BIOGRAPHICAL SKETCH

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NAME: Tracy G. Anthony

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

POSITION TITLE: Professor

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
Virginia Tech University, Blacksburg, VA	B.S.	08/93	Human Nutrition&Foods
University of Illinois, Urbana, IL	M.S.	05/95	Nutritional Sciences
University of Illinois, Urbana, IL	Ph.D.	05/98	Nutritional Sciences
Penn State College of Medicine, Hershey, PA	Postdoc	1998-2001	Cellular & Molecular Physiology

A. Personal Statement

The broad aim of my research program is to understand how altering the supply of amino acids, in total or individually, regulates metabolism and protein homeostasis in the whole animal. I have expansive training in biochemistry, endocrinology, immunology, kinesiology, metabolism, molecular biology and physiology, and I hold deep experience in the design and use of experimental diets, exercise modes and animal models to reflect the human condition. Over the years I have published numerous high impact publications which delineate mechanisms of metabolic and proteostasis control by diet, drugs, genetics and environmental stressors. These works have spanned many organ systems including endocrine, gastrointestinal, immune, lymphatic, muscular and nervous with particular emphasis in liver, skeletal muscle, pancreas, adipose, spleen, thymus, bone marrow and brain. I am especially interested in nutrient sensing and how affiliated signal transduction networks such as the integrated stress response, the endoplasmic reticulum stress response/unfolded protein response and the mammalian target of rapamycin pathways are coordinated to protect and preserve cell, tissue and organ function in response to nutritional insufficiency or environmental stress. My lab also uses big data approaches to examine the regulation of protein synthesis and gene expression.

B. Positions and Honors

Positions and Employment

1998-2001 American Diabetes Association Postdoctoral Research Fellow, Department of Cellular and Molecular Physiology, Penn State College of Medicine, Hershey, PA

2001-2005 Assistant Scientist/Assistant Professor, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine-Evansville, Evansville, IN.

2005-2010 Assistant Professor, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine-Evansville, Evansville, IN.

2010-2012 Associate Professor, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine-Evansville, Evansville, IN.

2012-2018 Associate Professor, Department of Nutritional Sciences, Rutgers University, New Brunswick, NJ.

2018-current Professor, Department of Nutritional Sciences, Rutgers University, New Brunswick, NJ.

Other Experiences and Professional Memberships

1994 – current	Member, American Society for Nutrition
1997 – current	Member, American Physiological Society
2004 – current	Member, American Society for Biochemistry and Molecular Biology
2010 – current	Editorial Board, *American Journal of Physiology Endocrinology and Metabolism*
2015 – current	Editorial Board, *Advances in Nutrition*
2016 – current	Editorial Board, *Annual Reviews in Nutrition*
2017 – current	Editorial Board, *Journal of Biological Chemistry*
2019	Attendee: 12th Annual Course on Isotope Tracers in Metabolic Research, Nashville, TN, October 21-25.
2019 - 2020	Visiting Scholar (sabbatical), laboratory of Josh Rabinowitz, Lewis-Sigler Institute for Integrative Genomics, Carl Icahn Laboratory, Princeton University, Princeton, NJ.

Honors and Awards

2003	American Society for Nutritional Sciences *Peter J. Reeds Young Investigator Award* for recognition of research which focuses on the regulation of somatic growth and the unique roles of amino acids in protein metabolism.
2010	*Trustees Teaching Award*, Indiana University School of Medicine
2014	*Fellow*, Dannon Institute Academic Mid-Career Nutrition Leadership Institute
2013-2018	*Standing Member*, Integrative Nutrition and Metabolic Processes Scientific Review Group, NIH
2017	*Invited Co-chair*, NIH/NIDDK Workshop on "Emerging Role of Branched-Chain Amino Acids in Human Diseases", May 25-26, 2017
2017	*"Editor's Pick"*, Research article [doi: 10.3945/jn.116.246710] selected in *Journal of Nutrition*.
2018	Research article highlighted in *Journal of Nutrition* 90th Anniversary supplement issue as one of the most cited and impactful papers published in the journal's history. J. Nutr. 130:2413-2419, 2000.
2019	*Fellow*, Higher Education Resource Services (HERS) academic leadership institute for women, Bryn Mawr, PA July 8-20.
2019	*"Editor's Pick"*, Research article (J. Biol. Chem. doi: 10.1074/jbc.RA119.009864) selected, awarded to the top 2 percent of manuscripts reviewed in a year in significance and overall importance.

