



Application

01962 - The GEM Challenge 2015

02109 - Silent IV- A wireless monitored and integrated IV fluid delivery system to increase nursing efficiency, information quality and patient comfort during intravenous medication and fluid therapy.

Collaborative awards with IEM

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Primary Contact

First Name*	Jeffrey	Burke	Halldorson
	<small>First Name</small>	<small>Middle Name</small>	<small>Last Name</small>
Degree	MD		
Faculty Rank*	Associate Professor		
		<small>Faculty Rank - Other</small>	
Email:	jhalldorson@ucsd.edu		
eRA Commons Name	jhalldorson		
Area of Specialty	Transplant Surgery		
<i>(If you are not currently a CTRI member, please fill out a membership application by clicking here.)</i>			
Are you a CTRI member?	Yes		
Address:	Suite 2-286		
	200 West Arbor Drive, #8401		
*	San Diego	92103	California
	<small>City</small>	<small>Postal Code/Zip</small>	<small>State/Province</small>
Fax:			
Phone:*	619-543-5870		
	<small>Phone</small>	<small>Ext.</small>	

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Information

PI Name (Last Name, First Name)

Halldorson, Jeffrey Burke

CO-PI Name (Last name, First name)

Project Title

Silent IV- A wireless monitored and integrated IV fluid delivery system to increase nursing efficiency, information quality and patient comfort during intravenous medication and fluid therapy.

PI Contact information - include email and campus phone number

Jeffrey Burke Halldorson M.D.
Associate Professor
Department of Surgery
Suite 2-286
200 West Arbor Drive, #8401
San Diego, CA 92103

PI Biosketch

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Silent IV.pdf

Silent I.V. narrative

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Halldorson, Jeffrey Burke	POSITION TITLE Associate Professor of Surgery Division of Transplantatoin		
eRA COMMONS USER NAME (credential, e.g., agency login)			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Michigan State University	B.S.	05/88	Biology
University of Michigan	M.D.	05/92	Medicine
University of Pennsylvania		06/99	Molecular Biology

Please refer to the application instructions in order to complete sections A, B, C, and D of the Biographical Sketch.

A. Personal Statement

The goal of the proposed research is to advance the translation of successful models of muscle directed gene therapy utilizing adeno-associated viral vectors into large animal models with an eventual goal of developing safe and effective gene therapy for treatment of Duchenne Muscular Dystrophy in humans. More specifically, our proposal first aims to optimize an isolated limb perfusion circuit to for delivery of adeno-associated viral vectors to skeletal muscle in a large animal model in preparation for future human trials for treatment of DMD.

My training and experience in both general and transplant surgery and gene therapy is particularly well suited to translational research in Gene Therapy. As a general and transplant surgeon I have a daily working knowledge of vascular anatomy and not uncommonly utilize venovenous bypass during liver transplant operations. Additionally, I work daily with our nephrologists managing renal failure and dialysis in our pre-and post transplant patients. I have had a long interest in Gene Therapy and spent 4 years during my surgical residency at the University of Pennsylvania enrolled in the Molecular Biology Ph.D. Program. My initial laboratory mentor was John Englehardt developing redox-gene therapy to liver utilizing recombinant adenoviruses. Unfortunately, Dr. Englehardt left the University of Pennsylvania midway through my PhD. and I was unable to move with him due to family considerations. I then switched labs to study under James Wilson and took up the study of immune responses to gene therapy vectors as well a significant amount of effort establishing a model demonstrating correction of dystrophin deficiency in mice utilizing recombinant adenoviral gene therapy. During this time I gained practical experience in all of the laboratory techniques necessary for successful animal experimentation in this model, including growing and purifying recombinant adenoviral and adeno-associated viral vectors, developing Immunological assays for host responses against transgenes and/or viral vector as well as basic techniques in molecular biology, histology and basic immunohistochemistry. Unfortunately, given the loss of time unavoidable from changing mentors the refusal by my surgery department in Minnesota to grant another year of research time, I was unable to complete my Ph.D. thesis as originally planned.

