BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Denise Ratzlaff Cooper, Ph.D., F.A.H.A.	Program Director/PI Senior Research Career Scientist
eRA COMMONS USER NAME (credential, e.g., agency login) DRCooper	

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)*	MM/YY	FIELD OF STUDY
Oklahoma State University, Stillwater, OK	B.S.	1972	Biochemistry
University of Oklahoma Health Sciences Center, OK	M.S.	1981	Biochemistry/Molecular Biology
University of Oklahoma Health Sciences Center, OK	Ph.D.	1983	Biochemistry/Molecular Biology
Oklahoma Medical Research Foundation Oklahoma City, OK	Post-Doc	1983-1985	Biology Protein kinases Insulin signaling and adipocyte function
University of South Florida, Tampa, FL	Post-Doc	1985-1986	

A. Personal Statement

Dr. Cooper is known for her laboratory's discovery of insulin regulation of alternative pre-mRNA splicing in adipogenesis, muscle, fibroblasts and liver. Her lab provided the first link of a cell surface receptor modifying alternate exon usage and 5' splice site selection on PKCßII via activation of Akt and the subsequent phosphorylation of serine-rich (SR) splicing factors. The phosphorylation of SR domains by Akt is now widely recognized. Her lab went on to demonstrate that Akt regulated CDC2-like kinase (Clk) activity by phosphorylating its SR domain. This pathway is important in adipogenesis, neurogenesis and skeletal muscle development. It will be a key factor in stem cell differentiation, because splicing of RNA is essential to signaling and development. Their identification of insulin signaling through Clk is the first pathway to be reported to alter splice variants in stem cells. She has a long record of isolating primary cells for culture. She recently isolated lncRNAs in the conditioned media of stem cells and initiated studies showing how they altered cell migration. She has recently focused on the use of flow cytometry to study signaling pathways in pre-adipocytes. She is qualified to be the Director of the REMexRNA Program due to her record of mentoring young investigators, review of VA, NIH and outside agency grants, ability to identify novel and innovative questions in cell signaling. She serves on various oversite committees dealing with the development of stem cell therapies for tissue regeneration. In addition to studying obesity and diabetes, Dr. Cooper has transitioned her work into developing the human adipocyte derived stem cell as a model to develop for tissue repair and has a personal investment in seeing that this research succeeds.

B. Positions and Honors

Positions and Employment

1973 - 1974 Lecturer in Dept. of Life Sciences, University of Missouri-Rolla, Rolla, MO
1974 - 1977 Senior Chemist, Hazleton Laboratories America, Dept. of Radiochemistry, Vienna, VA

1977 - 1978	Senior Research Assistant, Dept. of Obstetrics and Gynecology University of Oklahoma Health Sciences Center, Okla. City, OK
1978 - 1982	Predoctoral Fellow, Oklahoma Medical Research Foundation,Oklahoma City, OK
1982 - 1983	Samuel R. Noble Foundation Predoctoral Fellow, Oklahoma Medical Research Foundation, Oklahoma City, OK
1983 - 1985	Post-Doctoral Fellow, Biomembrane Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK
1985 - 1986	Postdoctoral Fellow, Dept. of Medicine, University of South Florida, and James A. Haley Veterans Hospital, Tampa, FL
1986 - 2002	Research Scientist/Investigator, James A. Haley Veterans Hospital, Tampa, FL
1992 - 1995	Assistant Professor, Dept. of Biochemistry and Molecular Biology University of South Florida College of Medicine, Tampa, FL
1995 – 2000	Associate Professor, Dept. of Biochemistry and Molecular Biology University of South Florida College of Medicine, Tampa, FL
1997 - 2000	Associate Professor, Dept. of Internal Medicine University of South Florida College of Medicine, Tampa, FL
2000-present	Professor, Dept. of Biochemistry and Molecular biology University of South Florida College of Medicine, Tampa, FL
2002-present	Research Career Scientist, James A. Haley Veterans Hospital, Tampa, FL Member, Moffitt Cancer Center, Tampa, FL

Other Experience and Professional Memberships:

