Faculty Mentor List

Basic Science faculty mentors

1. Joseph Takahashi, Ph.D.
   Professor and Chair, Department of Neuroscience
   Joseph.Takahashi@UTSouthwestern.edu
   Research Statement:
   The long-term goals of the Takahashi laboratory are to understand the molecular and genetic basis of circadian rhythms in mammals and to utilize forward genetic approaches in the mouse as a tool for gene discovery for complex behavior. We have focused our attention in three areas: 1) identification of circadian clock genes and assignment of their function in the molecular mechanism of the circadian pacemaker; 2) analysis of central and peripheral circadian oscillators using real-time circadian reporters; and 3) identification of genes defined by mutations isolated in the large-scale mutagenesis screens we have conducted on neural and behavioral phenotypes including psychostimulant responses and contextual and cue dependent fear conditioning. Recently, we have focused on the structural biology of circadian clock proteins and on genomewide analysis of transcription factor binding and gene expression using next generation sequencing methods. A comprehensive global analysis of circadian transcription factor binding in the mouse liver has been completed in which all core components of the clock gene pathway have been interrogated. In addition, we have also analyzed the genome-wide regulation of nascent transcription, RNA polymerase II occupancy and epigenomic regulation of chromatin by the circadian clock. We have recently identified genes involved in cocaine responsiveness using forward genetic approaches. My laboratory has demonstrated a successful record of research productivity and training in circadian biology, mammalian genetics, genomics and molecular biology.

   1. Huang, N, Y Chelliah, Y Shan, CA Taylor, S-H Yoo, C Partch, CB Green, H Zhang, JS Takahashi 2012 Crystal structure of the heterodimeric CLOCK:BMAL1 transcriptional activator complex. Science 337: 189-194. DOI:10.1126/science.1222804. PMCID: 3694778.
   2. Koike N, SH Yoo, HC Huang, V Kumar, C Lee, TK Kim, JS Takahashi 2012 Transcriptional architecture and chromatin landscape of the core circadian clock in mammals. Science 338:349-354. DOI:10.1126/science.1226339. PMCID: 3694775.
   3. Yoo S-H, JA Mohawk, SM Siepka, Y Shan, SK Huh, H-K Hong, I Kornblum, V Kumar, N Koike, M Xu, J Nussbaum, X Liu, Z Chen, ZJ Chen, CB Green, JS Takahashi 2013 Competing E3 ubiquitin ligases govern circadian periodicity by degradation of CRY in nucleus and cytoplasm. Cell 152:1091–1105. DOI:10.1016/j.cell.2013.01.055. PMCID: 3694781.
   4. Kumar V, K Kim, C Joseph, S Kourrich, SH Yoo, HC Huang, MH Vitaterna, FP de Villena, G Churchill, A Bonci, JS Takahashi 2013 C57BL/6N mutation in cytoplasmic FMRP interacting protein 2 regulates cocaine response. Science 342: 1508-1512.

2. Carla Green, Ph.D.
   Professor, Department of Neuroscience
   Carla.Green@UTSouthwestern.edu
   Research Statement:
   The general focus of my lab is to understand the molecular mechanism of the mammalian circadian clock and how it controls rhythmic biochemistry, physiology and behavior. My formal training in biochemistry, molecular biology and cell biology gave me a broad skill set that I have further expanded into new areas over my career including structural biology, genomics, proteomics and metabolic studies. As a result, my lab has expertise in many technical approaches at many levels of analysis, ranging from biochemistry and molecular biology to cell biology to whole animal physiology and behavior. We have used these approaches to study the core circadian mechanism, focused largely on the role of the CRY proteins in setting the circadian period, and to study the output rhythms of the clock that are regulated post-transcriptionally. My discovery of the Nocturnin gene provided the first insights into the importance of circadian post-transcriptional control in vertebrates and more recently have extended this finding into general poly(A) tail length control driven by the clock. Subsequent work built upon these findings to explore the mechanisms by which circadian control of poly(A) tail length and how this shapes the rhythmic proteome. More recently, we have begun to explore the molecular mechanisms that govern sleep and how the circadian clock exerts control on this critical physiological phenomenon. Together, these data, have revealed novel and surprising ways

about how the clock works and how it generates the many biological rhythms that are essential for the well-being of the organism. I have trained and supervised many undergraduate students, graduate students, postdoctoral fellows and technicians throughout these past years and have established a long track record of federal funding and productivity in this field of research.

