**KALEV FREEMAN**

## CURRICULUM VITAE

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| Position: |  | Associate Professor with Tenure |
|  |  | Department of Surgery |
|  |  |  |
| Address: |  | Room E301 Given Building, 89 Beaumont Ave |
|  |  | Department of Surgery |
|  |  | The Robert Larner, M.D. College of Medicine |
|  |  | University of Vermont |
|  |  | Burlington, VT 05405 |
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|  |  | website: http://www.med.uvm.edu/freemanlab |

**EDUCATION**

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| **Year** | **Institution** | **Degree** | **Area of Degree** |
| 2004-2007 | Boston University, Boston, MA | Residency | Emergency Medicine |
| 2003-2004 | University of Colorado, Denver, CO | Internship | Surgery |
| 1995-2003 | University of Colorado, Denver, CO | M.D. | Medicine |
| 1995-2000 | University of Colorado, Boulder, CO | Ph.D. | Molecular Biology |
| 1991-1995 | University of Michigan, Ann Arbor, MI | B.S. | Cellular and Molecular Biology |

**LICENSES, CERTIFICATION**

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| **Years** | **License/Certification** |
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| 2011-Present  2010-Present | Fellow of the American College of Emergency Physicians (FACEP)  Diplomat, American Board of Emergency Medicine, Board Certification |
| 2007-Present  2005-Present | Medical License, State of Vermont  Advanced Cardiac Life Support, Instructor Certification |
| 2005-Present | Pediatric Advanced Life Support, Instructor Certification |
| 2004-Present | Advanced Cardiac Life Support, Certification |
| 2004-Present | Pediatric Advanced Life Support, Certification |
| 2004-2007 | Medical License, State of Massachusetts |
| 2004-Present | Advanced Trauma Life Support, Certification |
| 2003-Present | Practitioner License, DEA |
| 2003-2004 | Medical License, State of Colorado |

**FACULTY POSITIONS HELD**

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| **Years** | **Institution** | **Academic Title** | **Department** |
| 2019-Present | University of Vermont,  Larner College of Medicine | Associate Professor  with Tenure | Surgery and Pharmacology |
| 2012-2019 | University of Vermont,  Larner College of Medicine | Assistant Professor (Secondary Appointment) | Pharmacology |
| 2011-2019 | University of Vermont,  Larner College of Medicine | Assistant Professor  Tenure Track | Surgery |
| 2007-2011 | University of Vermont,  Larner College of Medicine | Assistant Professor  Research Track | Surgery |

**OTHER POSITIONS AND MAJOR ADMINISTRATIVE POSITIONS HELD**

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| **Years** | **Location/Program Name** | **Role** |
| 2007-Present | University of Vermont Medical Center  Emergency Services | Attending Physician |

**HONORS AND AWARDS**

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| **Year** | **Name of Award** |
| 1993 | All Big-Ten Scholar-Athlete Academic Award, University of Michigan, Ann Arbor, MI |
| 1993 | Regional Finalist, Rhodes Scholarship, University of Michigan, Ann Arbor, MI |
| 1994 | Trainee Investigator Award, Clinical Research Meeting, San Diego, CA |
| 1994 | All Big-Ten Scholar-Athlete Academic Award, University of Michigan, Ann Arbor, MI |
| 1995 | All Big-Ten Scholar-Athlete Academic Award, University of Michigan, Ann Arbor, MI |
| 1995-2003 | NIH Fellowship, Medical Scientist Training Program, University of Colorado, Denver,  CO |
| 1997 | Excellence in Research award, Western Medical Student Research Forum, Western Medical Student Research Association, Carmel, CA |
| 1998 | Beverly Sears Student Research Award, University of Colorado, Boulder, CO |
| 2006 | Best Oral Presentation, 10th Annual New England Regional Social Academic Emergency Medical (SAEM) Conference, Boston, MA |
| 2007 | David A. Frommer Award for Academic Excellence, Boston University, Boston, MA |
| 2010 | James E. Demeules Surgical Research Award, University of Vermont, Burlington, VT |
| 2011 | James E. Demeules Surgical Research Award, University of Vermont, Burlington, VT |
| 2012  2014  2015 | Junior Researcher Award, University of Vermont Medical Group, Burlington, VT  Fletcher Allen Health Care’s Recognition Program, Faces of Fletcher Allen, Burlington, VT  Safety Partner Award, University of Vermont Risk Management and Safety, Burlington, VT |

**KEYWORDS/AREAS OF INTEREST**

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| Surgery; Emergency Medicine; Wounds and Injuries; Brain Injuries, Traumatic; Hemostasis; Thrombosis; Inflammation; Blood Vessels; Vasodilation; Endothelium; Ion Channels. |

**SUMMARY OF PROFESSIONAL ACTIVITIES**

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| I am the Principal Investigator leading an NIH-funded research program that works to improve outcomes for victims of trauma. Our work is addressing one of the most pressing problems in shock and trauma: the acute endotheliopathy which drives multiorgan failure through the combination of coagulopathy, barrier dysfunction, and disrupted regulation of microvascular blood flow. We employ cutting-edge vascular biology, electrophysiology, and immunobiology methods in animal models and bio samples from human subjects. By understanding the vascular responses to injury, we can identify and test therapeutic strategies that will ultimately benefit trauma patients. |

