OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Kilbaugh, Todd

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-4959-3092

Position Title: Professor of Anesthesiology, Critical Care, and Pediatrics

Organization and Location: Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States	Fellow	07/2005	07/2007	Pediatric Critical Care Medicine
The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States	Fellow	07/2004	07/2005	Pediatric and Pediatric Cardiac Anesthesiology
Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, United States	Resident	07/2002	07/2005	Anesthesiology and Critical Care Medicine
Louisiana State University Health Sciences Center, New Orleans, Louisiana, United States	Resident	07/1999	06/2002	Pediatrics
Medical University of South Carolina, Charleston , South Carolina, United States	Doctor of Medicine (MD)	08/1995	05/1999	Medicine
Wake Forest university, Winston-Salem, North Carolina, United States	Bachelor of Science (BS)	08/1990	05/1994	Biology

Appointments and Positions

2023 - present	Professor of Anesthesiology, Critical Care, and Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States
2026 - present	Timothy J. Raymond Endowed Chair in Pediatric Resuscitation Science, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States
2023 - present	Faculty Associate Director, Penn Center for Health, Devices and Technology, Penn Center for Health, Devices and Technology, Philadelphia, Pennsylvania, United States
2023 - present	Executive Leadership Team, Translational Medicine, Children's Hospital of Philadelphia Research Institute, Philadelphia, Pennsylvania, United States
2023 - present	William J. Greeley Endowed Chair in Pediatric Anesthesia and Critical Care Research, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States
2021 - present	Professor of Anesthesiology, Critical Care, and Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, United States
2021 - present	Associate Chair for Research, Department of Anesthesia and Critical Care, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States
2017 - present	Co-Director of The Resuscitation Science Program, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States
2017 - 2022	Associate Professor of Anesthesiology, Critical Care, and Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, United States
2016 - present	Director of the Anesthesia and Critical Care Mitochondrial Unit, The Center for Mitochondrial and Epigenomic Medicine, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States
2015 - present	Director of the Extracorporeal Life Support Center, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States
2014 - present	Co-Director Neurosurgical Critical Care, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States

Products

Products Closely Related to the Proposed Project

1. Senthil K, Ranganathan A, Piel S, Hefti MM, Reeder RW, Kirschen MP, Starr J, Morton S, Gaudio HA, Slovis JC, Herrmann JR, Berg RA, Kilbaugh TJ, Morgan RW. Elevated serum neurologic biomarker profiles after cardiac arrest in a porcine model. Resusc Plus. 2024 Sep;19:100726. PubMed Central PMCID: PMC11325790.
2. Guarnieri JW, Lie T, Albrecht YES, Hewin P, Jurado KA, Widjaja GA, Zhu Y, McManus MJ, Kilbaugh TJ, Keith K, Potluri P, Taylor D, Angelin A, Murdock DG, Wallace DC. Mitochondrial antioxidants abate SARS-COV-2 pathology in mice. Proc Natl Acad Sci U S A. 2024 Jul 23;121(30):e2321972121. PubMed Central PMCID: PMC11287122.
3. Kilbaugh TJ, Sutton RM, Karlsson M, Hansson MJ, Naim MY, Morgan RW, Bratinov G, Lampe JW, Nadkarni VM, Becker LB, Margulies SS, Berg RA. Persistently Altered Brain Mitochondrial Bioenergetics After Apparently Successful Resuscitation From Cardiac Arrest. J Am Heart Assoc. 2015 Sep 14;4(9):e002232. PubMed Central PMCID: PMC4599507.
4. McManus MJ, Zhu Y, Alves C, Kohli N, Prada-Dacasa P, Sanchez-Benito L, Sanz E, Yee I, Robinson L, Sheldon M, McHugh WJ, Ranganathan A, Meng J, Duncan N, Grönberg A, Wallace DC, Piel S, Karlsson M, Moss SJ, Webster L, Hansson MJ, Elmér E, Ehinger JK, Quintana A, Kilbaugh TJ. The succinate prodrug NV354 prevents brain lesions and late-stage motor dysfunction in mitochondrial complex I deficiency. iScience. 2026 Feb 20;29(2):114717. PubMed Central PMCID: PMC12907114.
5. Karlsson M, Pukenas B, Chawla S, Ehinger JK, Plyler R, Stolow M, Gabello M, Hugerth M, Elmér E, Hansson MJ, Margulies S, Kilbaugh T. Neuroprotective Effects of Cyclosporine in a Porcine Pre-Clinical Trial of Focal Traumatic Brain Injury. J Neurotrauma. 2019 Jan 1;36(1):14-24. PubMed Central PMCID: PMC6306685.

