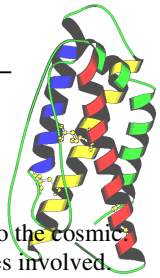

Background:

I believe there is structure in all things on all scales, from the sub-atomic to the cosmic. To understand basic mechanisms of actions requires knowing the structures involved. My scientific interests are related to understanding and defining relationships between molecular structure and biological activity with practical experience in protein engineering, molecular, structural and computational biology. Highlights of my background include initiating startup companies, working with NASA and protein structural work in Europe. I received my Master's degree in biochemistry and Ph.D. in pharmacology from Boston University. My post-doctoral work focused on interleukin-7 (IL-7), a protein important for B cell development and maintenance and T cell activation. Master thesis described the construction of a luciferase interleukin-2 fusion enzyme designed to measure cell surface receptors without the requirement of radioactive materials.

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Mobile Telephone: (205) 586-9163
E-mail: lcayp@hotmail.com, lcosenza@c2biotechnologies.com

Citizenship: USA

Languages: English (American, native), French (remedial)

Social Status: Married (Spouse: Annie Provan: Occupation Nurse Practitioner, two children)

Activities: Aviation (student pilot), cycling, hiking, skiing, travel, beer & wine, soccer, inventing, anthropology, paleontology, mathematics, goat farming.

Education:

2010 Certificate. Pennsylvania State University, Biotechnology Training Program, Fermentation Methods
1993 - 1998 Ph.D. (Pharmacology), Boston University, Boston, MA
1990 - 1992 M.A. (Biochemistry), Boston University, Boston, MA
1981 - 1986 B.A. (Biology) / (Math), State University of New York, New Paltz, NY
1976 – 1981 Kingston City High School, Kingston, NY

Professional Positions / Employment:

August 2006 – present
Founder and Chief Science Manager: C2 Biotechnologies, LLC a Research and Development Company. Focus on developing biological catalysis for the renewable energy markets.

March 2010-present
President: C2B Institutional Biosafety Committee (IBC). Volunteer IBC registered with the National Institutes of Health. This IBC is composed of C2 Biotechnologies company and community members that review projects involving the use of recombinant DNA technologies.

2004-2006 Co-founder and CSO: InSilicor, Inc. An informatics based company that develops artificial intelligence and smart algorithm solutions. Support from SBIR Phase II sponsored by NASA to develop pattern mining algorithms. Ownership in the company was purchased.

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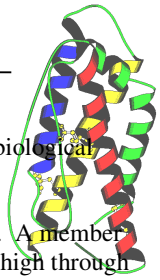
2001-2004 PI: Diversified Scientific, Inc. PI on Phase I and II SBIR from NASA (Trojan Phage Crystallization System). Other project involvements include developing peptides that



specifically bind pathogenic fungi using M13 phage display technology for a biological sensor for air born fungal spores.

Research Associate: University of Alabama at Birmingham, Birmingham, AL. A member of a small group of highly trained individuals focused on implementation of a high through put crystallographic system. I primarily acted as a systems integration specialist.

2000-2001 Chateaubriand Research Fellow: Institute de Biological Structural, Grenoble, France. Project: "X-ray crystal structure determination of human interleukin-7".

February 7 – 18, 2000: Institut fur Molekulare Biotechnologie (IMB), Postfach 100813, D-07745, Jena, Germany. Two week sabbatical at the Center for Design and Structure in Biology (CDSB). Utilized the equipment and reagents for initial sparse matrix screening of crystallization conditions for interleukin-7 and phosphodikinase (PPDK),

June 19 – 24, 2000: Laboratoire pour l'Utilisation du Rayonnement Electromagnetique (LURE). Utilize first generation synchrotron radiation source for diffraction and data collection for PPDK. This was my premiere experience using synchrotron radiation source. The event was successful and resulted in a complete data set used to solve the structure of PPDK.

