Curriculum Vitae


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| Date Prepared: | 10/1/2014 |
| Name: | Steven Jon Russell, M.D., Ph.D. |
| Office Address: | MGH Diabetes Center<br>50 Staniford St., Suite 301<br>Boston, MA 02114 |
| Home Address: | 32 Stonehedge Road<br>Lincoln, MA 01773 |
| Work Phone: | 617-726-1848 |
| Work Email: | sjrussell@partners.org |
| Work FAX: | 617-643-0697 |
| Place of Birth: | Lincoln, Nebraska, USA |


Education

| Year | Degree (Honors) | Fields of Study (Thesis advisor for doctoral research degrees) | Institution |
|---|---|---|---|
| 1990 | B.S. | Biochemistry | Trinity University |
| 2001 | M.D., Ph.D. | Medicine, Biological Chemistry | University of Texas Southwestern Medical Center |

Postdoctoral Training

| Year(s) | Title | Specialty/Discipline (Lab PI for postdoctoral research) | Institution |
|---|---|---|---|
| 7/2001-6/2003 | Resident | Internal Medicine | Massachusetts General Hospital |
| 7/2003-6/2006 | Clinical Fellow | Endocrinology | Massachusetts General Hospital |
| 7/2004-7/2008 | Research Fellow | C. Ronald Kahn | Joslin Diabetes Center |

Faculty Academic Appointments

| Year(s) | Academic Title | Department | Academic Institution |
|---|---|---|---|
| 7/2006-3/2012 | Instructor in Medicine | | Harvard Medical School |
| 4/2012-present | Assistant Professor of Medicine | | Harvard Medical School |

Appointments at Hospitals/Affiliated Institutions

| Year(s) | Position Title | Department (Division, if applicable) | Institution |
|---|---|---|---|
| 7/2006-present | Assistant in Medicine | Internal Medicine | Massachusetts General Hospital |

Other Professional Positions

| Year(s) | Position Title | Institution |
|---|---|---|

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|---|---|---|
| 1987-1990 | National Science Foundation Summer Undergraduate Research Fellow | Trinity University, San Antonio, TX |

Committee Service

Local

| Year(s) of Membership | Name of Committee<br>Dates of Role(s) | Institution/Organization<br>Title of Role(s) |
|---|---|---|
| 2003-2006 | Teaching and Training Council<br>2003-2006 | MGH Department of Medicine<br>Member (Fellow Representative) |
| 2005-2006 | Perioperative Diabetes Management Taskforce<br>2005-2006 | Massachusetts General Hospital<br>Member |

National and International

| Year(s) of Membership | Name of Committee<br>Dates of Role(s) | Institution/Organization<br>Title of Role(s) |
|---|---|---|
| 2012- | Initiative to Advance Pediatric Therapeutics<br>Member, Diabetes Core Group | National Institute of Child Health and Human Development |
| 2012-present | Clinical Development Advisory Panel | California Institute of Regenerative Medicine |
| 2013-present | Glu Research Advisory Board | T1D Exchange |

Professional Societies

| Year(s) of Membership | Society Name<br>Dates of Role(s) | <br>Title of Role(s) |
|---|---|---|
| 1991- | American Medical Association | |
| 2001- | American College of Physicians | |
| 2005- | Endocrine Society | |
| 2005-2012 | Longevity Consortium | |
| 2007-2012 | American Aging Association | |
| 2007- | American Diabetes Association | |

Grant Review Activities

| Year(s) of Membership | Name of Committee<br>Dates of Role(s) | Institution/Organization<br>Title of Role(s) |
|---|---|---|
| 2011 | Artificial Pancreas Study Section (SBIR)<br>2011 | NIH/NIDDK<br>Ad-hoc member |
| 2011-2012 | National Scientific Advisory Council<br>2011-2012 | American Foundation for Aging Research<br>Member |
| 2012 | Medical Research Council (UK) | Medical Research Council (UK) |