1986-present	Member: Endocrine Society
1987-present	Member: American Society for Biochemistry and Molecular Biology
1986-present	Member: American Diabetes Association
1997-present	Member: American Society for Cell Biology
2006	Member: American Heart Association
1992	Review Panel for JDF/NIDDM Study Section
1996	JDF/VA Diabetes Research Program Review Panel
1994-1995	Member of Research Advisory Group for R&D, Veterans Administration
1993-1997	American Heart Assoc. FL Affiliate Peer Review Panels
1996	American Institute of Cancer Research Review Panel
1999	Member of Endocrinology Review Committee and Ad Hoc Reviews for ALTX-1, NIH
1999	Member of Endocrinology Review Panel for VA Merit Review
1998-2002	Member of Research Committee, AHA-Florida and Puerto Rico Affiliate
2001-2004	Member of Peer Review Panel (Signaling) for AHA-Fl and PR Affiliate
2002-2005	Member, NASA Cell and Molecular Biology Peer Review Panel
2003-2006	Merit Review Subcommittee Endocrinology A, Veterans Health Administration
2005	Member, SBIR and STTR ZRG1 EMNR-E Study Section, NIH
2006	Member, ZRG1 EMNR-G 02: Diabetes Study Section, NIH
2004	Guest Editor, Journal of Clinical Ligand Assay Society
2004-2006	Annual Meeting Steering Committee, The Endocrine Society
2006-2010	American Heart Association Research Committee (National)
2007, 2009	*Member-Review of Diabetes Centers for RFA-DK-06-014*NIH
2007, 2009	*Member-Health of the Population Special Emphasis Panel* ZRG1 HOP B 50R (Building Interdisciplinary Research Careers in Women's Health) Panel. NIH
2010-2013	Oversight Committee for the AHA DeHaan Myogenesis Research Centers
2009	*Member-* ZRG1 EMNR-B Special Emphasis Panel, NIH-NIDDK
2008-2009	Member-Review of Extramural Loan Repayment Program for Clinical Researchers. NIH-NIDDK.
2009	Member-R4 Basic Cell and Molecular Biology 3 Peer Review Committee. AHA Natl.

2008 *Member-DDK-B2* Review of KO1, K99/R00, R03, T32 grants for NIDDK
2008 *Member- ZDKQ GRB-N* Peer Review Special Emphasis Panel for NIDDK
2009-2010 Ad Hoc Member Cellular Aspects of Diabetes and Obesity Peer Review Panel
2010-2014 Member Cellular Aspects of Diabetes and Obesity Peer Review Panel, NIH
2010 Chair-Stem Cell Subgroup of the AHA Research Committee (National)
2010-2012 Vice Chair of the AHA Southeast Affiliate Research Committee
2010 Co-Chair of the Innovative Research Grant Review Panel for AHA
2012-14 Chair of the AHA Greater Southeast Affiliate Research Committee
2012-present Member of the Board of Directors of the AHA Greater Southeast Affiliate

Honors:

1978-1982 Oklahoma Medical Research Foundation Pre-Doctoral Fellow
1982-1983.1 Samuel R. Noble Research Foundation Pre-Doctoral Fellow
2009 Founding Member, USF Academy of Inventors
2007 Research Mentor of the Year, McNair Scholars
2008 Fellow of the American Heart Association (FAHA)

C. Selected Peer-reviewed Publications (Selected from 96 peer-reviewed publications)

Most relevant to the current application

1. Chalfant, C., Mischak, H., Watson, J., Winkler, B.C., Goodnight, J., Farese, R.V., **Cooper, D.R.** Regulation of alternative splicing of PKCβ by insulin. J. Biol. Chem. 270: 13326-13332, 1995 (First report of insulin regulating splicing of mRNA.)
2. Yan, S.F., Lu, J., Zou, Y.S., Soh-Won, J., Cohen, D.M., Buttrick, P., **Cooper, D.R.**, Steinberg, S., Mackman, N., . Pinsky, D.J., Stern, D.M. Hypoxia-associated induction of EGR-1 gene expression is mediated by activation of protein kinase CβII isoform and ERK1/2. J. Biol. Chem. 274: 15030-15040, 1999. (Roles of hypoxia in activation of kinases.)
3. Patel, N., Chalfant, C.E., Watson, J.E., Taub, R., Wyatt, J., Dean, N., Manley, J., Eichler, D.C., **Cooper, D.R.** Insulin increases the phosphorylation state of nuclear serine/arginine (SR) splicing factor, SRp40, and alternative splicing of PKCßII through a PI-3 kinase-sensitive pathway. J. Biol Chem 276:22648-22654, 2001 (PI-3 kinase pathway for regulation of nuclear events)
4. Patel, N.A., Apostolatos, N.S., Mebert, K., Chalfant, C.E., Watson, J.E., T.S. Pillay, Sparks, J., **Cooper, D.R.** Insulin regulates PKCßII alternative splicing in multiple target tissues: Development of a hormonally responsive heterologous minigenes. Molecular Endocrinology 18(4):899-911, 2004. (development of minigenes to assess hormonal signals)
5. Patel, N.A., Apostolatos, N.S., Kaneko, S., Bae, S.S., Chappell, D., Davidowitz, K., Watson, J.E., M.E. Birnbaum, J.Q. Cheng**, Cooper, D.R**. Molecular and Genetic Studies Imply Akt-mediated Signaling Promotes PKCßII alternative splicing via Phosphorylation of SRp40. J. Biol. Chem. 280: 14302-14309, 2005 (Development of assays for signaling to mRNA splicing.)
6. Kleiman, E., Carter, G., Ghansah, T., Patel, N.A., ***Cooper, D.R***. Developmentally spliced PKCßII provides a possible link between mTORC2 and Akt kinase to regulate 3T3-L1 adipocyte insulin-stimulated glucose transport. BBRC 388:554-559, 2009. (signaling pathways, glucose transport, assay development)

Additional recent publications (in chronological order)