After returning to surgery training and completing my surgical training at the University of Minnesota, I trained in transplantation at the University of California, San Francisco where I initiated a project to develop SV40 based gene therapy vectors intended to be eventually used for modulation of immune responses to transplant organs using localized gene therapy. I continued this yet unpublished work with Dr. Chamberlain for the last number of years where I have also participated in the Chamberlain groups continuing efforts to translate muscle directed gene therapy to large animal models.

During my time at the University of Washington I have successfully published a number of clinical studies in collaboration with my colleagues in Nephrology and Hepatology. Motivated by my unique position to assist Dr. Chamberlain in his studies, I laid the groundwork for the proposed research by connecting the local experts in both dialysis (Dr. Ahmad and Bieber) with the experts in muscle directed gene therapy (Dr. Chamberlain and Odom). To this collaboration I will bring my unique perspective and surgical experience in vascular anatomy and physiology necessary for a successful project.

In summary, I have a longstanding interest in gene therapy and have demonstrated a record of accomplished and productive research projects in both clinical medicine and gene therapy. Surgical skills, experience with ex-vivo blood circuits and dialysis as well as gene therapy make me well qualified to help translate successful animal research in Duchenne muscular dystrophy into first the large animal model and hopefully human trials in the future.

B. Positions and Honors

FELLOWSHIP TRAINING

UCSF Transplant Surgery	2001-2003
University of Pennsylvania	Molecular Biology/Gene Therapy Post-Doctoral Fellowship.
	Research Mentors, James Wilson M.D., Ph.D. and John Englehardt Ph.D.

ACADEMIC APPOINTMENTS

UCSF	2001-2003 Instructor Transplant Surgery
University of Washington	2003 to 2007 Acting Assistant Professor Transplant Surgery
University of Washington	2007 to 2008 Clinical Assistant Professor of Transplant Surgery
University of Washington	2008 to Current Assistant Professor of Transplant Surgery

Other Experience and Professional Memberships

2011 – present	Member, Editorial Board – <i>World Journal of Transplantation</i>
2011 – present	Member, Editorial Board – <i>World Journal of Gastroenterology</i>
2011 – present	Member, Editorial Board – <i>Surgery: Current Research</i>
2011 – present	Member, Editorial Board – <i>HPB Surgery</i>

Honors

1991	AOA Honor Society	University of Michigan Medical School
2003	Board Certified in General Surgery	

C. Selected Peer-reviewed Publications

Most relevant to the current application

1. Zwacka RM, Zhang Y, **Halldorson J**, Schlossberg H, Dudus L, Engelhardt JF. CD4(+) T-lymphocytes mediate ischemia/reperfusion-induced inflammatory responses in mouse liver. *J Clin Invest*, 1997 Jul 15;100(2):279-289.
2. Zwacka RM, Zhou W, Zhang Y, Darby CJ, Dudus L, **Halldorson J**, Oberley L, Engelhardt JF. Redox gene therapy for ischemia/reperfusion injury of the liver reduces AP1 and NF- κ B activation. *Nat Med*, 1998 June;4(6): 698-704.
3. Zwacka RM, Zhang Y, Zhou W, **Halldorson J**, Engelhardt JF. Ischemia/reperfusion injury in the liver of BALB/c mice activates AP-1 and nuclear factor κ B independently of I κ B degradation. *Hepatology*, 1998 Oct;28(4):1022-1030.
4. Louboutin JP, Rouger K, Tinsley JM, **Halldorson J**, Wilson JM. iNOS expression in dystrophinopathies can be reduced by somatic gene transfer of dystrophin or utrophin. *Mol Med*, 2001;7(5):355-364.
5. Gregorevich P, Schultz BR, Allen JM, **Halldorson JB**, Blankinship ML, Mezmarich MA, Kuhr CS, Doremus C, Finn E, Liggett D and Chamberlain JS, Evaluation of vascular delivery methodologies to enhance rAAV6-mediated gene transfer to canine striated musculature. *Mol Ther*. 2009 Aug;17(8):1427-33. Epub 2009 May 26.

