BIOGRAPHICAL SKETCH

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NAME: Taylor VI, James G.

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

POSITION TITLE: Professor and Center Director

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Creighton University, Omaha, NE	BS	08/1989	05/1991	Biology
Medical College of Wisconsin, Milwaukee, WI	MD	08/1991	05/1995	Medicine
Washington University, St. Louis, MO	Resident	07/1995	06/1998	Pediatrics
Johns Hopkins University/NIH, Bethesda, MD	Fellow	07/1998	06/2001	Pediatric Hem/Onc
National Cancer Institute, Bethesda, MD	Postdoctoral Fellow	07/2001	06/2004	Genetics research
NHLBI, NIH, Bethesda, MD	Postdoctoral Fellow	07/2004	10/2004	Vascular medicine

A. Personal Statement

I have the necessary training, experience and motivation to successfully contribute to the Center for Hemoglobin Research in Minorities (CHaRM) program, including leadership of translational research projects. I am a pediatric hematologist/oncologist with more than a decade of clinical experience in adult hematology. Over the past five years, I have focused on sickle cell pain biology and genetics; especially the degree to which genetic admixture in African Americans influences sickle phenotypes. My laboratory has experience with experimental pain phenotyping including quantitative sensory testing (QST) and development of a custom genome wide SNP panel to study admixture in African Americans. I have recently been appointed as Director of the Center for Sickle Cell Disease, which is supported by CHaRM. My faculty appointment supports more than 50% of my time for directing translational research in the Center. I lead 24 employees in their mission to provide clinical care and perform research for 350 adults with sickle cell. I laid the groundwork for my present position by recruiting subjects for a large intramural NIH sickle cell registry from Howard over the last decade. Consequently, I already have an established rapport with the Center's patient population. Overall, I can utilize my position to leverage the resources of the Center for Sickle Cell Disease and our unique patient population towards a better understanding of factors leading to health disparities in medicine.

1. Darbari DS, Hampson JP, Ichesco E, Kadom N, Vezina G, Evangelou I, Clauw DJ, Taylor Vi JG, Harris RE. Frequency of Hospitalizations for Pain and Association With Altered Brain Network Connectivity in Sickle Cell Disease. J Pain. 2015 Nov;16(11):1077-86. PubMed PMID: 26291276; PubMed Central PMCID: PMC4986827.
2. Webb RC, Ma Y, Krishnan S, Li Y, Yoon S, Guo X, Feng X, Shi Y, Seidel M, Cho NH, Kurniawan J, Ahad J, Sheth N, Kim J, Taylor JG 6th, Darlington T, Chang K, Huang W, Ayers J, Gruebele A, Pielak RM, Slepian MJ, Huang Y, Gorbach AM, Rogers JA. Epidermal devices for noninvasive, precise, and continuous mapping of macrovascular and microvascular blood flow. Sci Adv. 2015 Oct;1(9):e1500701. PubMed PMID: 26601309; PubMed Central PMCID: PMC4646823.
3. Belfer I, Youngblood V, Darbari DS, Wang Z, Diaw L, Freeman L, Desai K, Dizon M, Allen D, Cunnington C, Channon KM, Milton J, Hartley SW, Nolan V, Kato GJ, Steinberg MH, Goldman D, Taylor JG 6th. A GCH1 haplotype confers sex-specific susceptibility to pain crises and altered endothelial function in adults with sickle cell anemia. Am J Hematol. 2014 Feb;89(2):187-93. PubMed PMID: 24136375; PubMed Central PMCID: PMC4281092.
4. Solovieff N, Hartley SW, Baldwin CT, Klings ES, Gladwin MT, Taylor JG 6th, Kato GJ, Farrer LA, Steinberg MH, Sebastiani P. Ancestry of African Americans with sickle cell disease. Blood Cells Mol Dis. 2011 Jun 15;47(1):41-5. PubMed PMID: 21546286; PubMed Central PMCID: PMC3116635.

