

BIOGRAPHICAL SKETCH

NAME: Eric B. Dammer

eRA COMMONS USER NAME: EDAMMER

POSITION TITLE: Research Associate, Bioinformatics

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YY	FIELD OF STUDY
Florida Gulf Coast University (FGCU)	B.A.	08/03	Liberal Arts, Molecular Biology focus
Georgia Institute of Technology (Georgia Tech)	PhD	12/08	Biology, Molecular Genetics focus
Emory University School of Medicine	postdoc	09/13	Mass Spectrometry, Neuroproteomics Analysis

A. Personal Statement

Dr. Dammer has established himself as an expert systems biology analyst with over 15 years of biochemistry, molecular biology, and mass spectrometry experience. For the past 12 years since joining Emory in 2008, he has routinely performed mass spectrometry experiments, validation and systems level analysis of mass spectrometric data. A major research focus of Dr. Dammer's is the analysis of differential expression and co-expression of proteins and protein post translational modifications (PTMs) in proteomic data sets, particularly those focused on mechanistic biomarkers of neurodegenerative disease such as Alzheimer's disease (AD) and ALS/FTD. Examples of his key contributions on systems analysis of genomic, transcriptomic, and proteomic systems level analysis can be found below, ranging from **(1)** validation metaanalysis of 1000s of proteomic case samples, to **(2)** the initial determination of cell type shifts in AD brain, to **(3)** visualizing protein interactions in synaptic AD networks, to **(4)** uncovering splicing effects in AD, and **(5)** revealing networks of (co-)aggregation in the ALS/FTD brain. These works demonstrate Dr. Dammer's eminence in the field of applied systems biology and neurodegeneration.

1. Johnson ECB, **Dammer EB**, Duong DM, Ping L, Zhou M, Yin L, Higginbotham LA, Guajardo A, White B, Troncoso JC, Thambisetty M, Montine TJ, Lee EB, Trojanowski JQ, Beach TG, Reiman EM, Haroutunian V, Wang M, Schadt E, Zhang B, Dickson DW, Ertekin-Taner N, Golde TE, Petyuk VA, De Jager PL, Bennett DA, Wingo TS, Rangaraju S, Hajjar I, Shulman JM, Lah JJ, Levey AI, Seyfried NT. "Large-scale Proteomic Analysis of Alzheimer's Disease Brain and Cerebrospinal Fluid Reveals Early Changes in Energy Metabolism Associated with Microglia and Astrocyte Activation." *Nat Med* 26(5): 769-780. 2020. PMID: 32284590
2. Seyfried NT, **Dammer EB**, Swarup V, Nandakumar D, Duong DM, Yin, L, Deng Q, Nguyen T, Hales CM, Wingo T, Glass J, Gearing M, Thambisetty M, Troncoso JC, Geschwind DH, Lah JJ, Levey AI. "A Multi-network Approach Identifies Protein-Specific Co-expression in Asymptomatic and Symptomatic Alzheimer's Disease." *Cell Systems* 4(1): 60-72. 2017. PMID: PMC5269514
3. Wingo AP, **Dammer EB**, Breen MS, Logsdon BA, Duong DM, Troncoso JC, Thambisetty M, Beach TG, Serrano GE, Reiman EM, Caselli RJ, Lah JJ, Seyfried NT, Levey AI, Wingo TS. "Large-scale proteomic analysis of human brain identifies proteins associated with cognitive trajectory in advanced age." *Nat Commun* 10(1): 1619. 2019. PMID: PMC6453881
4. Johnson ECB, **Dammer EB**, Duong DM, Yin L, Thambisetty M, Troncoso JC, Lah JJ, Levey AI, Seyfried NT. "Deep proteomic network analysis of Alzheimer's disease brain reveals alterations in RNA binding proteins and RNA splicing associated with disease." *Mol Neurodegen* 13(1): 52. 2018. PMID: 30286791. PMID: PMC6172707
5. Umoh ME, **Dammer EB**, Dai J, Duong DM, Lah JJ, Levey AI, Gearing M, Glass JD, Seyfried NT. "A Proteomic Network Approach across the ALS-FTD Disease Spectrum Resolves Clinical Phenotypes and Genetic Vulnerability in Human Brain." *EMBO Mol Med* 10(1): 48-62. 2018. PMID: PMC5760858