1998-2000 Post Doctorate: New England Medical Center, Department of Medicine, Division of Hematology / Oncology, Boston, MA, USA. My work concentrated on the cellular signal transduction properties of human interleukin-7.

Laboratory Radiation Safety Officer. Responsible for the daily accounting, use, security, safety and cleanup of radioactive chemicals used in the laboratory.

1993-1998 Pre-Doctoral Candidate: Boston University, Department of Pharmacology and Experimental Therapeutics, Boston, MA, USA.

1990-1992 Master of Arts Candidate: Boston University, Department of Biochemistry, Boston, MA, USA.

1990-1993 University Hospital, Department of Chemistry, Boston, MA, USA.
Laboratory Aid: Managed the collection and preparation of patient samples for analysis.

1988-1989 Boston University, Department of Dermatology, Boston, MA, USA.
Technician: Performed electron microscopy, histology and immune histochemistry on patient samples.

Teaching Experience:

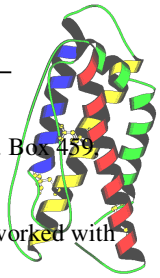
1980 – 1986: Martial Arts Instructor. I provided instruction in Fu Jow Pai kung fu under the supervision of Sifu Look, a high ranking member of the Fu Jow Pai Federation.

7/24/2002: Participated in the BioTeach / GENius Program: Developed by Dr. Stephen Hajduk, founding director of CORD, BioTeach has been offered since 1992 to high school biology teachers within the state of Alabama. I was responsible for seminars describing Crystallography and protein structure determination.

Spring 2007 Central Alabama Soccer League (CASL) Head Coach for the Panthers a U10 girl team.

Summer 2010: Industrial Molecular Biology Internship for High School Students.

Ivancic, Joanne. "C2Biotechnologies' High School Incubator with Lesson Plabs". WWW.advancedbiofuelsusa.info. Accessed September 29, 2014 http://advancedbiofuelsusa.info/education/c2biotechnologies-high-school-incubator-with-lesson-plans



2014-2015 Ski Season. Ski Instructor. Children Learning Center, Windham Mountain Resort, P.O. Box 459, Windham, NY 12496.

2013 – Current WyzAnt Tutor. Online based service that matches tutors with students. I have worked with teenagers and adults in various subjects ranging from algebra to organic chemistry.

Volunteer Experiences

Germantown Democratic Club (Germantown, NY) 2012
Participating in Steering Committee mission to improve communications for members and recruit new and younger individuals.

Stratton VA Medical Center (Albany, NY) 2015

Community Projects

High School / Business Incubator Profit Sharing Model to Cover State Public School Costs

Summary

State public educational systems are funded primarily by taxes to produce an educated workforce but conventionally do not generate revenue streams. This model defines a linkage between industry and high schools using a profit sharing agreement that when implemented on a state wide scale has the potential to reduce and or eliminate school tax. The high school – business incubator model differ from conventional incubators because public schools are funded and the quality of potential employees is low. The relationship between the high school and business is based on free access to operational space in exchange for profit sharing and development of intern training positions and programs.

Background

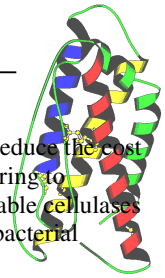
A model that links public schools with revenue streams from industry via a profit sharing arrangement becomes interesting because of the possibility for small business to support public education as they grow. A corollary result is a reduction or elimination of school tax without levying fines or taxes on industry. The basis for this innovation was the need for C2 Biotechnologies, LLC (C2B) for laboratory space and access to trained workforce and the willingness for a high school to allow a small company to operate on premise with the anticipation students may work in the company. Small start-up companies require many things including a space out of which to perform operations and trained employees but the financial support to obtain space and trained workforce is limited. Public schools have come under increased scrutiny and face economic cut backs which threaten the quality of services offered. A financial model where a small company agrees to share a small portion of potential future profits in return for access to space and labor suggests that public school costs could be completely derived from the relationship and both partners benefit. The model suggests that if this process is replicated over multiple schools, school districts, counties and states that public school costs nationally could be supported by industry performance.

