BIOGRAPHICAL SKETCH

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NAME: Delucas, Lawrence

eRA COMMONS USER NAME (agency login):

POSITION TITLE: Director

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Alabama at Birmingham, Birmingham, A	BS	06/1972	Chemistry
University of Alabama at Birmingham, Birmingham, AL	MS	06/1974	Chemistry
University of Alabama at Birmingham, Birmingham, AL	BS	10/1979	Physiological Optics
University of Alabama at Birmingham, Birmingham, AL	OD	05/1981	Optometry
University of Alabama at Birmingham, Birmingham, AL	PHD	05/1982	Biochemistry

A. PERSONAL STATEMENT

I have served as Director of the UAB Center for Biophysical Sciences and Engineering (CBSE) and Director of the UAB Comprehensive Cancer Center's Structural Biology Shared Facility since 1994. The CBSE is currently composed of 36 aerospace engineers and 52 scientists (9 faculty members, 7 post-doctoral students, 11 PhD-level graduate students, research technicians and administrative support staff. From 1994 until 2008 I was Director of the NASA-sponsored Center for Commercial Space Partnerships (CSP). Under my leadership from 1994-2008, my Center was rated as the top NASA CSP every year for the duration of these centers. Other management experience includes serving as the NASA Chief Scientist for the ISS (a 1-year rotating position), President of the Alabama Biotechnology Association and Director of the Comprehensive Cancer Center's Structural Biology Shared Facility. I have more than 30 years of experience investigating the structure/function roles of aqueous and membrane proteins. My current NASA-funded research involves use of ISS microgravity environment to produce higher quality protein crystals. I currently am PI on two NASA grants; 1) Comprehensive Evaluation of Microgravity Protein Crystallization", NNH10CAO001K; this project involves demonstrating the scientific and commercial value of protein crystallization using a long-duration microgravity mission (~20 weeks duration on ISS); and 2) "The Effect of Macromolecular Transport on Microgravity Protein Crystallization", NNH13ZTT001N; this project involves use of the LMM's planned confocal laser-scanning fluorescent microscope, compare in microgravity versus unit gravity, percentage incorporation of different molecular aggregates (protein impurities) into the crystalline lattice of growing crystals. Based on the % incorporation of larger aggregates within the crystals, the effect of molecular filtering based on differences in diffusion rates will be assessed. I am PI for the NIH award 1R01-GM095639-01 involving membrane protein structural studies, and PI and member of the Cystic Fibrosis Foundation's Structural Biology Consortium dedicated to understanding the structure/function of the cystic fibrosis transmembrane regulator protein (CFTR). My NIH-funded work involves the expression, purification, crystallization and structure determination of several membrane proteins implicated in different cancers. My interest in biotechnology includes development of a novel self-interaction and cross-interaction chromatography system (a technology that provides a rapid method to 1) determine optimum protein solubility solution conditions and 2) determine conditions to stabilize protein complexes).

B. POSITIONS AND HONORS

Positions and Employment

1981 - 1985 Assistant Professor , University of Alabama at Birmingham, Department of Optometry, Birmingham , AL

1983 - Member, Graduate Faculty, University of Alabama at Birmingham , Birmingham, AL

1984 - Senior Scientist, University of Alabama at Birmingham, Comprehensive Cancer Center , Birmingham, AL

1985 - 1989 Associate Professor, University of Alabama at Birmingham, Department of Optometry, Birmingham, AL

1989 -	Adjunct Professor, University of Alabama at Birmingham, Materials Science, Birmingham, AL
1989 - 2010	Adjunct Professor , University of Alabama at Huntsville, Materials Science
1989 -	Professor, University of Alabama at Birmingham, Department of Optometry, Birmingham, AL
1990 -	Professor (Secondary Appt), University of Alabama at Birmingham, Department of Biochemistry, Birmingham, AL
1990 - 2010	Adjunct Professor, University of Alabama at Birmingham, Department of Medical Genetics, Birmingham, AL
1994 -	Director, University of Alabama at Birmingham, Comprehensive Cancer Center, X-ray Core Facility , Birmingham, AL
1994 -	Director, University of Alabama at Birmingham, Center for Biophysical Sciences and Engineering, Birmingham, AL
1994 - 1995	Chief Scientist, NASA Headquarters, International Space Station
1996 -	Member, University of Alabama at Birmingham, Center for Metabolic Bone Disease, Birmingham, AL
2001 -	Adjunct Professor, University of Alabama at Birmingham, Physiology and Biophysics, Birmingham, AL
2002 -	Adjunct Professor, University of Alabama at Birmingham, Department of Biomedical Engineering, Birmingham, AL

