BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Ortlund, Eric Anthony

eRA COMMONS USER NAME (credential, e.g., agency login): EORTLUND

POSITION TITLE: Professor of Medicine

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of South Carolina	B.S.	05/1997	Chemistry
University of South Carolina	Ph.D.	05/2002	Chemistry, Biochemistry
University of North Carolina – Chapel Hill	Post-Doc	06/2007	Biochemistry Structural Biology

A. Personal Statement

Our laboratory is keenly interested in macromolecular signaling within the context of normal and disease-state cellular functions. We leverage structural, biochemical, and computational studies to assess protein-protein interactions enabling structure-guided studies to assess function in the context of inflammation, stress, homeostasis and disease. We are excited to leverage our expertise to tackle fundamental questions centered on how Flu vaccination may influence circulating strains. I have a strong track record of collaboration, which has led to numerous contributions to the protein signaling community. In addition to acting as PI of a laboratory in the Biochemistry Department, I serve as Director for Emory's Integrated Metabolomics and Lipidomics Core. I lead and participate in several National-level NIH-funded consortia efforts to generate a systems-level understanding of metabolism, immune function, and disease. Our lab is part of the NIH funded Rapid Acceleration of Diagnostics, or RADx center.

We are on the Variant Task Force and part of the RADx effort at Emory. Our objective is to assess the threat of variants with respect to their ability to evade detection in rapid COVID tests and to evade detection by neutralizing antibodies. For this effort, we work closely with members of the Variant Task Force and RADx through daily meetings which includes members from Emory University and the University of Washington and works with the NIH, FDA, DOD, CDC, DOE, and BARDA. Our current objectives are to map epitopes on the spike protein and N-protein for commercial detection reagents and to help develop system to score the threat of SARS-Cov2 mutations. We are taking a three-pronged approach which involves CryoEM, sophisticated mass spectrometry techniques and a high-throughput deep mutational screen containing over 28,000 SARS-COV2 variants.

Relative to this proposal, I have participated in two NIH-funded contracts through the NIH Vaccine Translation and Evaluations Unit mechanism to identify lipid biomarkers in clinical samples derived from vaccine trials (Ebola, Yellow Fever, Tularemia). This effort includes collaboration with Dr. Mehul Suthar resulting in publications in *Biomolecules* (2019) and *Vaccines* (2020). The VTEU-funded effort requires that we coordinate and collaborate with our proteomics, metabolomics, transcriptomics, bioinformatics, and genomics cores. Thus, we are currently working with leaders in these areas to integrate 'omics data to generate information on signaling pathways in disease. Dr. Suthar and I have also collaborated to describe the rapid generation of neutralizing antibodies in SARS patients (Cell Reports, 2020). Finally, I am also currently collaborating with Dr. Ahmed, Dr. Kaja and Dr. Chandele (ICGEB) to determine CryoEM structures of Indian patient derived antibodies in complex with the SARS-Cov2 spike protein. Our manuscripts describing this work has been published in *iScience* and *Structure*.

I am excited to leverage my expertise and resources to collaborate on this application focused on defining antigens and developing vaccine candidates for alpha and filoviruses.

Ongoing and recently completed projects that I would like to highlight include:

3U54EB027690-05S1/National Institutes of Health/NIH/NIBIB
Lam (contact mPI); Ortlund (MPI)
Emergency COVID-19 Variant Supplement for Atlanta Center for Microsystems Engineered Point-of-Care Technologies (ACME POCT)

HHSN272201300018I/HHSN27200009
Rouphael/ Anderson (PI)
NIH Vaccine Treatments Evaluation Unit (VTEU); Consultation and 'omics testing of clinical samples

1U24DK112341-01 (MPI)
Ortlund (contact mPI); Fernandez (MPI)
Georgia Comprehensive Metabolomics and Proteomics Unit for MoTrPAC

Citations:

a. Frank F, Keen MM, Rao A, Bassit L, Liu X, Bowers HB, Patel AB, Cato ML, Sullivan JA, Greenleaf M, Piantadosi A, Lam WA, Hudson WH, **Ortlund EA**. Deep mutational scanning identifies SARS-CoV-2 Nucleocapsid escape mutations of currently available rapid antigen tests. Cell. 2022;185(19):3603-16 e13. PMCID: PMC9420710.