Additional recent publications of importance to the field (in chronological order)

6. Jones JW, **Halldorson J**, Elick B, Granger DK, Matas AJ. Unrecognized health problems diagnosed during living donor evaluation: a potential benefit. *Transplant Proc*, 1993 Dec;25(6):3083-3084.
7. Limaye AP, Bakthavatsalam R, Kim HW, Kuhr CS, **Halldorson JB**, Healey PJ, Boeckh M. Late-onset cytomegalovirus disease in liver transplant recipients despite antiviral prophylaxis. *Transplantation*, 2004 Nov 15;78(9):1390-1396.
8. Limaye AP, Bakthavatsalam R, Kim HW, Randolph SE, **Halldorson JB**, Healey PJ, Kuhr CS, Levy AE, Perkins JD, Reyes JD, Boeckh M. Impact of cytomegalovirus in organ transplant recipients in the era of antiviral prophylaxis. *Transplantation*, 2006 Jun 27;81(12):1645-1652.
9. Chan EY, Olson LC, Kisthard JA, Perkins JD, Bakthavatsalam R, **Halldorson JB**, Reyes JD, Larson AM, Levy AE. Ischemic cholangiopathy following liver transplantation from donation after cardiac death donors. *Liver Transpl*, 2008 May 14(5):604-610.
10. Chan EY, Larson AM, Fix OK, Yeh MM, Levy AE, Bakthavatsalam R, **Halldorson JB**, Reyes JD, Perkins JD. Identifying risk for recurrent hepatocellular carcinoma after liver transplantation: implications for surveillance studies and new adjuvant therapies. *Liver Transpl*, 2008 Jul;14(7):956-965.
11. Perkins JD, **Halldorson JB**, Bakthavatsalam R, Fix OK, Carithers RL Jr, Reyes JD. Should liver transplantation in patients with model for end-stage liver disease scores ≤ 14 be avoided? A decision analysis approach. *Liver Transpl*, 2009 Feb;15(2):242-254.

12. **Halldorson JB**, Bakthavatsalam R, Fix O, Reyes JD, Perkins JD. D-MELD, a simple predictor of post liver transplant mortality for optimization of donor and recipient matching. *Am J Transplant*, 2009 Feb 9(2):318-326.
13. **Halldorson JB**, Bakthavatsalam R, Reyes JD, Perkins JD. The impact of consecutive operations on survival after liver transplantation. *Liver Transpl*, 2009 Aug;15(8):907-914.
14. **Halldorson JB**, Bakthavatsalam R, Salvalaggio PR, Pichler RH, Kendrick EA, Reyes JD, Davis CL, Leca N. Donor-recipient size matching influences early but not late graft function after pediatric en-bloc kidney transplantation. *Transplantation* 2010; 89(2): 208-214.
15. Spitzer AL, Dick AA, Bakthavatsalam R, **Halldorson JB**, Salvalaggio PR, Reyes JD, Perkins JD. Intraoperative portal vein blood flow predicts allograft and patient survival following liver transplantation. *HPB (Oxford)* 2010;12:166-173.
16. Spitzer AL, Lao OB, Dick AA, Bakthavatsalam R, **Halldorson JB**, Yeh MM, Upton MP, Reyes JD, Perkins JD. The biopsied donor liver: incorporating macrosteatosis into high-risk donor assessment. *Liver Transpl* 2010;16:874-884.
17. Park ES, Peccoud M, Wicks KA, **Halldorson JB**, Carithers RL Jr, Reyes, JD, Perkins JD. Use of an automated clinical management system improves outpatient immunosuppressive care following liver transplantation. *JAMIA* 2010;17:396-402
18. Rayhill S, Schwartz J, Ham J, Carithers R, Lei Y, Bhattacharya R, Liou I, Landis C, Limaye A, Rakita R, Dick A, Healey J, **Halldorson J**, Bakthavatsalam R, Perkins J, Reyes J. The use of hepatitis B core antibody-positive donor livers does not appear to have a deleterious effect on graft survival in liver transplantation for hepatitis C. *Transplant Proc* 42(10):4141-4144, 2010.
19. Cantafio A, Dick A, **Halldorson J**, Bakthavatsalam R, Reyes J, Perkins J. Risk stratification of kidneys from donation after cardiac death donors and the utility of machine perfusion. *Clin Transplant*, in press.
20. JP Roberts, HJ Paarsch A Segre and **Halldorson JB**, , Competition and Post-Transplant Outcomes in Cadaveric Liver Transplantation under the MELD Scoring System, *Collegio Carlo Alberto*, July 2011, No. 213.
21. **Halldorson J**, Dodge J, HJ Paarsch, A Segre and JP Roberts, *Center Competition and Outcome Following Liver Transplantation*, *Liver Transplantation* 2013 Jan;19(1):96-104.
22. Bieber S, **Halldorson J**, Finn E, Ahmad S, Chamberlain J and G Odom, *Extracorporeal Delivery of rAAV with Metabolic Exchange and Oxygenation*, *Scientific Reports*, 3: 1538, Mar 26, 2013.
23. Avolio AW, **Halldorson JB**, Burra P, Dutkowski P, Agnes S, Clavien PA., *Balancing Utility and Need by Means of Donor-to-Recipient Matching: A Challenging Problem*, *Am J Transplant*. 2013 Feb;13(2):522-3.
24. Avolio AW, **Halldorson JB**, Lirosi M, Lupo L, Nicoletti N, and S Agnes, *D-MELD, a Strong and Accurate Tool to Guide Donor-2-Recipient Matching*, *Ann Transplant*. 2013 Apr 8;18:161-2.