B. Positions and Honors

Positions and Employment

2002 - 2016	Attending Physician, Division of Pediatric Hematology, Johns Hopkins Hospital, Baltimore, MD
2004 - 2009	Staff Clinician, Vascular Medicine Branch, NHLBI, NIH, Bethesda, MD
2010 - 2016	Clinical Investigator, Genomic Medicine Section, Hematology Br, NHLBI, NIH, Bethesda, MD
2017 -	Director, Center for Sickle Cell Disease, Howard University, Washington, DC
2017 -	Professor of Medicine (Hem/Onc), Howard University College of Medicine, Washington, DC

Other Experience and Professional Memberships

2005 -	Member, American Society of Hematology
2008 - 2009	Reviewer, Clinical Hematology Special Emphasis Panel (ZRG1 HEM-D), CSR, NIH
2009 - 2009	Member, Clinical Center Pharmacy Department Operational Review Panel, NIH
2009 - 2016	Member, Biomedical Translational Research Information System (BTRIS) Data Access Committee, NIH
2010 -	Member, American Pain Society
2010 - 2010	Reviewer, Transfusion Medicine Special Emphasis Panel (ZRG1 VH-E 50), CSR, NIH
2011 - 2011	Reviewer, Indo-US Program on Maternal and Child Health and Human Development Research (MCHDR), CSR, NIH
2013 - 2014	Reviewer, Orphan Products Development Grant Program (Hematology), US FDA
2014 - 2016	Member, Data and Safety Monitoring Board (DSMB), National Human Genome Research Institute, NIH
2015 - 2015	Reviewer, Special Emphasis Panel, Early Detection Research Network (ZCA1 RPRB-B, NCI EDRN), NCI, NIH
2015 - 2016	Member, Search Committee for Chief, Biomedical Translational Research Information System, Clinical Center, NIH
2016 -	Associate Editor, BMC Hematology journal
2016 - 2017	Reviewer, Orphan Products Development Grant Program (Hematology), US FDA

Honors

1991	Achiever Award, Nebraska Trio Program
1991	BS Magna Cum Laude, Creighton University
1995	MD with Honors in Research, Medical College of Wisconsin
1995	Research Award, Medical College of Wisconsin
1998 - 2005	Loan Repayment Program, NIH
2009	Top Science Advance, NCI Center for Cancer Research
2014	Scientific Research and Service Award, Queens Sickle Cell Advocacy Network
2014	Citation, Office of the President, Borough of Brooklyn, NY
2014	Citation of Achievement, City Council, City of New York, NY

C. Contribution to Science

1. Epidemiology, Co-Morbidities and Mechanisms of Pain in Sickle Cell Anemia: The hallmark of SCA is pain. The most severe events require hospitalization for treatment with parenteral opioids. Frequent hospitalization for pain is also a risk factor for early death, and this association does not appear to have changed in recent decades despite the availability of hydroxyurea therapy. Few tools have been developed to objectify pain in SCA, and the mechanisms underlying acute and chronic pain have not been elucidated. My lab has recently shown that pain in SCA is likely related to altered processing in the central nervous system ("Central Sensitization") using functional MRI. Another study under review (presented in abstract format) used quantitative sensory tests in adults with SCA to also show an association between central sensitization and HbF. If validated, this could explain the high prevalence of co-morbidities (sleep disturbance, depression and emotional behavior) that are associated with other diseases of central sensitization like fibromyalgia. I have also participated in the development of wearable detectors to assess

changes in skin temperature and superficial blood flow in anticipation of using these methods to further elucidate mechanisms of pain in SCA. All of these tools can also serve as novel primary endpoints for clinical trials. If central sensitization represents a common mechanism for pain in SCA, it could fundamentally change the physician's clinical approaches to treatment as opioids are often ineffective for this type of pain.