1. Zhu, H., Conte, F. and Green, C.B. (2003) Nuclear localization and transcriptional repression are confined to separable domains in the circadian protein CRYPTOCHROME. Curr. Biol., 13: 1653-1658. (PMID: 13678599)
2. McCarthy, E.v., Baggs, J.E., Geskes, J.M., Hogenesch, J.B. and Green, C.B. (2009) Generation of a novel allelic series of cryptochrome mutants via mutagenesis reveals residues involved in protein:protein interaction and CRY2-specific repression. Mol Cell Biol, 29: 5465-5476 (PMCID:PMC2756885).
3. Yoo, S.-H., Mohawk, J.A., Siepka, S.M., Shan, Y., Huh, S.K., Hong, H.-K., Kornblum, M.S., Kumar, V., Koike, N., Xu, M., Nussbaum, J., Liu, X., Chen, Z., Chen, Z.J., Green, C.B., Takahashi, J.S. (2013) Competing E3 Ubiquitin Ligases Determine Circadian Period by Regulated Degradation of CRY in Nucleus and Cytoplasm. Cell, 152: 1091-1105 (PMCID: PMC3694781).
4. Nangle, S.N., Rosensweig, C., Koike, N., Tei, H., Takahashi, J.S.*, Green, C.B.*, and Zheng, N*. (2014) Molecular assembly of the period-cryptochrome circadian transcriptional repressor complex. Elife, 3: e03674. (*shared corresponding authorship; PMCID: PMC4157330)

3. Lora Hooper, Ph.D

Professor and Chair, Department of Immunology, Center for Genetics of Host Defense, Microbiology
Lora.Hooper@UTSouthwestern.edu

Research Statement:
The research in my laboratory centers around the question of how the intestinal microbiota interacts with the intestinal epithelium to regulate host physiology. To address this problem, we have studied gnotobiotic and genetically-manipulated mouse models using a variety of microbiological, cell biological, and molecular techniques. Over the past 15 years, we have used these approaches to gain new insight into the interactions between the immune system and the intestinal microbiota, and to understand how these interactions influence intestinal health and disease. We have particular expertise in the study of epithelial antimicrobial proteins that are induced by the microbiota and have remained at the forefront of this field, investigating both biochemical mechanisms and the immunological consequences of antimicrobial protein expression in the intestine. We have also carried out studies on the circadian clock transcription factor NFIL3, exploring both its impact on intestinal immune system development and its regulation of lipid metabolism.

During my 15 years on the faculty at UT Southwestern, I have acquired significant mentoring experience. I have graduated six Ph.D students. All of the graduates are currently in successful scientific careers, including NASA support scientist, scientific writer, radiology resident, industry research scientist, and academic post-doctoral fellow. All of the Ph.D trainees have had at least one first-authored, peer-reviewed publication in a top-tier journal such as Science, Proceedings of the National Academy of Sciences, Cell Host & Microbe, and eLife. All of the Ph.D. students completed their degrees in 5.5 years or less. Four of my former post-doctoral fellows have tenure-track faculty positions at top research institutions (Brown University, UT Southwestern, University of Colorado, and Bar-Ilan University (Israel)). Others are flourishing in careers in industry and academia.