**SUMMARY OF ACCOMPLISHMENTS**

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| 1. Adrenergic signaling, cardiomyopathy and exercise physiology. My Ph.D. work in molecular biology, with Dr. Leslie Leinwand, lead to novel insights into the mechanisms by which adrenergic receptor-mediated signaling pathways impact exercise performance and cardiomyopathy in humans and model systems. Most significantly, we found that mice harboring a myosin heavy chain mutation show evidence of beta-adrenergic dysfunction during development of cardiomyopathy. We crossbred the animals with other strains that overexpressed the beta-2 adrenergic receptor in the heart, expressed a beta-adrenergic receptor kinase inhibitor in the heart, or were genetically ablated for phospholamban. All of these perturbations increased cardiac contractility, but as the animals aged, phospholamban ablation rescued the cardiomyopathy, whereas adrenergic receptor overexpression proved lethal. Because phospholamban acts to inhibit the sarcoplasmic reticulum Ca2+ ATPase, our results pointed to Ca2+ cycling as a potential therapeutic target in cardiomyopathy. This early work provided me with the opportunity to interact with and co-author papers with eminent scientists including Dr. Robert Lefkowitz (Nobel Prize in Chemistry, 2012), established my expertise in cell signaling, and provided the foundation for me to develop my independent research program. 2. **Freeman K**, Farrow S, Schmaier A, Freedman R, Schork T, and Lockette W. Genetic polymorphism of the α2 -adrenergic receptor is associated with increased platelet aggregation, baroreceptor sensitivity, and salt excretion in normotensive humans, The American Journal of Hypertension (1995, 8:863-869). PMID: 8541000 3. **Freeman K**, Lerman I, Kranias EG, Bohlmeyer T, Bristow MR, Lefkowitz RJ, Iaccarino G, Koch WJ, Leinwand LA. Alterations in cardiac adrenergic signaling and calcium cycling have markedly different effects on the progression of hypertrophic cardiomyopathy, The Journal of Clinical Investigation (2001, 107: 967-974). PMID: 11306600 4. **Freeman K**, Colon-Rivera C, Olsson MC, Moore RL, Weinberger HD, Grupp IL, Vikstrom K, Iaccarino G, Koch WJ, Leinwand LA. Progression from hypertrophic to dilated cardiomyopathy in mice that express a mutant myosin transgene, The American Journal of Physiology (2001, 280: H151-H159). PMID: 11123229 5. Lerman I, Harrison B, **Freeman K**, Hewett TE, Allen DL, Robbins J, Leinwand LA. Genetic variability in forced and voluntary endurance exercise performance in seven inbred mouse strains, The Journal of Applied Physiology(2002, 92: 2245-2255). PMID: 12015333 6. Identifying theinteractions between DAMPs and cell membranesin acute endotheliopathy**.**   We discovered that a particular damage-associated molecular pattern (DAMP), extracellular histones, provoke massive Ca2+ transients in intact human and mouse endothelium, which, paradoxically, do not activate endothelial nitric oxide synthase, but instead, disrupt endothelial-dependent vasodilation. In other experiments, we used electrophysiology, pressure myography, and intravital imaging approaches to understand how brain injury alters vascular function. We showed that abnormal function of a specific lipid-gated subset of potassium channels, the inward-rectifier (Kir2.1) channel, on cerebrovascular endothelium prevents the cells from sensing extracellular K+ and disrupts the capillary-to-arterial electrical signaling needed for control of local blood flow. We recently found that addition of PIP2 to rescues Kir2.1 channel function in endothelial cells after a TBI. These works established that trauma produces sustained deficits on endothelial functions and evidence that histones are an important DAMP in acute endotheliopathy.   * 1. Sackheim AM, Villalba N, Sancho M, Harraz OF, Bonev AD, D’Alessandro AD, Nemkov T, Nelson MT, and **Freeman K**. Traumatic brain injury impairs systemic vascular function through altered lipid metabolism and disruption of inward-rectifier potassium (kir2.1) channels. Function, 2021 *(in press*).   2. Mughal A, Sackheim AM, Sancho M, Longden TA, Russell S, Lockette W, Nelson MT, **Freeman K.** Impaired capillary-to-arteriolar electrical signaling after traumatic brain injury. Journal of Cerebral Blood Flow and Metabolism. (2020: Oct 13; online ahead of print). PMID: 33050826.   3. Collier DM, Villalba N, Sackheim AM, Bonev AD, Miller ZD, Moore JS, Shui B, Lee JC, Lee FK, Reining S, Kotlikoff MI, Nelson MT, **Freeman K**. Extracellular histones induce calcium signals in the endothelium of resistance-sized mesenteric arteries and cause loss of endothelium-dependent dilation. American Journal of Physiology Heart Circulatory Physiology. (2019: Jun 1;316(6):H1309-H1322.) PMID: 30848676.  1. Vascularcell signal responses to histone and other DAMPsresulting in severe injury**.** Understanding the vascular responses to acute insults such as shock and trauma is a complex physiological problem, involving multiple organ systems, with important public health significance. We use animal models of isolated traumatic brain injury as a paradigm to examine effects of acute sterile inflammation on remote microvascular tissue beds. Our recent work has shed light on mechanisms of vascular injury including changes in reactive oxygen species, endothelial nitric oxide production, and calcium signals. These results have demonstrated basic mechanisms of sterile inflammation after trauma and suggest novel targets for endothelial protection during inflammation.    1. Haines L, Villalba N, Sackheim AM, Collier DM, **Freeman K**. Myogenic tone contributes to the regulation of permeability in mesenteric microvessels. Microvascular Research. 2019 Apr 8. PMID: 30974113.    2. Villalba N, Sackheim A, Nunez I, Hill-Eubanks D, Nelson MT, Wellman GC, **Freeman K.** Traumatic brain injury causes endothelial dysfunction in the systemic microcirculation through arginase-1-dependent uncoupling of endothelial nitric oxide synthase. Journal of Neurotrauma. (2017; Jan 1;34(1):192-203.) PMID: 26757855.    3. Villalba N, Sonkusare SK, Longden TA, Tran TL, Nelson MT, Wellman GC, **Freeman K.** Traumatic brain injury disrupts cerebrovascular tone through endothelial iNOS expression and nitric oxide gain-of-function. Journal of the American Heart Association (2014; 2014 Dec 19;3(6): e001474).PMID: 25527626. 2. Reactions to DAMPs leading to blood clotting: Mechanisms of trauma-induced coagulopathy. Trauma surgeons have long struggled to manage the acute trauma-induced coagulopathy which occurs in as many as one-fourth of patients after severe multi-system trauma. Refractory coagulopathy prevents optimal surgical management and can lead to death from otherwise survivable injuries. Building on my experience as a board-certified Emergency Physician, I have led or collaborated on several studies of trauma patients, including the NHLBI Trans-Agency Consortium for Trauma-Induced Coagulopathy (TACTIC) program. Our efforts have provided novel insights into the mechanisms driving coagulopathy in trauma and sterile inflammation.    1. Coleman JR, Moore EE, **Freeman K**, Cohen MJ , Samuels JM, Hansen K. Actin is associated with tissue injury in trauma patients and produces a hypercoagulable profile. Journal of Trauma and Acute Care Surgery. 2020 Jul; 89(1):87-95. PMID: 32574484 .    2. Dow N, Coleman JR, Moore H, Osborn Z, Sackheim A, Hennig G, Butenas S, Nelson MT, Moore EE, **Freeman K**. Dense and dangerous: the tissue plasminogen activator (t-PA)-resistant fibrinolysis shutdown phenotype is due to abnormal fibrin polymerization. Journal of Trauma and Acute Care Surgery. 2020 Feb;88(2):258-265. PMID: 31999655    3. Prior SM, Mann KG, **Freeman K,** Butenas S. Continuous thrombin generation in whole blood: new applications for assessing activators and inhibitors of coagulation, Analytical Biochemistry, 2018 Jun 15;551:19-25. PMID: 29746819. 3. Clinical research: Improving emergency care of trauma patients. In the chaotic environment of a busy emergency department, there is a critical need for robust diagnostic tests and clinical algorithms that help providers manage patients quickly and safely. As a board-certified Emergency Physician, I have served as PI or co-I on clinical trials of emergency department-based diagnostic platforms and clinical algorithms that have improved care for trauma patients. I am also engaged in the NIH-funded (UM1/ NHLBI) Trans-Agency Consortium for Trauma-Induced Coagulopathy (TACTIC) program, which is working to elucidate the mechanisms driving trauma-induced coagulopathy.    1. Mann KG, **Freeman K**. TACTIC: Trans-Agency Consortium for Trauma-Induced Coagulopathy. Journal of Thrombosis and Haemostasis. (2015; 13:S63-71). PMID: 26149052    2. Neal MD, Moore HB, Moore EE, **Freeman K**, Cohen MJ, Sperry JL, Zuckerbraun BS, Park MS; TACTIC Investigators. Clinical assessment of trauma-induced coagulopathy and its contribution to postinjury mortality: A TACTIC proposal. Journal of Trauma and Acute Care Surgery. 2015;79(3):490-492. PMID: 26307885    3. Watts R, Thomas A, Filippi CG, Nickerson JP, **Freeman K**. Potholes and molehills: Bias in diagnostic performance of diffusion tensor imaging in concussion. Radiology (2014; 272(1):217-23). PMID: 24635677. |

**PROFESSIONAL SERVICE**

COLLEGE SERVICES

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| **Years** | **Service Committee** | **Role** |
| 2017-Present | Medical Student Research Committee | Member |
| 2018-Present | Physician Scientist Working Group | Member |
| 2018-2019 | Medical School Admissions | Interviewer |
| 2019-2020 | Faculty Search, Tenure Track Position, Department of Pharmacology | Member |
| 2021-present | Faculty Search, Tenure Track Position, Department of Pharmacology | Member |

MEDICAL CENTER SERVICE

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| **Years** | **Service Committee** | **Role** |
| 2014-2016 | Jeffords Institute for Quality, Concussion Care Committee | Member |

UNIVERSITY SERVICE

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| **Years** | **Service Committee** | **Role** |
| 2008-2011 | Committee on Human Subjects Research in Medical Sciences (Institutional Review Board) | Standing Member |
| 2012-2015 | Committee on Human Subjects Research in Medical Sciences (Institutional Review Board) | Alternate Member |
| 2015-2019 | Committee on Human Subjects, Research in Medical Sciences (Institutional Review Board) | Standing Member |

NATIONAL INSTITUTE OF HEALTH

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| **Years** | **Committee** | **Role** |
| 2020  2021 | NHLBI Working Group, Mechanistic Studies Center, ACTIV-4 Initiative  Integrative Vascular Physiology and Pathology Study Section | Committee Member  Reviewer (Ad Hoc) |
| 2021 | Surgery Anesthesiology and Trauma Study Section | Reviewer (Ad Hoc) |

GOVERNMENT

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| **Years** | **Service Committee** | **Role** |
| 2015-Present | Physician Representative, Vermont Alcohol and Drug Abuse Council | Gubernatorial Appointment |

SOCIETY MEMBERSHIPS

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| **Years** | **Society** | **Role** |
| 2006-Present | American College of Emergency Physicians | Fellow |
| 2015-2017 | Society of General Physiology | Member |
| 2016-Present  2018-Present | Shock Society  North American Vascular Biology Organization | Member  Member |

SERVICE TO PROFESSIONAL PUBLICATIONS

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| **Years** | | **Journal/Publication/Board** | **Role** |
| 2005-2007 | Case Management column, MACEP News (Massachusetts College of Emergency Physicians) | | Section Editor | |
| 2006-2007 | Annals of Emergency Medicine | | Editorial Board (Resident Fellow) | |
| 2006-Present | Annals of Emergency Medicine | | Peer Reviewer | |
| 2011-2013 | Annals of Emergency Medicine | | Editorial Board (Research Methodology Editor) | |
| 2017-Present  2020-Present  2020-Present  2021-Present  2021-Present | Annals of Emergency Medicine  Journal of Thrombosis and Hemostasis  Proceedings of the National Academy of Sciences  Surgery  SHOCK | | Editorial Board (Research Methodology Editor)  Peer Reviewer  Peer Reviewer  Peer Reviewer  Peer Reviewer | |

PUBLIC SERVICE

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| **Years** | **Service Role** |
| 2005-2007 | Music Therapy Program Coordinator, Boston University  and Berklee College of Music, Boston, MA |
| 2011-2015 | Medical Director, Mark O’Connor / Berklee College of Music Summer String Program, Boston, MA |
| 2016-present | Board Member, The Children’s Early Learning Space non-profit organization, Duxbury, VT |