a. Darbari DS, Hampson JP, Ichesco E, Kadom N, Vezina G, Evangelou I, Clauw DJ, Taylor Vi JG, Harris RE. Frequency of Hospitalizations for Pain and Association With Altered Brain Network Connectivity in Sickle Cell Disease. J Pain. 2015 Nov;16(11):1077-86. PubMed PMID: 26291276; PubMed Central PMCID: PMC4986827.
b. Wallen GR, Minniti CP, Krumlauf M, Eckes E, Allen D, Oguhebe A, Seamon C, Darbari DS, Hildesheim M, Yang L, Schulden JD, Kato GJ, Taylor JG 6th. Sleep disturbance, depression and pain in adults with sickle cell disease. BMC Psychiatry. 2014 Jul 21;14:207. PubMed PMID: 25047658; PubMed Central PMCID: PMC4223647.
c. Darbari DS, Wang Z, Kwak M, Hildesheim M, Nichols J, Allen D, Seamon C, Peters-Lawrence M, Conrey A, Hall MK, Kato GJ, Taylor JG 6th. Severe painful vaso-occlusive crises and mortality in a contemporary adult sickle cell anemia cohort study. PLoS One. 2013;8(11):e79923. PubMed PMID: 24224021; PubMed Central PMCID: PMC3818240.
d. Darbari DS, Onyekwere O, Nouraie M, Minniti CP, Luchtman-Jones L, Rana S, Sable C, Ensing G, Dham N, Campbell A, Arteta M, Gladwin MT, Castro O, Taylor JG 6th, Kato GJ, Gordeuk V. Markers of severe vaso-occlusive painful episode frequency in children and adolescents with sickle cell anemia. J Pediatr. 2012 Feb;160(2):286-90. PubMed PMID: 21890147; PubMed Central PMCID: PMC3258348.

2. Physiologic Consequences and Manifestations of Hemolysis in Sickle Cell Anemia: Red cells filled with sickle hemoglobin are misshapen, rigid and fragile. The central pathologic event in SCA is believed to be occlusion of sickled erythrocytes during hypoxia within post-capillary venules resulting in acute pain. However, red cell fragility also results in high levels of intravascular hemolysis. I have been a major contributor to studies investigating the hypothesis that red cell hemolysis induces a series of physiologic alterations and SCA complications via altered nitric oxide (NO) bioavailability. One of these studies was the first to suggest that hemolysis might also influence pain crises, as opposed to the vascular complications of SCA like elevation of pulmonary pressures, leg ulceration and priapism. One of the figures from this study is often used to visually summarize data in support of the NO bioavailabilty/hemolysis hypothesis, as this has emerged as a polarizing controversy in SCA.

a. Milton JN, Rooks H, Drasar E, McCabe EL, Baldwin CT, Melista E, Gordeuk VR, Nouraie M, Kato GR, Minniti C, Taylor J, Campbell A, Luchtman-Jones L, Rana S, Castro O, Zhang Y, Thein SL, Sebastiani P, Gladwin MT, Steinberg MH. Genetic determinants of haemolysis in sickle cell anaemia. Br J Haematol. 2013 Apr;161(2):270-8. PubMed PMID: 23406172; PubMed Central PMCID: PMC4129543.
b. Kato GJ, Taylor JG 6th. Pleiotropic effects of intravascular haemolysis on vascular homeostasis. Br J Haematol. 2010 Mar;148(5):690-701. PubMed PMID: 19958359; PubMed Central PMCID: PMC3210728.
c. Taylor JG 6th, Nolan VG, Mendelsohn L, Kato GJ, Gladwin MT, Steinberg MH. Chronic hyper-hemolysis in sickle cell anemia: association of vascular complications and mortality with less frequent vasoocclusive pain. PLoS One. 2008 May 7;3(5):e2095. PubMed PMID: 18461136; PubMed Central PMCID: PMC2330070.
d. Kato GJ, McGowan V, Machado RF, Little JA, Taylor J 6th, Morris CR, Nichols JS, Wang X, Poljakovic M, Morris SM Jr, Gladwin MT. Lactate dehydrogenase as a biomarker of hemolysis-associated nitric oxide resistance, priapism, leg ulceration, pulmonary hypertension, and death in patients with sickle cell disease. Blood. 2006 Mar 15;107(6):2279-85. PubMed PMID: 16291595; PubMed Central PMCID: PMC1895723.

3. Identification of VCAM1, GCH1 and FGFR4 as Functional Genetic Modifiers in Rare Diseases: The clinical manifestations of sickle cell anemia (SCA) are protean with a wide phenotypic expression. As a post-doctoral fellow, I initiated one of the first studies to determine if single nucleotide polymorphisms in VCAM1 were associated with stroke in SCD. The study included a sequence based discovery phase with newly

identified markers being submitted to dbSNP, and highlighted my ability to use to principles of population genetics for rational support of hypothesis generating association studies. In addition, study of GCH1 not only identified a unique SCA pain association, but also included analysis of genetic admixture as confounder. This in turn has become the focus for our current genome wide studies using admixture mapping. In pediatric rhabdomyosarcoma, we similarly reasoned that mutations were also likely to be a mechanism by which a receptor tyrosine kinase could be activated to promote turmorigenesis and metastases. Genetic and functional analysis of FGFR4 has significantly influenced the direction of pediatric oncology, as our work successfully illustrated a paradigm for target discovery and personalized medicine.