B. Positions and Honors

Positions and Employment

1998-2000 Operations Manager, Moneyline Telerate, New York, NY
2002 Tutor and Teaching Assistant, Organic Chemistry, Florida Gulf Coast Univ., Fort Myers, FL
2013-2017 Instructor, Research Track
2017-Current Research Associate, Bioinformatics

Other Experience and Professional Memberships

2009-current Member, American Society for Mass Spectrometry (ASMS)
Ongoing Reviewer on proteomics and neurodegeneration in various journals

Academic and Professional Honors

2002 HHMI Summer Intern (at Georgia Tech School of Biology)
2002 FGCU Campbell Engineering Scholarship
2002 Golden Key National Honor Society Inductee
2003-07 Georgia Tech President's Fellowship
2006 Travel Award, Keystone Symposia Nuclear Receptors Conference
2007 Best Presentation, College of Sciences, 3rd Ann. Graduate Student Govt. Research Symposium
2018 Travel Award, American Neurological Association Conference

C. Contribution to Science

1. Eric has excelled at in-depth analysis of, and biological inference from, involved biochemical methods such as (cross-linking) immunoprecipitation (IP) and chromatin IP coupled to MS or next generation sequencing of RNA or DNA, building proteogenomic databases of in silico predictions of splicing for unbiased discovery of splicing events at the protein level in MS data. He has performed PTM identification, quantification, and/or confirmation by MS such as that afforded by histone derivatization workflows. He has also identified a role for ubiquitination in aggregation of TDP-43, further confirming AD-associated ubiquitin pathology in dystrophic neurites and neurofibrillary tangles via IHC of postmortem tissue. Proteostasis of cotranslationally folded proteins was also examined in yeast proteomics performed in collaboration with the lab of Judith Frydman. Citations a. b. and d. each have more than 100 citations.

- a. **Dammer EB**, Xu P, Seyfried NT, Rees HD, Gearing M, Lah JJ, Levey AI, Peng J. "Polyubiquitin Linkage Profiles in Three Models of Proteolytic Stress Suggest Etiology of Alzheimer Disease." *J Biol Chem* 286(12): 10457-65. 2011. PMID: PMC3060499
- b. Sephton CF, Cenik C, Kucukural A, **Dammer EB**, Cenik B, Han YH, Dewey CM, Roth FP, Herz J, Peng J, Moore MJ, Yu G. "Identification of Neuronal RNA Targets of TDP-43-containing Ribonucleoprotein Complexes." *J Biol Chem* 286(2): 1204-15. 2011. *F1000 "must read."* PMID: PMC3020728
- c. **Dammer EB**, Fallini C, Gozal YM, Rossoll W, Xu P, Duong DM, Lah JJ, Levey AI, Peng J, Bassell GJ, Seyfried NT. "Coaggregation of RNA-binding Proteins in a Cellular Model of TDP-43 Proteinopathy with Selective RGG Motif methylation and RRM Domain Ubiquitination." *PLoS One* 7(6): e38658. 2012. PMID: PMC3380899
- d. Willmund F, Del Alamo M, Pechmann S, Chen T, Albanèse V, **Dammer EB**, Peng J, Frydman J. "The Cotranslational Function of Ribosome-associated Hsp70 in Eukaryotic Protein Homeostasis." *Cell* 152(1-2): 196-209. 2013. PMID: 22332755

2. As a Ph.D candidate, Eric studied the molecular genetics of a model cytochrome P450 gene (CYP17) that undergoes Steroidogenic Factor-1 (SF-1) nuclear receptor mediated transcription in a cyclic AMP (cAMP)-inducible manner. Eric was involved in the validation of the discovery of the lipid sphingosine as an antagonistic ligand of SF-1. Chromatin IP of transcription and splicing factors in α -amanitin-synchronized adrenal cortex steroidogenic cells revealed a temporal order of chromatin modification by post-translational modification (PTM) of histones via transcriptional coregulator binding culminating in cycles of RNA polymerase II recruitment to the CYP17 promoter. Later, Eric demonstrated phosphorylation- and metabolite- dependent regulation of CYP17 transcription through the E1A C-terminal Binding Protein (CtBP) transcriptional coregulator, confirming *in silico* molecular dynamic predictions of phosphorylation-dependent heterodimerization of CtBP1 and 2 via