25. Jia N, Liou I, **Halldorson J**, Carithers C, Perkins J, Reyes J, Yeh M, Stohr E, Rao S and E Lin, *Phase I Adjuvant Trial of Sorafenib in Patients with Hepatocellular Carcinoma after Orthotopic Liver Transplantation*, In Press for Anti-Cancer Research (2013).
26. **Halldorson JB** and JP Roberts, *Decadal Analysis of Deceased Organ Donation in Spain and the U.S., Linking Increased Donation Rate and Utilization of Older Donors*, In Press for Liver Transplantation (2013).
27. Leca N, Warner P, Bakthavatsalam R, Nelson K, **Halldorson JB**, , Rayhill S, Kendrick E, Davis C and JD Reyes, *Outcome of Simultaneous Liver and Kidney Transplantation in Relation to a High Level of Preformed Donor-Specific Antibodies*. Transplantation. 2013 Nov 27; 96(10):914-8.
28. Lang J, Smith A, Brandon A, Bradley K, Liu Y, Li Y, Crowe D, Jhala N, Cross R, Frenette L, Martay K, Vater Y, Vitin A, Dembo G, DuBay D, Bynon J, Szychowski J, Reyes J, **Halldorson J**, Rayhill S, Dick A, Bakthavatsalam R, Brandenberger J, Broeckel-Elrod J, Sissons-Ross L, Jordan T, Chen L, Siriussawakul A, Eckhoff D and R. Patel, A randomized clinical trial testing the anti-inflammatory effects of pre-emptive inhaled nitric oxide in human liver transplantation, PLoS ONE 9(2): e86053. doi:10.1371/journal.pone.0086053
29. Montenovo M, Vaidya S, Bakthavatsalam RB and **JB Halldorson**, *Pseudoaneurysm after Combined Kidney/Pancreas Transplantation Presenting with Sentinel Bleeding. A Case Report and Review*, Ann Transplant 2014;19:317-319.
30. **Halldorson JB**, Bakthavatsalam R, Dick A, Rayhill S, Perkins JD and JD Reyes, *Differential Rates of Ischemic Cholangiopathy and Graft Survival Associated with Induction Therapy in DCD Liver Transplantation*. Manuscript accepted for publication, Am J Transplant.
31. **Halldorson JB**, Carithers R, Bakthavatsalam R, Dick A, Bhattacharya R, Liou I, Reyes J and James D. Perkins, *D-MELD Risk Capping Improves Post Liver Transplant Survival and Overall Mortality after Listing, A Markov Microsimulation Analysis*. World J Transplant. 2014 September 24; 4(3): 206-215.
32. **Halldorson JB**, *The Impact of Market Forces on Liver Transplant Allocation*, Surgery Curr Res 2014, 4:6.
33. **Halldorson JB**, Bakthavatsalam R, Dick A, Rayhill S, Perkins JD and JD Reyes. *Serum Alkaline Phosphatase and Bilirubin are Early Surrogate Markers for Ischemic Cholangiopathy and Graft Failure after DCD Liver Transplantation*. Manuscript accepted for publication, Transplant Proceedings

D. Research Support

Prior Research Support

Completed Research Support

- 2002 PPTA “Impact of Intra-operative Human Serum Albumin (HSA) vs. Crystalloid in the reduction of Delayed Graft Function following Kidney Transplantation.” Co-investigator with Sandy Feng MD, PhD
Amount: \$90,000
- 1997-00 NRSA “Mechanisms of redox regulation in LPS mediated TNFa secretion”
Amount: \$180,000

Silent IV- A wireless monitored and integrated IV fluid delivery system to increase nursing efficiency, information quality and patient comfort in intravenous fluid delivery system monitoring.