a. Belfer I, Youngblood V, Darbari DS, Wang Z, Diaw L, Freeman L, Desai K, Dizon M, Allen D, Cunnington C, Channon KM, Milton J, Hartley SW, Nolan V, Kato GJ, Steinberg MH, Goldman D, Taylor JG 6th. A GCH1 haplotype confers sex-specific susceptibility to pain crises and altered endothelial function in adults with sickle cell anemia. Am J Hematol. 2014 Feb;89(2):187-93. PubMed PMID: 24136375; PubMed Central PMCID: PMC4281092.

b. Taylor JG 6th, Cheuk AT, Tsang PS, Chung JY, Song YK, Desai K, Yu Y, Chen QR, Shah K, Youngblood V, Fang J, Kim SY, Yeung C, Helman LJ, Mendoza A, Ngo V, Staudt LM, Wei JS, Khanna C, Catchpoole D, Qualman SJ, Hewitt SM, Merlino G, Chanock SJ, Khan J. Identification of FGFR4-activating mutations in human rhabdomyosarcomas that promote metastasis in xenotransplanted models. J Clin Invest. 2009 Nov;119(11):3395-407. PubMed PMID: 19809159; PubMed Central PMCID: PMC2769177.

c. Idelman G, Taylor JG, Tongbai R, Chen RA, Haggerty CM, Bilke S, Chanock SJ, Gardner K. Functional profiling of uncommon VCAM1 promoter polymorphisms prevalent in African American populations. Hum Mutat. 2007 Aug;28(8):824-9. PubMed PMID: 17431880.

d. Taylor JG 6th, Tang DC, Savage SA, Leitman SF, Heller SI, Serjeant GR, Rodgers GP, Chanock SJ. Variants in the VCAM1 gene and risk for symptomatic stroke in sickle cell disease. Blood. 2002 Dec 15;100(13):4303-9. PubMed PMID: 12393616.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/james.taylor.4/bibliography/52088088/public/

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

Ongoing Research Support

Institutional award, Howard University College of Medicine and Center for Sickle Cell Disease
Taylor VI, James G. (PI) 01/16/16-12/31/19 2.4 Cal
Translational analysis of mechanisms of pain in sickle cell disease
The goal of this project is to identify mechanisms of acute and chronic pain in sickle cell disease using experimental pain phenotype, genomic and pharmacologic approaches in human subjects.
Role: PI

P50 HL118006, NIH/NHLBI
Taylor, Robert E. (PI) 08/22/13-06/30/18 1.2 Cal
Center For Hemoglobin Research In Minorities (CHARM)
The goal of this program is to further develop a center of excellence for the study of hemoglobinopathies, iron metabolism, and oxygen sensing.
Role: Co-Investigator

Completed Research Support

1 ZIA HL006012 , NIH - Division of Intramural Research
Taylor VI, James G. (PI)
02/10/10-10/05/16
Prevalence and Prognosis of Secondary Pulmonary Hypertension in Adults with Sickle Cell Disease

The goal of this 15 year study (the Bethesda Sickle Cell Cohort Study) was to identify clinical determinants of pulmonary hypertension and related sickle cell disease complications in 795 subjects.
Role: PI

1 ZIA HL006160, NIH - Division of Intramural Research
Taylor VI, James G. (PI)
02/10/10-10/05/16
Genomic Determinants of Phenotypes of Sickle Cell Disease
The goal of this lab based study was to identify genetic determinants of complications of sickle cell disease as part of the Bethesda Sickle Cell Cohort Study. A biorepository of DNA, RNA and plasma was established. A significant focus was also to develop new tools for quantifying pain in sickle cell disease.
Role: PI

Bench to Bedside Award, NIH Clinical Center
Taylor VI, James G. (PI)
01/01/09-12/31/10
Gene Expression Profiling to Predict Sickle Cell Anemia Sub-Phenotypes
The goal of this study was to refine methods of cell isolation and analysis of gene expression in sickle cell anemia with a team of extramural investigators, and then to compare gene expression profiles between 2 sub-phenotypes of sickle cell anemia.
Role: PI