4. Genevieve Konopka, Ph.D.

Associate Professor, Department of Neuroscience
Genevieve.Konopka@UTSouthwestern.edu

Statement of Research:
The overarching research goal of my lab is to elucidate the molecular signaling pathways involved in brain disorders in order to develop improved therapeutics for these devastating disorders. I am identifying novel genes and signaling pathways implicated in brain disorders through the study of transcription and splicing factors as well as through comparative genomics and other computational approaches. I am also carrying out functional studies of these factors and their target genes in human cells and animal models. I have a successful track record in publishing and productive research projects related to understanding gene expression, gene co-expression, gene methylation, and alternative splicing in the nervous system. My lab has recently published several research papers related nervous system genomics. In the past two years, we have also developed extensive wet and dry bench tools for the analysis

of single-cell RNA-sequencing. I currently have two post-doctoral fellows in the lab with PhDs in bioinformatics, four postdocs who carry out both dry and wet-bench experiments, five PhD students, and two research technicians. My lab has generated a flexible pipeline for analysis of large-scale gene expression datasets, most importantly, weighted gene co-expression network analyses and single-cell RNA-seq analyses. I have seven years' experience mentoring both graduate students and postdoctoral fellows and have published both primary science and review articles with trainees in my lab. My students and postdocs have also received several training awards or individual fellowships (e.g. NSF GRF, NIH F30, Autism Science Foundation Fellowship). Four of my previous postdoctoral fellows have transitioned to faculty positions, and three of my graduate students have received their PhDs. In addition, I have a long-standing interest in sleep and circadian rhythms as it pertains to autism spectrum disorders as well as brain evolution. Trainees in my lab have published a number of papers related to these topics. Thus, I believe my lab provides a strong training environment especially with regards to neurogenomics of brain disorders and related phenotypes.

5. Qinghua Liu, Ph.D.
   Associate Professor, Department of Neuroscience
   Qinghua.Liu@UTSouthwestern.edu
   Research Statement:
   My laboratory focused on elucidation of the molecular mechanisms of the RNA interference (RNAi) and microRNA pathways. We identified a number of important components or regulators of Drosophila and human RNAi/microRNA pathways by classical biochemical fractionation and genetic screening. We developed the first in vitro reconstitution systems for Drosophila and human RNA-induced silencing complex (RISC) to understand the in-depth mechanism of RISC assembly and function. We characterized the enzymes, co-factors, and modulators of microRNA biogenesis. Furthermore, we discovered that the mitogen activated protein kinase (MAPK)/Erk pathway targets human microRNA machinery to effect mitogen-induced growth signaling.

   Despite the ubiquity of sleep behavior among animals, the function and regulatory mechanism of sleep remain unknown. We recently established a collaboration with Dr. Masashi Yanagisawa, who has conducted a forward genetic screen to identify Sleepy and Dreamless mutant mice. We applied cutting-edge quantitative mass spectrometry technology to analyze whole brain proteome and phosphoproteome of sleep-deprived mice and Sleepy mutant mice. We believe that these studies should reveal novel and important insights into the molecular mechanism of sleep function and regulation. The combination of forward genetic screening and quantitative mass spectrometry will have a transformative impact on understanding the genetic basis of and developing novel therapeutic interventions for human sleep disorders.

6. Beverly Rothermel, Ph.D.
   Associate Professor, Department of Internal Medicine, Division of Cardiology
   Beverly.Rothermel@UTSouthwestern.edu
   Research Statement:
   My laboratory has a long-standing interest in metabolic and structural remodeling of cardiac and skeletal muscle during development and disease. Our studies center on calcium-regulated signal transduction pathways with a focus on the calcium/calmodulin activated protein phosphatase calcineurin. My lab identified the protein RCAN1.4 as a feed back inhibitor of calcineurin activity and demonstrated RCAN1's ability to influence remodeling of both heart and skeletal muscle. Experiments in my lab are designed to better understand the biochemistry of the RCAN/calcineurin interaction, identify transcriptional and posttranscriptional mechanisms controlling RCAN levels, and determine the biological consequences of RCAN regulation of the calcineurin signaling cascade in the heart and other organs. One of the remarkable characteristics of RCAN1 is its strong circadian expression in the heart, and we have recently shown that RCAN1 protects the heart from I/R damage at specific times of the day. My approach to basic research is highly collaborative and this has provided many opportunities to integrate work in the cardiovascular system from my laboratory with that of researchers in other fields. This has opened opportunities for my lab to contribute to new discoveries relative in the fields of circadian biology, mitochondrial dynamics, metabolism, and synaptic plasticity. I am firmly committed to advancing the careers of my trainees. I feel that as a mentor one of my most important jobs is to help students identify and prepare themselves for the next step in the