mutagenesis and immunoprecipitation time courses. As a postdoc, Eric revisited this system in collaboration with my former PI where I performed discovery by mass spectrometry of immunoprecipitates which was later validated biochemically, revealing phosphorylation-dependent dynamics of cAMP-dependent mitochondria-endoplasmic reticulum interactions which are required for efficient adrenocortical cortisol production.

- e. Urs AN, **Dammer E**, Sewer MB. "Sphingosine Regulates the Transcription of CYP17 by Binding to Steroidogenic Factor-1." *Endocrinology* 147(11): 5249-58. 2006. PMID: 16887917
 - f. **Dammer EB**, Leon A, Sewer MB. "Coregulator Exchange and Sphingosine-Sensitive Cooperativity of Steroidogenic Factor-1, General Control Nonderepressed 5, p54, and p160 Coactivators Regulate Cyclic Adenosine 3',5'-Monophosphate-Dependent Cytochrome P450c17 Transcription Rate." *Mol Endocrinol* 21(2): 415-38. 2007. PMID: 17121866
 - g. **Dammer EB**, Sewer MB. "Phosphorylation of CtBP1 by PKA Modulates Induction of CYP17 by Stimulating Partnering of CtBP1 and 2." *J Biol Chem* 283(11): 6925-34. 2008. PMCID: PMC2730192
 - h. Li D, **Dammer EB**, Lucki NC, Sewer MB. "cAMP-stimulated Phosphorylation of Diaphanous 1 Regulates Protein Stability and Interaction with Binding Partners in Adrenocortical Cells." *Mol Biol Cell* 24(6): 848-57. 2013. PMCID: PMC3596254
3. As a postdoctoral investigator, Eric developed biochemical and analytic methods for examining roles of RNA-binding proteins and RNA splicing in neurodegeneration, and hypothesized a later confirmed role of U1 snRNA in AD pathology after identifying U1 spliceosome components in the AD insoluble proteome. Eric analyzed Nanostring and RNA-Seq data sets for splicing defects in AD, which in combination with the above findings has led to a growing appreciation of RNA splicing machinery deficits in AD. In a closely related biochemical method coupled to MS, membrane (synaptic enriched) proteome was also examined and membrane proteome of blood platelets was examined for potential biomarkers of AD.
- i. Donovan LE, Higginbotham L, **Dammer EB**, Gearing M, Rees H, Xia Q, Duong D, Seyfried NT, Lah JJ, Levey AI. "Analysis of a Membrane Enriched Proteome from Post-mortem Human Brain Tissue in Alzheimer's Disease." *Proteomics Clin Appl* 6(3-4): 201-11. 2012. PMCID: PMC3338199
 - j. Donovan LE, **Dammer EB**, Duong DM, Hanfelt JJ, Levey AI, Seyfried NT, Lah JJ. "Exploring the Potential of the Platelet Membrane Proteome as a Source of Peripheral Biomarkers for Alzheimer's Disease." *Alz Res Ther* 5(3). *Published online June 2013*. PMCID: PMC4054949
 - k. Bai B, Hales CM, Chen P-C, Gozal YM, **Dammer EB**, Fritz JJ, Wang X, Xia Q, Duong DM, Street C, Cantero G, Cheng D, Jones DR, Wu Z, Li Y, Diner I, Heilman CJ, Rees HD, Wu H, Lin L, Szulwach KE, Gearing M, Mufson EJ, Bennett DA, Montine TJ, Seyfried NT, Wingo TS, Sun YE, Jin P, Hanfelt J, Willcock DM, Levey AI, Lah JJ, Peng J. "U1 Small Nuclear Ribonucleoprotein Complex and RNA Splicing Alterations in Alzheimer's Disease." *Proc Natl Acad Sci USA* 110(41): 16562-7. 2013. PMCID: PMC3799305
 - l. Hales CM, **Dammer EB**, Diner I, Yi H, Seyfried NT, Gearing M, Glass JD, Montine TJ, Levey AI, Lah JJ. "Aggregates of Small Nuclear Ribonucleic Acids (snRNAs) in Alzheimer's Disease." *Brain Pathology* 24(4): 344-51. 2014. PMCID: 4096308
4. Eric continued to explore the role of PTMs in AD, such as phosphorylation crosstalk with heat shock protein oligomerization in AD, and actively pursued development of methods to couple fluorescence activated nuclei sorting (FANS) of nuclei to proteomics for future applications in discovery of nuclear protein changes in neurodegeneration. He has also excelled at collaborative science, and has lent technical support and expertise in analysis of MS and RNA-seq datasets to collaborators. For example, Eric was able to confirm specificity of an engineered histone H4 expression product for acetylation at a particular residue using a histone derivatization workflow. In another example of biological findings from collaborative analysis, his analysis uncovered proteome changes in stable isotope labeled dopaminergic cell lines engineered to mimic a deficiency in hypoxanthine-guanine phosphoribosyltransferase (HGPRT) which defines Lesch-Nyhan Disease.
- m. **Dammer EB**, Lee AK, Duong DM, Gearing M, Lah JJ, Levey AI, Seyfried NT. "Quantitative Phosphoproteomics of Alzheimer's Disease Reveals Cross-talk between Kinases and Small Heat Shock Proteins." *Proteomics* 15(2-3): 508-19. 2015. PMCID: PMC4404162