Other Significant Products Highlighting Contributions to Science

1. Kilbaugh TJ, Karlsson M, Byro M, Bebee A, Ralston J, Sullivan S, Duhaime AC, Hansson MJ, Elmér E, Margulies SS. Mitochondrial bioenergetic alterations after focal traumatic brain injury in the immature brain. Exp Neurol. 2015 Sep;271:136-44. PubMed Central PMCID: PMC4586357.
2. Kilbaugh TJ, Karlsson M, Duhaime AC, Hansson MJ, Elmer E, Margulies SS. Mitochondrial response in a toddler-aged swine model following diffuse non-impact traumatic brain injury. Mitochondrion. 2016 Jan;26:19-25. PubMed Central PMCID: PMC4752861.
3. Slovis JC, Morgan RW, Landis WP, Roberts AL, Marquez AM, Mavroudis CD, Lin Y, Ko T, Nadkarni VM, Berg RA, Sutton RM, Kilbaugh TJ. The physiologic response to rescue therapy with vasopressin versus epinephrine during experimental pediatric cardiac arrest. Resusc Plus. 2020 Dec;4:100050. PubMed Central PMCID: PMC8244440.
4. Mavroudis CD, Karlsson M, Ko T, Hefti M, Gentile JI, Morgan RW, Plyler R, Mensah-Brown KG, Boorady TW, Melchior RW, Rosenthal TM, Shade BC, Schiavo KL, Nicolson SC, Spray TL, Sutton RM, Berg RA, Licht DJ, Gaynor JW, Kilbaugh TJ. Cerebral mitochondrial dysfunction associated with deep hypothermic circulatory arrest in neonatal swine. Eur J Cardiothorac Surg. 2018 Jul 1;54(1):162-168. PubMed Central PMCID: PMC7448940.
5. Volk LE, Mavroudis CD, Ko T, Hallowell T, Delso N, Roberts AL, Starr J, Landis W, Lin Y, Hefti M, Morgan RW, Melchior RW, Rosenthal TM, Chappell A, Fisher D, Dreher M, Licht DJ, Chen J, Gaynor JW, Mascio CE, Kilbaugh TJ. Increased cerebral mitochondrial dysfunction and reactive oxygen species with cardiopulmonary bypass. Eur J Cardiothorac Surg. 2021 Jun 14;59(6):1256-1264. PubMed PMID: 33367535; NIHMSID: NIHMS1674104.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

Certified by Kilbaugh, Todd in SciENcv on 2026-07-27 12:38:55

NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Kilbaugh, Todd

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-4959-3092

Position Title: Professor of Anesthesiology, Critical Care, and Pediatrics

Organization and Location: Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States

Personal Statement

I am a Professor of Anesthesiology, Critical Care, and Pediatrics at the Children's Hospital of Philadelphia (CHOP) and the University of Pennsylvania, Associate Chair of Research in the Department of Anesthesia and Critical Care Medicine at CHOP, Co-Director of the CHOP Resuscitation Science Center (RSC), William J. Greeley Endowed Chair in Pediatric Anesthesia and Critical Care Research, Timothy J. Raymond Endowed Chair in Pediatric Resuscitation Science, and the Director of the Anesthesia and Critical Care Mitochondrial Unit at the CHOP Center for Mitochondrial and Epigenomic Medicine (CMEM). I am also an attending intensivist and anesthesiologist at CHOP and am internationally recognized for my work defining mitochondrial bioenergetic dysfunction s a driver of brain injury after hypoxia-reperfusion.