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|---|---|---|
| | 2012 | Ad-hoc reviewer |
| 2012 | Strategic Partnership Awards review panel | California Institute for Regenerative Medicine |
| | 2012 | Member |
| 2012-present | Clinical Development Awards Panel | California Institute for Regenerative Medicine |
| | 2012-present (meetings in 2012 and 2014) | Member |
| 2013 | A*Star Biomedical Engineering Programme (BEP) grant | Center for Integration of Engineering and Medicine |
| | 2013 | Ad-hoc reviewer |
| 2013 | CIRM Translational Portfolio Assessment | California Institute for Regenerative Medicine |
| | 2013 | Panel Member |
| 2013-present | Grants Working Group | California Institute of Regenerative Medicine |
| | 2013- | Member |
| 2013 | Disease Team Therapy Development III Awards review panel | California Institute for Regenerative Medicine |
| | 2013 | Member |
| 2014 | Fellowship Grant Evaluation Committee | The Danish Diabetes Academy |
| | 2014 | Member |
| 2014 | Women's Health Research at Yale (Internal Grant Program) | Yale University School of Medicine |
| | 2014 | External Reviewer |
| 2014 | Stem Cell Alpha Clinics review panel | California Institute for Regenerative Medicine |
| | 2014 | Panel Member |

Editorial Activities

| Journals for which you serve as a reviewer |
|---|

In alphabetical order:
Aging Cell
Annals of the New York Academy of Sciences
BioEssays
Diabetes
Diabetes Care
Diabetes Technology and Therapeutics
The FASEB Journal
The Journal of Diabetes Science and Technology
The Lancet
The Lancet Diabetes & Endocrinology
Molecular and Cellular Endocrinology
The New England Journal of Medicine
PLoS ONE

Other Editorial Roles

| Year(s) | Role | Journal Name |
|---|---|---|
| 2010 | Co-editor - Symposium: Glucagon | Journal of Diabetes Science and |

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|---|---|---|
| | Physiology and Pharmacology (Volume 4, Issue 6, November 2010) | Technology |
| 2012-present | Section Editor - Technological Developments in Diabetes Therapies (Volume 12, Issue 6, December 2012) | Current Diabetes Reports |
| 2012-present | Advisory Board member | diaTribe, diabetes Close Up, and CloserLook (Close Concerns) |

Honors and Prizes

| Year | Name of Honor/Prize | Awarding Organization | Achievement for which awarded (if unclear from award title) |
|---|---|---|---|
| 1986-1990 | National Merit Scholarship | Trinity University | National Merit Finalist |
| 1986-1990 | President's / Trustee Scholarship | Trinity University | |
| 1994 | High Pass | University of Texas Southwestern Medical Center, Biochemistry and Molecular Biology Graduate Program | Outstanding qualifying exam proposal in NIH grant form |
| 1997 | Young Scientists' Program Fellowship | American Society for Biochemistry and Molecular Biology / International Union of Biochemistry and Molecular Biology | Abstract competition |
| 1997-1998 | Presenter | 29th and 3oth Annual Sigma Xi Graduate Student Research Forum | Abstract competition |
| 1997 | Sigma Xi Membership | Sigma Xi | |
| 1997 | Exceptional presentation | Graduate Student Illustrations and Presentations Session | Poster competition |
| 2000 | Alpha Omega Alpha Membership | Alpha Omega Alpha | |
| 2008 | Scholarship to MBL Molecular Biology of Aging Course | Ellison Medical Foundation | |
| 2013 | Granite Gala Honoree | Juvenile Diabetes Research Founation – Northern New England Chapter | |

Report of Funded and Unfunded Projects
Funding Information
Past

| Grant title | Grant title<br>Grant type and number<br>Role on Project (if PI or site PI, total indirect costs)<br>Description of the major goals |
|---|---|
| 2006-2007 | Adipocyte Insulin Signaling in Metabolism and Aging |

NIH, Ruth L. Kirschstein National Research Service Award (1 F32 AG028265-01)
PI ($52,048)
The goal of this study was to investigate how insulin signaling in adipocytes regulates lifespan in long-lived fat-specific insulin receptor knockout (FIRKO) mice.

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2007

Closed-loop blood-glucose regulation in type 1 diabetes: A clinical trial
Wallace H. Coulter Foundation, Translational Partners Award
MGH PI ($0 - full budget of $100,000 spent on preclinical development at Boston University site)
The goal of this project was to complete preclinical experiments on a closed-loop blood glucose control system and to prepare an IDE application for human studies.