- n. **Dammer EB**, Duong DM, Diner I, Gearing M, Feng Y, Lah JJ, Levey AI, Seyfried NT. "Neuron Enriched Nuclear Proteome Isolated from Human Brain." *J Proteome Res* 12(7): 3193-206. 2013. PMID: PMC3734798
- o. Kallappagoudar S, **Dammer EB**, Duong DM, Seyfried NT, Lucchesi JC. "Expression, Purification and Proteomic Analysis of Recombinant Histone H4 Acetylated at Lysine 16." *Proteomics* 13(10-11): 1687-91. 2013. PMID: PMC3771349
- p. **Dammer EB**, Göttle M, Duong DM, Hanfelt J, Seyfried NT, Jinnah HA. "Consequences of Impaired Purine Recycling on the Proteome in a Cellular Model of Lesch-Nyhan Disease." *Mol Genet Metab* 114(4): 570-9. 2015. PMID: PMC4390545

Complete List of Published Work in MyBibliography (79 references):

<http://www.ncbi.nlm.nih.gov/sites/myncbi/eric.dammer.1/bibliography/41167974/public/?sort=date&direction=ascending>

D. Research Support

Ongoing Research Support

U01AG061357-02 (PI: Levey)	09/30/2018-08/31/2023	2.4 CM
NIH/NIA	\$3,337,106	

AMP-AD Brain Proteomic Network Enhancement, Validation, and Translation into CSF Biomarkers

In this proposal, we use next generation proteomic methods and systems biology to validate protein targets and networks altered in postmortem AD brain, including phosphorylation sites and interacting protein partners. Networks and targets experimentally tested in model systems will be translated into actionable biomarkers in the CSF. Ultimately, this will establish an innovative pipeline for discovery and validation of AD therapeutic targets.

Role: Co-Investigator

U24DK112341-04 (PI: Ortlund)	12/08/2016-11/30/2022	0.24 CM
NIH/NIDDK	\$4,902,401	

Georgia Comprehensive Metabolomics and Proteomics Unit for MoTrPAC

This is a comprehensive metabolomics and proteomics chemical analysis site to support the Molecular Transducers of Physical Activity Consortium (MoTrPAC). Advanced analytical methods, including mass spectrometry, bioinformatics and chemical forensics are used to provide targeted and global analysis of small molecules, lipids, proteins to develop a molecular transducer map for physical activity.

