BIOGRAPHICAL SKETCH

NAME: Eltzschig, Holger K

eRA COMMONS USERNAME: eltzschig.h

POSITION TITLE: Professor of Anesthesiology

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)*	MM/YY	FIELD OF STUDY
University of Tübingen, Germany	MD, PhD	06/96	Medicine
University of Tübingen, Germany	Residency	07/96-06/98	Anesthesiology
Harvard Medical School Boston, MA	Internship, Residency	07/98-06/02	Anesthesiology
Harvard Medical School, Boston, MA	Fellowship	07/02-06/03	Cardiac Anesthesia
Harvard Medical School. Boston, MA	Post Doc	01/02-10/04	Vascular Biology

A. Personal Statement

As a physician-scientist trained in anesthesiology, cardiac anesthesia, and critical care medicine, my research has been funded by the NIH over many years to study perioperative organ injury. Many surgical patients experience acute organ injury in the perioperative period, leading to morbidity and mortality (1-5). Our research laboratory is interested in endogenous adaptive pathways that are controlled by hypoxia-inducible factors (HIFs). We have shown that activation of hypoxia-signaling during inflammatory conditions represents an endogenous adaptive pathway that can be targeted therapeutically. We have applied these molecular concepts to diseases that are important to the field of perioperative medicine, including acute kidney injury, myocardial or hepatic ischemia, intestinal inflammation and acute lung injury. Our studies point towards an adaptive role for HIFs, for example by attenuating hypoxia-associated inflammation or promoting ischemia tolerance. It is our hope that these studies will contribute to novel pharmacologic approaches to prevent or treat acute organ injury. For example, we are currently performing a multi-center, randomized, placebo-controlled clinical trial in ARDS patients using the HIF activator vadadustat for ARDS prevention or therapy.

My research laboratory is particularly devoted to research training and mentoring. Many of my previous trainees became independently funded investigators or obtained academic leadership roles.

Citations:

1.) **Eltzschig, H.K.**, and P. Carmeliet. 2011. Hypoxia and Inflammation. ***N Engl J Med*** 364:656-665 (PMID 21323543, PMCID: PMC3930928).
2.) **Eltzschig, H.K.**, M.V. Sitkovsky, and S.C. Robson. 2012. Purinergic signaling during inflammation. ***N Engl J Med*** 367:2322-2333 (PMID: 23534573).
3.) Idzko, M., Ferrari, D., and **Eltzschig, H.K.** 2014. Nucleotide signalling during inflammation. ***Nature*** 509:310-317 (PMID: 24828189 PMCID: PMC4222675).
4.) Ruan W, Yuan X, **Eltzschig HK**. Circadian rhythm as a therapeutic target. Circadian rhythm as a therapeutic target. ***Nat Rev Drug Discov.*** 2021;20(4):287-307 (PMID: 33589815 and PMCID: PMCID: PMC8525418).

Pending, ongoing and recently completed projects that I would like to highlight include:

T32GM135118 (PI: Eltzschig; Multi-PI: Ju) TBD (pending)
NIGMS
Research Training of Anesthesiology Physician-Scientists

Parker B. Francis Fellowship (PI: Yuan; Mentor: Eltzschig) 07/01/2020 – 06/30/2023
Parker B. Francis Foundation
microRNA-147 Controls the Lipopolysaccharide-Induced Inflammatory Response in Macrophages

CA-622265 (PI: Yuan; Mentor: Eltzschig) 07/01/2019 – 06/30/2021
American Lung Association
The role of miR-147 in acute respiratory distress syndrome

T32GM120011 (PI: Dessauer; Mentee: Nathaniel Berg; Mentor: Eltzschig) 11/01/2018 – 06/30/2021
NIH/NIGMS
Training Interdisciplinary Pharmacology Scientists

R01HL154720 (PI: Eltzschig) 09/01/2020 – 11/30/2024
NIH/NHLBI
MicroRNA miR-147 Dampens Alveolar Epithelial Inflammation during ARDS