Ivancic, Joanne. "Creating a High School Incubator in Biofuels Development from Lab Technique to Grant Writing—Sounds Impossible? See C2B's Project in Green County, New York." WWW.Advancedbiofuelsusa.info. . Published July 22, 2011, Accessed September 29, 2014.

http://advancedbiofuelsusa.info/creating-a-high-school-incubator-in-biofuels-development-from-lab-technique-to-grant-writing%E2%80%94sounds-impossible-see-c2b%E2%80%99s-project-in-green-county-new-york

Awards and Research Projects:

2009-2010, SBIR Phase I, Institution: DOE, Organization: **C2 Biotechnologies, LLC,** Role: PI
Duration: 9 months, Requested Support: $100,000, CFDA Number: 81.049, Opportunity Number: DE-FOA-0000350, Status: Completed.
Title: Cellulosic Fusion Enzyme Development: The proposed research will develop fusion enzymes that will improve the conversion of cellulose to fuel ethanol while reducing manufacturing costs. The milestone required to prepare this research for potential commercialization is design, construction and characterization of cellulosic fusion enzyme activity. This proposal outlines a research program to accomplish these goals, which if successful



are major steps toward commercialization of this cellulosic fusion enzyme which potentially can reduce the cost of cellulosic biomass conversion by 30%. The technical objectives include: a) use protein engineering to combine two required cellulosic enzymatic activities that complement current commercially available cellulases into one molecule, b) test the biological activities of the fusion enzyme and c) use a recombinant bacterial expression system to develop a scalable production process capable of producing gram quantities.

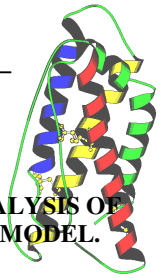
2004 SBIR Phase I & II Hamrick, D. (PI), Cosenza (Co-PI). Sponsor: NASA. Performance Site: Diversified Scientific, Birmingham, AL, USA. Duration: 6 months, 01/01/02 - 06/30/04. Total Support: $670,000.00. Project: Neural Network Enhanced Structure Determination of Osteoporosis, Immune System, and Radiation Repair Proteins. This project investigates the use of neural nets and second viral coefficient to predict and optimize conditions for crystallization of proteins involved in osteoporosis, immune system disease, and DNA radiation damage. Primary function has been assisting in selecting the neural net architecture used for predicting crystallization conditions "*in silico*" and developing tools for the analysis of protein crystallization screening.

2001 Phase I & II, Small Business Innovative research (SBIR) grant. Sponsor: NASA. PI: Cosenza, L. Duration: 6 months for Phase I, 24 months for Phase II (October 1, 2002 -2004). Title: TROJAN PHAGE CRYSTALLIZATION SYSTEM. Major goal: Utilizing protein engineering technologies to construct a novel system for the mass crystallization of small proteins (patents section 2 and 4). The system is derived from the X-ray crystallographic known capsid structure of an enterovirus that has been genetically engineered to display protein on interior surface. Hypothesis: Embedding structurally unknown and previously un-crystallized protein inside a crystallizable viral shell will facilitate structure determination of target molecules. Major goal: To develop an expression system for a unique chimeric capsid as a universal protein crystallization vehicle. This is an exciting novel technology that can guarantee crystallizing protein molecules for 1/10 the cost. A picornavirus with known crystallization parameters has been engineered to display protein molecules on the interior surface. Because the molecules of interest are displayed in the interior, the exterior viral surface should remain unaltered. Hence, the hypothesis is that the crystallization parameters will remain constant, that is similar to the native complex, and the display molecule will co-crystallize along with the viral protein shell. Therefore, this system has the potential to crystallize any suitable protein for structure determination without having to screen conditions for protein crystal growth.

