Tara Lynne Davis, Ph.D.

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Education

The University of Texas Southwestern Medical Center, Dallas, TX

1997-2004

- **Ph.D. in Molecular Biophysics Advisor: Dr. Stephen Sprang**
- Dissertation Title: Heterotrimeric G Protein Beta:Gamma bound to a Biologically Active Peptide: Structural Definition of a Preferred Protein Interaction Surface

The University of Texas at Austin, Austin, TX

1991-1996

- **B.S. Honors in Biochemistry**
  - Minor: Chemistry
  - Areas of Concentration: English, Music Performance (Bassoon)

Postgraduate Training

Postdoctoral Fellow, Dhe-Paganon Lab

2004-2009 Structural Genomics Consortium, Toronto, Ontario, Canada

- Lead scientist on projects designed to focus on the structures of human enzymes involved in insulin related signaling and the pathology of diabetes. Highlights of published research include:
  - Human peptidyl prolyl isomerases have striking specificity for substrate/ligand despite encoding similar structural elements.
  - The receptor tyrosine kinase EPHA3 is regulated by spatially coupled set of residues that connect the solvent-accessible juxtamembrane segment directly to the activation loop segment.
  - The calcium-dependent calpain proteases undergo dynamic conformational rearrangement in the presence of substrate.
  - The galactolipase HPLRP2 is structurally and biochemically distinct from the classical lipases, thereby rationalizing next-generation obesity drug design.

Postdoctoral Fellow, Jurica Lab, Center for RNA Biology

2009-2012 University of California Santa Cruz, Santa Cruz, CA

- Senior scientist performing independently designed research program centering on the composition and functional role of human cyclophilins in spliceosomal complexes.
- Completed the K99 mentored phase of a K99/R00 grant.

Employment History and Faculty Appointments

Assistant Professor, Department of Biochemistry and Molecular Biology

2012-present Drexel University College of Medicine, Philadelphia PA 19102

Honors and Awards

NRSA Training Grant Recipient	**1999 – 2002**
Graduate Student Organization President	**2000 – 2001**
Poster award, GSO Poster Session	**2000**
Ida M. Green Service Award	**2001**
(note: this is the highest honor given for a student at UT-Southwestern for academic achievement and service to the community and University)	
Finalist, Martin Luther King Jr. Award for Community Service	**2001**
Best of Show, GSO Poster Session	**2002**
Poster award, UTSWMC Biophysics Program	**2004**

Memberships and Offices in Professional Societies

Current:

RNA Society, 2010-
ACA (American Crystallographic Association), 2001-

Professional Committees and Administrative Services

Institutional:

Drexel University College of Medicine Women in Medicine and Science Committee, 2013-

Extramural:

Organized inaugural session "Professional Directions", ACA National Meeting, 2008.

Educational Activities

Courses (organized by year):

2014

- Macromolecular Structure and Function (Graduate Level Course), "Nuclear Magnetic Resonance".
- Core Course, 1st semester (Graduate Level Course), "Nucleic Acids"
- Core Course, 1st semester (Graduate Level Course), "Nucleic Acid Techniques"
- Adv. Topics, 1st semester (Graduate Level Course), "Techniques: Nucleic Acids"
- IFM (1st year Medical School), "Ethylene Glycol Case Study", directed discussion group.
- IFM (1st year Medical School), "Glycolytic Diseases Case Study", directed discussion group.
- IFM (1st year Medical School), "Diabetes Case Study", directed discussion group.
- IFM (1st year Medical School), "Human Disease Presentations", directed discussion group.
- Introduction to Biochemistry (Undergraduate),"Basic Properties of Amino Acids and Protein Structure".

2013

- Core Course, 1st semester (Graduate Level Course), "Nucleic Acids"
- Core Course, 1st semester (Graduate Level Course), "Nucleic Acid Techniques"
- Adv. Topics, 1st semester (Graduate Level Course), "Techniques: Nucleic Acids"
- Adv. Topics, 2nd semester (Graduate Level Course), "Advances in RNA Biology".
- IFM (1st year Medical School), "Ethylene Glycol Case Study", directed discussion group.
- IFM (1st year Medical School), "Diabetes Case Study", directed discussion group.
- IFM (1st year Medical School), "Human Disease Presentations", directed discussion group.
- Introduction to Biochemistry (Undergraduate),"Basic Properties of Amino Acids and Protein Structure".

2012

- Adv. Topics, 1st semester (Graduate Level Course), "Techniques: Nucleic Acids".