Summary of Service Activities

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| I have strived to consistently provide a high level of quality service to my University, profession and community. I have served the University for nearly a decade as a standing member on the Committee on Human Research in the Medical Sciences (CHRMS). This entails reviewing proposed clinical trials and participating in monthly board meetings. I serve my professional discipline-related through service as the Research Methodology Editor on the Editorial Board of the *Annals of Emergency Medicine* (Impact factor 5.8). In this capacity, I assist in editorial decisions, reviewing approximately one manuscript per week for quality and consistency in methodology and statistics. I have also served my community through public and government service. As a volunteer board member for The Children’s Early Learning Space non-profit organization, I advocate for childhood safety and education. I have served as the Physician Representative to the Vermont Alcohol and Drug Abuse Council since my appointment by Governor Shumlin in 2016. |

**TEACHING**

Formal scheduled Classes

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| **Year** | **Course Title** | **Course**  **R E** | | **Hours** | **Number of Learners** | **Learner Level** |
| 2007-2019 | SURG9502 Emergency Medicine Clerkship |  | X | 24 | 7-35 | G |
| 2008-2011 | SURG195/196/197 EMS Research |  | X | 60 | 24-47 | UG |
| 2011-2017 | SURG200 Introduction to Emergency Medicine Research |  | X | 60 | 25-41 | G |
| 2011-2017 | SURG201 Emergency Medicine Research II |  | X | 60 | 5-11 | G |
| 2011-2017 | SURG220 Advanced Topics in Emergency Medicine Research |  | X | 60 | 4-12 | G |
| 2016- present | PHARM200 Cannabis Pharmacology |  | X | 6 | 58-99 | G |

R-required; E-elective; Hours-approx. per semester; G-graduate studies (instruction as per the COM Teaching Academy Portfolio)

CURRICULUM DEVELOPMENT

Course Director, SURG 195, 196, 197, 220, 201 and 220. I established and directed the Emergency Medicine Research Associate Program (EMRAP) and associated UVM courses in 2008, initially listed as “SURG195 Section C EMS Research” in Spring 2009. The course attracted 27 students the first semester; by Fall 2009 the class met the target enrollment of 50 participants, including 47 registered students and 3 continuing-education students. The courses became very popular with pre-medical students, so in 2010 I added a second and third semester (SURG 196 and 197) to accommodate the requests of those students seeking additional involvement. In 2011, I received approval the graduate college to list the course at the 200 level, and the courses were re-listed as SURG 200, 201, and 220. In Fall 2011, I cross-listed the course to serve as an introductory core class for graduate students in the Research Management Masters / Clinical Translational Sciences Program. I continued to serve as course director until Fall 2017, when UVMMC recruited a new faculty member to oversee the continued success of EMRAP.

PREDOCTORAL STUDENTS SUPERVISED OR MENTORED

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| **Dates** | **Name** | **Program  School** | **Role** | **Current Position** |
| 2020-present | Amanda Sidwell | University of Vermont | Graduate Research Advisor | PhD Candidate at the University of Vermont |
| 2020-present | Michael Lawson | University of Vermont | Medical Student Advisor | Medical Student at the University of Vermont |
| 2017-2019 | Nathan Dow | University of Vermont | Graduate Research Advisor | Medical Student at the University of Vermont |
| 2016-2019 | Zachary Osborn | University of Vermont | Post-Baccalaureate Pre-Medical Advisor | Medical Student at the University of Vermont |
| 2015-2017 | David Polson | University of Vermont | Undergraduate Research Advisor | Pharmacy Student at the Albany College of Pharmacy |
| 2015-2016 | Pamela Derickson | University of Vermont | Undergraduate Research Advisor | Medical Student at the University of Vermont |
| 2015-2016 | Nathan Dreyfus | University of Vermont | Undergraduate Research Advisor | Medical Student at the University of Vermont |
| 2013-2017 | Laurel Haines | University of Vermont | Undergraduate Research Advisor | Doctor of Veterinary Medicine DVM-PhD Student at Colorado State University |
| 2013-2015 | Ivette Nunez | University of Vermont | Graduate  Research Advisor | Ph.D. Student at University  of Texas in Austin |
| 2013-2015 | Eric Curran | University of Vermont | Undergraduate Research Advisor | Medical Student at Temple University |
| 2012-2015 | Chelsea Manning | University of Vermont | Undergraduate Research Advisor | Medical Student at Dartmouth |
| 2012-2015 | Tom Sewatsky | University of Vermont | Post-Baccalaureate pre-Medical Advisor | Medical Student, Geisinger |
| 2011-2013 | Jacob Buinewicz, M.D. | University of Vermont | Undergraduate Research Advisor | Medical Student, Thomas  Jefferson |
| 2010-2013 | Alex Thomas, M.D. | University of Vermont | Undergraduate  Honors College Advisor | Internal Medicine Resident, Yale University |
| 2010-2013 | Tram L. Tran, M.D. | University of Vermont | Undergraduate  Honors College Advisor | Orthopedic Surgery Resident, University of Arizona |
| 2010-2011 | Ali Sadeghi | University of Vermont | Undergraduate  Honors College Advisor | Masters of Public Health (MPH) Student, New York University |
| 2009-2011 | Hunter Moore, M.D. | University of Vermont | Medical Student Advisor | Surgery Resident, University of Colorado |
| 2009-2010 | Nicholas Larochelle, M.D. | University of Vermont | Medical Student Advisor | Emergency Medicine Physician, Concord Hospital |
| 2008-2010 | John Soltys, M.D., Ph.D. | University of Vermont | Undergraduate Research  Advisor | Neurology Resident, University of South Alabama |
| 2008-2011 | Angus Beal, M.D. | University of Vermont | Medical Student Advisor | Emergency Medicine Physician, Bangor Medical Center |
| 2008-2009 | Jared Blum, M.D. | University of Vermont | Medical Student Advisor | Emergency Physician, Central Vermont Medical Center |

DISSERTATION/THESIS COMMITTEE MEMBERSHIP

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| **Dates** | **Name** | **Program  School** | **Degree** | **Current Position** |
| 2018 | Joseph Charles | University of Vermont, Department of Pharmacology | Masters of Science | Research Technician at the University of Vermont |
| 2015 | Ivette Nunez | University of Vermont, Department of Pathology | Masters of Science | Ph.D. Student at University  of Texas in Austin |

POSTDOCTORAL FELLOWS AND RESIDENTS DIRECTLY SUPERVISED OR MENTORED

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| **Dates** | **Name** | **Fellow** | **Faculty Role** | **Current Position** |
| 2011-2017 | Nuria Villalba-Isabel, Ph.D. | University of Vermont Pharmacology | Postdoctoral Advisor | Faculty Scientist, University of Florida |
| 2013-2014 | Emilia Krol, M.D. | University of Vermont Surgery Resident | Resident Advisor | General Surgeon, Norfolk, VA |
| 2010-2011 | David Stockwell, M.D. | University of Vermont Neurosurgery Resident | Resident Advisor | Neurosurgeon, Indiana University |
| 2014-2015 | Katrina Ducis, M.D. | University of Vermont Neurosurgery Resident | Resident Advisor | Pediatric Neurosurgery Fellow, Indiana University |

FACULTY MENTORED

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| **Dates** | **Name** | **Position while Mentored** | **Faculty Role** | **Current Position** |
| 2019-present | Dev Majumdar, Ph.D. | University of Vermont Assistant Professor | Department of Surgery Mentoring Committee | Assistant Professor, University of Vermont |
| 2017-2019 | Daniel Collier, Ph.D. | University of Vermont Assistant Professor | Mentoring Committee on NIH K99/R00 award | Assistant Professor, University of Tennessee |

TEACHING AIDS

1. **Standardized patient workshop teaching the informed consent process for research studies.** I developed a novel curriculum to help train students to perform informed consent in the emergency department setting, including lectures, small group discussions, and a standardized patient workshop in the simulation laboratory. This workshop is part of the SURG200 curriculum.
2. **Trauma simulations for resident physician training.** I participated in an academic working group that developed a teaching aid to simulate and evaluate trauma residents’ ability to run a trauma code.

SUMMARY OF TEACHING ACTIVITIES

My teaching interest is clinical research ethics and study design. I designed the Emergency Medicine Research Associate Program (EMRAP) and associated University courses (SURG 200, 201, and 220) to teach the foundations of human subjects research and EMS research. I also teach medical students in the Emergency Medicine Clerkship (SURG9502). The University courses stress ethics, responsibility, and professionalism. The introductory level course (SURG 200) was designed for pre-health students interested in learning the foundations of human subject research. Students who successfully complete the first semester of the class may continue in the program as Research Associates through subsequent courses (SURG 201 and 220). The Research Associates (RAs) screen and enroll emergency department patients for ongoing clinical research and quality improvement projects under the supervision of UVMMC emergency physicians. All of the research projects are aimed at improving patient outcomes. As such, RAs participate daily in the innovation of emergency medical practice. Thus, EMRAP provides a valuable resource that is able to provide ED-based subject recruitment, while at the same time, creating a bridge between UVM medical faculty and students interested in clinical research.

My teaching philosophy is based to a large extent on my personal experiences. I believe we learn best by doing. Therefore, I believe that students in my class will retain information best by actually performing hands-on clinical research. Throughout the semester, the students work through real problems with clinical research methodology and protocol development. In sharing my knowledge and enthusiasm for clinical research, I hope to ignite research interests in my students. By active discussion and clinical experiences throughout the course, I create for my students a unique learning environment. I strive to encourage natural curiosity and to instill a yearning for knowledge and passion for biomedical research.