C. Contributions to Science

1. Identified in vivo mechanisms by which dietary protein stimulates protein synthesis. Our group was the first to show that feeding protein after endurance exercise stimulates protein synthesis and translation initiation in the skeletal muscle of rodents. We then described how the leucine content of a complete meal is a determining factor for initiating the anabolic response to dietary protein. Our group was also the first to show that the branched chain amino acid leucine was unique in its potency to stimulate mechanistic/mammalian target of rapamycin complex 1 (mTORC1) activity in vivo. We were also the first to show control of mRNA translation initiation by leucine in mammalian tissue. One of these papers (**marked below) was highlighted in 2018 by the journal as one of the most impactful in its 90 year history. I was involved in all aspects of these experiments and took a lead or supporting role in manuscript preparation.

a) **Gautsch TA**, Anthony JC, Kimball SR, Paul GL, Layman DK, Jefferson LS. Availability of eIF4E regulates skeletal muscle protein synthesis during recovery from exercise. Am J Physiol. 1998 Feb;274(2 Pt 1):C406-14. PMID: 9486130
b) Anthony JC, **Anthony TG**, Kimball SR, Vary TC, Jefferson LS. Orally administered leucine stimulates protein synthesis in skeletal muscle of post-absorptive rats in association with increased eIF4F formation. J Nutr. 2000 Feb;130(2):139-45. PMID: 10720160
c) **Anthony JC, Yoshizawa F, **Anthony TG**, Vary TC, Jefferson LS, Kimball SR. Leucine stimulates translation initiation in skeletal muscle of postabsorptive rats via a rapamycin-sensitive pathway. J Nutr. 2000 Oct;130(10):2413-9. PMID: 11015466
d) **Anthony TG**, Anthony JC, Yoshizawa F, Kimball SR, Jefferson LS. Oral administration of leucine stimulates ribosomal protein mRNA translation but not global rates of protein synthesis in the liver of rats. J Nutr. 2001 Apr;131(4):1171-6. PMID: 11285321

2. Identified novel events to amino acid insufficiency. My group uncovered early and seminal evidence revealing how reduced dietary amino acid supply is sensed by GCN2. We were the first to report altered control of mTORC1 signaling by GCN2 status in tissues of mammals. We were also the first to report a vital role for GCN2 in brain development and control of feeding behavior. On the other hand, we were the first to show that dietary sulfur amino acid restriction in mice alters protein synthesis and body composition independently of eIF2 phosphorylation by GCN2. One of these papers (**marked below) was selected as an "Editor's Pick" for its scientific quality and impact. I served as the principal or co-investigator on these projects and was involved in all aspects of this work including manuscript preparation.

a) **Anthony TG**, McDaniel BJ, Byerley RL, McGrath BC, Cavener DR, McNurlan MA, Wek RC. Preservation of liver protein synthesis during dietary leucine deprivation occurs at the expense of skeletal muscle mass in mice deleted for eIF2 kinase GCN2. J Biol Chem. 2004 Aug 27;279(35):36553-61. Epub 2004 Jun 22. PMID: 15213227
b) Hao S, Sharp JW, Ross-Inta CM, McDaniel BJ, **Anthony TG**, Wek RC, Cavener DR, McGrath BC, Rudell JB, Koehnle TJ, Gietzen DW. Uncharged tRNA and Sensing of Amino Acid Deficiency in Mammalian Piriform Cortex. Science. 2005 Mar 18;307(5716):1776-8. PMID: 15774759
c) She P, Bunpo P, Cundiff JK, Wek RC, Harris RA, **Anthony TG**. General control nonderepressible 2 (GCN2) kinase protects oligodendrocytes and white matter during branched-chain amino acid deficiency in mice. J. Biol. Chem. Oct 25;288(43):31250-60. doi: 10.1074/jbc.M113.498469. PMID: 24019515; PMC3829435
d) **Pettit AP, Jonsson WO, Bargoud AR, Mirek ET, Peelor FF 3rd, Wang Y, Gettys TW, Kimball SR, Miller BF, Hamilton KL, Wek RC, **Anthony TG**. Dietary Methionine Restriction Regulates Liver Protein Synthesis and Gene Expression Independently of Eukaryotic Initiation Factor 2 Phosphorylation in Mice. J Nutr. 2017 Jun;147(6):1031-1040. doi: 10.3945/jn.116.246710. Epub 2017 Apr 26. PMID: 28446632, PMCID: PMC5443467