W81XWH2110032 (PI: Eltzschig) 01/01/2021 – 12/31/2022
Department of Defense
A randomized, phase 2 clinical trial of HIF-activator Vadadustat for prevention or treatment of ARDS

1R01DK122796-01A1 (PI: Ju; Multi-PI: Eltzschig) 05/11/2020 – 03/31/2024
NIH-NIDDK
Targeting microRNA miR-122 for the treatment of perioperative liver injury

1R01HL133900-01 (PI: Eltzschig) 06/08/2017 – 03/31/2022
NIH-NHLBI
MicroRNA Shuttling during Acute Respiratory Distress

R01HL155950 (PI: Yuan; Co-I: Eltzschig) 02/01/2022 – 01/31/2027
NIH/NHLBI
Targeting Myeloid Dependent MicroRNAs in Acute Respiratory Distress Syndrome

75N91019D00021 (PI: Brown, Bailey, McAllister; Co-I: Eltzschig) 09/21/2020 – 09/14/2023
NCI/National Institutes of Health
Preclinical Testing of CD73 Inhibitors for Pancreatic Cancer Immunoprevention

R21CA249924 (PI: Bailey; Co-I: Eltzschig) 01/01/2021 – 12/31/2022
NIH
Defining the role of Mst1/Mst2 in regulating metabolic alterations in Ras driven NSCLC

1R01CA237327 (PI: Lee; Co-I: Eltzschig) 02/06/2020 – 01/31/2025
NIH/NCI
PEA15 in Development of Liver cancer and Its Therapeutic Implication

1R01DK109574 (PI: Ju; Multi-PI: Eltzschig) 09/21/2016– 06/30/2021
NIH-NIDDK
Hypoxia-Inducible Factors in Acetaminophen-Induced Injury

5R01HL109233-08 (PI: Herzog, Co-PI: Eltzschig) 07/01/2016 – 04/30/2020
NIH-NHLBI
Neuronally Active Proteins in IPF

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2017 - today Professor and Tenure, Department of Anesthesiology, McGovern Medical School, Houston
2016 - today Chairman, Department of Anesthesiology, McGovern Medical School, Houston
2016 - today Associate Vice President for Translational Research, McGovern Medical School, Houston
2016 - today Director, Center for Perioperative Medicine, McGovern Medical School, UTHealth, Houston
2011 - 2013 Vice Chair for Research, Department of Anesthesiology, University of Colorado, Denver
2010 - 2016 Professor and Tenure, Department of Anesthesiology, University of Colorado, Denver
2007 - 2010 Associate Professor, Department of Anesthesiology, University of Colorado, Denver
2004 - 2007 Assistant Professor, Department of Anesthesiology, University of Tübingen, Germany
2002 - 2004 Post Doc (Vascular Biology) Brigham and Women's Hospital, Harvard Medical School, Boston
2002 - 2003 Fellowship, Cardiac Anesth. Brigham and Women's Hospital, Harvard Medical School, Boston
1999 - 2002 Residency, Anesthesiology Brigham and Women's Hospital, Harvard Medical School, Boston
1998 - 1999 Internship, Cardiac Surgery Brigham and Women's Hospital, Harvard Medical School, Boston

