Inhibitor. **Biochemistry** **30**, 3356-3364.
- Werner, M. H. & Wemmer, D. E. (1992) Three-dimensional Structure of Soybean Trypsin/Chymotrypsin Bowman-Birk Inhibitor in Solution. **Biochemistry** **31**, 999-1010.
- Werner, M. H. & Wemmer, D. E. (1992) Identification of a Protein-binding Surface by Differential Amide Hydrogen-exchange Measurements: Application to Bowman-Birk Serine-Protease Inhibitor. **J. Mol. Biol.** **225**, 873-889.
- Werner, M. H., Clore, G. M., Gronenborn, A. & Nash, H. A. (1994) Symmetry and Asymmetry in the Function of E. coli Integration Host Factor: Implications for target identification by DNA-binding proteins. **Curr. Biol.** **4**, 477-487.
- Werner, M.H., Clore, G. M., Gronenborn, A., Kondoh, A & Fisher, R. J. (1994) Refolding Proteins by Gel Filtration. **FEBS Lett.** **345**, 125-130.
- Werner, M. H., Huth, J., Gronenborn, A., Clore, G.M. (1995) Molecular Basis of 46X,Y Sex Reversal Revealed from the Three-Dimensional Structure of the SRY/DNA Complex. **Cell** **81**, 705-714.
- Werner, M. H., Bianchi, M., Gronenborn, A., Clore, G. M. (1995) NMR Spectroscopic Analysis of DNA Conformation Induced by the Human Testis Determining Factor SRY. **Biochemistry** **34**, 11998-12004.
- Werner, M. H., Clore, G. M., Fisher, C. L., Fisher, R. J., Trinh, L., Shiloach, J., Gronenborn, A. M. (1995) The Solution Structure of the Human ETS1-DNA Complex Reveals a Novel Mode of Binding and True Sidechain Intercalation. **Cell** **83**, 761-771.
- Werner, M. H., Clore, G. M., Fisher, C. L., Fisher, R. J., Trinh, L., Shiloach, J., Gronenborn, A. M. (1997) Correction of the NMR structure of the ETS1-DBD/DNA Complex. **J. Biomol. NMR** **10**, 317-328.
- Groft, C. M., Uljon, S., Wang, R, Werner, M. H. (1998) Structural homology between the Rap30 DNA-binding domain and linker histone H5: implications for pre-initiation complex assembly. **Proc. Natl. Acad. Sci. USA** **95**, 9117-9122.
- Nagata, T., Gupta, V., Sorce, D., Kim, W-Y., Sali, A., Chait, B., Shigesada, K, Ito, Y. and Werner, M.H. (1999) Immunoglobulin motif DNA recognition and heterodimerization for the PEBP2/CBF Runt Domain. **Nat. Struct. Biol.** **6**, 615-619.
- Goger, M., Gupta, V., Kim, W-Y., Shigesada, K., Ito, Y. and Werner, M. H. (1999) Molecular insights into PEBP2/CBF β -SMMHC associated acute leukemia revealed from the three-dimensional structure of PEBP2/CBF β . **Nat. Struct. Biol.** **6**, 620-624.
- Werner, M. H., Gupta, V., Lambert, L., Nagata, T. (2001) Uniform DNA Labeling by Tandem Repeat Amplification. **Methods Enzymol.** **338**, 233-240.
- Nagata, T. and Werner, M. H. (2001) Functional Mutagenesis of AML1/RUNX1 and PEBP2 β /CBF β Define Distinct, Non-overlapping Sites for DNA Recognition and Heterodimerization by the Runt domain **J. Mol. Biol.** **308**, 191-201
- Lambert, L J., Schirf, V., Demmeler, B., Cadene, M. and Werner, M. H. (2001) Flipping a genetic switch by subunit exchange. **EMBO J.** **20**, 7149-7159.
- Hill, J. M., Ramos, J., Ginsberg, M., Werner, M. H. (2002) The interaction of the death motif protein PEA-15 with ERK MAP kinase reveals a common docking site for protein interaction with the death domain/death effector domain fold. **EMBO J.**, **21**, 6494-6504.
- Chou, F-L, Hill, J. M., Hsieh, J-C., Pouyssegur, J., Glading, A. B. A., Ramos, J. W., Werner, M. H., Ginsberg, M. H. (2003) PEA-15 Binding to ERK1/2 MAP Kinases is Required for its Modulation of Integrin Activation. **J. Biol. Chem.** **278**, 52587-52597
- Hill, J. M., Morisawa, G., Kim, T., Huang, T. (2003) Identification of an expanded binding surface on the FADD death domain responsible for interaction with CD95/Fas. **J. Biol. Chem.** **279**, 1474-1481.
- Lambert, L. J., Schirf, V., Demeler, B. and Werner, M. H. (2003) Molecular analysis of activator engagement with RNA polymerase. **Methods Enzymol.** **370**, 505-521.
- Lambert L. J., Schirf, V., Demeler, B. and Werner, M. H. (2004) T4 AsiA blocks DNA recognition by remodeling σ^{70} region 4. **EMBO J.** **15**, 2952-2962.
- Lausen, J., Cho, S., Liu, S., Werner, M. H. (2004) The nuclear repressor co-repressor (N-CoR) utilizes repression domains I and II for interaction and co-repression with ETO. **J. Biol. Chem.** **279**, 49281-49288.

Sandu, C., Gavathiotis, E., Huang, T., Wegorzewska, I, Werner, M. H. (2005) A mechanism for death receptor discrimination of death adaptors. **J. Biol. Chem.** **280**, 31974-31980.

Lausen, J., Liu, S., Fliegau, M., Lübbert, M., Werner, M. H. (2006) ELA2 is regulated by hematopoietic transcription factors but not repressed by AML1-ETO. **Oncogene**, **25**, 1349-1357.

Carrington, P. E., Morisawa, G., Hill, J. M., Wei, Y-f., Sandu, C., Huang, T., Kim, T., Wei, Y., Werner, M. H. (2006) The structure of FADD and its interaction with procaspase-8. **Mol. Cell** **22**, 599-610.

Sandu, C., Morisawa, G., Hill, J. M., Huang, T., Kim, T., Werner, M. H. (2006) FADD self-association is required for stable interaction with an activated death receptor. **Cell Death Differ.** **13**, 2052-2061.

Wei, Y., Werner, MH (2006) iDC: A comprehensive toolkit for the analysis of residual dipolar couplings for macromolecular structure determination. **J. Biomol. NMR** **35**, 17-25.

Werner MH, Wu C, Walsh CM. (2006) Emerging roles for the death adaptor FADD in death receptor avidity and cell cycle regulation. **Cell Cycle** **5**, 2332-2338.

Wei, Yf., Liu, S., Lausen, J., Cho, S., Biris, N., Kobayashi, N., Yokoyama, S., Werner, MH (2007) A TAF4-homology domain from the the co-repressor Eight Twenty-One (ETO) is a docking platform for positive and negative regulators of transcription. **Nat. Struct. Mol. Biol.**, in press.

Wu, C., Sandu, C., Werner, M. H. (2007) Death receptor mimicry by enforced oligomerization reveals the origin of CD95/Fas receptor clustering. **PLoS Biology**, under revision.

Gavathiotis E., Sandu C., Huang T., Hill J. M., Werner M. H. (2007) A common mechanism for initiator procaspase and c-FLIP entry into FADD-mediated signaling complexes. **Mol. Cell**, submitted.

Presentations

Since 2004, I have given more than 100 lectures at Universities, National and International Conferences in my fields of biology and in biophysics.