Other Experience and Professional Memberships

1995 - 2002	Member, Science Advisory Board, National Space Development Agency of Japan
1996 - 2002	Member, Structural Biology Working Group, University of Alabama at Birmingham
1996 - 2005	Board Member and Co-founder, Diversified Scientific, Inc
1997 - 2004	Member, Research Foundation and Technology Transfer Committee, University of Alabama at Birmingham
1998 - 1999	Chairman, Search Committee for V.P. of Development, Helen Keller Eye Research Foundation
1998 - 2007	Member, Helen Keller Research Foundation Board
1999 - 2000	Member, Alabama Information Technology Association (AITA), Board of Directors
1999 - 2000	President, Board of Directors, Alabama State Biotechnology Association
1999 - 2003	Chair, Scientific Advisory Board, Spacehab, Inc
2000 - 2008	Member, Board of Trustees, Illinois College of Optometry
2001 - 2004	Member, Review Committee, Crystal Growth and Design Journal
2003 - 2008	Member, Board of Directors, Birmingham Area Technology Leadership Alliance
2003 -	Member, Board of Governors, Indian Springs School
2003 - 2008	Member, Scientific Advisory Board, Fluidigm Corporation
2004 -	Board Member, Vivo Biosciences, Inc
2004 - 2014	Member, External Advisory Committee, Res. Infrastructure in Minority Institutions, RIMI, Alabama State University
2008 -	Member, Biomatrix Engineering and Regenerative Medicine Center
2008 - 2014	Member, Biochemistry and Structural Biology Graduate Student Admissions Committee
2008 -	Board Member and Co-founder, Soluble Therapeutics, LLC
2008 -	Member, Center for Computational and Structural Dynamics
2008 -	Board member, Space Energy, Inc
2009 -	Board Member, Alabama Chapter for the Cystic Fibrosis Foundation
2009 -	Member, Science and Technology Honors Program Leadership Council
2011 -	Member, Scientific Advisory Board, Minerva Biotechnologies, Inc

Honors

1991	"Distinguished Alumnus Award", University of Alabama at Birmingham
1992	NASA Space Flight Medal. Payload Specialist/Astronaut for United States Microgravity Laboratory-1 (Space Shuttle launch date: June 25, 1992); established new record for longest duration space shuttle flight, National Aeronautics and Space Administration
1993	Distinguished Crystallography Lecturer, Pittsburgh Diffraction Society Lectures, Pittsburgh, PA.
1994	Appointed NASA Chief Scientist for the International Space Station, National Aeronautics and

	Space Administration Headquarters, Washington, D.C.
1997	NASA Public Service Medal for exemplary performance in support of the Microgravity Projects Office, National Aeronautics and Space Administration
1999	Honorary Doctor of Science degree, Ohio State University
1999	Recipient of the Howell Heflin Statesmanship award for Technology, State of Alabama
2000	Distinguished Faculty Lecturer, University of Alabama at Birmingham
2011	President's Award for "Best Teacher, 2011", University of Alabama at Birmingham

C. Contribution to Science

1. I was the first US scientist to demonstrate the potential of a microgravity environment to enhance protein crystal quality (PMID:2510297). Publication of the results from our initial four space flights led to a major program within the National Aeronautics and Space Administration (NASA) to support fundamental theoretical and laboratory-based studies on protein crystallization. It also led to a major program supporting microgravity protein crystallization for more than 100 investigators world-wide (funded by space agencies from the USA and several other countries including Germany, France, Spain, Italy, Japan, Canada, Russia and China). More than 200 peer-reviewed publications resulted from the NASA-funded program. Improved microgravity-grown protein crystals have benefitted more than 100 researchers in the USA, Canada, Japan and several European countries. In 1999, I conceived of a fully automated x-ray generator/data collection, crystal mounting and analysis system (Crystallography Facility) as part of an effort to incorporate a X-ray crystallography system on the International Space Station (ISS). The facility occupied a full space station rack (Figure 1). Although this facility was never placed on the ISS, it demonstrated to the scientific community that crystals could be remotely manipulated (including mounting in cryo-loops, cryo-freezing and placement on a goniometer for X-ray data collection). I believe that this contribution stimulated the development of automated crystal manipulation systems at synchrotron facilities and in some cases home laboratories (McDonald, WT, Smith, CD, Nordness, JE, Fountain, JA, and DeLucas, LJ; “Protein Crystallography Facility for the International Space Station", American Institute of Aeronautics and astronautics Space Programs and Technology Conference and Exhibit, Huntsville, Alabama 1995 September: 95-3661).

Figure 1: X-ray Crystallography Facility. Includes: X-ray data collection with CCD detector, crystal manipulation/mounting, -180^{o}C freezer & cryo-preservation.

   a. DeLucas LJ, Smith CD, Smith HW, Vijay-Kumar S, Senadhi SE, et al. Protein crystal growth in microgravity. Science. 1989 Nov 3;246(4930):651-4. PubMed PMID: 2510297.