b. Maner-Smith, K.M., Goll, J.B., Ford, D.A., Jensen, T.L. Khadka, M., Colucci, J.K., Gelber, C.E., Albert, C.J., Bosinger, S., Franke, S., Natrajan, M., Rouphael, N., Johnson, R., Zanz, P., Anderson, E.J., Hoft, D.F., Mulligan, M., **Ortlund, E.A.**, Alterations in the human plasma lipidome in response to Tularemia vaccination. *Vaccines*, 2020, Jul 24; 8(3):E414 PMCID: PMC7564507

c. Kumar S, Patel A, Lai L, Chakravarthy C, Valanparambil R, Reddy ES, Gottimukkala K, Davis-Gardner ME, Edara VV, Linderman S, Nayak K, Dixit K, Sharma P, Bajpai P, Singh V, Frank F, Cheedarla N, Verkerke HP, Neish AS, Roback JD, Mantus G, Goel PK, Rahi M, Davis CW, Wrammert J, Godbole S, Henry AR, Douek DC, Suthar MS, Ahmed R, **Ortlund E**, Sharma A, Murali-Krishna K, Chandele A. Structural insights for neutralization of Omicron variants BA.1, BA.2, BA.4, and BA.5 by a broadly neutralizing SARS-CoV-2 antibody. Sci Adv. 2022;8(40):eadd2032. PubMed PMID: 36197988.

d. Suthar, M.S., Zimmerman, M., Kauffman, R., Mantus, G. Linderman, S, Hudson, W.H., Vanderheiden, A, Nyhoff, L., Davis, C., Adekunle, S., Affer, M., Sherman, M., Reynolds, S., Verkerke, H., Alter, D., Guarner, J., Bryksin, J., Horwath, M., Arthur, C., Saakadze, N., Smith, G., Edupuganti, S., Scherer, E., Hellmeister, K., Cheng, A., Morales, J., Neish, A., Stowell, S., Frank, F., **Ortlund, E.A.**, Anderson, E., Menachery, V., Rouphael, N., Mehta, A., Stephens, D., Ahmed, R., Roback, J., Wrammert, J., Rapid generation of neutralizing antibody responses in COVID-19 patients, *Cell Reports*, 2020, May 8:2020.05.03.20084442. PMCID: PMC7276302

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2002-02	Postdoctoral Fellow, Laboratory of Lukasz Lebioda; Dept of Chemistry, University of South Carolina, Columbia, SC
2003-07	Postdoctoral Fellow, Laboratory of Matthew Redinbo; Department of Chemistry, University of North Carolina, Chapel Hill; Lineberger Comprehensive Cancer Center, UNC
2007-	Associate Professor; Department of Biochemistry, Emory University, Atlanta, GA
2009-	Member, Executive Committee, Molecular Systems Pharmacology Graduate Program
2016-2018	Founder and Director of Emory Integrated Lipidomics Core

2019- Founder and Director of Emory Integrated Metabolomics and Lipidomics Core
2010-14 PC4 and PC2 study section, American Heart Association
2012 RFA study section NIH Blood and Vascular Branch, National Heart, Lung, and Blood Institute, NIH
2012-13 French National Research Agency Grant Reviewer
2012-13 Foundation for Polish Science Grant Reviewer
2014 NIH Molecular and Cellular Endocrinology study section, NIH, *Ad hoc*
2012- Editorial Board, ASPET, Molecular Pharmacology
2012- Reviewer Board, Journal of Pediatric Biochemistry
2013- Editorial Board, Nuclear Receptor Research
2013- Editorial Board, Hepatology
2015 NIH LCMI Special Emphasis Panel/Scientific Review Group
2015 NIH SEP ZRG1 EMNR-R(56), Cellular Mechanisms of Metabolism and Obesity
2016 Austrian Science Fund, study section
2016- NIH Molecular and Cellular Endocrinology study section, Chair
2017 NIH ZRG1 EMNR A 07, Molecular and Cellular Endocrinology, Chair

Honors and awards

2000 Bayer Corporation Award for Excellence in Chemistry, 2000
2002 College of Science and Mathematics Dissertation Fellowship
2004 Lineberger Comprehensive Center NIH NSRA Postdoctoral Fellowship
2013 American Crystallographic Association Margaret C. Etter Early Career Award
2013 Albert E. Levy Scientific Research Award for Junior Faculty
2013 Department of Biochemistry, Emory University Outstanding Teaching Award
2015 Awarded the W. M. Keck Foundation Medical Research Grant
2017 Postdoctoral Office “One in a hundred” Mentor of the Year Award
2017 “Special Recognition for Outstanding Research” Emory University School of Medicine

C. Contributions to Science

1. ‘omics and Lipid Signaling

Leveraging our expertise in lipid structure, biochemistry and signaling we founded the Emory Integrated Lipidomics Core which uses cutting edge LC-MS/MS based approaches to identify and quantify lipids biological samples. We have collaborated with many groups at Emory and abroad to understand how lipids drive and are modulated both normal biology and disease. We have developed robust quantitative methods to identify and quantify bioactive lipids (e.g. oxylipins, cannabinoids), bile acids, short and long chain fatty acids, carnitines, CoAs and polyunsaturated lipids. We have also developed high-resolution methods for untargeted lipidomics leveraging scheduled MS/MS methods.