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2007-2010

Utility of Continuous Glucose Monitoring for Maintenance of Normoglycemia in ICU Patients
Abbott Diabetes Care
PI ($110,000)
The goal of this study was to test the accuracy of a continuous glucose monitoring device that measures interstitial fluid glucose (Abbott Navigator) in critically ill ICU patients.

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2009-2011

Development and preclinical testing of a closed-loop control system for blood-glucose regulation in the ICU
Wallace H. Coulter Foundation, Translational Partners Award
MGH PI ($0 - full budget of $200,000 spent on preclinical development at Boston University site)
The objective of this program was to perform pre-clinical experiments on a closed-loop control system for regulating blood glucose in critically ill patients.

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2009-2011

Adipocyte Insulin Signaling in Metabolism and Aging
NIH/NIA, ARRA Supplement (3 K08 AG032869-02S1)
PI ($99,937)
This is an American Reinvestment and Recovery act supplement to 1 K08 AG032869-01 to fund hiring of a research assistant and purchase of equipment.

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2007-2011

Closed-loop glucose control for automated management of type 1 diabetes
Juvenile Diabetes Research Foundation, Clinical Investigations Research Grant
MGH PI ($1,034,092)
The objective of this project was to test the ability of a closed-loop control system to regulate blood glucose in adults with type 1 diabetes.

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2010-2012

In-patient trials of automated glucose control in children with type 1 diabetes
Leona M. and Harry B. Helmsley Charitable Trust,
MGH PI ($640,635)
The objective of this project is to test the ability of a closed-loop control system to regulate blood glucose in children with type 1 diabetes.

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2008-2013

Adipocyte Insulin Signaling in Metabolism and Aging
NIH/NIA-American Foundation for Aging Research, Paul Beeson Career Development Award in Aging Research (1 K08 AG032869-01)
PI ($799,719)
The goal of this study is to investigate how insulin signaling in adipocytes regulates lifespan in long-lived fat-specific insulin receptor knockout (FIRKO) mice.

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2009-2013 Clinical trials of a closed-loop control system for type 1 diabetes management
NIH/NIDDK (1R01DK085633-01)
MGH PI ($1,812,925)
The goal of this trial is to test the safety and efficacy a bi-hormonal closed-loop blood glucose control system in adults with type 1 diabetes.

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2010-2014 Selecting Insulin Analogs for Closed-loop Control Using Multiplex Pharmacokinetic Profiling
Leona M. and Harry B. Helmsley Charitable Trust (09-T1D038)
PI ($526,700)
The objective of this study is to determine whether the pharmacokinetic characteristics of rapid acting insulin preparations vary within a single individual.

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2011-2013 Subcutaneous continuous glucose monitoring and intravenous dosing of insulin and dextrose for automated glycemic control in the in-patient setting: A clinical trial in the MGH CRC
Wallace H. Coulter Foundation, Translational Partners Grant
MGH PI ($90,000)
This is a first-in-man closed-loop blood glucose control system for inpatient application using interstitial fluid continuous glucose monitoring intravenous insulin and dextrose.

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2012-2014 Pharmacokinetic Comparison of Intradermal vs. Sub-cutaneous Insulin and Glucagon Delivery in Volunteers with Type 1 Diabetes
Leona M. and Harry B. Helmsley Charitable Trust
PI ($87,959)
This study is designed to determine the impact on insulin and glucagon pharmacokinetics of intradermal vs. subcutaneous delivery.

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2013-2014 Testing a bi-hormonal bionic pancreas in an outpatient study in children with type 1 diabetes at the Clara Barton/Joslin Camps
Helmsley Trust Foundation (2014PG-T1D006)
MGH PI ($416,000)
The goal of this project is to test the ability of a wearable bihormonal bionic pancreas to provide BG control in pediatric volunteers with type 1 diabetes (ages 12-20) in the setting of a summer diabetes camp outpatient study.

Current

| Grant title | Grant title<br>Grant type and number<br>Role on Project (if PI or site PI, total indirect costs)<br>Description of the major goals |
|---|---|

2012-2016 Translational studies of a bionic pancreas for out-patient diabetes management
NIH/NIDDK (1R01DK097657-01)
PI ($2,911,229)
The project will test a fully automated, wearable, bi-hormonal closed-loop bionic pancreas in adults and children over extended periods (up to six days of wear) in environments that will approximate the rigors of the outpatient environment. Adults experiments will last five days while subjects live in a hotel and interact with the city environment, experiments in children will last six days in a diabetes camp environment.