2. I submitted the first patent (patent#6,579,358; “Method of Growing Protein Crystals") for high throughput nano-crystallization (Figure 2). This led to a partnership with the Fluidigm Corporation (the company licensed my patent thereby enabling them to produce and sell a high-throughput fluidic nano-crystallization system) where I served on their science advisory board for a period of approximately 10 years. Today high-throughput nano-crystallization systems (droplet dispensing and fluidic systems) are utilized by hundreds of laboratories throughout the world. I also patented and developed the first automated crystal imaging and analysis system (CrystalScoreTM) that was licensed to a local spinoff company called Diversified Scientific Inc. (patent#6,529,612; “Method for Acquiring, Storing and Analyzing Crystal Images”). One of my other patents associated with this technology (patent #7,250,305; “Use of Dye to Distinguish Salt in Protein Crystals under Micro Crystallization Conditions”) includes the ability to detect protein crystals using dye or UV light. This company sold approximately 30 CrystalScore systems in the US and in Europe. Today there are several companies that sell similar high-throughput crystal imaging and analysis systems, incorporating brightfield and UV imaging.

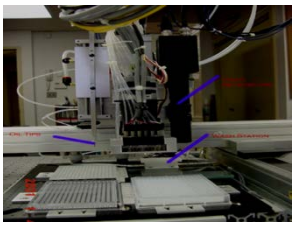

Figure 2: High-throughput nano-crystallization System

3. More recently I and a colleague (Dr. WW Wilson, Mississippi state University) conceived of and developed a high-throughput system that can rapidly determine solution conditions that enhance protein solubility and stability (PMID: 24817708; PMID: 20057048; PMID: 18923812; PMID: 15652246; PMID:12718931 and Wilson, WW, Henry, see, Johnson, D and DeLucas, LJ; “Tools to Enhance Membrane Protein Crystallization" Membrane Protein Crystallization, Elsevier Inc., Editor: L. DeLucas. 2009, volume 63 page 151 -178). This technology led to the spin out of a new company, Soluble Therapeutics Inc. that is currently

located in Birmingham, Alabama (lab and commercial versions of the technology shown in Figure 3). The technology, called HSCTM, has applications for protein crystallization as well as protein-based therapeutics (most protein therapeutics require high solubility, often more than 100 mg/mL without inducing nonspecific aggregation). The HSC utilizes a miniaturized form of self-interaction chromatography (performed in chromatography columns that are 0.3 mm in diameter) combined with an artificial neural network to rapidly survey a variety of additives and additive combinations to determine the optimum solution conditions that provide maximum protein solubility and physical stability. This technology is currently being used by a number of UAB CCC members (although not part of the structural biology shared facility, the device is available to any UAB investigator provided they cover all supply-related costs).

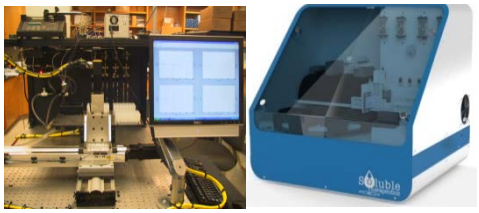

Figure 3: 2nd and 3rd Generation HSC™

a. Delucas LJ, Hamrick D, Cosenza L, Nagy L, McCombs D, et al. Protein crystallization: virtual screening and optimization. Prog Biophys Mol Biol. 2005 Jul;88(3):285-309. PubMed PMID: 15652246.

b. Johnson DH, Parupudi A, Wilson WW, DeLucas LJ. High-throughput self-interaction chromatography: applications in protein formulation prediction. Pharm Res. 2009 Feb;26(2):296-305. PubMed PMID: 18923812.

c. Gabrielsen M, Nagy LA, DeLucas LJ, Cogdell RJ. Self-interaction chromatography as a tool for optimizing conditions for membrane protein crystallization. Acta Crystallogr D Biol Crystallogr. 2010 Jan;66(Pt 1):44-50. PubMed PMID: 20057048.

d. Wilson WW, Delucas LJ. Applications of the second virial coefficient: protein crystallization and solubility. Acta Crystallogr F Struct Biol Commun. 2014 May;70(Pt 5):543-54. PubMed PMID: 24817708; PubMed Central PMCID: PMC4014317.