7. Perrotti, D., Bonatti, S., Trotta, R., Martinez, R., Skorski, T., Salomonim, P., Grassilli, E., Iozzo, R.V., **Cooper, D.R.**, Calabretta, B. TLS/FUS, a pro-oncogene involved in multiple chromosomal translocations, is a novel regulator of BCR/ABL-mediated leukemogenesis. EMBO J. 17: 4442-4455, 1998. (linking PKCb to signling in tumorigenesis)
8. **Cooper, D.R.,** Patel, N.A. Glucose-regulated mRNA Instability element. U.S. Serial No. 6,852,529. Issued: Feb. 8, 2005 ***(mRNA stability)***

9. Patel, N.A., Song, S., **Cooper, D.R.** Retinoic acid regulation of alternatively spliced PKCdelta promotes neurogenesis in NT2 cells. Genes Expr 13: 73-84, 2006 (cellular differentiation, neurogenesis)
10. Ghosh, N., Patel, N.A., Jiang, K., Watson, J.E., Cheng, J., Chalfant, C.E., **Cooper,D.R**. Ceramide Activated Protein Phosphatase (CAPP) Targets Akt, SRp40 and Alternative Pre-mRNA Splicing of PKCßII in L6 Skeletal Muscle Cells. Endocrinology 148: 1359-66, 2007. (ability to link ceramide to signaling pathways, measurements of lipids)
11. Jiang, K., Patel, N.A., James E. Watson, Hercules Apostolatos, Eden Kleiman, Olivia Hanson, Masatoshi Hagiwara, **Denise R. Cooper.** Akt2 regulation of Cdc2-like kinases (Clk/Sty), serine/arginine-rich (SR) protein phosphorylation, and insulin-induced alternative splicing of PKCßII mRNA. Endocrinology 150(5):2087-97, 2009 (expertise in PI3K/Akt and linkage to Clk kinase)
12. Chappell, D.S., Patel, N.A., Jiang, K., Li, P., Watson, J.E., Byers, D.M., ***Cooper, D.R.*** Functional involvement of protein kinase C-ßII, and its substrate, MARCKS, in insulin-stimulated glucose transport in L6 rat skeletal muscle cells. Diabetologia 52:901-911, 2009. (Expertise in cellular trafficking.)
13. **D.R. Cooper** and N.A. Patel in **Methods in Alternative Splicing:** Manipulation of splicing events: Changing signals to the spliceosome. May 2011. Editors: Stefan Stamm, Chris Smith, Reinhard Luhrmann. (Demonstrates expertise with RNA.)
14. Apostolatos, A.,Song, S., Acosta, S., Peart, M., Watson, J., Bickford, P., **Cooper, D.R.,** Patel, N.A., Insulin promotes neuronal survival via the alternatively spliced protein kinase C delta isoform. J. Biol. Chemistry.285:23987-95, 2012. (Expertise in neurogenesis, mRNA splicing, work with Bickford and Patel.)

15. Sanchez-Ramos, J., Song, S., Cardozo-Pelaez, F., Hazzi, C., Stedeford, T., Willing, A., Freeman, T., Saporta, S., Janssen, W., Patel, N., **Cooper, D.,** Sanberg, P. Adult bone marrow stromal cells differentiated into neural cells in vitro. Exp Neurology 164: 247-56, 2000. (Demonstrates expertise with stem cells and neural differentiation.)

D. Research Support

VA BLRD Senior Research Career Scientist (PI) Salary support 4/1/12-3/31/19

NIH-NIDDK R01-54393-08 PI 1/1/08-1/31/13 (NCE)
Title: Insulin Signaling Pathways regulating PKCß splicing
This grant had 3 supplements for Diversity, Undergraduate Summer Student, and Equipment. It examines the role of Akt phosphorylation of Clk kinases in regulating splicing.
Pending:
ADA (PI) 1/31/13-1/15
Title: Long non-coding RNAs functioning in alternative splicing during adipogenesis
This grant examines the roles of NEAT1 and MALAT1 in splicing of PKCbII during adipogenesis in normal, obese and diabetic subjects. (no overlap)
VA BLRD (PD/PI) 4/01/13-3/31/17
Title: Regenerative Medicine and Stem Cell Biology Group
This program project examines the role of conditioned media and hADSC on wound healing and traumatic brain injury. There is partial overlap with one aim of one project.
VA Merit (PI) 4/01/13-3/31/17
Title: Akt regulated kinases in cellular differentiation
This grant examines the role of Akt regulated Clk in adipogenesis. No overlap.
Completed Projects:
AHA-SE Affiliate (Kleiman) Mentor 7/06-7/08
Title: PKCbeta promoter-mediated alternative splicing: bypassing the insulin receptor
VA Merit Review PI 04/01/08- 03/31/12
Title: Regulation of PKCßII splicing
This proposal examines RNA splicing in muscle cells and differentiating adipocytes adipocytes.
VA Merit Review PI 04/01/03- 03/31/08
Title: Mechanisms involved in TNF-alpha nduction of insulin resistance
VA Merit Rev Entry Mentor 5/1/05-4/31/08
Title: RA regulation of PKCdelta splicing,