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2013-2015 A multicenter outpatient trial of a bihormonal bionic pancreas

NIH/NIDDK (1DP3DK101084)
PI ($2,880,000)
The goal is to test fully automated, wearable, bi-hormonal closed-loop bionic pancreas in ad over extended periods (12 days of wear) at home and at work in four US centers with MGH the coordinating center.

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2014 Testing a bionic pancreas in an outpatient study in preadolescent children with type 1 diabetes at the Clara Barton/Joslin Camps
Helmsley Trust Foundation (2014PG-T1D032)
MGH PI ($514,300)
The goal of this project is to test the ability of a wearable bihormonal bionic pancreas to provide BG control in pediatric volunteers (ages 6-11) with type 1 diabetes in the setting of a summer diabetes camp outpatient study.

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2012-2015 Bionic Pancreas with Minimally Invasive Continuous Insulin Monitoring
Juvenile Diabetes Research Foundation – JDRF (17-2013-485)
PI ($765,360)
The goal of this project is to develop continuous insulin monitor. The device will use a probe about the same size as an infusion set. It will continuously sample the insulin that has been absorbed from the blood into the tissues using microdialysis and measure it will a flow-through microfluidic immunoassay.

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2014 Equivalence of a Stable Liquid Glucagon Formulation with Freshly Reconstituted Lyophilized Glucagon
Helmsley Trust Foundation (2014PG-T1D006)
PI ($174,130)
The goal of this project is to test the equivalence of a stable glucagon formulation with freshly reconstituted samples of a formulation that has been used successfully in a bionic pancreas, but it not stable enough for prolonged use.

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2012-2015 Closed loop micodose glucogon administration for the automated prevention and treatment of hypoglycemia
American Diabetes Association (7-12-HYPO-07)
PI ($499,998)
This project is a randomized, double-blinded, placebo controlled trial of automated, closed-loop microdose glucagon delivery for prevention and treatment of hypoglycemia in patients with type 1 diabetes.

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Report of Local Teaching and Training
Teaching of Students in Courses

| Year(s) | Course Title<br>Type of student/audience | Location<br>Level of Effort |
|---|---|---|
| 2005-2006 | Patient-Doctor II<br>2nd year medical students | Harvard Medical School<br>Examiner, Endocrine section of OSCE |
| 2007 | Human Systems<br>1st year medical students | Harvard Medical School<br>Substitute tutor, Endocrine section |

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|---|---|---|
| 2014 | HST-060 (Endocrinology)<br>1st year HST (MD/PhD) students | Harvard Medical School<br>75 minute lecture on type 1 diabetes |

Formal Teaching of Residents, Clinical Fellows and Research Fellows (post-docs)

| Year(s) | Title<br>Type of student/audience | Location<br>Level of Effort |
|---|---|---|
| 2012-present | Tools of Human Investigation<br>Course for Internal Medicine Residents | Massachusetts General Hospital<br>90 minute lecture 4 times per year |

Clinical Supervisory and Training Responsibilities

| Year(s) | Type of responsibility | Level of Effort |
|---|---|---|
| 2008-present | Endocrine Consult Service Attending | Rounds 8:30-10:00 daily, writing attending notes on new consults, 3 weeks annually |
| 2010-present | Endocrine Fellow Diabetes Clinic Preceptor | Occasional preceptor of fellows in clinic |

Laboratory and Other Research Supervisory and Training Responsibilities

| Year(s) | Type of responsibility | Level of Effort |
|---|---|---|
| 1995-1998 | Supervision of 1st and 2nd year graduate students rotating through laboratory, University of Texas Southwestern Medical Center | Daily supervision of 7 rotation students for 3 months each |
| 2007-2012 | Supervision of research assistants Joslin Diabetes Center | Daily supervision and mentoring of two research assistants. To date, one former RA is a PhD student in Biology at Boston University starting in 2011-2012 academic year, one will be applying to medical school for the 2014-2015 academic year |
| 2012-present | Co-mentorship of Lindy Kahanovitz with Tania Konry (Lindy is a graduate student doing thesis work at MGH while still matriculating at Ben Gurion University because her husband took a postdoctoral fellowship at HMS) | At least weekly meetings, supervision of research progress on development and testing of a microfluidic device for continuous insulin monitoring in vivo using microdialysis fluid from the subcutaneous space |
| 2012-present | Research mentor for Manasi Sinha, MD, MPH, who completed her clinical fellowship in Pediatric Endocrinology. | Primary mentoring and supervision of her research efforts. We have at least weekly meetings and more typically meet 2-3X per week. |
| 2014-present | Research mentor for Laya Eklaspour, MD, who completed her clinical fellowship in Pediatric Endocrinology. | Primary mentoring and supervision of her research efforts. We have intermittent meetings. She will begin working full time when her clinical fellowship is complete. |