2000 Chateaubriand Fellowship
Title: X-Ray Crystal Structure Determination of Human Interleukin-7. Chateaubriand Research Fellow: Lawrence Cosenza. Agency: French Government. Period: January 2000 - January 2001. Major goal: To solve the structure of human interleukin-7 and foster international exchange of ideas and techniques. This project has fostered collaborations between America and France. IL-7 biology and structure activity relationships were a major focus of interest during my graduate and post doctoral work (see dissertation section). Major contributions made to the field was a structural hypothesis for IL-7, identification of surface of ligand important for receptor activation and the generation of a potential IL-7 receptor antagonist.

References

John R. Murphy, Ph.D. Chief, Section of Biomolecular Medicine, Boston University, Boston, MA 02118 (617) 638-6010 E-mail: jmurphy@med1-mail.bu.edu	FMD Vellieux Ph.D., Ing. Tenured Scientist, Laboratoire de Biophysique Moléculaire, Institut de Biologie Structurale, 41 Rue Jules Horowitz, 38027 Grenoble, Cedex 01, France (33) (0) 47 688-9605, E-mail: vellieux@ibs.fr
Sandy L. Kelly-Schultz, Ph.D Groton School 22 Adams Avenue Groton, MA 01450 (978)448-9545 E-mail: sschultz@groton.org	Temple F. Smith, Ph.D. Prof Director, Molec. Eng. Res. Ctr., ENG Biomedical Boston University, 111 Cummington Street Boston, MA 02215, (617) 353-3577 E-mail: tsmith@darwin.bu.edu



Pre Doctorial Dissertation Project:

COMPUTATIONAL MOLECULAR MODELING AND STRUCTURE-FUNCTION ANALYSIS OF INTERLEUKIN-7: ON THE PATH TO A THREE DIMENSIONAL ATOMIC SCALE MODEL.

Lawrence W. Cosenza, Jr.
Boston University School of Medicine, 1997
Major Professor: John R. Murphy, Chief, Section of Biomolecular Medicine

ABSTRACT

A combination of theoretical structure predictions and experimental disulfide bond assignments in human interleukin-7 (hIL-7) resulted in the construction and analysis of an atomic scale model with enough resolution to identify receptor binding residues by site-directed mutagenesis. Human IL-7 has a bioactive tertiary structure dependent on disulfide bond formation. Matrix-assisted laser desorption ionization (MALDI) mass spectroscopy of hIL-7 digested with trypsin and site-directed cysteine (C)-to-serine (S) mutagenesis data demonstrate that (C3, C142) forms a disulfide bond. Further mutational analyses defined disulfide bonds between cysteine residues (C3, C142) and (C48, C93). Incorporation of disulfide bond assignments in the construction of the hIL-7 model increases resolution of the structure. Structural prediction for the hIL-7 amino acid sequence suggested an alpha parallel bundle folding motif, similar to that of human interleukin-4 (hIL-4). A three dimensional structural model of hIL-7 was constructed by homologous extension, using the known crystal structure of hIL-4 as a template. Predicted alpha helices of hIL-7 derived from the structure analysis were constructed, and superimposed upon the hIL-4 template in an up-up down-down topology similar to that of other cytokines. Loops were constructed to connect the helices which form the core of the model. The IL-7 model was optimized for three disulfide bonds between Cys residues (C3, C142), (C48, C93), and (C35, C130). The entire structure was energetically minimized. Structural analysis of the hIL-7 model indicated an atypical structural phenomenon in helix D. The hydrophobic moment of the predicted helix D appears to be directed toward bulk solvent. To test if the calculated hydrophobic moment of helix D in the IL-7 model is suggestive of a region of protein sequence important for receptor binding, site-directed alanine (A) substitution scanning mutational analysis was performed. This scanning mutational analysis probed the solvent exposed surface of helix D and identified lysine (K) 121, and leucine (L) 136, K140, and tryptophan (W) 143 which form a patch near the carboxyl terminal of predicted helix D, as important for stimulating 2E8 pre-B cell proliferation, as measured using a MTT assay. An important suggestion that now needs to be tested is weather hIL-7(W143A), which is biologically inactive, can act as an antagonist to the hIL-7 receptor.