Other Experience/Activities and Professional Memberships

2021 - Elected Member, Association of American Physicians (AAP)
2020 - Member, Academy of Research Mentors, Foundation for Anesthesia Education and Research (FAER)
2019 - John P. and Kathrine G. McGovern Distinguished University Chair
2019 - Franz-Koehler Inflammation Award, Berlin, Germany
2017 - John P. and Kathrine G. McGovern Distinguished Chair
2016 - today: Member, NIH Study Section, Surgery, Anesthesia and Trauma (SAT)
2015 - *John Hedley-Whyte Lecture: The Hypoxia-Inflammation Link*, Harvard Medical School, Boston
2013 - today: Associate Editor *Anesthesiology*
2012 - 2017: Associate Editor *The Journal of Molecular Medicine*
2011 - Elected Member, American Society of Clinical Investigation (ASCI)
2011 - Heinrich-Dräger Research Award for Critical Care Medicine, Hamburg, Germany
2010 - 2015: Academic Editor *PLoS One*
2010 - 2015 Associate Editor, 2015 - 2018 Section Editor *The Journal of Immunology*
2009 - Member, Association of University Anesthesiologists
2007 - Karl-Thomas Research Award for Anesthesiology and Critical Care Medicine, Hamburg
2006 - Hanse Research Award for Critical Care Medicine, Bremen, Germany
2006 - Heinrich - Dräger Research Award for Critical Care Medicine, Leipzig, Germany
2004 - Hanse Research Award for Critical Care Medicine, Bremen, Germany
2004 - Habilitation, Eberhard Karls University of Tübingen, Germany
2003 - *Thomas Smith Lecture: Nucleotide Metabolism and Signaling*, Harvard Medical School, Boston
1992 - Member of the German National Scholarship Foundation

C. Contributions to Science

1. **Hypoxia-inducible transcription factors during myocardial ischemia and reperfusion injury.** Studies from our laboratory have shown that myocardial ischemia and reperfusion injury is associated with profound changes in metabolic supply and demand leading up to the stabilization of hypoxia-inducible transcription factors. Our studies were among the first to identify a link between circadian rhythm regulation and hypoxia signaling during ischemia and reperfusion injury of the heart.

    a. Eckle T, Hartmann K, Bonney S, Reithel S, Mittelbronn M, Walker LA, Lowes BD, Han J, Borchers CH, Buttrick PM, Kominsky DJ, Colgan SP, **Eltzschig HK**. Adora2b-elicited per2 stabilization promotes a HIF-dependent metabolic switch crucial for myocardial adaptation to ischemia. ***Nat Med.*** 2012;18(5):774-82 (PMID: 22504483, PMCID: PMC3378044).
    b. **Eltzschig, H.K.**, Bratton, D.L., and Colgan, S.P. 2014. Targeting hypoxia signalling for the treatment of ischaemic and inflammatory diseases. ***Nat Rev Drug Discov*** 13:852-869 (PMID: 25359381 PMCID: PMC4259899)

c. Koeppen M, Lee JW, Seo SW, Brodsky KS, Kreth S, Yang IV, Buttrick PM, Eckle T, **Eltzschig HK**. HIF2A-dependent induction of amphiregulin dampens myocardial ischemia-reperfusion injury. ***Nat Commun.*** 2018;9(1):816 (PMID: 29483579 PMCID: PMC5827027).

d. Li J, Conrad C, Mills TW, Berg NK, Kim B, Ruan W, Lee JW, Zhang X, Yuan X, and **Eltzschig HK**. PMN-derived netrin-1 attenuates cardiac ischemia-reperfusion injury via myeloid ADORA2B signaling. ***J Exp Med***. 2021;218(6):e20210008 (PMID: 33891683 PMCID: PMC8077173).

2. **Identification of HIFs as a therapeutic target to dampen ischemic tissue injury or harmful inflammation.** Our work has examined the functional role of hypoxia-dependent signaling during ischemia or inflammation, and indicates that tissue-specific functions of HIFs are geared towards dampening uncontrolled inflammation. These studies also identified genes that are under the control of HIFs and can be targeted to promote the resolution of inflammation as well as their to ischemic tissue injury resistance.

a. Eckle T, Köhler D, Lehmann R, El Kasmi K, **Eltzschig HK**. Hypoxia-inducible factor-1 is central to cardioprotection: a new paradigm for ischemic preconditioning. ***Circulation.*** 2008;118(2):166-75. (PMID: 18591435).

b. **Eltzschig HK**, Eckle T. Ischemia and reperfusion--from mechanism to translation. ***Nat Med.*** 2011;17(11):1391-1401 (PMID:22064429, PMCID: PMC3886192; currently over 2500 citations).