Local Invited Presentations

| Year(s) | Title of presentation/ Type of presentation<br>Department and Institution where presented (Sponsor, if any) |
|---|---|

No presentations below were sponsored by outside entities

1997 Molecular Gears of Circadian Clocks / Biochemistry Department Graduate Student/Post-doctoral Fellow Colloquium, University of Texas Southwestern Medical Center

2005 Diabetic Complications / Department Seminar
Podiatry, Massachusetts General Hospital

2007 Continuous Glucose Monitoring / Special Interest Group Seminar
Nursing, Massachusetts General Hospital

2008 Continuous Glucose Monitoring: Update / DRC Research Meeting
Diabetes Research Center, Massachusetts General Hospital

2008 Closed-loop Blood Glucose Control / DRC Research Meeting
Diabetes Research Center, Massachusetts General Hospital

2008 Closed-loop Blood Glucose Control / Pediatric Endocrinology conference, Massachusetts General Hospital

2009 Closed-loop Blood Glucose Control – Update on Clinical Trials / DRC Research Meeting
Diabetes Research Center, Massachusetts General Hospital

2009 Bi-hormonal Closed-loop Blood Glucose Control for Type 1 Diabetes Mellitus /
Pediatric Endocrinology conference, Massachusetts General Hospital

2009 Bi-hormonal Closed-loop Blood Glucose Control for Type 1 Diabetes Mellitus / Grand Rounds, Endocrine Unit, Massachusetts General Hospital

2010 Regulation of Aging by Insulin Signaling in Mammals / Grand Rounds
Geriatric Medicine, Massachusetts General Hospital

2010 Regulation of Aging by Insulin Signaling in Fat / Internal Seminar Series
Joslin Diabetes Center, Boston, MA

2011 Sponsoring and Conducting Research Under an IDE / Clinical Research Program Seminar Series, Massachusetts General Hospital

2011 “Compelling Applications” panel / panelist discussing Continuous Glucose Monitoring and Closed-loop Blood Glucose Control
CIMIT Innovation Workshop on Next Generation Drug Delivery, Monitoring and Adherence Systems in Chronic Disease Management, Boston, MA

2011 Automated Glucose Management in Type 1 Diabetes with a Bi-hormonal Bionic Pancreas
The Center for Engineering in Medicine, Massachusetts General Hospital

2011 Continuous Glucose Monitoring and Closed-loop Blood Glucose Control in the ICU / Pulmonary and Critical Care Division Research Conference, Massachusetts General Hospital

2011 Automated Glucose Management in Type 1 Diabetes With a Bi-hormonal Bionic Pancreas / Endocrine Grand Rounds, Beth Israel Deaconess Medical Center, Boston, MA

2011 Continuous Glucose Monitoring and Artificial Pancreas Update / Diabetes Research Center Research Meeting, Massachusetts General Hospital

2012 Automated Glucose Management in Type 1 Diabetes with a Bi-hormonal Bionic Pancreas / Pediatric Endocrinology conference, Massachusetts General Hospital

2012 Automation of Blood Glucose Management in Diabetes Mellitus with a Bionic Endocrine Pancreas / Medical Grand Rounds, Massachusetts General Hospital

2012 Continuous Glucose Monitoring and Automate Glucose Control / Diabetes Research Center Research Meeting, Massachusetts General Hospital

2013 Medical Devices: Sponsoring and Conducting Trials Under an IDE / Design and Conduct of Clinical Trials course, MGH Clinical Research Program

2013 Automated Blood Glucose Management with a Bi-hormonal Bionic Pancreas / Division of Endocrinology Clinical Seminar, Boston Children’s Hospital

2014 Update on Continuous Glucose Monitoring and Automated Glycemic Regulation / Diabetes Research Center Research Meeting, Massachusetts General Hospital