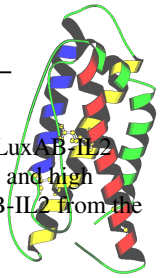
Master Thesis:

GENETIC CONSTRUCTION AND CHARACTERIZATION OF AN INTERLEUKIN-2 BACTERIAL LUCIFERASE FUSION PROTEIN: A POTENTIALLY SENSITIVE PROBE FOR THE DETECTION OF INTERLEUKIN-2 RECEPTOR BEARING CELLS

Lawrence W. Cosenza, Jr.
Boston University School of Medicine, 1992
Major Professor: John R. Murphy, Chief, Section of Biomolecular Medicine

Abstract

To date, there are no published reports describing the genetic fusion of a polypeptide ligand to bacterial luciferase. It is the intent of this project to genetically construct, purify, and characterize a new molecule that is anticipated to be used to probe the cell surface for interleukin-2 receptors. Interleukin-2 is a pleiotropic cytokine that is 133 amino acid residues long, with a predicted molecular weight of 15,418 Daltons. Interleukin-2 stimulates T-cell proliferation and natural killer cell activity. The interleukin-2 receptor is a heterodimeric complex of two subunits which associate together on the cell surface to form the high affinity interleukin-2 receptor. High affinity interleukin-2 receptors are expressed on the cell surface of activated T-cells, the surface of abnormal T-cells in patients with certain lymphoid malignancies, autoimmune disorders and individuals rejecting allographs. Luciferase is a heterodimeric bacterial enzyme composed of a 30,000 Dalton alpha subunit and a 45,000 Dalton beta subunit that associate together which is capable of producing photons. Under the appropriate conditions there is a direct correlation between the number of molecules present in the assay and the number of photons produced. Two fusion molecules, LuxAB-IL2 and IL2-LuxAB, have been constructed and expressed under the control of a T7 RNA polymerase in recombinant *E. coli*. LuxAB-IL2 molecules, partially purified from the insoluble fraction, refolded under conditions which produce bifunctional molecules.



Luciferase activity was used as a reporter of the number of LuxAB-IL2 bound to the cell surface. LuxAB-IL2 was shown to bind to the surface of MT-1 and HUT102/6TG cell lines which over express the low and high affinity interleukin-2 receptors on their cell surface respectfully. Unlabeled rIL-2 displaced LuxAB-IL2 from the surface of HUT102/6TG cells.

Patents
Current patent applications: Provided on request

Publications / Presentations:

Cosenza, L. Design, Construction and Characterization of an Amylase Fusion Enzyme: a simple solution for an industrial problem. 2014 In Preparation.

Delucas LJ, Hamrick D, **Cosenza L**, Nagy L, McCombs D, Bray T, Chait A, Stoops B, Belgovskiy A, William Wilson W, Parham M, Chernov N. Protein crystallization: virtual screening and optimization. Prog Biophys Mol Biol. 2005 Jul;88(3):285-309. Epub 2004 Sep 30.

L. J. DeLucas, T. L. Bray, L. Nagy, D. McCombs, N. Chernov, D. Hamrick, **L. Cosenza**, A. Belgovskiy, B. Stoops, and A. Chait. Efficient protein crystallization. J.Struct.Biol. 142 (1):188-206, 2003.

Adriana Irimia, Christine Ebel, Frédéric M.D. Vellieux, Stéphane B. Richard, **Lawrence W. Cosenza**, Giuseppe Zaccaï and Dominique Madern. The oligomeric states of Haloarcula marismortui malate dehydrogenase are modulated by solvent components as shown by crystallographic and biochemical studies. J. Mol. Biol., 2003, 318:1417-1432.