**RESEARCH AND SCHOLARLY ACTIVITIES**

**RESEARCH AWARDS AND GRANTS**

\* Indicates peer-reviewed by panels of national experts (National Institutes of Health, Department of Defense).

**Ongoing Research Support**

\* NIH/NIGMS (RO1 GM123010 PI: Kalev Freeman)

9/30/17-8/1/22 $193,000 (Annual direct costs)

Title: Impact of Trauma and its Factors on Vascular Endothelial Function

Role: Principal Investigator (40%FTE)

Brief description: This project will define functions of the endothelium in detecting and responding to injury and elucidate mechanisms that contribute to maladaptive vascular responses after severe trauma.

\* Department of Defense (DM190028 PI: Moore)

Subcontract to the University of Vermont (PI: Kalev Freeman)

1/1/2020-12/31/2022 $24,375 (Vermont annual direct costs)

Title: Impact of REBOA and Tranexamic Acid on Clot Structure and Secondary Brain Injury Following Severe Polytrauma, Hemorrhagic Shock, and Traumatic Brain Injury

Role: Co-investigator (1%FTE)

Brief description: This project will determine the impact of REBOA and tranexamic acid on outcomes of severe trauma and shock in a porcine model.

\* Department of Defense/ The Henry M. Jackson Foundation for the Advancement of Military Medicine (HU001-18-2-0016 PI: Daniel Perl)

Subcontract to the University of Vermont (PI: Kalev Freeman)

9/1/2018-7/30/22 $220,220 (Vermont annual direct costs)

Cardiovascular Consequences of Traumatic Brain Injury

Role: Co-Principal Investigator (10%FTE)

Brief description: The thrust of the overarching research project at the Uniformed Services University for the Health Sciences is to study the pathologic and physiologic consequences of traumatic brain injury with special attention to the pathogenesis and sequalae of chronic traumatic encephalomalacia and interface astroglial scarring induced by concussive, impact and/or blast injury. The goal of this subaward is to study the chronic effects of a traumatic brain injury on small blood vessel function in the brain.

\* NIH/NHLBI (UM1 HL120877 PIs: James Morrissey)

Subcontract to the University of Vermont (PI: Mark Nelson)

7/1/19-6/30/21 $200,000 (Project 7 UVM Annual direct costs)

Title: Analysis and Characterization of Trauma-Induced Coagulopathy

Role: Co-investigator (7.5%FTE)

Brief description: The Trans-Agency Research Consortium for Trauma-Induced Coagulopathy (TACTIC) grant’s global objective is to elucidate the mechanisms driving trauma induced coagulopathy. This project is focused on the role of scramblase TMEM16f in trauma induced coagulopathy.

\* NIH/NHLBI (ACTIV COVID-19 Administrative Coordinating Center PI: James Morrissey)

Subcontract to the University of Vermont (PI: Kalev Freeman)

1/1/21-12/31/22 $50,000 (UVM Annual direct costs)

Title: Mechanisms of Endotheliopathy in SARS-CoV-2 Infection

Role: Principal Investigator (1%FTE)

Brief description: We are using a pharmacological strategy featuring two polyanionic molecules, heparin and suramin – one anti-coagulant and the other without anti-coagulant effects – to dissect their efficacy in protecting endothelial cells during SARS-CoV-2 infection.

BioDirection, Inc. (PI: Kalev Freeman)

1/1/21-12/31/21 $125,000 (Approximate direct costs depending on enrollment)

Title: Pivotal Trial of Diagnostic Performance of Tbit System in Screening for CT-positive TBI

Role: Principal Investigator

Brief description: The Tbit system is a point of care test including recently FDA-approved biomarkers for traumatic brain injury, assayed using nano-wire based biosensor technology. This multi-center trial will validate sensitivity and specificity of the Tbit system compared to head CTs in screening for traumatic brain injury.

Masimo Corporation (PI: Kalev Freeman)

1/1/21-12/31/21 $100,000 (Approximate direct costs depending on enrollment)

Title: Data Collection of Non-Invasive Carboxyhemoglobin and Total Hemoglobin Measurements in Emergency Department Patients

Role: Principal Investigator

Brief description: This project will evaluate the performance characteristics of non-invasive pulse oximetry platforms for measurement of carboxyhemoglobin and total hemoglobin in the emergency department setting.

**Completed Research Support**

\* NIH/NHLBI (UM1 HL120877 PIs: Kenneth Mann, Charles Esmon)

Subcontract to the University of Vermont (PI: Mark Nelson)

9/30/13-6/30/19 $162,847 (Project 12 UVM Annual direct costs)

Title: Analysis and Characterization of Trauma-Induced Coagulopathy

Role: Co-investigator (7.5%FTE)

Brief description: The Trans-Agency Research Consortium for Trauma-Induced Coagulopathy (TACTIC) grant’s global objective is to elucidate the mechanisms driving trauma induced coagulopathy. Our work within this multi-investigator study focuses on the effects of trauma on endothelial function studied in animal models.

\* NIH/NIGMS (K08 GM098795-01 PI: Kalev Freeman)

8/1/11-2/28/17 Annual direct costs $109,239

Title: Endothelial Ca2+ signals and vasodilatory function after traumatic brain injury

Role: Principal Investigator (80%FTE)

Brief description: The goal of this project is to understand fundamental mechanisms and functional consequences of endothelial vasodilatory signal changes that occur in a remote tissue bed – the mesenteric artery circulation – after a brain injury. We will determine effects of trauma on endothelial calcium and vasodilatory signal in a rodent model of traumatic brain injury.

\* Department of the Army (W911NF-10-1-0376 PI: Kenneth Mann)

3/1/10-8/31/16 Vermont annual direct costs $685,000

Title: Systems biology for biological responses to severe hemorrhage

Role: Co-investigator (5%FTE)

Brief description: We propose to use a multicenter approach to systematically examine and characterize the multiple aspects of the biology of coagulation and coagulopathy after traumatic and burn injury using existing databases, prospective collection and analysis of samples from patients, multiple animal models and in vitro systems. Data from these studies will be used to develop a comprehensive mathematical model of the human coagulation cascade and advanced analysis techniques will be used to interrogate the coagulation model to determine key mechanisms in the coagulation architecture.

UVM College of Medicine Internal Grant Program (PI: Kalev Freeman)

1/1/15-12/31/16 Annual direct costs $75,000

Title: Histone-induced endothelial calcium signals and sterile inflammation

Role: Principal Investigator

Brief description: The overall goal of this project is to test the effects of extracellular histones on endothelial calcium signals, inflammatory cytokines, and immune cell activation in a mouse model.

Luoxis Corporation (PI: Kalev Freeman)

8/1/14-7/31/16 Annual direct costs $85,151

Title: Measurement of oxidation-reduction potential in trauma and sepsis

Role: Principal Investigator

Brief description: The major goal of this project is to determine the diagnostic performance characteristics of oxidation-reduction potential measurements in patients with severe trauma or infections.

Haemonetics Corporation (PI: Kalev Freeman)

11/1/14-10/31/16 Annual direct costs $41,000

Title: The Role of Factor XIa in Trauma-Induced Coagulopathy

Role: Principal Investigator

Brief description: This project seeks to evaluate the role of factor XIa in trauma-induced coagulopathy using viscoelastic measurements of whole blood clotting in trauma patients.

UVMMG Research and Education Committee Grant (Co-PIs: Isabelle Desjardins, Kalev Freeman)

1/1/2013-12/31/2014 $75,000

Title: Building an expert system to evaluate suicide risk: replicating the expert judgement of experienced psychiatrists to optimize patient safety and resource utilization

Role: Co-Principal Investigator

Brief description: The major goal of this project is to test the predictive validity of a screening algorithm developed by nationally recognized suicide experts for modeling critical thinking of experienced physicians.

UVM College of Medicine Surgical Research Award (PI: Kalev Freeman)

7/1/09-6/30/11 Total $17,744

Title: Cardiac MRI to determine left ventricular function in a rodent model of traumatic brain injury

Role: Principal Investigator

Brief description: The goal of this project is to determine the acute effects of traumatic brain injury on cardiac function.

Masimo Corporation (PI: Kalev Freeman)

4/1/11-3/31/14 Annual direct costs $100,000

Title: Evaluation of Masimo noninvasive carboxyhemoglobin testing in ED patients with suspected carbon monoxide poisoning.

Role: Principal Investigator

Brief description: The major goal of this project is to determine the accuracy of noninvasive carboxyhemoglobin testing in the emergency department setting.

\* NIH (P20 RR16435/ P30 GM103498 PI: Rodney Parsons)

Center for Neuroscience Excellence, Pilot Project

7/1/11-6/30/12 Annual direct costs $69,393

Title: Endothelial Ca2+ signals and blood brain barrier permeability following traumatic brain injury

Role: Principal Investigator (Pilot Project)

Brief description: The objective of this proposal is to understand the molecular basis and functional consequences of altered cerebral artery endothelial calcium (Ca2+) signaling and impaired neurovascular coupling after TBI.

UVM College of Medicine Surgical Research Award (PI: Kalev Freeman)

7/1/11-6/30/13 Total $24,950

Title: A randomized controlled trial of cognitive therapy to enhance neural repair and improve outcomes following traumatic brain injury.