a. Sanford, J.A., Nogiec, C.D., Lindholm, ME, Adkins, JN, Amar, D, Dasari, S, Drugan, JK, Fernández, F.M., Radom-Aizik, S., Schenk, S., Snyder, M.P., Tracy, R.P., Vanderboom, P., Trappe, S., Walsh M.J.; Molecular Transducers of Physical Activity Consortium. Molecular Transducers of Physical Activity Consortium (MoTrPAC): Mapping the Dynamic Responses to Exercise, *Cell*, 2020, Jun 25;181(7):1464-1474 ***Ortlund, E.A.** part of MoTrPAC Consortium Research and Writing group
b. Mhadka, M., Todor, Andrei, A., Maner-Smith, K.M., Colucci, J.K., Tran, ViLinh, T., Gaul, D.A., Anderson, E., Natrajan, M., Rouphael, N., Mulligan, M.J., McDonald, C., Suthar, M., Li, S., **Ortlund, E.A.**, The effect of anticoagulants, temperature and time on the human plasma metabolome and lipidome from healthy donors as determined by liquid chromatography-mass spectrometry. *Biomolecules*, 2019, 23:9(5)
c. Tillman, M.C., Imai, N., Li, Y., Khadka, M., Okafor, C.D., Juneja, P., Adhiyaman, A., Hagen, S.J., Cohen, D.E., **Ortlund, E.A.**, Allosteric regulation of Thioesterase Superfamily Member 1 lipid sensor domain by free fatty acids and lysophosphatidylcholine, *Proceedings of the National Academy of Sciences U S A*, 2020, 117(36):22080-22089, PMCID: PMC7486800
d. Cordy R.J., Lili L, Cabrera-Mora M, Chien J-T, Meyer E.V.S., Lapp S.A., Joyner C.J., Banton S., Tran V., Luvira V., Rungin S., Saeseu T., Rachaphaew N., Garcia A., Khadka M., Pakala S., Tharp G., MaHPIC Consortium, DeBarry J.D., Kissinger J.C., Bosinger S., Li S., **Ortlund, E.A.**, Jones D.P.,

Sattabongkot J., Uppal K., Barnwell J.W., Patrapuvich R., Moreno A., Galinski M.R., Distinct amino acid and lipid perturbations characterize acute versus chronic malaria. *JCI Insight*, 2019, ePub 10.1172/jci.insight.125156 PMCID: PMC6538326

2. Phospholipid-regulated gene expression

During my postdoctoral training, I tackled the characterization of liver receptor homologue -1 (LRH-1), an orphan nuclear receptor involved in glucose homeostasis, reverse cholesterol transport, lipid absorption, hormone synthesis, and cell proliferation. My structural and functional studies identified phospholipids as *bona fide* LRH-1 ligands, identifying LRH-1 as the first mammalian phospholipid-sending transcription factor. We have continued to pursue this challenging project attempting to link phospholipid sensing with glucose, lipid, and bile acid homeostasis. We have recently established a collaboration with Dr. David Cohen (Harvard Medical School/BWI) centered on the action of START domain containing proteins and their connection to phospholipid-driven gene regulation. Together, we have discovered that PC-TP stimulates LRH-1 transcriptional activity making PC-TP a critical player in the phosphatidylcholine signaling pathway that impacts glucose homeostasis. Thus, we are well positioned to elucidate the molecular mechanisms that drive the unique biology of phospholipid to control metabolism.

a. **Ortlund EA**, Lee Y, Solomon IH, Hager JM, Safi R, Choi Y, Guan Z, Tripathy A, Raetz CR, McDonnell DP, Moore DD, Redinbo MR. Modulation of human nuclear receptor LRH-1 activity by phospholipids and SHP. Nat Struct Mol Biol. 2005:12:357-63. PMID: 15723037
b. Lee JM, Lee YK, Mamrosh JL, Busby SA, Griffin PR, Pathak MC, **Ortlund EA**, Moore DD. A nuclear-receptor-dependent phosphatidylcholine pathway with antidiabetic effects. Nature. 2011:474:506-10 PMCID: PMC3150801.
c. Musille PM, Pathak MC, Lauer JL, Hudson WH, Griffin PR, **Ortlund EA**. Antidiabetic phospholipid-nuclear receptor complex reveals the mechanism for phospholipid-driven gene regulation. Nat Struct Mol Biol. 2012:19:532-7. PMCID: PMC3960984.
d. Musille PM, Pathak M, Lauer JL, Griffin PR, **Ortlund EA**. Divergent sequence tunes ligand sensitivity in phospholipid-regulated hormone receptors. J Biol Chem. 2013:288:20702-12 PMCID: PMC3711333.