c. Clambey ET, McNamee EN, Westrich JA, Glover LE, Campbell EL, Jedlicka P, de Zoeten EF, Cambier JC, Stenmark KR, Colgan SP, **Eltzschig HK**. Hypoxia-inducible factor-1 alpha-dependent induction of foxp3 drives regulatory t-cell abundance and function during inflammatory hypoxia of the mucosa. ***Proc Natl Acad Sci U S A.*** 2012;109(41):E2784-93 (PMID: 22988108 PMCID: 3478644).

d. Gao RY, Wang M, Liu Q, Feng D, Wen Y, Xia Y, Colgan SP, **Eltzschig HK**, Ju C. Hypoxia-Inducible Factor-2α Reprograms Liver Macrophages to Protect Against Acute Liver Injury Through the Production of Interleukin-6. ***Hepatology.*** 2020; 71(6):2105-2117 (PMID: 31529728; PMCID: PMC7075728).

3. **Hypoxia-inducible transcription factor during acute respiratory distress syndrome (ARDS).** Research on the control of alveolar-epithelial inflammation led us to the surprising discovery that hypoxia-inducible transcription factor HIF1A is stabilized during conditions of lung inflammation. Particularly alveolar-epithelial HIF1A is involved in adapting the alveolar epithelium to injurious or inflammatory conditions, and can be targeted for ARDS treatment.

a. Eckle T, Brodsky K, Bonney M, Packard T, Han J, Borchers CH, Mariani TJ, Kominsky DJ, Mittelbronn M, **Eltzschig HK**. HIF1A reduces acute lung injury by optimizing carbohydrate metabolism in the alveolar epithelium. ***PLoS Biol.*** 2013;11(9):e1001665 (PMID: 24086109, PMCID: PMC3782424).

b. Gao R, Peng X, Perry C, Sun H, Ntokou A, Ryu C, Gomez JL, Reeves BC, Walia A, Kaminski N, Neumark N, Ishikawa G, Black KE, Hariri LP, Moore MW, Gulati M, Homer RJ, Greif DM, **Eltzschig HK**, Herzog EL. Macrophage-derived netrin-1 drives adrenergic nerve-associated lung fibrosis. ***J Clin Invest.*** 2021;131(1):e136542 (PMID: 33393489; PMCID: PMC7773383).

c. Berg NK, Li J, Kim B, Mills T, Pei G, Zhao Z, Li X, Zhang X, Ruan W, **Eltzschig HK**, Yuan X. Hypoxia-inducible factor-dependent induction of myeloid-derived netrin-1 attenuates natural killer cell infiltration during endotoxin-induced lung injury. ***FASEB J.*** 2021;35(4):e21334 (PMID: 33715200 PMCID: PMC8251729).

d. Vohwinkel CU, Coit EJ, Burns N, Elajaili H, Hernandez-Saavedra D, Yuan X, Eckle T, Nozik E, Tuder RM, **Eltzschig HK**. Targeting alveolar-specific succinate dehydrogenase A attenuates pulmonary inflammation during acute lung injury. ***FASEB J.*** 2021;35:e21468 (PMID: 33687752 PMCID: PMC8250206).

4. **Roles of microRNAs in attenuating mucosal or alveolar inflammation during ARDS.** Several of our studies have implicated functional roles of microRNAs in attenuating harmful inflammatory responses by repressing pro-inflammatory target genes. These studies implicate miRNAs as therapeutic targets to prevent or treat alveolar inflammation during ARDS or organ injury. They also demonstrate that HIFs can play a functional role in inducing tissue-protective miRNAs.