Role: Principal Investigator

Brief description: This pilot study evaluated the impact of cognitive therapy in human on outcomes in subjects after a traumatic brain injury.

**PENDING**

SCHOLARSHIP

**Peer Reviewed Publications**

*H-Index:16*

*Total citations 1450*

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**Google Scholar**

*https://scholar.google.com/citations?user=NlxKrfEAAAAJ&hl=en*

Original Research

1995

1. **Freeman K**, Farrow S, Schmaier A, Freedman R, Schork T, and Lockette W. Genetic polymorphism of the 2 -adrenergic receptor is associated with increased platelet aggregation, baroreceptor sensitivity, and salt excretion in normotensive humans, The American Journal of Hypertension (1995, 8:863-869). PMID: 8541000

2001

1. **Freeman K**, Nakao K, Leinwand LA. Low sequence variation in the human cardiac -myosin heavy chain gene, Genomics (2001, 76: 73-80). PMID: 11549319
2. **Freeman K**, Colon-Rivera C, Olsson MC, Moore RL, Weinberger HD, Grupp IL, Vikstrom K, Iaccarino G, Koch WJ, Leinwand LA. Progression from hypertrophic to dilated cardiomyopathy in mice that express a mutant myosin transgene, The American Journal of Physiology (2001, 280: H151-H159). PMID: 11123229
3. **Freeman K**, Lerman I, Kranias EG, Bohlmeyer T, Bristow MR, Lefkowitz RJ, Iaccarino G, Koch WJ, Leinwand LA. Alterations in cardiac adrenergic signaling and calcium cycling have markedly different effects on the progression of hypertrophic cardiomyopathy, The Journal of Clinical Investigation (2001, 107: 967-974). PMID: 11306600

2002

1. Lerman I, Harrison B, **Freeman K**, Hewett TE, Allen DL, Robbins J, Leinwand LA. Genetic variability in forced and voluntary endurance exercise performance in seven inbred mouse strains, The Journal of Applied Physiology (2002, 92: 2245-2255). PMID: 12015333

2006

1. Sandhu H, Carpenter C, **Freeman K**, Nabors SG, Olson A. Clinical decision making: opening the black box of cognitive reasoning. Annals of Emergency Medicine. (2006 Dec;48(6):713-9)

2007

1. **Freeman K**, Dewitz A, Baker W. Ultrasound-guided hip arthrocentesis in the emergency department. The American Journal of Emergency Medicine (2007, 25: 80-86).

2008

1. **Freeman K**, Feldman JA, Mitchell P, Donovan J, Dyer KS, Eliseo L, White L, Temin E. Effects of clinical presentation and initial electrocardiogram on time-to-treatment in emergency department patients with hyperkalemia, Academic Emergency Medicine (2008, 5(3):239-49). PMID: 18304054
2. **Freeman K**, Feldman JA. Cocaine, myocardial infarction, and beta blockade: Time to rethink the equation? Annals of Emergency Medicine (2008,51(2):130-4.) PMID: 17933425

2009

1. Blum JA, **Freeman K**, Dart RC, Cooper RJ. Requirements and definitions in conflict of interest policies of medical Journals. The Journal of the American Medical Association (2009; 302(20):1-5). PMID: 19934424

2012

1. Wyne KT, Soltys JN, O'Keefe MF, Wolfson D, Wang HE, **Freeman K**. King LTS-D use by EMT-intermediates in a rural prehospital setting without intubation availability. Resuscitation. (2012; 83(7):e160-1). PMID: 22484435
2. Larson BA, Stockwell D, Boas S, Andrews T, Wellman G, Lockette W, **Freeman K**. Cardiac reactive oxygen species after traumatic brain injury. The Journal of Surgical Research (2012 Apr;173(2):e73-81). PMID: 22172132. PMCID: PMC3299814

2013

1. Larochelle N, Okeefe MF, Wolfson D, **Freeman K**. Cellular technology improves transmission success of pre-hospital electrocardiograms, American Journal of Emergency Medicine (2013, 31(11):1564-70.) PMID: 24075803. PMCID: PMC3874289
2. Moore HB, DeStigter KK, Mann-Gow T, Dorf L, Streeter MH, Ebert G, Crookes B, Leffler SM, O’Keefe M, **Freeman K**. Airway, Breathing, CT Scanning: Duplicate computed tomography imaging after transfer to trauma center. Journal of Trauma and Acute Care Surgery (2013, 74(3):813-7). PMID: 23425740 PMCID: PMC4104067
3. Jones CA, Petrozzino JJ, Hoesche J, Krol EM, **Freeman K**. Perceptions about time for normalization of international normalized ratio in patients requiring acute warfarin reversal when using fresh frozen plasma. American Journal of Emergency Medicine (2013; 31(5):878-9). PMID: 23478117

2014

1. Watts R, Thomas A, Filippi CG, Nickerson JP, **Freeman K.** Potholes and molehills: bias in diagnostic performance of diffusion tensor imaging in concussion. Radiology (2014; 272(1):217-23). PMID: 24635677. PMCID: PMC4263643
2. Moody BJ, Liberman C, Zvara P, Smith PP, **Freeman K**, Zvarova K. Acute lower urinary tract dysfunction (LUTD) following traumatic brain injury (TBI) in rats. Neurourol & Urodynamics; (2014;33(7):1159-64). PMID: 24038177
3. Villalba N, Sonkusare SK, Longden TA, Tran TL, Nelson MT, Wellman GC, **Freeman K**. Traumatic brain injury disrupts cerebrovascular tone through endothelial iNOS expression and nitric oxide gain-of-function. Journal of the American Heart Association (2014;3(6): e001474.). PMID: 25527626.

2015

1. Wylie G, **Freeman K**, Thomas A, Shpaner M, Okeefe M, Watts R, Naylor MR. Cognitive improvement after mild traumatic brain injury measured with functional neuroimaging during the acute period. PLOS One (2015;10(5):e0126110). PMID: 25962067. PMCID: PMC4427352
2. Abar B, Ogedegbe C, Dalawari P, **Freeman K**, Boudreaux ED, Illuzzi F, Carro-Kowalcyk S, Molloy M, Bradley K. Promoting cessation utilizing pre-health professional students as research associates in the emergency department. Addict Behav. (2015; 40:73-6). PMID: 25226592. PMCID: PMC5120677
3. Mann KG, **Freeman K**. TACTIC: Trans-Agency Consortium for Trauma-Induced Coagulopathy. Journal of Thrombosis and Haemostasis (2015;13(Suppl. 1): S63–S71). PMID: 26149052. PMCID: PMC4498273
4. Neal M, Moore H, Moore E, **Freeman K**, Sperry J, Mann K. Clinical assessment of trauma-induced coagulopathy and its contribution to post-injury mortality: A TACTIC Proposal. Journal of Trauma and Acute Care Surgery (2015, 79(3):490-2.) PMID: 26307885
5. Jones CA, Petrozzino P, Weimersheimer P, Fung MK, Sarkar IN, Boutrus A, Pochal B, Clark E, Peters C, Krol E, Ducis K, **Freeman K**. Prevention of treatment-related fluid overload reduces estimated effective cost of prothrombin complex concentrate in patients requiring rapid vitamin k antagonist reversal. Expert Review of Pharmacoeconomics & Outcomes Research 2015 Jul 29:1-5. PMID: 26211539

2016

1. Manning CT, Buinewicz JD, Sewatsky TP, Zgonis E, Gutierrez K, O'Keefe MF, **Freeman K.**Does routine midazolam administration prior to nasogastric tube insertion in the emergency department decrease patients' pain? (A Pilot Study). Acad Emerg Med. 2016 Jul 23(7):766-71. PMID: 26211539

2017

1. Villalba N, Sackheim A, Nunez I, Hill-Eubanks D, Nelson MT, Wellman GC, **Freeman K**. Traumatic brain injury causes endothelial dysfunction in the systemic microcirculation through arginase-1-dependent uncoupling of endothelial nitric oxide synthase. Journal of Neurotrauma. 2017 Jan 1;34(1):192-203. PMID: 26757855. PMCID: PMC5198065
2. Curran EJ, Wolfson DL, Watts R, **Freeman K**. Cold blooded: evaluating brain temperature by mri during surface cooling of human subjects. Neurocritical Care. 2017 Mar 28. PubMed PMID: 28352966.
3. Price M, van Stolk-Cooke K, Ward HL, O'Keefe M, Gratton J, Skalka C, **Freeman K**. Tracking post-trauma psychopathology using mobile applications: A usability study. Journal of Technology Behavioral Science. 2017 Mar;2(1):41-48. PMID: 29109968. PMCID: PMC5669390
4. Sackheim AM, Stockwell D, Villalba N, Haines L, Scott CL, Russell S, Hammack SE, **Freeman K**. Traumatic brain injury impairs sensorimotor function in mice. Journal of Surgical Research. 2017 Jun 1;213:100-109. PMID: 28601302
5. Thomas AW, Watts R, Filippi CG, Nickerson JP, Andrews T, Lieberman G, Naylor MR, Eppstein MJ, **Freeman K**. Dynamic changes in diffusion measures improve sensitivity in identifying patients with mild traumatic brain injury. PLoS One. 2017 Jun 12;12(6):e0178360. PMID: 28604837. PMCID: PMC5467843
6. Desjardins I, Cats-Baril W, Maruti S, **Freeman K**, Althoff R. Suicide risk assessment in hospitals: an expert system-based triage tool. J Clin Psychiatry. 2016 Jul;77(7):e874-82. PMID: 27314465
7. Preston K, Harm S, Dreyfus N, Villalba N, **Freeman K**. Packed red blood cells accumulate oxidative stress with increased storage duration. Shock. 2017 Aug;48(2):270-271. PMID: 28709159. PMCID: PMC5512443