process toward contributing as scientists, physicians, and teachers. I am actively involved in the selection and training of graduate students, medical students, and postdoctoral fellows.

7. Todd Roberts, Ph.D.
   Assistant Professor, Department of Neuroscience
   Todd.Roberts@UTSouthwestern.edu
   Statement of Research
   The Roberts lab is interested in understanding the circuit and cellular mechanisms for vocal learning, how the brain encodes memories of auditory experiences, uses auditory feedback to shape vocal behaviors and the role of sleep-based consolidation in this process. Our research seeks to identify general mechanisms and principles for how brain circuits learn from experience and how neurodevelopmental disorders known to impede speech and social development in children derail the learning process.

8. Benjamin Tu, Ph.D.
   Associate Professor, Department of Biochemistry
   Benjamin.Tu@UTSouthwestern.edu
   Statement of Research:
   My lab is investigating critical but often overlooked mechanisms by which fundamental cellular processes are coupled to the metabolic and nutritional state of the cell. Our studies of the yeast metabolic cycle system have provided a wealth of information regarding the changes in gene expression and metabolites that occur as a function of the growth and metabolic state of a cell. They predict that many important regulatory decisions will ultimately be linked in one way or another to metabolism, which may reveal an underlying metabolic basis of the circadian and sleep-wake cycles. We utilize both yeast and mammalian systems to elucidate how biological oscillatory systems are coupled to metabolism.

9. Shin Yamazaki, Ph.D.
   Associate Professor, Department of Neuroscience
   Shin.Yamazaki@UTSouthwestern.edu
   Statement of Research:
   The goal of this proposal is to determine the anatomical locus of the food-entrainable oscillator (FEO). I will use luminescence real-time gene reporting and whole brain microscopy to complete this project. I have been an active researcher studying circadian rhythms for over 25 years. As a postdoctoral fellow at the University of Virginia, I developed the technology for real-time monitoring of circadian gene expression and discovered that mammalian peripheral tissues contain self-sustained circadian oscillators. This discovery laid the groundwork for my studies investigating the organization of the circadian system and how an experimental protocol that approximates chronic jet-lag or shift-work disrupts the phase relationship among circadian clocks. As a PI, I have continued to investigate the organization of the circadian system using real-time gene expression monitoring. With their anatomical loci unknown and their outputs not expressed under normal physiological conditions, the FEO and methamphetamine-sensitive circadian oscillator (MASCO) are “black box” mysteries. My lab has shown that the FEO and MASCO are functional in mice lacking all three paralogs of the *Period* gene (their canonical circadian system is disabled). These mice are a novel and unique tool for revitalizing the search for the FEO and MASCO. My expertise in time-lapse brain imaging led to my position as Director of the Imaging Facility in the Department of Neuroscience at UT Southwestern, and to my collaboration with the UT Southwestern Whole Brain Microscopy Facility. This project is the culmination of my circadian expertise and data and toolsets collected over 25 years. My lab, in collaboration with the UT Southwestern Whole Brain Microscopy Facility, is ideally positioned to discover the locus of the FEO. By combining circadian mouse models, which I have characterized, with cutting-edge whole brain imaging technology, we will elucidate the neural substrate(s) of food anticipatory activity.
   a) **Yamazaki S**, Numano R, Abe M, Hida A, Takahashi RI, Ueda M, Block GD, Sakaki Y, Menaker M, Tei H (2000) Resetting central and peripheral circadian oscillators in transgenic rats. ***Science*** 288 (5466):682-685. *PMCID: PMC1635489*