2014 Closing the Loop: Developing New Treatment for Type I Diabetes and Insights that Apply to Current Therapy/ Lecture to an audience of chairs of endocrine departments in Chinese hospitals for the Harvard School of Public Health China Initiative, Harvard School of

Public Health

Report of Regional, National and International Invited Teaching and Presentations
Invited Presentations and Courses
Regional

| Year(s) | Title of presentation or name of course/ Type of presentation/role(s) (note if presentation the result of a selected abstract)<br>Location (Sponsor, if any) |
|---|---|
| | No presentations below were sponsored by outside entities |
| 1996 | Do the Protein Expression and Degradation Machineries of the Cell Share Common Components? / Biology Department Seminar<br>Trinity University, San Antonio |
| 2010 | Closed-loop Blood Glucose Control for Type 1 Diabetes and Critical Illness / Endocrinology Grand Rounds<br>University of Massachusetts Medical Center, Worcester |
| 2010 | Regulation of Aging by Insulin Signaling in Mammals / invited lecture<br>MGH Geriatric Medicine Research Conference |
| 2010 | Regulation of Aging by Insulin Signaling in Fat / invited lecture<br>Joslin Diabetes Center Internal Seminar Series |
| 2010 | On the Road to a Prosthetic Endocrine Pancreas / invited lecture (speakers chosen by Editor of Nature Medicine)<br>SciCafe (Nature Publishing Group) |
| 2011 | A Bi-Hormonal Closed-Loop Artificial Pancreas for Type 1 Diabetes / invited lecture, Pediatric Endocrinology<br>University of Massachusetts Medical Center, Worcester |
| 2011 | A Bi-Hormonal Closed-Loop Artificial Pancreas for Type 1 Diabetes / Pediatric Grand Rounds<br>Brown University Medical School, Providence, RI |
| 2011 | A Bi-hormonal Bionic Pancreas for Blood Glucose Control in Type 1 Diabetes / Endocrine Grand Rounds - Yale University Medical School, New Haven, CT |
| 2014 | A Bionic Endocrine Pancreas for Automated Management of Glycemia in Diabetes Mellitus / Grand Rounds<br>Emerson Hospital, Concord, MA |

National

| Year(s) | Title of presentation or name of course/ Type of presentation/role(s) (note if presentation the result of a selected abstract)<br>Location (Sponsor, if any) |
|---|---|
| | Presentations below were not sponsored by outside entities except as noted by (Sponsor) |
| 1996 | Sug1 and Sug2 Proteins, Putative Transcriptional Co-activators, Are Components of the 26S Proteasome / abstract selected for oral presentation<br>11th Annual M. D./ Ph. D. Student Conference, Aspen, CO |
| 1997 | Sug1 and Sug2: ATPase Family Components of the Yeast 26S Proteasome / abstract selected for oral presentation<br>Young Scientist Program, International Congress of Biochemistry and Molecular Biology, |

Asilomar, CA

1999 A Novel Approach For Selective Inactivation of AAA Proteins / abstract selected for oral presentation
Third International Conference on Cellular Functions of AAA Proteins, La Jolla, CA

1999 The 19S Regulatory Complex of the Proteasome Functions Independently of Proteolysis in Nucleotide Excision Repair / invited lecture
Third International Conference on Cellular Functions of AAA Proteins, La Jolla, CA

2000 Role of the Proteasome and the Ubiquitin-like Domain of Rad23 in Nucleotide Excision Repair / abstract selected for oral presentation
FASEB Summer Research Conference on Ubiquitin and Intracellular Protein Degradation, Saxton's River, VT

2004 Molecular Mechanisms of Aging in Mammals / invited lecture
University of Texas Southwestern Medical Center Merck Scholars Symposium, Boston, MA (Merck)

2007 Clinical Parameters for Closed-Loop Studies / invited lecture
Juvenile Diabetes Research Foundation Artificial Pancreas Consortium Meeting, San Francisco, CA

2008 Design of Closed-loop Human Studies / invited lecture
Juvenile Diabetes Research Foundation Artificial Pancreas Consortium Meeting, San Francisco, CA

2008 Design of Closed-loop Blood Glucose Control Trials In Human Subjects / invited lecture
Towards an Artificial Pancreas: An FDA-NIH-JDRF Workshop, Bethesda, MD