2018

1. Prior SM, Mann KG, **Freeman K**, Butenas S. Continuous thrombin generation in whole blood: new applications for assessing activators and inhibitors of coagulation, Analytical Biochemistry, 2018 Jun 15;551:19-25. PMID: 29746819. PMCID: PMC5993644
2. Price M, van Stolk-Cooke K, Legrand AC, Brier ZMF, Ward, HL, Connor, JP, Gratton, J, **Freeman K**, Skalka C. Implementing assessments via mobile phone during the acute posttrauma period: feasibility, acceptability, and strategies to improve response rates. European Journal of Psychotraumatology. 2018 Jul 31;9(Suppl 1):1500822. PMID: 30083303.
3. Polson D, Villalba N, **Freeman K**. Optimization of a diagnostic platform for oxidation-reduction potential (ORP) measurement in human plasma. Redox Report, 2018 Dec;23(1):129. PMID: 29606080.

2019

1. Osborn ZT, Villalba N, Derickson PR, Sewatsky TP, Wager AP, **Freeman K**. Accuracy of point-of-care testing for anemia in the emergency department. Respir Care. 2019 Mar 26. PMID: 30914492.
2. Collier DM, Villalba N, Sackheim AM, Bonev AD, Miller ZD, Moore JS, Shui B, Lee JC, Lee FK, Reining S, Kotlikoff MI, Nelson MT, **Freeman K**. Extracellular histones induce calcium signals in the endothelium of resistance-sized mesenteric arteries and cause loss of endothelium-dependent dilation. American Journal of Physiology Heart Circulatory Physiology. 2019 Mar 8. PMID: 30848676
3. Haines L, Villalba N, Sackheim AM, Collier DM, **Freeman K**. Myogenic tone contributes to the regulation of permeability in mesenteric microvessels. Microvasc Res. 2019 Apr 8. PMID: 30974113
4. Shupp JW, Brummel-Ziedins KE, Cohen MJ, **Freeman K**, Hammamieh R, Mudunuri US, Orfeo T, Moffatt LT, Brownstein BH, Mann KG, Jett M, Pusateri AE. Assessment of coagulation homeostasis in blunt, penetrating, and thermal trauma:Guidance for a multicenter systems biology approach. Shock. 2019 Oct;52 (Military Supplement):84-91. PMID: 30339633
5. Villalba N, Osborn Z, Derickson P, Manning C, Herrington R, Kaminsky D, **Freeman K**. Diagnostic performance of pulse cooximetry in the emergency department. Respiratory Care. 2019 Nov; 64(11):1351-1357. PMID: 31040204.

2020

1. Dow N, Coleman JR, Moore H, Osborn Z, Sackheim A, Hennig G, Butenas S, Nelson MT, Moore EE, **Freeman K**. Dense and Dangerous: The Tissue Plasminogen Activator (t-PA)-Resistant Fibrinolysis Shutdown Phenotype is Due to Abnormal Fibrin Polymerization. Journal of Trauma and Acute Care Surgery. 2020 Feb;88(2):258-265. PMID: 31999655
2. Coleman JR, Moore EE, **Freeman K**, Cohen MJ , Samuels JM, Hansen K. Actin is associated with tissue injury in trauma patients and produces a hypercoagulable profile. Journal of Trauma and Acute Care Surgery. 2020 Jul;89(1):87-95. PMID: 32574484

2021

1. Mansour Gergi, Goodwin A, **Freeman K**, Colovos C, Volod O. Viscoelastic hemostasis assays in septic, critically ill coronavirus disease 2019 patients: a practical guide for clinicians. Blood Coagulation and Fibrinolysis. 2021 Apr 1;32(3):225-228. PMID: 33443923
2. **Freeman K,** Miller Z, Herrington RR, Dreyfus N, Buttaravoli P, Burgess A, Nickerson JP, Daphtary N, and Bates JHT. An oropharyngeal device for airway management of conscious and semiconscious patients: a randomized clinical trial. JACEP Open. 2021 Apr 29;2(2):e12440. PMID: 33969347
3. Mughal A, Sackheim AM, Sancho M, Longden TA, Russell S, Lockette W, Nelson MT, **Freeman K.** Impaired capillary-to-arteriolar electrical signaling after traumatic brain injury. Journal of Cerebral Blood Flow and Metabolism. 2021 Jun;41(6):1313-1327. PMID: 33050826.
4. Sackheim AM, Villalba N, Sancho M, Harraz OH Bonev AD, D’Alessandro A, Nemkov T, Nelson MT, **Freeman K**. Traumatic brain injury impairs systemic vascular function through disruption of inward-rectifier potassium channels. Function. (2021, in press).