b) Pendergast JS, Oda GA, Niswender KD, **Yamazaki S** (2012) Period determination in the food-entrainable and methamphetamine-sensitive circadian oscillator(s). ***Proc Natl Acad Sci U S A.*** 109(35): 14218-14223. *PMCID: PMC3435193* Participating Faculty Biosketches
c) Pendergast JS, **Yamazaki S** (2013) The complex relationship between the light-entrainable and methamphetamine-sensitive circadian oscillators: evidence from behavioral studies of Period-mutant mice. ***Eur J Neurosci*** 38 (7): 3044-3053. *PMCID: PMC3899104*
d) Pendergast JS, **Yamazaki S** (2014) Effects of light, food, and methamphetamine on the circadian activity rhythm in mice. ***Physiol Behav*** 128: 92-98. *PMID: 24530262*

Translational Science faculty mentors:

1. Robert Greene, M.D., Ph.D.
Professor, Departments of Psychiatry and Neuroscience
RobertW.Greene@UTSouthwestern.edu
Statement of Research:
My entire research career has involved sleep research and the control of behavioral state using both *in vivo* and *in vitro* electrophysiological and molecular approaches. An important focus of this work has been a characterization of the sleep homeostatic phenotype and its underlying mechanisms as distinct from time spent in sleep or wake. In addition we have worked on mechanisms responsible for arousal and attention. My lab has developed novel electrophysiological and molecular methodology directed towards this end and have characterized the critical role of the adenosine system in sleep homeostasis suggesting functionally important aspects of sleep related to adenosine's role at the cellular and synaptic levels to maintain an electrophysiological balance with metabolic state. Currently we are pursuing mechanisms responsible for altered gene expression programs controlled by sleep.

2. Kathleen Bell, M.D.
Professor and Chair, Department of Physical Medicine and Rehabilitation
Kathleen.Bell@UTSouthwestern.edu
Research Statement:
My research over the past 15 years has involved symptom characterization after traumatic brain injury (TBI) and interventions for treatment of mild and severe TBI and stroke and co-morbid conditions. In particular, mood disorders, pain, and sleep disorders have been of interest. I have an early publication on sleep apnea after TBI and a number of papers on the association of sleep disorders with co-morbid conditions after TBI. Currently, I am the co-PI of a trial of phototherapy for improving sleep efficiency in patients with acute TBI and a PCORI grant evaluating diagnostic techniques for obstructive sleep apnea in persons with acute TBI. I have successfully directed a number of single-site and multi-center studies with excellent retention of subjects and am currently an investigator with the TBI Model System program with 16 centers across the United States.

3. Sherwood Brown, M.D. Ph.D.
Professor, Department of Psychiatry
Sherwood.Brown@UTSouthwestern.edu
Research Statement:
My research focuses on comorbidities of mood disorders including medical illness, cortisol elevations and substance use. I have mentored trainees on projects in this area since the earliest stages of my career. This mentoring has included three post-doctoral fellows all of whom joined the faculty at UT Southwestern. In addition, I have mentored four graduate students on clinical psychology Ph.D dissertations (two as dissertation advisor), 54 undergraduate interns from UT Dallas, nine other undergraduate students, nine high school students, six residents in Psychiatry or Internal Medicine, and 37 medical students. This mentoring has resulted in 52 papers, some with more than one trainee as authors. Many of the trainees were from underrepresented racial or ethnic groups and four were funded through a NIDA summer research program for underrepresented minority students. A total of 16 of these trainees are from racial and ethnic groups underrepresented in biomedical sciences. I also serve as director of the Psychiatry Clinical Research Infrastructure at UT Southwestern. This is a system of resources (e.g. administrative, statistical, database, biomarkers) and training (e.g. presentations on topics