3. Phospholipid transport and signaling

Since 2006, I have studied how phospholipids are sensed and signal though interaction with the Sec14 family of proteins. This has largely been a collaborative effort between our lab and Dr. Vytas Bankaitis (Texas A&M Health Science Center). I was responsible for discovering the molecular mechanism driving both phosphatidylcholine and phosphatidylinositol recognition in the protein family. We were able to develop mutant variants with selective disruptions in their ability to transport either PC or PI and tie specific lipid shutting abilities to cell functions such as proliferation, vesicle maturation, and protein synthesis. We have extensive experience in manipulating the phospholipid transfer ability of most known soluble phospholipid transport proteins in both yeast and mammals and are eager to apply this knowledge to understand the mechanisms that underlie exercise adaptation.

a. Schaaf G, **Ortlund EA**, Tyeryar KR, Mousley CJ, Ile KE, Garrett TA, Ren J, Woolls MJ, Raetz CR, Redinbo MR, Bankaitis VA. Functional anatomy of phospholipid binding and regulation of phosphoinositide homeostasis by proteins of the sec14 superfamily. Mol Cell. 2008:29:191-206. PMID: 18243114.
b. Schaaf G, Dynowski M, Mousley CJ, Shah SD, Yuan P, Winklbauer EM, de Campos MK, Trettin K, Quinones MC, Smirnova TI, Yanagisawa LL, **Ortlund EA**, Bankaitis VA. Resurrection of a Functional Phosphatidylinositol Transfer Protein from a Pseudo-Sec14 Scaffold by Directed Evolution. Mol Biol Cell. 2011:22:892-905. PMCID: PMC3057712.
c. Ren J, Pathak MC, Temple BRS, Lin C, Nile AH, Mousley CJ, Duncan MC, Eckert DM, Leiker TJ, Ivanova PT, Meyers MS, Murphy RC, Brown HA, Verdaasdonk J, Bloom KS, **Ortlund EA**, Neiman AM, Bankaitis VA A Phosphatidylinositol Transfer Protein Integrates Phosphoinositide Signaling With Lipid Droplet Metabolism To Regulate a Developmental Program of Nutrient Stress-Induced Membrane Biogenesis. Molecular and Cellular Biology. 2014:25(5): 712-727. PMCID: PMC3937096

d. Flynn, A.R., Mays, S.G., **Ortlund, E.A.**, Jui, N.T., Development of Hybrid Phospholipid Mimics as Effective Agonists for Liver Receptor Homolog-1, *ACS Med Chem Lett*., 2018, 9(10):1051-1056. PMID PMC6187417

4. Immunology and RADx

Our lab has a long-standing intertest in how signaling lipids (e.g. corticoids, oxylipins, phospholipids) control the immune singling though nuclear receptors and lipid transport proteins.

a. Creager, Richard S, Blackwood, John, Pribyl, Thomas, Bassit, Leda, Rao, Anuradha, Frank, Filipp, Lam, Wilbur, **Ortlund, Eric A**, Schinazi, Raymond, Greninger, Alexander L, Cirrincione, Mia, Gort, Dale, Kennedy, Emily, Samuta, Adam, Shaw, Megan, Walsh, Brian, Lai, Eric, "RADx Variant Task Force Program for Assessing the Impact of Variants on SARS-CoV-2 Molecular and Antigen Tests," in *IEEE Open Journal of Engineering in Medicine and Biology*, doi: 10.1109/OJEMB.2021.3116490.
b. Folick A, Oakley HD, Yu Y, Armstrong EH, Kumari M, Sanor L, Moore DD, Zechner R, **Ortlund EA**, Wang MC. Lysosomal Signaling Molecules Regulate Longevity in Caenorhabditis elegans. *Science*. 2014:347(6217):83-6. PMCID: PMC4425353.
c. Druzak S, Iffrig E, Roberts BR, Zhang T, Fibben KS, Sakurai Y, Verkerke HP, Rostad CA, Chahroudi A, Schneider F, Wong AKH, Roberts AM, Chandler JD, Kim SO, Mosunjac M, Mosunjac M, Geller R, Albizua I, Stowell SR, Arthur CM, Anderson EJ, Ivanova AA, Ahn J, Liu X, Maner-Smith K, Bowen T, Paiardini M, Bosinger SE, Roback JD, Kulpa DA, Silvestri G, Lam WA, **Ortlund EA**, Maier CL. Multiplatform analyses reveal distinct drivers of systemic pathogenesis in adult versus pediatric severe acute COVID-19. Nat Commun. 2023 Apr 4;14(1):1638. doi: 10.1038/s41467-023-37269-3. PMID: 37015925; PMCID: PMC10073144.
d. Farmer S, Razin V, Peagler AF, Strickler S, Fain WB, Damhorst GL, Kempker RR, Pollock NR, Brand O, Seitter B, Heilman SS, Nehl EJ, Levy JM, Gottfried DS, Martin GS, Greenleaf M, Ku DN, Waggoner JJ, Iffrig E, Mannino RG, F Wang Y, **Ortlund E**, Sullivan J, Rebolledo PA, Clavería V, Roback JD, Benoit M, Stone C, Esper A, Frank F, Lam WA. Don't forget about human factors: Lessons learned from COVID-19 point-of-care testing. Cell Rep Methods. 2022 May 23;2(5):100222. doi: 10.1016/j.crmeth.2022.100222. Epub 2022 May 3. PMID: 35527805; PMCID: PMC9061138.