Aim: Improve I.V. fluid and drug delivery information and efficiency while improving patient comfort using wireless technology. The system would consist of two parts. The first component would consist of an I.V. fluid and drug delivery monitor equipped with a wireless transmitter. The second component would be a smart-phone receiver and software app that would provide user-friendly information directly to the bedside nurse. Drug delivery and IV infusion information could be linked to continuous monitoring of vital signs allowing for more rapid identification and treatment of adverse reactions. (See diagram) A remote nursing directed or automated safety stop function could be incorporated into the device.

Rationale: Current generation IV delivery units have archaic and non-integrated information delivery systems, largely limited to audible alarms that sound at the bedside when intravenous flow is interrupted. Essentially, the patient, who cannot act on the alarm, is disturbed from rest while the nurse, often not in the room, does not receive the information in a timely and efficient manner. Typically, as floor nurses care for several patients simultaneously and bedside alarms largely result in frequent patient disturbances and not infrequently patient self-muting the alarm system. An optimized system would deliver higher quality information directly to the nurse who is responsible for drug and IV fluid delivery while simultaneously leaving the patient undisturbed.

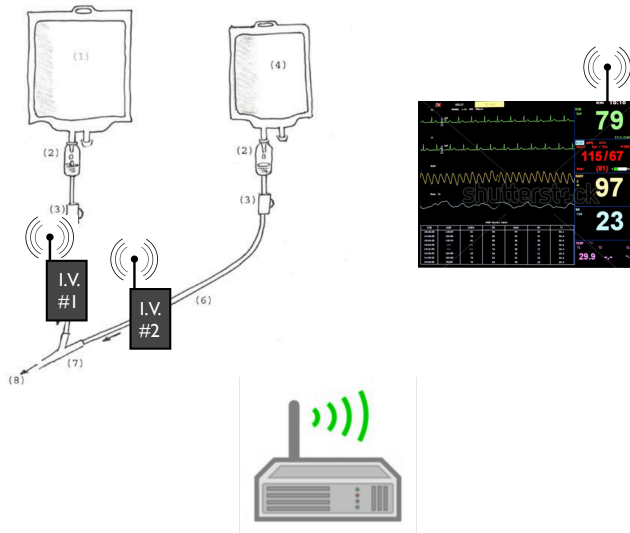
Challenge/Need and Significance: Almost all hospital inpatients receive intravenous fluid delivery, often with multiple infusing agents/drugs being delivered simultaneously. Maintenance of I.V. lines and timing of drugs is a manually intensive and time consuming process with multiple pathways for error. Integration of I.V. fluid and medication delivery, monitoring coordinated with real time patient clinical data could increase nursing efficiency, improve patient satisfaction and speed identification and treatment of adverse drug reactions or adverse reactions to blood product infusions.

Innovation, Feasibility: A flow monitor/transmitter and smart-phone based receiver system could use current technology that is readily available. There is no equivalent product currently used in the hospital. Development of such a system would be widely applied to improve care for all hospitalized patients.

Investigator Qualifications: The investigator is known for publishing several sentinel articles with innovative approaches to clinical problems. Additionally, I have organized multi-specialty approaches to engineering problems in gene therapy most recently at the University of Washington where I initiated a project to develop an ex-vivo perfusion circuit to optimize adeno-associated gene delivery for treatment of Duchenne Muscular Dystrophy. (reference: [Sci Rep](#). 2013;3:1538. *Extracorporeal delivery of rAAV with metabolic exchange and oxygenation*. Bieber S1, Halldorson JB, Finn E, Ahmad S, Chamberlain JS, Odom GL.)

Schematic Drawing

A. Bedside Transmitters.



B. Smartphone Nursing App.