relevant to researchers, mock study sections) for departmental researchers. The services are provided at no charge for junior researchers. I am also Vice Chairman for Faculty Research Development and chief of the Division of Clinical Research. Thus, I have extensive experience both clinical research and in the career development of junior researchers. I am currently PI on an R01 grant from NIMH that examines the treatment of people with bipolar disorder and alcohol use disorder. A second R01 in this population recently received a priority score of 14, 1 percentile. The ongoing R01 study and this new grant, should it be funded, would provide potential research projects for fellows. Examples of publications with trainees are below with trainee names designed with an asterisk throughout this biosketch.

1. Desai S*, Khanani S *, Shad MU, Brown ES: Attenuation of amygdala atrophy with lamotrigine in patients receiving corticosteroid therapy. Journal of Clinical Psychopharmacology 29:284-287(2009). PMID:19440084; PMCID: PMC161623
2. Caldera-Alvarado G*, Khan DA, DeFina LF, Pieper A, Brown ES: Relationship between asthma and cognition: The Cooper Center longitudinal study. Allergy 68:545-548 (2013). PMID: 23409872
3. Xiao H*, Wignall N*, Brown ES: An open-label pilot study of icariin for bipolar disorder and alcohol use disorder. The American Journal of Drug and Alcohol Abuse 42:162-167 (2016).PMID: 26809351
4. Carlson SM*, Kim J*, Khan DA, King K, Lucarelli RT, McColl R, Peshock R, Brown ES. Hippocampal Volume in Patients with Asthma: Results from the Dallas Heart Study. Journal of Asthma (In press).

4. Marc Diamond, M.D., Ph.D.
Professor, Department of Neurology, Director, Center for Alzheimer's and Neurodegenerative Diseases
Marc.Diamond@UTSouthwestern.edu
Research Statement:
My laboratory is focused on basic research to develop novel diagnostic and therapeutic approaches to neurodegenerative diseases. We are especially interested in targeting abnormal protein conformational change, which plays a key role in neurodegenerative diseases such as Alzheimer's disease. We use a range of approaches: biochemistry, cell and molecular biology, and animal models. AD features deposition of aggregated tau protein, and exhibits inexorable spread of pathology. In patients with AD, sleep disturbances feature prominently, and this may relate back to progression of disease, as production and clearance mechanisms of protein aggregates may be related to the sleep cycle Our work on tau suggests that the aggregates are not static within the cell. Rather, aggregates are taken up by vulnerable cells where they can trigger fibrillization of endogenous, natively folded protein. The newly formed aggregates are capable of moving to neighboring cells to spread pathology. During the process of spread between cells, aggregates may be cleared by sleep-dependent systems such as the glymphatics. As diseases impact sleep, thus they may also impair pathological protein clearance. Prion-like mechanisms of pathology represent a potentially new paradigm in our understanding of neurodegenerative diseases, and could enable a host of new therapeutic strategies based on blocking propagation of misfolding, and improving clearance. In terms of my dedication to training, all of my significant publications have involved my students and postdoctoral fellows. I have helped place my students in prestigious postdoctoral fellowships, and my postdocs have gone on to industry positions and to productive careers in tenure-track academic appointments.