Role: Co-Investigator

P30CA138292-12 (PI: Curran)	04/07/2009 – 03/31/2022	1.2 CM
NIH/NCI	\$25,086,481	

Winship Cancer Institute Cancer Center Support Grant

Winship's mission is to lessen the burden of cancer for the citizens of Georgia, its primary catchment area. This will be accomplished by: (1) seeking greater insights into the molecular, genetic, and epigenetic basis of cancer; (2) discovering new knowledge that drives improvements in cancer detection, prevention, and/or therapy; (3) developing or defining novel therapeutic targets and/or agents as a pathway to better cancer therapies; and (4) studying and implementing population-based strategies to lessen the cancer burden in the state.

Role: Research Associate, Bioinformatics

R01NS089719-04 (PI: Rye)	09/01/2015 – 08/31/2020	1.2 CM
NIH/NINDS	\$2,375,857	

Characterization of an endogenous GABA-ergic mechanism underlying hypersomnia

In this R01 proposal, we employ an unbiased proteomic screen of CSF from controls and humans with primary hypersomnia (PH) that present in the clinic with excessive sleepiness and include patients with narcolepsy. CSF from individuals with PH mimics the pharmacological actions of sedative-hypnotics and anesthesia. Identification of the bioactive CSF peptides in patients with PH offers an opportunity from which to derive novel mechanistic insights into natural sleep patterns as well as potential therapies for sleep disorders.

Role: Research Associate, Bioinformatics

Pending – None

Completed Research Support

5/1/14-4/30/20

U01AG046161

Discovery of Novel Proteomic Targets for Treatment of Alzheimer's Disease

The aim of this project is to employ large-scale, unbiased proteomics analysis of postmortem Alzheimer's disease (AD) brain tissues to discover and then validate novel molecular targets for therapeutic intervention in AD. Eric Dammer performs systems biology to discern brain changes co-occurring with amyloid pathology and/or clinical disease. He analyzes all quantitative proteomics collected for this project in collaboration with the UCLA and other AMP-AD site teams.

PI: Levey AI Role: Investigator

9/1/16-6/30/19

P30NS055077

Emory Neuroscience NINDS Core Facilities

Emory Neuroscience NINDS Core provides subsidized support for NINDS funded investigators to utilize five core operations on the Emory campus including Proteomics, Viral Vector, Imaging, Neuropath/Histochem, and Rodent Behavior services. Eric provides analytical and bioinformatic support for projects generating data at the Emory Integrated Proteomics Core (EIPC) subsidized by this grant.

PI: Levey AI Role: Co-Investigator

8/1/15-7/31/17

R21NS087488-01A1

Decoding the RGS14 Interactome/Signalosome in CA2 Hippocampal Neurons

The goal of these studies is to define the overall signaling environment present in RGS14-expressing CA2 hippocampal neurons, and the specific signaling proteins/pathways that native RGS14 interacts with to regulate synaptic plasticity.

9/30/2011-09/29/2013

F32AG038259

Defining Mechanisms of TDP-43 Ubiquitination for QC and Aggregation

Neurodegeneration in frontotemporal lobar dementia with ubiquitinated inclusions (FTLD-U), amyotrophic lateral sclerosis (ALS), and other delayed-onset diseases associated with degeneration of aging neurons involves a deficit in the degradation of the TAR DNA binding protein (TDP-43). A determinant of TDP-43 aggregation was hypothesized to be K63-linked polyubiquitin. Novel interactions relevant to disease progression were identified in a cell model of TDP-43 with extensive K63 ubiquitin linkages. Measurements of ubiquitin chains and identification of novel disease-related proteins relied on quantitative MS and software developed by the PI and mentors at the Emory CNS proteomics facility.

7/01/2010-6/30/2011

T32NS007480

Training in Translational Research in Neurology

To understand protein oligomerization and associated dysregulation of cellular processes relevant to AD, Dr. Dammer confirmed that the U1 snRNP complex is involved in the development of pathology, including neurofibrillary tangles either containing Tau pathology, or concurrent with this pathology. The hypothesis that U1 snRNP loss of function is associated with cytoplasmic retention and development of U1 component-containing tangles, and with biochemical insolubility in MCI not yet associated with visible pathology was examined. Further, we hypothesized that function of U1, the first essential spliceosome component complex in the major eukaryotic splicing pathway (98% of splicing events), leads to increased exon inclusion or skipping.