3. Established asparaginase as a model of amino acid starvation. Asparaginase is used to treat acute lymphoblastic leukemia, the most common childhood cancer, but unpredictably causes adverse metabolic toxicities that lead to treatment failure. Our group was the first to show that asparaginase activates the amino acid response/integrated stress response via GCN2 in mammalian tissues (PMID:19783659). We also revealed the protective function of GCN2 during asparaginase treatment and described the mechanism by which loss of GCN2 predisposes to immunosuppression (PMID: 20861212), liver steatosis (PMID: 24002574, 25491724) and pancreatitis (PMID: 26968207), providing the first mechanistic explanation for adverse events by asparaginase. We then detailed the role of activating transcription factor 4 (ATF4) in mediating the transcriptional response to asparaginase and then used asparaginase to further describe control of mTORC1 by GCN2 during amino acid starvation. My group also delineated the effect of age on the liver transcriptome, work which was highlighted as an "Editor's Pick" for its high quality and impact (**marked below). I served as principal investigator on these projects and was involved in all aspects of this work including manuscript preparation.

a) Nikonorova IA, Al-Baghdadi RJT, Mirek ET, Wang Y, Goudie MP, Wetstein BB, Dixon JL, Hine C, Mitchell JR, Adams CM, Wek RC, **Anthony TG**. Obesity challenges the hepatoprotective function of the integrated stress response to asparaginase exposure in mice. J Biol Chem. 2017 Apr 21;292(16):6786-6798. doi: 10.1074/jbc.M116.768408. Epub 2017 Feb 27. PMID: 28242759, PMC5399125
b) Al-Baghdadi RJT, Nikonorova IA, Mirek ET, Wang Y, Park J, Belden WJ, Wek RC, **Anthony TG**. Role of activating transcription factor 4 in the hepatic response to amino acid depletion by asparaginase. Sci Rep. 2017 Apr 28;7(1):1272. doi: 10.1038/s41598-017-01041-7. PMID: 28455513, PMCID: PMC5430736
c) Nikonorova IA, Mirek ET, Signore CC, Goudie MP, Wek RC, **Anthony TG**. Time-resolved analysis of amino acid stress identifies eIF2 phosphorylation as necessary to inhibit mTORC1 activity in liver. J Biol Chem. 2018 Apr 6;293(14):5005-5015. doi: 10.1074/jbc.RA117.001625. Epub 2018 Feb 15. PMID: 29449374
d) **Nikonorova IA, Zhu Q, Signore CC, Mirek ET, Jonsson WO, Kong B, Guo GL, Belden WJ, **Anthony TG**. Age modulates liver responses to asparaginase-induced amino acid stress in mice. J Biol Chem. 2019 Sep 20;294(38):13864-13875. doi: 10.1074/jbc.RA119.009864. Epub 2019 Aug 14. PMID: 31413113

4. Characterized novel elements within the integrated stress response. Activation of eIF2 kinases to environmental stress triggers the integrated stress response to promote cellular adaptation and proteome resilience. Our group described novel and key features of the integrated stress response and its relationship to ER stress and the unfolded protein response in mice. Specifically, we describe the role of the eIF2 kinase PERK in regulating selective mRNA translation during ER stress, and we reveal the role of activating transcription factor 4 in regulating antioxidant stress defenses and metabolic responses in liver. I served as the principal or co-investigator on these projects and was involved in all aspects of this work including manuscript preparation.

a) Teske BF, Wek SA, Bunpo P, Cundiff JK, McClintick JN, **Anthony TG**, Wek RC. The eIF2 kinase PERK and the integrated stress response facilitate activation of ATF6 during endoplasmic reticulum stress. Mol Biol Cell. 2011 Nov;22(22):4390-405. doi: 10.1091/mbc.E11-06-0510. Epub 2011 Sep 14. PMID: 21917591; PMC3216664
b) Baird TD, Palam LR, Fusakio ME, Willy JA, Davis CM, McClintick JN, **Anthony TG**, Wek RC. Selective mRNA translation during eIF2 phosphorylation induces expression of IBTKα. Mol Biol Cell. 2014 May;25(10):1686-97. doi: 10.1091/mbc.E14-02-0704. Epub 2014 Mar 19. PMID: 24648495; PMC4019499
c) Fusakio ME, Willy JA, Wang Y, Mirek ET, Al Baghdadi RJ, Adams CM, **Anthony TG**, Wek RC. Transcription factor ATF4 directs basal and select induced gene expression in the unfolded protein response and cholesterol metabolism in liver. Mol Biol Cell. 2016 May 1;27(9):1536-51. doi: 10.1091/mbc.E16-01-0039. Epub 2016 Mar 9. PMID: 26960794; PMC4850040
d) Jonsson WO, Margolies NS, **Anthony TG**. Dietary Sulfur Amino Acid Restriction and the Integrated Stress Response: Mechanistic Insights. Nutrients. 2019 Jun 15;11(6). pii: E1349. doi: 10.3390/nu11061349. PMID: 31208042