This proposal addresses a question I believe is the central obstacle to neuroprotective therapy for hypoxic brain injury: more than Thiry Phase III trials have failed by targeting single nodes of the secondary-injury cascade, and I believe this reflects a failure to first define the injury's true control point. My laboratory has spent over a decade building the gyrencephalic swine asphyxial cardiac arrest platform that makes this question testable: a model my group has used to characterize the time course of cerebral mitochondrial bioenergetic failure after resuscitation and, more recently, to link that failure to neuroinflammatory and neuropathologic injury across a multi-day post-arrest window. This application draws directly on an existing 7-day post-arrest biobank generated by my team, together with our recent demonstration that mitochondrial reactive oxygen species drive HIF-1a stabilization, mitochondrial DNA release, and innate-immune activation in a manner reversible by mitochondrially targeted antioxidants. This work anchors the mechanistic premise of this proposal linking Complex I dysfunction to the two-signal microglial NLRP3 inflammasome response.

As Principal Investigator, I will oversee all aspects of the proposed work at the CHOP Resuscitation Science Center and CMEM, including asphyxia cardiac-arrest model implementation, the pre-registered analysis of our existing biobank, the focused acute cohort resolving mPTP verses BAK/BAX-mediated mitochondrial DNA release, and the pre-registered 2x2 pharmacological-probe factorial testing the necessity of Signal 1 (cyclosporine A) and Signal 2 (ketone monoester) in driving microglial pyroptosis. My laboratory's high-resolution respirometry, mitochondrial H_2O_2 flux, digital-PCR, and multiplex-immunofluorescence platforms, together with our established collaboration with Dr. Marco Hefti's neuropathology group at the University of Iowa, provide the infrastructure to resolve this causal architecture at the level of the individual animal and to adjudicate, for the first time, whether these two signals are non-redundant in vivo. I am well positioned to lead this work to conclusion and to translate its findings toward the broader set of hypoxic exposures: blast, altitude, hemorrhage, and cardiac arrest that the FY26 PRMRP Hypoxia Topic Area is intended to address.

Honors

2023	NINDS Faculty Mentor Award Finalist, NINDS
2023	Greeley Endowed Chair in Research, The Children's Hospital of Philadelphia
2020	Young Investigator Award, 48th Critical Care Congress, Society of Critical Care Medicine
2019	Star Research Achievement, 48th Critical Care Congress, Society of Critical Care Medicine
2018 - 2019	Faculty Honor Roll, Division of Critical Care Medicine, Department of Anesthesiology and Critical Care Medicine, Children's Hospital of Philadelphia
2017	Young Investigator Award, Resuscitation Science Symposium, American Heart Association
2017	C. Walton Lillehei MD, PhD Young Investigator Award, 31st European Association for Cardio-Thoracic Surgery
2017	Star Research Achievement Award, 46th Critical Care Congress, Society of Critical Care Medicine
2015	Joyce Massey Traumatic Brain Injury Summit Junior Investigator, University of Michigan
2014	Teaching Award, Department of Anesthesia and Critical Care Medicine, Children's Hospital of Philadelphia
2013	Research Citation Finalist, Neurotrauma Society
2011 - 2014	Faculty Honor Roll, Children's Hospital of Philadelphia

2009 - 2011	Anesthesiology and Critical Care Medicine Educator of the Year, Children's Hospital of Philadelphia
2005	Chief Resident, Department of Anesthesiology, University of Pennsylvania
2002	Excellence in Pediatric Research, LSU Health Science Center

Contributions to Science

1. Alterations in Mitochondrial Bioenergetics Following Acute Brain Injury: Defining the Paradigm of Mitochondrial Resuscitation in Pediatric Acute Brain Injury

   My scientific contributions include leading and contributing to studies that define how mitochondrial bioenergetic dysfunction evolves following acute brain injury in the immature brain. Using translational large animal models of pediatric traumatic brain injury and cardiac arrest, this work has characterized injury-induced disruptions in mitochondrial energy production, respiratory capacity, and metabolic flexibility that are not fully captured in small animal systems.