2008 Regulation of Stress Resistance by Insulin Signaling In Fat / invited lecture
Nathan Schock Aging Center Conference on Aging, Bandera, TX

2008 Validation of the Via Medical GlucoScout For Closed-loop Blood Glucose Control Trials / invited lecture
Juvenile Diabetes Research Foundation Artificial Pancreas Consortium Meeting, Washington, DC

2009 A Clinical Feasibility Trial of Bi-hormonal Closed-loop Blood Glucose Control for Type 1 Diabetes / abstract selected for oral presentation
American Diabetes Association Annual Scientific Session, New Orleans, LA

2010 The Artificial Pancreas: Closing the Loop on Insulin Delivery in the Treatment of Diabetes / invited lecturer and panelist
BIO International Convention, Chicago, IL (Abbott Diabetes Care)

2010 Bi-hormonal closed-loop blood glucose control using subcutaneous infusions of insulin and glucagon / invited lecture
10th Annual Rachmiel Levine Diabetes and Obesity Symposium, Las Vegas, NV

2010 Key Areas of Innovation in Artificial Pancreas Development / invited lecture
Medical Device Technology Innovation Partnership (MD-TIP) Project Workshop, U.S. Food and Drug Administration, Center for Devices and Radiological Health, Bethesda, MD

2010 Cell Non-autonomous Regulation of Aging by Insulin Resistant Adipose Tissue / invited lecture
Gerontological Society of America, 63rd Annual Scientific Meeting, New Orleans, LA

2010 Better Hormones for Fully Automated Glucose Control: Role of Glucagon / invited lecture
Diabetes Technology Meeting, Bethesda Maryland

2011 Artificial Pancreas Platform Panel Discussion / panelist
NIH / Juvenile Diabetes Research Foundation Artificial Pancreas Consortium Meeting, San Diego, CA (concurrent with American Diabetes Association Annual Scientific Sessions)

2012 Automated Management of Blood Glucose with a Closed-loop Bi-hormonal Bionic Pancreas / Invited lecture
Phacilitate Autoimmune and Inflammation Leaders' Forum (Workshop – Picking the

Winning Modalities in the Race to Address Type 1 Diabetes), San Francisco, CA

2012 Automated glucose management in type 1 diabetes with a bi-hormonal bionic pancreas / Invited lecture
Pediatric Endocrine Society Annual Meeting, Boston, MA

2012 A Bionic Pancreas Delivering Insulin and Microdose Glucagon Automates Blood Glucose Control in Type 1 Diabetes / Invited lecture
American Diabetes Association Annual Scientific Session, Philadelphia, PA

2012 A Comparative Analysis of Three Continuous Glucose Monitors: Not All Are Created Equal / Abstract selected for oral presentation
American Diabetes Association Annual Scientific Session, Philadelphia, PA

2012 A Bionic Pancreas Delivering Insulin and Microdose Glucagon Automates Blood Glucose Control in Type 1 Diabetes / Invited lecture (with Ed Damiano)
Lilly & Co, Indianapolis, IN (Eli Lilly)

2012 Automated Glucose Control with a Bi-hormonal Bionic (Artificial) Pancreas in Children and Adults with Type 1 Diabetes / Invited lecture - Sumner J. Yaffe Memorial Lecture Series in Pediatric Clinical Pharmacology
Webinar sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Human Development

2013 Automated Blood Glucose Control with a Bi-hormonal Bionic Pancreas / Invited lecture
University of North Carolina School of Medicine, Endocrinology and Metabolism Research Conference, Chapel Hill, North Carolina

2013 Automatic Blood Glucose Control with a Bi-hormonal Bionic Pancreas / Keynote lecture
JDRF 6th Annual 'Diabetes Today and Tomorrow' Conference, Belleville, MI

2013 Real World Insights / Panelist
T1D Exchange Annual Meeting: What Does it Take to Get Therapies and Devices to Market?, Boston, MA

2013 A Robustly Adaptive Bi-Hormonal Bionic Pancreas For Automated Glucose Control in Children and Adults / Abstract selected for oral presentation
American Diabetes Association Annual Scientific Session, Chicago, IL

2013 A Comparative Analysis of Three Continuous Glucose Monitors / Abstract selected for oral presentation
American Diabetes Association Annual Scientific Session, Chicago, IL