a. Neudecker V, Brodsky KS, Clambey ET, Schmidt EP, Packard TA, Davenport B, Standiford TJ, Weng T, Fletcher AA, Barthel L, Masterson JC, Furuta GT, Cai C, Blackburn MR, Ginde AA, Graner MW, Janssen WJ, Zemans RL, Evans CM, Burnham EL, Homann D, Moss M, Kreth S, Zacharowski K, Henson PM, **Eltzschig HK**. Neutrophil transfer of *miR-223* to lung epithelial cells dampens acute lung injury in mice. ***Sci Transl Med.*** 2017;9(408)eaah5360 (PMID: 28931657 PMCID: PMC5842431).
b. Neudecker V, Haneklaus M, Jensen O, Khailova L, Masterson JC, Tye H, Biette K, Jedlicka P, Brodsky KS, Gerich ME, Mack M, Robertson AAB, Cooper MA, Furuta GT, Dinarello CA, O'Neill LA, **Eltzschig HK**, Masters SL, McNamee EN. Myeloid-derived miR-223 regulates intestinal inflammation via repression of the NLRP3 inflammasome. ***J Exp Med.*** 2017;214(6):1737-1752 (PMID: 28487310 PMCID: PMC5460990).
c. Lee TJ, Yuan X, Kerr K, Yoo JY, Kim DH, Kaur B, **Eltzschig HK**. Strategies to Modulate MicroRNA Functions for the Treatment of Cancer or Organ Injury. ***Pharmacol Rev.*** 2020;72(3):639-667 (PMID: 32554488 PMCID: PMC7300323).
d. Ju C, Wang M, Tak E, Kim B, Emontzpohl C, Yang Y, Yuan X, Kutay H, Liang Y, Hall DR, Dar WA, Bynon JS, Carmeliet P, Ghoshal K, **Eltzschig HK**. Hypoxia-inducible factor-1α-dependent induction of miR122 enhances hepatic ischemia tolerance. ***J Clin Invest.*** 2021;131(7):e140300 (PMID:33792566; PMCID: PMC8011886).

5. **Hypoxia-control of extracellular adenosine signaling.** Our research work has provided fundamental insight into how conditions of hypoxia – such as occur during alveolar inflammation or ischemia and reperfusion injury – influence purinergic signaling events. Our findings highlight that extracellular adenosine signaling functions as an endogenous feedback mechanism to dampen mucosal inflammation.

a. Rosenberger P, Schwab JM, Mirakaj V, Masekowsky E, Mager A, Morote-Garcia JC, Unertl K, **Eltzschig HK**. Hypoxia-inducible factor-dependent induction of netrin-1 dampens inflammation caused by hypoxia. ***Nat Immunol.*** 2009;10(2):195-202 (PMID: 19122655).
b. Aherne CM, Saeedi B, Collins CB, Masterson JC, McNamee EN, Perrenoud L, Rapp CR, Curtis VF, Bayless A, Fletcher A, Glover LE, Evans CM, Jedlicka P, Furuta GT, de Zoeten EF, Colgan SP, **Eltzschig HK**. Epithelial-specific A2B adenosine receptor signaling protects the colonic epithelial barrier during acute colitis. ***Mucosal Immunol.*** 2015;8(6):1324-38. (PMID: 25850656; PMCID: PMC4598274).
c. Hoegl S, Brodsky KS, Blackburn MR, Karmouty-Quintana H, Zwissler B, **Eltzschig HK**. Alveolar Epithelial A2B Adenosine Receptors in Pulmonary Protection during Acute Lung Injury. ***J Immunol.*** 2015;195(4):1815-24. (PMID: 26188061; PMCID: PMC4530072).
d. Aherne CM, Collins CB, Rapp CR, Olli KE, Perrenoud L, Jedlicka P, Bowser JL, Mills TW, Karmouty-Quintana H, Blackburn MR, **Eltzschig HK**. Coordination of ENT2-dependent adenosine transport and signaling dampens mucosal inflammation. ***JCI Insight.*** 2018;3(20)e121521. (PMID: 30333323; PMCID: PMC6237472).

Complete List of Published Work in MyBibliography
(currently over 300 peer reviewed publications; h-index 89; 29,675 citations):

https://www.ncbi.nlm.nih.gov/sites/myncbi/holger.eltzschig.1/bibliography/42995756/public/?sortby=pubDate&sdirection=descending