Complete List of Published Works (101 total):

https://pubmed.ncbi.nlm.nih.gov/?term=ortlund&sort=date

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Patel, Anamika

eRA COMMONS USER NAME (credential, e.g., agency login): ANAMIKAPATEL

POSITION TITLE: Assistant Professor (Research Track), Department of Biochemistry

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Mohanlal Sukhadia University, India.	B.S.	07/1997	Chemistry, Botany, Zoology
Mohanlal Sukhadia University, India.	M.S.	07/1999	Chemistry
Central Salt & Marine Chemicals Research Institute, India	Ph.D.	11/2004	Chemistry
Technical University, Munich, Germany	Postdoctoral	10/2005	Biochemistry
Syracuse University, Syracuse, NY.	Postdoctoral	12/2009	Biochemistry

A. Personal Statement

I began my scientific training in the field of biochemistry and structural biology in 2001 and was intrigued by how you could visualize 3-D structures of proteins and link form to function. Since then, I've remained interested in studying the structure-function relationship of proteins. During my postdoctoral training I got exposed to the interesting questions relating to the epigenetic transcriptional regulation through chromatin modifying enzymes and their implication in numerous diseases. My research on the topic changed the central dogma in field and led to several publications.

After joining Department of Biochemistry at Emory University as an Assistant Professor (Research track), I remained focused in the area of transcriptional regulation and worked on a highly diverse class of transcription factors containing a tandem array of C2H2-type Zinc fingers in Dr. Xiaodong Cheng's group. I solved several structures by X-ray crystallography and published few high-profile papers explaining how Zinc-fingers deviate from their conventional code of DNA recognition to achieve high sequence specificity without any gross penalties on DNA-binding. However, in year 2017, I shifted my effort towards cryoEM due to two main reasons: first, my persistent interest in visualizing large protein complexes and second, the technological advancement in cryoEM now allow high-resolution structure determination of tough to crystallize protein targets. Driven by these interests, I have invested time in building in my expertise in cryoEM by attending various workshops and training courses with a focus on transcription regulation of nuclear receptor coregulator complexes in Dr. Eric Ortlund's group at Emory. During the emergence Covid-19, our lab was asked to participate in NIH funded Rapid Acceleration of Diagnostics (RADx) project with aim of epitope mapping on Spike and N-protein. Leveraging on my expertise in cryoEM, I was able to solve high resolution structures of SARS-CoV2 spike protein in complex with several potently neutralizing antibodies to map their epitopes that explained their mechanism of neutralization (in collaboration with Dr. Rafi Ahmed's lab at Emory Vaccine Center). This led me to explore a new area of research involving structural immunology. In past two year, I have seeded several collaborations involving antigenic targets of SARS-COV2, Anthrax, Zika and Dengue with the aim of studying their immune responses with respect to natural infection or vaccination via monoclonal/polyclonal epitope mapping. Building on these accomplishments, I feel highly confident in my ability to deliver on current application.