**Abstracts**

1. **Freeman K**, Nakao K, Lerman IR, Leinwand LA*.* Strong selective pressure at the human beta-myosin heavy chain gene locus, *Circulation* (1998; 98(17):I-380). Poster presentation at American Heart Association Scientific Sessions, Dallas, TX, November 1998.
2. **Freeman, K**, Weinberger HD, Jackson TM, Grupp IL, Iaccarino G, Koch WJ, Vikstrom KL, Leinwand LA. Beta-adrenergic uncoupling, ventricular dysfunction, and exercise intolerance in a transgenic model of hypertrophic cardiomyopathy, *Circulation* (1998; 98(17): I-69). Oral presentation at American Heart Association Scientific Sessions, Dallas, TX, November 1998.
3. **Freeman K,** Iaccarino G, Bohlmeyer T, Leinwand LA. Overexpression of the beta-2-adrenergic receptor accelerates heart failure in hypertrophic cardiomyopathy mice, *Circulation* (1999; 100(18): I-493). Oral presentation at American Heart Association Scientific Sessions, Atlanta, GA, November 1999.
4. **Freeman K,** Kranias L, Leinwand LA. Phospholamban ablation rescues cardiac dysfunction in a mouse model of hypertrophic cardiomyopathy, *Circulation* (2000; 102(18): I-280). Featured oral presentation at American Heart Association Scientific Sessions, New Orleans, LA, November 2000.
5. **Freeman K**, Feldman JA, Mitchell P, Donovan J, Dyer KS, Eliseo L, White L, Temin E. Effects of clinical presentation and initial electrocardiogram on time-to-treatment in emergency department patients with hyperkalemia.  Oral presentation at 10th Annual New England Regional SAEM Meeting, Shrewsbury, MA, March 2006.
6. **Freeman K**, Feldman JA, Mitchell P, Donovan J, Dyer KS, Eliseo L, White L, Temin E. Effects of clinical presentation and initial electrocardiogram on time-to-treatment in emergency department patients with hyperkalemia.  *Academic Emergency Medicine* (2006; 13(5): I-185). Poster presentation at Society for Academic Emergency Medicine Annual Meeting, San Francisco, CA, May 2006.
7. Blum J, **Freeman K**, Cooper R, Dart RC. Inconsistent Conflict of Interest Policies Across Peer-reviewed Biomedical Journals. *Annals of Emergency Medicine* (2008; 52(4): S82). Poster presentation at American College of Emergency Medicine Scientific Assembly, Chicago, IL, October 2008.
8. Larson B, Beal A, Ahari A, Russell S, **Freeman, K**. Beta-adrenergic blockade prevents myocardial oxidative stress due to traumatic brain injury. *Annals of Emergency Medicine* (2008; 54(3): S142-143. Poster presentation at American College of Emergency Medicine Scientific Assembly, Boston, MA, October 2008.
9. Moore HB, Dorf L, Streeter MH, DeStigter KK, Ebert G, Crookes B, Leffler SM, O’Keefe M, **Freeman K**. Airway, Breathing, CT Scanning; Duplicate computed tomography imaging after transfer to trauma center. February 2011 *Journal of Surgical Research* Vol. 165, Issue 2, Page 341. Oral presentation at the Western Association for Surgical Trauma meeting, Telluride CO February 2012.
10. Loadholt CD, Larson BE, Andriakos PG, Boas S, Trahan TE, Tran TL, Falls WA, Hammack SE, **Freeman K**. Inter-rater reliability of a novel neurobehavioral scale for outcomes assessment in rats following traumatic brain injury. *FASEB J* (2011; 25; 856.5 abstract). Poster presentation at the American Society for Pharmacology and Experimental Therapeutics meeting, Washington DC, April 2011.
11. Larson BE, Hannah RM, Sonkusare SK, Wellman GC, Nelson MT, **Freeman K**. Endothelial Ca2+ signals and vasodilatory function following traumatic brain injury. *FASEB J* (2011; 25; 641.24 abstract). Poster presentation at the American Society for Pharmacology and Experimental Therapeutics meeting, Washington DC, April 2011.
12. Villalba N, Tran TL, Nelson MT, Wellman GC, **Freeman K.** Cerebral vascular dysfunction following traumatic brain injury. *FASEB J* (2013 27:875.6 abstract). Poster presentation at the American Society for Pharmacology and Experimental Therapeutics meeting, Boston MA, April 2013.
13. Tran TL, Villalba N, Nelson MT, Wellman GC, **Freeman, K**. Increased endothelial calcium signals in cerebral vessels following traumatic brain injury. FASEB J (2013 27:875.9 abstract). Poster presentation at the American Society for Pharmacology and Experimental Therapeutics meeting, Boston MA, April 2013.
14. Villalba N, Tran TL Nelson MT, Wellman GC, **Freeman, K**. Inhibition of nitric oxide synthase restores cerebral artery tone in a rodent model of traumatic brain injury. Poster presentation at the Society for Neuroscience, San Diego, CA, October 2013.
15. Sonkusare SK, Villalba V, **Freeman K,** Bonev AD, Sanana LF, Nelson MT.  Cooperative gating and sensitivity of TRPV4 channels are regulated by distinct factors in different vascular beds. FASEB J (2014). Poster presentation at the American Society for Pharmacology and Experimental Therapeutics meeting, San Diego, CA, April 2014.
16. Villalba N, Longden T, Nelson MT, Wellman GC, **Freeman K**. Enhanced endothelial production of nitric oxide impairs cerebrovascular tone after brain trauma. FASEB J (2014). Poster presentation at the American Society for Pharmacology and Experimental Therapeutics meeting, San Diego, CA, April 2014.
17. Villalba N, Nuñez I, Sackheim A, Sonkusare SK, Nelson MT, Wellman GC, **Freeman K.** Impaired vasodilatory function of systemic resistance vessels following traumatic brain injury.  Poster presentation at the International Symposium on Resistance Arteries, Calgary Canada, October 2014.
18. Sackheim A, Villalba N, Sonkusare SK, Esmon C, Wellman GC, Nelson MT, **Freeman K**. Effects of extracellular histones on vascular endothelium are mediated by TRPV4 and TLR4 pathways in mouse mesenteric resistance arteries. Poster presentation at the International Symposium on Resistance Arteries, Calgary Canada, October 2014.
19. **Freeman K**, Collier D, Sackheim A, Villalba N, Sackheim A, Bonev A, Nelson MT. Histone-induced endothelial calcium signals: a novel mechanism for detection of tissue injury. Poster presentation at the Society of General Physiologists, Annual Meeting and Symposium, Woods Hole, MA, September 2015.
20. Villalba N, Sackheim A, Nunez I, Nelson MT, Wellman GC, **Freeman K.** Arginase inhibition improves endothelial dysfunction in the systemic microvasculature following TBI. Poster presentation at the World Congress on Microcirculation, Kyoto Japan, September 2015.
21. Sackheim A, Haines L, Kuzma R., Silver C, Villalba N, **Freeman K.** Automated methodology for ex-vivo measurement of vascular permeability. Poster presentation at the World Congress on Microcirculation, Kyoto Japan, September 2015.
22. Villalba N, Polson, D, Richards A, Sackheim A., **Freeman K.** Traumatic brain injury increases plasma and microvascular reactive oxygen species. Poster presentation at the World Congress on Microcirculation, Kyoto Japan, September 2015.
23. Collier D, Villalba N, Sackheim A, Sonkusare S, Nelson MT, **Freeman K.** Extracellular histones activate local and propagating endothelial calcium signals. Poster presentation at the World Congress on Microcirculation Kyoto, Japan, September 2015.
24. Butenas S, Prior SM, **Freeman K**. Tissue Factor Initiated Thrombin Generation in Trauma Patient Plasma. Journal of Thrombosis and Haemostasis (2016 14:S1 abstract). Poster presentation at the International Symposium on Thrombosis and Haemostasis, Montpellier, France,June 2016.
25. **Freeman K**, Collier DM, Villalba N, Harraz O, Sonkusare S, Bonev AD, Nelson MT. Regulation of cerebral artery endothelial TRPV4 channel function by cGMP-dependent protein kinase. Poster presentation at the Society of General Physiologists, Annual Meeting and Symposium, Woods Hole, MA, September 2016.
26. Collier D, **Freeman K**, Nelson MT. Trauma levels of extracellular histones cause endothelial cell Ca2+ overload, cell death, and loss of endothelial dependent dilation. Poster presentation at the Society of General Physiologists, Annual Meeting and Symposium, Woods Hole, MA, September 2016.
27. Sackheim AM, Villalba N, **Freeman K**. Traumatic brain injury causes inward rectifier potassium channelopathy and alters flow-mediated vasodilatory signaling pathways in rat mesenteric arteries. Poster presentation at the 19th International Vascular Biology Meeting, Boston, MA. November 2016.
28. Villalba N, Haines L, Sackheim A, Freeman K. Increased vascular permeability after extracellular histone exposure. Poster presentation at the 19th International Vascular Biology Meeting, Boston, MA. November 2016.
29. Collier DM, Villalba N, Sackheim AM, Nelson MT, **Freeman K**. Extracellular histone proteins cause Ca2+ influx and endothelial cell death in resistance-sized mouse mesenteric arteries. Shock (2017 47:6S.36P abstract). Poster presentation at the 40th Annual Conference on Shock, Fort Lauderdale, FL, June 2017.
30. Laurel A. Haines LA, Villalba N, Sackheim AM, Kasten M, **Freeman K**. Extracellular histone exposure increases endothelial-dependent permeability in systemic blood vessels. Shock (2017 47:6S.38P abstract). Poster presentation at the 40th Annual Conference on Shock, Fort Lauderdale, FL, June 2017.
31. Miller Z, Burgess A, Daphtary N, Bates J, Nickerson J, Buttaravoli P, **Freeman K**.  Airflow resistance of a novel airway compared to the standard oropharyngeal airway. Shock (2017 47:6S.45P abstract). Poster presentation at the 40th Annual Conference on Shock, Fort Lauderdale, FL, June 2017.
32. Sackheim AM, Villalba N, Bonev A, Nelson MT, **Freeman K**. Traumatic brain injury causes inward rectifier potassium channelopathy in rat mesenteric arteries. Shock (2017 47:6S.73P abstract). Poster presentation at the 40th Annual Conference on Shock, Fort Lauderdale, FL, June 2017.
33. Dow NE, Prior SN, Butenas S, **Freeman K**. Thrombin generation correlates with fibrinolysis phenotype after trauma. Shock (2017 47:6S.97P abstract). Poster presentation at the 40th Annual Conference on Shock, Fort Lauderdale, FL, June 2017.
34. Sackheim A, Villalba N, Bonev A, Nelson MT, **Freeman K**. Increased Hydrogen Peroxide After Traumatic Brain Injury Disrupts Phosphatidylinositol 4,5-Bisphosphate Metabolism Causing Impaired Endothelial Inward Rectifier Potassium Channel (KIR) Function. Oral presentation at the Microcirculatory Society session, Experimental Biology, April 2018.
35. **Freeman K**, Burgess A, Miller Z, Dreyfus N, Herrington R, Nickerson J, Daphtary N, Bates J, Buttaravoli P. Abstract # MHSRS-18-1963 - Research in Prolonged Field Care and Pre-Hospital Tactical Combat Casualty Care - Novel oropharyngeal device designed to improve the airway status of a conscious casualty under a delayed evacuation scenario. Oral presentation at