Advising/Mentoring:

Undergraduates/Medical Students/Summer Students (indicates funded position)*

David (Jau-Ann) Tsai, Drexel CoM (2014-)*
Ashley Bupp, junior, Drexel (2014-)
Alyssa Lipcsey, sophomore, Drexel (2014-)
Anh Trinh, sophomore, Drexel (2014-)*
Gabrielle Ann Habina, junior, Drexel (2013-)
Alexander Kaznel, sophomore, Dickinson College (2013,2014)*
Alexander Molchansky, sophomore, Drexel (2013)*
Damie Juat, sophomore, Drexel (2013)*
Elena Brindley, sophomore, Notre Dame (2012)*
Brent Dembo, medical student, Drexel CoM (2012)*

Support

NIH K99/R00 4R00GM094293-03 Davis (PI) 8/20/10 – 8/20/15

Title: Functional and structural characterization of spliceosomal cyclophilins.

Project Goals: The goals of this project are to functionally characterize the roles of spliceosomal cyclophilins in the process of mRNA splicing and to identify the molecular partners of cyclophilins in order to map the interaction networks of cyclophilins within the spliceosome.

Bibliography

*Davis TL, Bonacci TM, Sprang SR, Smrcka AV. Structural and molecular characterization of a preferred protein interaction surface on G protein beta gamma subunits. Biochemistry. 2005 Aug 9;44(31):10593-604

*Davis TL, Walker JR, Finerty PJ Jr, Mackenzie F, Newman EM, Dhe-Paganon S. The crystal structures of human calpains 1 and 9 imply diverse mechanisms of action and auto-inhibition. *J Mol Biol*. 2007 Feb 9;366(1):216-29.

*Davis TL, Walker JR, Ouyang H, Mackenzie F, Butler-Cole C, Newman EM, Eisenmesser EZ, Dhe-Paganon S. The crystal structure of human WD40 repeat-containing peptidylprolyl isomerase (PPWD1). *FEBS J*. 2008 May;275(9):2283-95.

The highlight of this work was the finding that PPWD1, a nuclear cyclophilin that is an active peptidyl-prolyl isomerase, is capable of binding an internal proline-containing sequence of another PPWD1 molecule *in trans*. This interaction was first observed in the crystal structure, and then replicated using peptide sequences in solution. Surprisingly, this peptide was able to bind the PPWD1 active site but was not a substrate for *cis/trans* isomerization, the first time this phenomenon was described for any prolyl isomerase. Considering that there are seven nuclear cyclophilins (including PPWD1) associated stably with active spliceosomes, the finding that internal cyclophilin sequences can act as substrates or as protein docking sites may one day hold great significance.

*Thai V, Renesto P, Fowler CA, Brown DJ, Davis T, Gu W, Pollock DD, Kern D, Raoult D, Eisenmesser EZ. Structural, biochemical, and in vivo characterization of the first virally encoded cyclophilin from the Mimivirus. *J Mol Biol*. 2008 Apr 18;378(1):71-86.

*Eydoux C, Spinelli S, Davis TL, Walker JR, Seitova A, Dhe-Paganon S, De Caro A, Cambillau C, Carrière F. Structure of Human Pancreatic Lipase-Related Protein

2 with the Lid in an Open Conformation. *Biochemistry*. 2008 Sep 9;47(36):9553-64.

*Davis TL, Walker JR, Loppnau P, Butler-Cole C, Allali-Hassani A, Dhe-Paganon S. Autoregulation by the Juxtamembrane Region of the Human Ephrin Receptor Tyrosine Kinase A3 (EPHA3). *Structure*. 2008 Jun;16(6):873-84.

*Davis TL, Walker JR, Allali-Hassani A, Parker, SA, Turk, BE, Dhe-Paganon S. Structural recognition of an optimized substrate for the ephrin family of receptor tyrosine kinases. *FEBS J.* 2009 Aug;276(16):4395-404.

The previous two papers provide a powerful reminder of the relationship between the observations provided by an x-ray crystallographic experiment and the functional hypotheses that can be driven by these observations. In this case, a series of carefully designed crystallization experiments on the physiologically important receptor tyrosine kinase EPHA3 led to a greater understanding of both autoregulatory mechanisms within the kinase and juxtamembrane regions, and provided leads on potential substrate specificity for this enzyme.

*Littler DR, Walker JR, Davis T, Wybenga-Groot LE, Finerty PJ Jr, Newman E, Mackenzie F, Dhe-Paganon S. A conserved mechanism of autoinhibition for the AMPK kinase domain: ATP-binding site and catalytic loop refolding as a means of regulation. *Acta Crystallogr Sect F Struct Biol Cryst Commun*. 2010 Feb 1;66(Pt 2):143-51.

*Davis TL, Walker JR, Campagna-Slater V, Finerty Jr. PJ, Paramanathan R, Bernstein G, Tempel W, Ouyang H, Lee, WH, Eisenmesser E, Dhe-Paganon S. The Human Cyclophilin Family of Peptidyl-Prolyl Isomerases. *PLoS Biol.* 2010 July; 8(7).