   A central aspect of this contribution is the development and application of novel methodologies to assess mitochondrial bioenergetics within the context of clinically relevant organ injury. These approaches enable high-resolution measurement of mitochondrial function across injury phases, providing insight into the temporal dynamics of primary and secondary mitochondrial failure following acute neurologic insults. By integrating bioenergetic profiling with physiologic and outcome-based measures, this work has helped establish mitochondrial dysfunction as a key determinant of injury severity and recovery potential in pediatric brain injury.

   Collectively, these studies have contributed to the emerging paradigm of "mitochondrial resuscitation," reframing post-injury care to include restoration and preservation of mitochondrial function as a therapeutic target. This body of work informs the design of pre-clinical intervention studies and supports the translation of mitochondrial-directed therapies aimed at improving neurologic outcomes following pediatric acute brain injury.

2. Mitochondria and Mechanisms of Disease

   My scientific contributions center on advancing the understanding of mitochondrial dysfunction as a fundamental mechanism underlying pediatric disease. As a member of the Center for Mitochondrial and Epigenomic Medicine at the Children's Hospital of Philadelphia, I work collaboratively with investigators across disciplines to study mitochondrial biology in both health and disease, with a particular focus on how disruptions in mitochondrial function contribute to disease pathogenesis and clinical outcomes in children.

   This work addresses both primary mitochondrial disorders and secondary mitochondrial dysfunction arising from acute injury, critical illness, or metabolic stress. By integrating mechanistic studies with clinically relevant models and patient-centered research approaches, these efforts aim to define how mitochondrial impairments influence cellular energetics, stress responses, and recovery trajectories. Emphasis is placed on identifying shared and disease-specific mitochondrial pathways that may serve as biomarkers of disease severity or targets for therapeutic intervention.

   Through multidisciplinary collaboration and translational research, this contribution supports the development of strategies to improve diagnosis, risk stratification, and treatment of mitochondrial-related diseases in pediatric populations. Collectively, this work underscores the central role of mitochondrial health in pediatric disease mechanisms and highlights opportunities to translate fundamental mitochondrial science into clinically meaningful advances for children.

3. Large Animal Model Development for Objective Metrics in Acute Brain Injury Diagnosis, Outcomes, and Pre-clinical Trial Design

   My scientific contributions focus on the development and implementation of translational large animal models of acute brain injury designed to bridge the gap between rodent studies and human clinical trials. Recognizing the limitations of small animal models in predicting clinical efficacy, this work emphasizes high-fidelity, clinically relevant injury platforms that more closely replicate human neurophysiology, injury mechanisms, and standards of care.

These large animal models incorporate real-world clinical management strategies, including intensive care–level monitoring and supportive interventions, enabling the evaluation of therapeutic candidates under conditions that mirror human acute care. A central component of this contribution is the development and validation of objective, minimally invasive and non-invasive diagnostic and outcome measures. These metrics are designed to quantify injury severity, track longitudinal recovery, and assess pharmacodynamic responses to investigational therapies with greater precision and reproducibility than traditional behavioral or histologic endpoints alone.

By integrating clinically translatable biomarkers and physiologic monitoring tools into pre-clinical trial design, this work supports more rigorous efficacy assessment and improves the predictive value of pre-clinical studies. Collectively, these efforts advance the design of large animal pre-clinical trials that better inform decisions, optimize therapeutic dosing strategies, and reduce translational failure as interventions progress from laboratory discovery to human clinical testing.

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