G. Gorgun, Spek J. van der, **L. Cosenza**, A. Menevse, and F. Foss. Altered biological activity associated with C-terminal modifications of IL-7. Cytokine 20 (1):17-22, 2002.

Larry W. Cosenza, Frederic Bringaud, Theo Baltz, and Frederic MD Vellieux. The 3.0 Å resolution crystal structure of glycosomal pyruvate phosphate dikinase from *Trypanosoma brucei*. J. Mol. Biol., 2002, 318:1417-1432.

Cosenza, L., Gorgun, G., Urbano, A., and Foss, F. Interleukin-7 receptor expression and activation in nonhaematopoietic neoplastic cell lines. Cellular Signaling, 2002, 14: 317-325.

Cosenza, L, Bringaud, F, Baltz, T, Vellieux, F.M.D. Crystallization and preliminary crystallographic investigation of pyruvate phosphate dikinase isolated from *Trypanosomia brucei.* Acta D,. 2000, D56, 1688-1690.

Cosenza, L., Rosenbach, A., White, J., Murphy, J.R. and Smith, T., Comparative model building of interleukin-7 using interleukin-4 as a template: A structural hypothesis that displays atypical surface chemistry in helix D important for receptor activation. Protein Science 2000, 9:916-926.

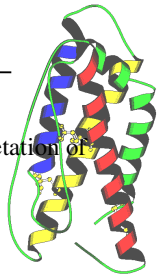
Cosenza, L., Sweeney, É., Murphy, J.R., Disulfide bond assignment in human interleukin-7 by MALDI mass spectroscopy and site-directed cysteine to serine mutational analysis. The Journal of Biological Chemistry, 1997, 272:32995-33000.

vanderSpek, J., **Cosenza, L**., Woodworth, T., Nichols, J. C. and Murphy, J. R., Diphtheria toxin-related cytokine fusion proteins: elongation factor 2 as a target for the treatment of neoplastic disease. Molecular and Cellular Biochemistry, 1994, 138: p. 151-156.

Invited Seminars:

Guest Speaker, Bard College: Environmental and Urban Studies Practicum. Title: Waste-to-energy: An integrated approach. April 10, 2014.

Cool Communities / Living Economies Conference 2007. Sponsored by Sustainable Hudson Valley Location: Ulster County Community College. Economic Panelist.



Protein crystallization in 10 dimensions: Regression models for optimization, analysis and interpretation of screening experiments. University of Alabama, Birmingham Alabama, USA.
Department of Mathematics
April 11, 2003

Trojan Phage: A System for Small Protein Crystallization
University of Alabama at Birmingham, Birmingham Alabama, USA
Center for Biophysical Sciences and Engineering
September 20, 2001

3D structure (determination) of a glycosomal pyruvate phosphate dikinase from *trypanosoma brucei*.
Athersys Inc. 3201 Carnegie Avenue, Cleveland, Ohio, USA.
March 7, 2001

3D structure determination of a glycosomal pyruvate phosphate dikinase from *trypanosoma brucei*.
University of Alabama at Birmingham, Alabama, USA
Special CBSE seminar
January 26, 2001

3-D structure (determination) of glycosomal pyruvate dikinase from *Trypanosoma brucei*.
32nd Microsymposium "Glycosomes and Drug Design"
Christian de Duve Institute of Cellular Pathology (ICP), Research Unit for Tropcal Diseases (TROP)
Avenue Hippocrate 74, B-1200, Brussels, Belgium.
December 1, 2000

Structure function analysis of human interleukin-7: a structural hypothesis with implications for receptor binding and activation.
New England Medical Center, Department of Medicine, Division of Hematology / Oncology
Boston, MA 02111, USA
Date: November 1999.

Molecular modeling and structure-function analysis of interleukin-7.
Institut de Biologie Structural J. -P. Ebel CEA CNRS, 41 rue Jules Horowitz, 38027, Grenoble Cedex, France
Date: June 5, 1998