5. Joseph Garcia, M.D., Ph.D.
Professor, Department of Internal Medicine, Division of Cardiology
Joseph.Garcia@UTSouthwestern.edu
Research Statement:
My laboratory uses molecular, biochemical, cellular, and physiological approaches to study mammalian stress signaling. The focus of our studies is Hypoxia Inducible Factor 2 (HIF-2), the second of three related stress activated transcription factors in vertebrates. Our overall objective is to discern the molecular basis and role for HIF-2 in mammalian physiology. In our mechanistic studies to date, we learned that maximal HIF-2 stress signaling requires two opposing post-translational modifications, acetylation and deacetylation, which occur in a cyclical manner during stress signaling. The rate-limiting step for acetylation is availability of a specific pool of acetyl CoA used in acetylation of HIF-2, which is produced by an acetate-dependent acetyl CoA generator, acetyl CoA synthetase 2 (Acss2). In our translational studies to date, we found that Acss2 confers optimal HIF- 2 signaling not only in anemia, but also in tumor growth and development. Although predominantly cytosolic, we discovered that Acss2 also

possesses a novel nuclear signaling ability that is induced upon stress exposure. We are currently defining novel mechanistic and functional roles for Acss2 in HIF-2 stress signaling.

- Xu M, Nagati JS, Xie J, Li J, Walters H, Moon Y-A, Gerard RD, Huang C-L, Comerford SA, Hammer RE, Horton JD, Chen R, Garcia JA. A mammalian acetate switch regulates stress erythropoiesis. Nature Medicine, 20(9):1018-26 (2014), PMID: 25108527.
- Chen R, Xu M, Nagati JS, Hogg RT, Das A, Gerard RD, Garcia JA. The acetate/ACSS2 switch regulates HIF-2 stress signaling in the tumor cell microenvironment. PLoS One, 10(2):e0116515 (2015), PMID: 25689462.

6. Ron Mitchell, M.D., Ph.D.
   Professor and Vice Chairman, Department of Otolaryngology, Head and Neck Surgery
   Ron.Mitchell@UTSouthwestern.edu
   Statement of Research:
   I have been involved in research into the clinical aspects of obstructive sleep apnea (OSA) in children for the last 15 years and have the experience to mentor and support trainees. I have previously mentored more than 40 former trainees and junior faculty of whom more than 10 remain in academic positions and 4 have become independent researchers. I have previous experience as a site PI for the Childhood Adenotonsillectomy Study (CHAT) study, which randomized more than 460 children with OSA to early adenotonsillectomy or watchful waiting with supportive care. I have also been the PI in several prospective outcomes studies on efficacy of adenotonsillectomy for OSA in children. I therefore have extensive experience in practical aspects of performing studies. I have more than 100 peer reviewed publications (as well as books, book chapters, editorials, and reviews) on OSA in children. I served as an Assistant Chair for the American Academy of Otolaryngology, Head & Neck Surgery Guideline Workgroup to establish clinical indications for tonsillectomy in children and have chaired the update for this document that is to be published in 2019. I also served as a member and consultant for the American Academy of Otolaryngology, Head & Neck Surgery Guideline Workgroup to establish clinical indications for polysomnography in children. Clinically, I direct the otolaryngology and sleep medicine divisions at UT Southwestern/Dallas Children's Medical Center as well as a 12-bed sleep center with over 2,000 sleep studies per annum. In conclusion, I have the clinical and research background to contribute positively to this grant.