This manuscript highlighted the novel structures of seven human cyclophilin domains, including five nuclear cyclophilins. Full enzymatic and biochemical analyses were performed for 15 of the 17 human cyclophilins; this included defining the affinities for the small molecular inhibitor cyclosporine A, measuring the ability of each cyclophilin to bind to and turn over proline-containing peptide sequences, and the definition of a previously unappreciated pocket in the active site that can be exploited to design novel specificity into next-generation inhibitors and substrates for this class of enzyme.

*Nguyen TG, Honson NS, Arns S, Davis TL, Dhe-Paganon S, Kovacic S, Kumar NS, Pfeifer TA, Young RN. Development of Fluorescent Substrates and Assays for the Key Autophagy-Related Cysteine Protease Enzyme, ATG4B. *Assay Drug Dev. Technol.* 2014 April; 12(3).

Presentations

"Spliceosomal Cyclophilins." Departmental Seminar Series, Drexel University Department of Biology, May 2013.

"Nuclear Cyclophilins: Splicing from a Protein's Point of View?" Departmental Seminar Series, Department of Biochemistry and Molecular Biology, Drexel University College of Medicine, November 2012.

Tara L. Davis and Melissa Jurica. "Spliceosomal Cyclophilins Impact Splicing in an in vitro Assay System: Implications for Spliceosomal Assembly and Catalysis". Poster: 2011 RNA Society Meeting, June 14th - 18th, 2011.

Tara L. Davis and Melissa Jurica. "Spliceosomal Cyclophilins: From Structure to Function and Back Again". Poster: 2010 RNA Society Meeting, June 22nd - 26th, 2010.

"Spliceosomal Cyclophilins: Can Structure Lead to Function?" Lecture: University of California – Santa Cruz, October 30th, 2009.

"Structures of EphA3 kinase and the human cyclophilins: using structural genomics to probe function". Lecture: University of Colorado Health Sciences Center, November 5th 2008.

Organized the inaugural "Professional Directions" Panel Discussion: 2008 ACA meeting, May 31st – June 5th, 2008.

Tara L. Davis, John R. Walker, Christine Butler-Cole, Abdellah Allali-Hassani, Benjamin E. Turk, Sirano Dhe-Paganon. "EphA3 Kinase: Activation, Regulation, and Mechanistic Insights from Structure". Poster: 2007 ACA meeting, July 21st – 26th, 2007.

"Structural Genomics and the Single Girl: Structures from the SGC-Toronto Pipeline". Lecture: University of Texas Southwestern Medical Center, December 19th 2006.

Tara L. Davis, John R. Walker, Patrick Finerty Jr., Elena Newman, Alexey Botchkarev, Cheryl Arrowsmith, Aled Edwards, Sirano Dhe-Paganon. "Human Peptidyl Prolyl Isomerases". Poster: 2006 Keystone Symposia in Structural Genomics, January 29th – February 3rd, 2006.

"Calpains: Exploring Mechanism(s) of Activation", Lecture: University of Toronto, November 2nd, 2005.

Tara Davis, Tabetha M. Bonacci, Alan V. Smrcka, and Stephen R. Sprang. "Crystal Structure of a Biologically Active Peptide Bound to a G Protein β1γ2 Heterodimer." Poster: Structural Biology Symposium, April 2004. Poster: 2004 ACA meeting, July 17th – 22nd, 2004.

Public Databases

PDB entries organized by enzyme class or signaling pathway (39 depositions)

- **Peptidyl-prolyl isomerases (cyclophilins and FKBPs)**
  - 2ESL (PPIC+CsA); 2R99 (PPIE); 2GW2 (PPIG); 2A2N (PPWD1); 2HE9 (NK-TR); 2HQ6 (SDCCAG-10); 1ZKC (PPIL2B); 2PBC (FKBP02); 3B7X (FKBP06); 2AWG (FKBP08); 2KFV (FKBP03)
- **Receptor tyrosine kinases**
  - 2GSF, 2QO2, 2QO7, 2QO9, 2QOB, 2QOC, 2QOD, 2QOF, 2QOI, 2QOK, 2QOL, 2QON, 2QOO, 2QOQ (all EPHA3); 3FXX, 3FY2 (EPHA3 + peptides)
- **Lipases**
  - 2PPL (HPLRP1); 2OXE (HPLRP2)
- **Calpains**
  - 2ARY (CAPN01); 2NQA (CAPN08); 1ZIV, 2P0R (CAPN09); 2I7A (CAPN13)
- **Components of the autophagy pathway**
  - 2P82 (APG4A); 2R2Q (GABARAP-L); 3ECI (MAP1LC3A)
- **Isoprenoid biosynthetic pathway**

- 2PNY (IDI2); 3FON (MVD)

Websites/Online

LinkedIn: http://www.linkedin.com/in/taradavis

ResearcherID: A-9858-2010 Scopus Author ID: 23969859800

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