4. In collaboration with Dr. John Kappes (CCC member), I have also worked for the past seven years on the development of an expression technology for integral membrane proteins. I am currently utilizing this technology for the expression of cystic fibrosis transmembrane regulator protein (CFTR), PMID:25065669 and PMID:22119790; syndecan-1 (a protein implicated in cancer metastasis, PMID:22298773) and chemokine receptor-1 (CCR1). Our latest modification of our lentivirus inducible expression system includes the ability to separate fully matured membrane protein that exists only in the plasma membrane (unpublished)

   a. McClure M, DeLucas LJ, Wilson L, Ray M, Rowe SM, et al. Purification of CFTR for mass spectrometry analysis: identification of palmitoylation and other post-translational modifications. Protein Eng Des Sel. 2012 Jan;25(1):7-14. PubMed PMID: 22119790; PubMed Central PMCID: PMC3276306.

   b. Ramani VC, Pruett PS, Thompson CA, DeLucas LD, Sanderson RD. Heparan sulfate chains of syndecan-1 regulate ectodomain shedding. J Biol Chem. 2012 Mar 23;287(13):9952-61. PubMed PMID: 22298773; PubMed Central PMCID: PMC3322978.

   c. Hildebrandt E, Zhang Q, Cant N, Ding H, Dai Q, et al. A survey of detergents for the purification of stable, active human cystic fibrosis transmembrane conductance regulator (CFTR). Biochim Biophys Acta. 2014 Nov;1838(11):2825-37. PubMed PMID: 25065669; PubMed Central PMCID: PMC4170525.

5. Finally, Dr. Chattopadhyay (CCC-member) and I are collaborating on two other cancer-related projects: 1) crystallization and structure determination and inhibitor development for ubiquitin specific protein (USP2a); this collaboration has led to the highest resolution structure reported (coordinates deposited in PDB). Ubiquitinin specific protease 2a (USP2a) is a deubiquinating protein implicated in prostate cancer. This project involves collaboration with medicinal chemists at the NIH NCATS (Dr. Matthew Boxer and colleagues); 2) structure determination and inhibitor development for protein phosphatase-5. PP5, a member of the PPP-family of ser/thr phosphatases, is a key regulator of cell growth. PP5 interacts with several proteins that influence intracellular signaling cascades initiated by glucocorticoids or cellular stress. This project involves collaboration with Dr. Richard Honkanen at the Univ. of South Alabama Mitchell Cancer Institute); NIH 1R21NS071553. At this early stage (we began this collaboration approximately 1 year ago) we have determined the native structure as well as structures with three different inhibitors for PP5 (Figure 4).

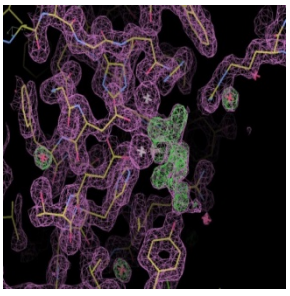

Figure-4:**Crystal structure at 1.96Å of the complex of PP5 with an active site inhibitor**. Location of active site Mn^{2+} ions are shown in white. The difference (Fo-Fc) electron density at 3σ-counter level is shown in green wire map represents the binding site of the inhibitor.

Complete List of Published Work in My Bibliography:

http://www.ncbi.nlm.nih.gov/pubmed/?term=delucas+LJ

D. RESEARCH SUPPORT

Ongoing Research Support

2013/06/01-2018/05/31
NNH13ZTT001N, NASA
DeLucas, Lawrence (PI)
The Effect of Macromolecular Transport on Microgravity Protein Crystallization
Study the effect of a diffusive environment on aggregate incorporation into gravity protein crystals.
Role: PI

2012/01/01-2016/12/31
NNH10CAO001K, NASA
DeLucas, Lawrence J (PI)
Enabling Support Equipment and Services for International Space Station (ISS) as a National Lab
Demonstrate the scientific and commercial value for protein crystallization on a long-duration microgravity mission. This will be accomplished using flight hardware that accommodates a statistically relevant number of high-value proteins combined with comprehensive crystal quality analysis for microgravity versus 1-g control experiments.
Role: PI

2013/09/01-2015/08/31
DELUCA05XX0, Cystic Fibrosis Foundation
DeLucas, Lawrence (PI)
Innovative Solutions toward a 3D CFTR Structure
To produce preparative amounts of CFTR to support Dr. DeLucas' crystallization efforts and to supply protein to pharmaceutical companies working with the CFF as well as other CFF-funded crystallographers.
Role: PI

2010/09/30-2015/07/31
R01 GM095639-04, National Institute of General Medical Sciences (NIGMS)
DeLucas, Lawrence J (PI)
Production & Crystallization of Membrane Protein for 3D Structure
Role: PI

2006/06/05-2015/03/31
5P30CA13148-40, NIH/National Cancer Center
DeLucas, Lawrence (PI)
Comprehensive Cancer Center Core Support Grant – X-Ray Crystallography
This Shared Facility supports UAB cancer center members who require three-dimensional structure information for macromolecules and drug discovery.
Role: PI

2015/04/01-2016/03/31
1R41GM109565-01A1, NIH
DeLucas, Lawrence (PI)
Soluble Therapeutics, Inc.
Development of a Novel Membrane Protein Solubilization/Stabilization Screen
Role: PI