Citations:

1. Sanjeev Kumar, **Anamika Patel** (co-first), Lilin Lai, Chennareddy Chakravarthy, Rajesh Valanparambil, Meredith E. Davis-Gardner, Venkata Viswanadh Edara, Susanne Linderman, Elluri Seetharami Reddy, Kamalvishnu Gottimukkala, Kaustuv Naya, Kritika Dixit, Pragati Sharma, Prashant Bajpai, Vanshika Singh, Filipp Frank, Narayanaiah Cheedarla, Hans P. Verkerke, Andrew S. Neish, John D. Roback, Grace Mantus, Pawan Kumar Goel, Manju Rahi, Carl W. Davis, Jens Wrammert, Mehul S. Suthar, Rafi Ahmed, Eric Ortlund, Amit Sharma, Kaja Murali-Krishna, Anmol Chandele. Structural insights for neutralization of BA.1, BA.2, BA.4 and BA.5 Omicron variants by a broadly neutralizing SARS-CoV-2 antibody. *Science Advances*. 2022 Oct 7;8(40):eadd2032. doi: 10.1126/sciadv.add2032. Epub 2022 Oct 5. PMID: 36197988; PMCID: PMC9534492.
2. Frank F, Keen MM, Rao A, Bassit L, Liu X, Bowers HB, **Patel Anamika**, Cato ML, Sullivan JA, Greenleaf M, Piantadosi A, Lam WA, Hudson WH, Ortlund EA. Deep mutational scanning identifies SARS-CoV-2 Nucleocapsid escape mutations of currently available rapid antigen tests. *Cell*. 2022 Sep 15;185(19):3603-3616.e13. doi: 10.1016/j.cell.2022.08.010. Epub 2022 Aug 29. PMID: 36084631; PMCID: PMC9420710.
3. **Patel Anamika**, Kumar S, Lai L, Chakravarthy C, Valanparambil R, Reddy ES, Gottimukkala K, Bajpai P, Raju DR, Edara VV, Davis-Gardner ME, Linderman S, Dixit K, Sharma P, Mantus G, Cheedarla N, Verkerke HP, Frank F, Neish AS, Roback JD, Davis CW, Wrammert J, Ahmed R, Suthar MS, Sharma A, Murali-Krishna K, Chandele A, Ortlund EA. Molecular basis of SARS-CoV-2 Omicron variant evasion from shared neutralizing antibody response. Structure. 2023 May 6:S0969-2126(23)00133-8. doi: 10.1016/j.str.2023.04.010. Epub ahead of print. PMID: 37167972; PMCID: PMC10171968.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

1999-2001: Project Assistant at Central Salt & Marine Chemicals Research Institute, Bhavnagar, India.
2006-2009: Postdoctoral Research Fellow at Department of Biology, Syracuse University, Syracuse, NY.
2010-2011: Assistant Professor (Research Track), Department of Biology, Syracuse University, Syracuse, NY
2012-2013: Assistant Professor (Research Track), Department of Biochemistry and Molecular Biology, SUNY Upstate Medical University, Syracuse, NY
2013-present: Assistant Professor (Research Track), Department of Biochemistry, Emory University School of Medicine, Atlanta
2022- Topic Editor, Frontiers in Virology

Other Experience and Professional Memberships

Member of American Association of Advancement of Science (AAAS)
Member of American Association of Cancer Research (AACR)

Honors

2005: DAAD Short Term Research Fellow at Physics department, Technical University, Munich, Germany.

C. Contributions to Science

1. LRH-1 transcription regulation by coregulatory proteins.
LRH-1 is a phospholipid sensing nuclear receptor that works in conjunction with multiple coregulatory protein to regulate metabolic gene program. In Ortlund lab, I focused my study on regulation of LRH-1 by its corepressor partner protein SHP, with the aim of determining the structure of LRH-1-SHP complex. My research in the lab showed that SHP regulate LRH-1's action by forming a trimer. We plan to apply this knowledge in understanding the mechanism of LRH-1-SHP signaling axis in metabolic gene regulation.

a. Cato ML, Cornelison JL, Spurlin RM, Courouble VV, **Patel Anamika**, Flynn AR, Johnson AM, Okafor CD, Frank F, D'Agostino EH, Griffin PR, Jui NT, Ortlund EA. Differential Modulation of Nuclear Receptor LRH-1 through Targeting Buried and Surface Regions of the Binding Pocket. *J Med Chem*. 2022 May 12;65(9):6888-6902. PMID: 35503419.

b. Suzzane Mays; Emma D'Agostino; Autumn Flynn; Xiangsheng Huang; Guohui Wang; Xu Liu; Elizabeth Millings; C. Denise Okafor; **Anamika Patel**; Michael Cato; Jeffrey Cornelison; Diana Melchers; Rene Houtman; David Moore; John Calvert; Nathan Jui; Eric Anthony Ortlund. A novel phospholipid mimetic targeting LRH-1 ameliorates colitis. *Cell Chemical Biology*. 2022 March 21; S2451-9456(22)00089-7. doi: 10.1016/j.chembiol.2022.03.001. Online ahead of print. PMID: 35316658

c. Jeffery L Cornelison , Michael L Cato , Alyssa M Johnson , Emma H D'Agostino, Diana Melchers, **Anamika B Patel** , Suzanne G Mays , René Houtman , Eric A Ortlund , Nathan T Jui. Development of a new class of liver receptor homolog-1 (LRH-1) agonists by photoredox conjugate addition. *Bioorg Med Chem Lett*. 2020 Aug 15;30(16) PMID: 32631515