5. Metabolomics and metabolic control. I have collaborated with several groups to study the effect of exercise and amino acids on metabolism and metabolic control. These efforts have produced several high profile papers which describe how the branched chain amino acids are metabolized as energy substrates, how glutamine is a driver of tumor growth and how sex affects whole body substrate selection by exercise. My role on these projects ranged from principal investigator (a) to collaborator (b-d).

a) Klein DJ, McKeever KH, Mirek ET, **Anthony TG**. Metabolomic Response of Equine Skeletal Muscle to Acute Fatiguing Exercise and Training. Front Physiol. 2020 Feb 18;11:110. doi: 10.3389/fphys.2020.00110. eCollection 2020. PMID: 32132934
b) Neinast MD, Jang C, Hui S, Murashige DS, Chu Q, Morscher RJ, Li X, Zhan L, White E, **Anthony TG**, Rabinowitz JD, Arany Z. (2018) Whole-body metabolic fate of branched chain amino acids in health and insulin resistance. Cell Metab. 2018 Nov 12. pii: S1550-4131(18)30645-4. doi: 10.1016/j.cmet.2018.10.013. PMID: 30449684
c) Bott AJ, Shen J, Tonelli C, Zhan L, Sivaram N, Jiang YP, Yu X, Bhatt V, Chiles E, Zhong H, Maimouni S, Dai W, Velasquez S, Pan JA, Muthalagu N, Morton J, **Anthony TG**, Feng H, Lamers WH, Murphy DJ, Guo JY, Jin J, Crawford HC, Zhang L, White E, Lin RZ, Su X, Tuveson DA, Zong WX. Glutamine Anabolism Plays a Critical Role in Pancreatic Cancer by Coupling Carbon and Nitrogen Metabolism. Cell Rep. 2019 Oct 29;29(5):1287-1298.e6. doi: 10.1016/j.celrep.2019.09.056. PMID: 31665640
d) Tuazon MA, Campbell SC, Klein DJ, Shapses SA, Anacker KR, **Anthony TG**, Uzumcu M, Henderson GC. Effects of ovariectomy and exercise training intensity on energy substrate and hepatic lipid metabolism, and spontaneous physical activity in mice. Metabolism. 2018 Jun;83:234-244. doi: 10.1016/j.metabol.2018.02.011. Epub 2018 Mar 6. PMID: 29522773

NCBI My Bibliography URL:
http://www.ncbi.nlm.nih.gov/sites/myncbi/tracy.anthony.1/bibliography/40896220/public/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

ACTIVE AWARDS

1 R01DK109714-01A1 (MPI: Anthony/Wek) 09/20/16 – 06/30/21
NIH/NIDDK
Homeostatic Responses to Amino Acid Insufficiency
Define the contribution of the integrated stress response to the early molecular and physiological responses that function to maintain proteostasis during dietary amino acid insufficiency.
Role: Lead PI

Multistate NC1184 10/01/17 – 09/30/18
USDA NIFA
Molecular Mechanisms Regulating Skeletal Muscle Growth and Differentiation
My portion of this project examines the role of dietary protein and exercise on the skeletal muscle of horses and mice.
Role: NJ Station PI

COMPLETED IN PAST 3 YEARS:

2 R01DK096311-05A1 (Gettys) 04/01/2017 – 03/31/2019
NIH/NIDDK
The major goal of this project is to examine the impact of PERK deletion on the metabolic phenotype associated with dietary methionine restriction.
Role: Subcontract PI

1 R01 DK105032 12/01/15 – 11/30/2017
NIH/NIDDK (PI: Morrison)
FGF21 is an Endocrine Signal of Protein Restriction.
This project examines the role of the hepatokine FGF21 on mediating the metabolic responses to dietary protein restriction.
Role: Subcontract PI

1 R01 HD070487-06 7/25/2011 – 4/30/2016 (NCE to 4/30/2017)
NIH/NICHD
Molecular Mechanisms of Adverse Metabolic Events by Asparaginase
The major goal of this project is to investigate key molecular events that modulate hepatic dysfunction by the anti-leukemic agent, asparaginase.
Role: PI