7. Lance Terada, M.D., Ph.D.
   Professor and Division Chief, Department of Internal Medicine, Division of Pulmonary and Critical Care Medicine
   Lance.Terada@UTSouthwestern.edu
   Statement of Research:
   I have had a sustained research focus on fundamental signaling pathways relevant to vascular and lung diseases, particularly those which control cytoskeletal dynamics and cell fate. Since 2007 I have directed the division of Pulmonary and Critical Care Division. A major focus has been the building of a clinical and research infrastructure which has allowed us to establish specific research and research training programs. An important clinical focus we have developed over the past 7 years is the Sleep and Breathing Disorders Center (SBDC), which attracts a large number of subjects with a variety of sleep related disorders. This Center offers a valuable clinical population suitable for a variety of clinical and translational studies. Other new clinical centers which now support robust disease-specific research are in lung cancer, interstitial lung disease, cystic fibrosis, COPD, interventional pulmonology, and pulmonary hypertension. In addition, I have obtained and currently direct a T32 research training program which trains lung and vascular scientists. My own laboratory is now focused upon the epigenetic and molecular control of matrix anchorage and its direct implications for cancer cell metastasis. Invited reviews which support my visibility in these fields include:
   1. **Terada LS**. Specificity in reactive oxidant signaling: think globally, act locally. J Cell Biol. 2006 Aug 28; 174(5):615-23. PubMed PMID: 16923830; PubMed Central PMCID: PMC2064304.
   2. Ma Z, Liu Z, Myers DP, **Terada LS**. Mechanotransduction and anoikis: death and the homeless cell. Cell Cycle. 2008 Aug 15; 7(16):2462-5. PubMed PMID: 18719379; PubMed Central PMCID:PMC2730734.
   3. **Terada LS**, Nwariaku FE. Escaping Anoikis through ROS: ANGPTL4 controls integrin signaling through Nox1. Cancer Cell. 2011 Mar 8; 19(3):297-9. PubMed PMID: 21397852.

4. **Terada LS**, Liu Z. Aiolos and lymphocyte mimicry in lung cancer. Molecular & Cellular Oncology. 2014 July; 1(1):e29912.

5. Jeffrey Zigman, M.D., Ph.D.
Professor, Department of Internal Medicine, Division of Endocrinology, and Department of Psychiatry
Jeffrey.Zigman@UTSouthwestern.edu
Statement of Research:
I have actively participated in research on metabolism, behavior, and islet biology for many years, beginning as a Medical Scientist Training Program trainee, resuming as a fellow, and continuing now as a full Professor with tenure at UT Southwestern Medical Center. In over 11 years as an independent investigator, I have combined my backgrounds in endocrinology and neuroscience to establish an internationally recognized profile for my research investigating ghrelin secretion and control of complex eating behaviors by ghrelin. My group was the first to show essential roles for ghrelin in mediating reward-based eating of various types. We were first to characterize ghrelin as a natural antidepressant. We showed that ghrelin's antidepressant actions rely on protection of adult hippocampal neurogenesis, leading us to identify potent antidepressant-like efficacy for the P7C3 class of rapid-acting neuroprotective compounds. We have helped highlight the essential actions of ghrelin in defending against life-threatening hypoglycemia in starvation-like states and in infants treated with beta blockers. We have identified key sites of ghrelin's orexigenic, antidepressant and glucoregulatory actions by comprehensively determining the pattern of ghrelin receptor expression in the rodent brain and by using mouse genetics to target ghrelin receptor expression to selective cell-types and to manipulate the activity of ghrelin receptor-expressing neurons. We also have led the field in identifying key elements of the ghrelin cell molecular machinery mediating ghrelin secretion, demonstrating an essential role played by ghrelin cell-expressed β_1-adrenergic receptors in that process. Substantive collaborative efforts have helped identify central sites of action for kisspeptin, leptin and serotonin, and roles for the ghrelin system in mediating the metabolic responses to exercise. I have been invited to speak on these topics at several universities and international meetings, including the annual scientific sessions of the Endocrine Society, American Diabetes Association, Obesity Society, and Society for Neuroscience. I have served in a major leadership position for The Obesity Society as the Chair of the Annual Program Committee, directing the development of the content for the society's annual scientific meeting in 2017. I also maintain a half-day per week clinical endocrinology practice. I currently serve as the mentor for three postdoctoral fellows and an instructor. Previously, I trained a graduate student, an F32 Individual NRSA-supported postdoctoral fellow, and nine other postdoctoral fellows including two who now run their own labs as faculty in their home countries. I also have mentored numerous undergraduate and medical school summer students and have won several teaching awards. I continue to support my former trainees in varying capacities, for instance helping to secure funding via a Fogarty International Research Collaboration – Basic Biomedical Research Award application for one of my former trainees. I am highly dedicated to my trainees' success.