2. Zinc Finger proteins and sequence specific DNA recognition.

The C2H2 type zinc finger (ZF) proteins belong to the largest and most diverse family of transcription factors in human. They have well documented functional role in DNA binding. Despite being the largest family, the molecular targets and the biological function for the majority of them remains elusive. Based on structural knowledge of 2-3 tandem ZF, algorithms are derived to predict their DNA binding sequences. Yet, often they do not match with experimentally identified sequences, specifically in case of ZF array containing large number of tandem fingers. This suggesting the need for the structural studies of a tandem ZFs-DNA complex to enhance our understanding in their code of DNA recognition. My structure-function studies on two of these ZF proteins PRDM9 and ZFP568, each containing 13 and 11 tandem ZF, respectively, help to decipher the molecular basis of their DNA recognition. PRDM9 that directs the sequence specific binding to meiotic recombination hotspots and showed adaptability in their ZFs by flipping two differently positioned residue to the variations in DNA sequence and thus, allows them to respond to the variation in DNA sequences without any gross penalties in their binding affinities. My studies help to explain genetic data on how allelic variants of PRDM9 could influence their DNA binding targets and therefore, their meiotic recombination landscape. Along this line, I worked on a project in collaboration with Dr. Todd Macfarlan at NIH on a ZF protein ZFP568 that directly regulates the expression of a placental growth factor Igf2-P0 and is required for embryonic development in mice. I determined the structure of ZFP568 in complex with DNA, this is first structure available to date showing the largest number of ZFs in complex with DNA. The structures, I determined are of significant importance as they show deviations at several levels from the classical C2H2 type ZF DNA recognition code. The structures propose flexibility in the ZF by 2-,3-or 4-base pair specific recognition per zinc finger to enhance the binding capacity and also respond to the specific DNA shape. Collectively, these structures provide additional layers of adaptable binding ability between ZFs and DNA.

a. **Anamika Patel**, Peng Yang, Matthew Tinkham, Mihika Pradhan, Ming-An Sun, Yixuan Wang, Don Hoang, Gernot Wolf, John R. Horton, Xing Zhang, Todd Macfarlan and Xiaodong Cheng. DNA Conformation Induces Adaptable Binding by Tandem Zinc Finger Proteins (2018). *Cell*, 147(1) 221-233. PMCID:PMC5877318

b. **Anamika Patel,** Xing Zhang, Robert Blumenthal and Xiaodong Cheng. Structural basis of human PR/SET domain 9 (PRDM9) allele C-specific recognition of its cognate DNA sequence (2017). *Journal of Biological Chemistry*, 292(39) 15994-16002.PMCID:PMC5625032

c. **Anamika Patel**, J.R. Horton, G.G. Wilson, X. Zhang, X. Cheng. Structural basis for human PRDM9 action at recombination hot spots (2016). *Genes & Development*. 2016. 30: 257-265. *(This work was featured on the journal's cover.)* PMCID:PMC4743056

d. **Anamika Patel**, H. Hashimoto, Xing Zhang, Xiaodong Cheng. Characterization of How DNA Modifications Affect DNA Binding by C2H2 Zinc Finger Proteins (2016). *Methods in Enzymology, 573 387-403*

3. MLL1-WDR5-RbBP5-Ash2L-DPY30: a core complex responsible for histone H3 lysine 4 tri-methylation

The disruption of Mixed Lineage leukemia-1 (MLL1) is frequently observed in acute lymphoblastic or acute mylogenous leukemia, which results in either increased or decreased MLL1's function. The MLL1 protein catalyzes histone H3 lysine 4 tri-methylation and regulates chromatin structure for active gene expression. The catalytic activity of MLL1 is tightly regulated by its core components. One question of significant importance in the field is that how MLL1's activity is regulated by its core components. My work showed that unlike other methyltransferase MLL1 core complex uses a novel mechanism involving two active sites to regulate its activity. We have identified a interaction motif in MLL1, which we named as "WIN" motif (also present in other family members: MLL2/3/4, SET1A and SET1B) required for binding with one of its regulatory subunit WDR5 and solved the first structure of MLL1 WIN motif in complex with WDR5. We also showed that targeting the interaction surface of MLL1-WDR5 successfully inhibits MLL1's activity and thus, provide a novel approach to target MLL1's activity in leukemia. As evidence of the high impact of this work, this research was published in several peer-reviewed journal articles as mentioned below. One article was pushed for accelerated publication and was featured on the cover of the Journal of Biological Chemistry. A second paper was highlighted as the paper of the week in the same journal.