2018 Military Health System Research Symposium (MHSRS), Kissimmee, FL, August 2018.

1. **Freeman K**, Dow N, Villalba N, Olson A, Prior S, Butenas S. Increased Thrombin Generation and Abnormal Clot Structure in Trauma Patients with Fibrinolysis Shutdown. Poster presentation at 2018 Military Health System Research Symposium (MHSRS), Kissimmee, FL, August 2018.
2. Osborn Z, Evans P, Miller Z, Villalba N, **Freeman K**. Pre-hospital Evaluation and Care of moderate/severe TBI in the Austere Environment Seeking Occult Shock in Traumatic Brain Injury (TBI): Diagnostic Performance of Plasma Oxidation-Reduction Potential in Neurotrauma. Poster presentation at 2018 Military Health System Research Symposium (MHSRS), Kissimmee, FL, August 2018.
3. **Freeman K**, Sackheim A, Villalba N, Nemkov T, D’Alessandro A, Banerjee A. Developing Traumatic brain injury (TBI) alters the metabolome 24 hours after injury. Poster presentation at Military Health System Research Symposium (MHSRS), Kissimmee, FL, August 2018.
4. Sackheim A, Villalba N, Bonev A, Nelson MT, **Freeman K.** Increased H2O2 After TBI Disrupts PIP2 Metabolism Causing Impaired Endothelial KIR Function. Oral presentation at the 11th World Congress for Microcirculation (WCM2018), Vancouver, BC, Canada, September 2018.
5. **Freeman K**, Dow N, Olsen A, Butenas S, Coleman JR, Moore HB, Moore EE. Dense and Dangerous: The Tissue Plasminogen Activator (t-PA)-Resistant Fibrinolysis Shutdown Phenotype is due to Thrombin-Induced Clot Strength. Oral presentation at the Western Trauma Association Annual Meeting, Snowmass, CO, March 2019.
6. Villalba N, Sackheim AM, Haines L, Ma YT, Li J, Ather JL, Poynter ME, Poynter ME, Sonkusare SK, Hennig G, Nelson MT, **Freeman K**. Suramin Neutralizes Cytotoxic Histones and Prevents Vascular Injury, Edema, And Death. Poster presentation at the 42nd Annual Conference on Shock, San Diego, CA, June 2019.
7. Osborn Z, Prior S, Dow N, Butenas S, Brummel-Ziedins K, **Freeman K**. Factor XIa, Factor IXa and Tissue Factor Contribute to Endogenous Procoagulant Activity in Trauma Patients. Poster presentation at the 42nd Annual Conference on Shock, San Diego, CA, June 2019.
8. **Freeman K**, Longden T, Mughal A, Boucher M, Sackheim A, Hennig G, Lockette W, Nelson MT. Traumatic brain injury impairs cerebral blood flow regulation through disruption of inside-out signaling between capillaries and upstream arterioles. Poster presentation at the 42nd Annual Conference on Shock, San Diego, CA, June 2019.
9. **Freeman K**, Disruption of inside-out signaling between capillaries and upstream arterioles after traumatic brain injury is due to a pervasive endothelial inward rectifier potassium channelopathy, Poster presentation at the 43rd Annual Conference on Shock, Portland, OR, October 2021
10. **Freeman K**, et al. A novel mechanism to neutralize circulating histones and prevent pulmonary endothelial cell icam-1 expression, neutrophil infiltration, and edema in histone infusion and acute lung injury models. Poster presentation at the 43rd Annual Conference on Shock, Portland, OR, October 2021
11. **Freeman K**, et al. Histones and LPS produce endothelial injury through distinct mechanisms. Poster presentation at the 43rd Annual Conference on Shock, Portland, OR, October 2021
12. **Freeman K**, Endothelial dysfunction and calcium channel signaling after trauma, invited talk at the 43rd Annual Conference on Shock, Toronto, Portland, OR, October 2021

**Non-Peer Reviewed Publications**

1. Bouchard B.A., **Freeman K.** (2021) Thrombin Formation. In: Moore H.B., Neal M.D., Moore E.E. (eds) Trauma Induced Coagulopathy. Springer, Cham. <https://doi.org/10.1007/978-3-030-53606-0_6>

**Patents Issued or Pending**

**Small molecule inhibitor of cytotoxic circulating histones in acute inflammation.** Patent application, July 2018 (UVM Ref. No. C717). We discovered a novel mechanism to bind and neutralize cytotoxic histone proteins, utilizing a small molecule inhibitor, and our data supports its therapeutic use in acute inflammatory conditions characterized by high levels of circulating histone. Potential targets include severe sepsis, trauma, major surgery, acute lung injury, systemic lupus, and stroke.

SUMMARY OF SCHOLARLY ACTIVITIES

My most significant recent scholarship activity is the transition from K award to R01 funding from the NIH. The successful funding of my first independent NIH grant represented the critical next step in the NIH-funded physician scientist career trajectory, building on my 8-year Medical Scientist Training Program fellowship and subsequent 5-year K08 Career Development Award. This award provides a secure pathway forward for my research program, which will continue to benefit from additional extramural funding from the Department of Defense, American Heart Association, and industry. My major activity during the course of the K award was conducting basic science research under the direct supervision of Mark Nelson, PhD. I conducted experimental series that established my technical expertise in vascular biology and ion channel physiology. During the period of the K award, I also developed my laboratory, setting up equipment and recruiting a post-doctoral scientist, technician and graduate student. The RO1 award, and my publication record as the senior author on all of the papers from my laboratory, demonstrates that I have successfully established a distinct and separate line of research from the Nelson laboratory. I have impacted the field of trauma through presentations, publications, and participation as an Investigator on the Trans-Agency Consortium for Trauma Induced Coagulopathy (TACTIC), the largest NIH grant in the field of trauma in history.

INVITED PRESENTATIONS

**Regional**

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| Years  2008  2009  2009  2010  2011  2011  2012  2012  2012  2013  2013  2013  2013  2013  2013  2013  2013  2014  2014  2015  2015  2015  2016  2017  2017  2018  2018 | Host Organization  UVM, Department of Surgery, Grand Rounds  Continuing Medical Education, Emergency Medicine Update  UVM, Department of Surgery, Grand Rounds  Vermont Emergency Nursing Association Conference  UVM, Neuroscience, Behavior, and Health Transdisciplinary Research  UVM, Pharmacology Retreat  Boston University, Department of Emergency Medicine, Resident Lecture, “Updates in Traumatic Brain Injury”  Cafe Scientifique, ECHO After Dark, ECHO Lake Aquarium & Science Center, “Sports Injuries and Brain Trauma”  Vermont Public Television, “Emerging Science: Traumatic Brain Injury In Sports”  Fletcher Allen CEO Meeting, “Emergency Medicine Research”  Boston University, Department of Emergency Medicine, Resident Lecture, “Trauma-Induced Coagulopathy”  Vermont Public Television, “Confronting Traumatic Brain Injury in Sports: On-Line Video Engagement Experience  WCAX Television, Healthwatch, “Researchers look for clues in concussions”  Vermont Public Television, “Damage Control: Concussions in Vermont Sports”  UVM, Department of Surgery, Grand Rounds, “Trauma Induced Coagulopathy”  WCAX Television, Healthwatch, “UVM Researchers Study Mysterious Bleeding Syndrome”  UVM, Center for Clinical and Translational Science Seminar, “Trauma induced coagulopathy and endothelial dysfunction”  UVM, Division of Emergency Medicine, Grand Rounds, “Coagulopathy in the emergency department trauma patient”  Boston University, Department of Emergency Medicine, Grand Rounds, “Trauma-induced coagulopathy and the vascular endothelium”  UVM, Department of Surgery, Grand Rounds, “Histone-induced endothelial calcium signals: a novel mechanism for detection of tissue injury”  UVM, Department of Pharmacology Retreat, “Sensory functions of the vascular endothelium in response to danger signals”  UVM, Department of Biochemistry Seminar, “Sensory functions of the vascular endothelium in response to danger signals”  Collaborative Meeting of the Vermont Medical Society, American Academy of Pediatrics VT, Vermont Academy of Family Physicians and the Vermont Psychiatric Association  UVM, Department of Surgery, Inaugural Catamount Surgeon Celebration, UVM Alumni House, “Trauma induced coagulopathy”  UVM, Department of Pharmacology Retreat, “A Model of Sterile Injury Reveals Mechanisms of Endothelial Dysfunction in Small Blood Vessels”  30th Annual Brain Injury Conference, “Emergency Care of Brain Trauma – Concepts and Controversies”  American College of Physicians Vermont Chapter 2018 Annual Meeting, “Medical Marijuana: Evidence-based Treatment” | Location  Burlington, VT  Stowe, VT  Burlington, VT  Berlin, VT  Burlington, VT  Stowe, VT  Boston, MA  Burlington, VT  Burlington, VT  Burlington, VT  Boston, MA  Burlington, VT  Burlington, VT  Burlington, VT  Burlington, VT  Burlington, VT  Burlington, VT  Burlington, VT  Boston, MA  Burlington, VT  Stowe, VT  Burlington, VT  Burlington, VT  Burlington, VT  Stowe, VT  Stowe, VT  Stowe, VT |

**National**

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| Years  2014  2015  2017  2018  2019 | Host Organization  American Association for the Surgery of Trauma, National Meeting / Optional Session: Trans-agency Research Consortium for Trauma Induced Coagulopathy, “Effects of histones, polyphosphates, and thrombin on native endothelium in trauma.”  San Francisco General Hospital, Trauma Surgery Research Conference, “Endothelial calcium signals and trauma-induced coagulopathy.”  University of Colorado, Department of Emergency Medicine Seminar, “Impact of Trauma and Its Factors on Vascular Endothelial Function.”  Military Health System Research Symposium (MHSRS), “Research in Prolonged Field Care and Pre-Hospital Tactical  Combat Casualty Care - Novel oropharyngeal device designed to improve the airway status of a conscious casualty under a delayed evacuation scenario.”  Western Trauma Association Annual Meeting, 2019 Podium Paper, “Dense and Dangerous: The Tissue Plasminogen Activator (t-PA)-Resistant Fibrinolysis Shutdown Phenotype is due to Thrombin-Induced Clot Strength.” | Location  Philadelphia, PA  San Francisco, CA  Denver, CO  Kissimmee, FL  Snowmass, CO |

**International**

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| Years  2018  2020 | Host Organization  Diagnostica Stago, International Webcast  “Code Red: Coagulation Testing in Trauma”  Shock Society Annual Meeting, “Endotheliopathy of Trauma” [POSTPONED DUE TO COVID-19] | Location  Asnières-sur-Seine, France  Toronto, Canada |