a. **Anamika. Patel**, V.E. Vought, V. Dharmarajan and M.S. Cosgrove (2011) A novel non-SET domain multi-subunit methyltransferase required for sequential nucleosomal histone H3 methylation by the MLL1 core complex. *Journal of Biological Chemistry* **286**(5): 3359-3369. PMCID: PMC3030342

b. **Anamika. Patel,** V. Dharmarajan, V.E. Vought and M.S. Cosgrove (2009) On the mechanism of multiple lysine methylation by the human Mixed Lineage Leukemia Protein-1 (MLL1) core complex. *Journal of Biological Chemistry* **284**(36): 2424-24256. PMCID: PMC2782018 *(**selected as the paper of the week and spotlight the first author**).*

c. **Anamika. Patel,** V. Dharmarajan and M.S. Cosgrove (2008) Structure of WDR5 bound to Mixed Lineage Leukemia Protein-1 peptide. *Journal of Biological Chemistry* **283**(47): 32158-32161. PMID: 18829459. (***Accelerated Publication*****,*** ***Featured on the Journal Cover***).

d. **Anamika. Patel,** V.E. Vought, V. Dharmarajan and M.S. Cosgrove (2008) A conserved arginine containing motif crucial for the assembly and enzymatic activity of the Mixed Lineage Leukemia protein-1 core complex. *Journal of Biological Chemistry* **283**(47): 32162-32175. PMID: 18829457. (***Featured on the Journal Cover***).

4. Analytical Ultracentrifugation (AUC) to study protein-protein interaction and conformational switch

I used my expertise in Analytical Ultracentrifugation to study Protein-Protein interactions and conformational changes in proteins in collaboration with various groups.

a. S. Zhong, F. Hsu, C.J. Stefan, X. Wu, **Anamika. Patel**, M.S. Cosgrove and Y. Mao (2012) Allosteric activation of the phosphoinositide phosphatase sac1 by anionic phospholipids. *Biochemistry* **51**(15): 3170-7. PMCID: PMC3329130

b. M. Mbantenkhu, X. Wang, S. Wilkens, E. Hoffman, **Anamika. Patel**, M.S. Cosgrove and X.J. Chen (2011) Mgm101 - a DNA recombinase essential for the mitochondrial DNA maintenance. *Journal of Biological Chemistry* **286**(49): 42360-70. PMCID: PMC3234957.

c. T. Wollert, **Anamika. Patel**, Y.-L. Lee, V.E. Vought, M.S. Cosgrove, J.A. Mercer and G.M. Langford (2011) Myosin5a tail associates directly with Rab3A-containing compartments in neurons. *Journal of Biological Chemistry* **286**(16): 14352-14361. PMCID: PMC3077635.

5. Bili-proteins in cyanobacteria as photo-optical switch

My earlier work showed biochemical and structural characterization of photosynthetic bili-proteins in cyanobacteria from marine and fresh water environment. I showed that bili-proteins isolated from marine cyanobacterial species have higher thermal stability and antioxidant potential compared to fresh water species. We were able to determine for the first time a structure of a photo-optical switch of so-called E-isomer in bili-proteins.

a. M. Schmidt, **Anamika. Patel**, Y. Zhao and W. Reuter (2007) Structural Basis for the Photochemistry of R-Phycoerythrocyanin. *Biochemistry* **46**: 416-423. PMID: 17209552

b. L. Satyanarayana, C.G. Suresh, **Anamika. Patel**, S. Mishra and P.K. Ghosh (2005) X-ray crystallographic studies on C-phycocyanin from the cyanobacteria of different habitats: marine & fresh water. *Acta Crystallographica Section F: Structural Biology and crystallization communications* F61: 844-847. PMCID: PMC1978106.

c. B.T. Paul, **Anamika. Patel**, G.S. Selvam, S. Mishra, P.K. Ghosh and R. Murugesan (2006) Photodynamic action of C-phycocyanins obtained from marine and fresh water cyanobacterial cultures: A comparative study using EPR spin trapping technique. *Free Radical research* **40**: 821-825. PMID: 17015260

d. **Anamika. Patel**, S. Mishra, R. Pawar, S. Sonawane and P. K. Ghosh (2005) Purification and characterization of C-Phycocyanin from cyanobacterial species of marine and fresh water habitats. *Protein Expression and Purification* **40**: 248-255. PMID: 15766866

Complete List of Published Works (28 total):

https://www.ncbi.nlm.nih.gov/myncbi/collections/mybibliography/