2013 Standardization of Trial Reporting / Panelist
JDRF/NIH Closed-Loop Research Meeting, Chicago, IL (concurrent with American Diabetes Association Annual Scientific Sessions)

2013 A Bionic Pancreas in the Wild: The Beacon Hill and Summer Camp Studies / Keynote presentation
14th North American Conference on Diabetes and Exercise "New Frontiers in Diabetes and Sport", San Diego, CA (Tandem Diabetes Care)

2014 A Bionic Pancreas in the Wild: Outpatient Studies / Invited lecture
14th Annual Rachmiel Levine Diabetes and Obesity Symposium, Pasadena, CA

2014 Why Endocrinology? Themes of a Career Journey / Keynote lecture
Close Concerns Alumni Summit, Aspen, CO

2014 Outpatient Glycemic Control in Type 1 Diabetes with a Bihormonal Bionic Pancreas / Invited lecture
Eli Lilly Grand Rounds, Indianapolis, IN

2014 Automated Glycemic Control In Diabetes with a Bihormonal Bionic Pancreas / Invited lecture
Celebrating Chemistry at Trinity – Research Symposium, Trinity University, San Antonio, TX

2014 Multiday Outpatient Glycemic Control in Adolescents with Type 1 Diabetes Using a Bihormonal Bionic Pancreas: The Barton Center Summer Camp Study / Abstract selected

for oral presentation
74th Annual American Diabetes Association Scientific Session, San Francisco, CA

2014 Outpatient Glycemic Control in Type 1 Diabetes with a Bihormonal Bionic Pancreas / Invited lecture
Clinical Application of Real-Time CGM: Professional Use, Pediatrics and the Pathway to the Artificial Pancreas (Corporate Symposium held during the 74th Annual American Diabetes Association Scientific Sessions) / San Francisco, CA

2014 Managing Hyperglycemia on the Ward and in the ICU: Challenges, Controversy, and New Technology / Invited Meet the Professor lecture (delivered twice)
Endocrine Society Diabetes Diagnosis and Management workshop / Chicago, IL

2014 Artificial and Bionic Pancreas Technology / Invited lecture
Endocrine Society Diabetes Diagnosis and Management workshop / Chicago, IL

2014 Multiday Outpatient Glycemic Control in Adults with Type 1 Diabetes Using a Bihormonal Bionic Pancreas: The Beacon Hill Study / Abstract selected for oral presentation
ICE/ENDO 2014 (International Congress of Endocrinology / Endocrine Society's 96th Annual Meeting) / Chicago, IL

International

| Year(s) | Title of presentation or name of course/ Type of presentation/role(s) (note if presentation the result of a selected abstract)<br>Location (Sponsor, if any) |
|---|---|

Presentations below were not sponsored by outside entities except as noted by (Sponsor)

1997 Isolation and Characterization of Sug2, a Novel ATPase Family Component of the Yeast 26S Proteasome / invited lecture
EMBO Workshop on Cellular Functions of AAA Proteins, Tutzing, Germany

2010 Diabetes, Thyroid Disease, and Osteoporosis / invited lecturer
International Medical Corps CME course for displaced Iraqi physicians, Amman, Jordan

2010 A Bi-Hormonal Closed-Loop Artificial Pancreas for Type 1 Diabetes / invited lecture
Sanofi Aventis, Frankfurt, Germany (Sanofi Aventis)

2012 Automated Management of Blood Glucose in Type 1 Diabetes with a Bi-hormonal Bionic Pancreas / invited lecture
Bringing the Artificial Pancreas Home (AP@home) meeting, Barcelona, Spain

2012 Automated Management of Blood Glucose in Type 1 Diabetes with a Bihormonal Bionic Pancreas / abstract selected for oral presentation
Advanced Technologies & Treatment for Diabetes meeting, Barcelona, Spain

2013 Continuous Glucose Monitoring and Automated Glucose Control / invited lecture to Clinical Endocrinology 2013, Boston, MA (ACCME accredited CME course by MGH/HMS; participants were from US, Europe, Asia, and Latin America)

2013 Progress Towards Automated Glucose Control in Type 1 Diabetes With a Bi-hormonal Bionic Endocrine Pancreas / invited lecture
6th Accu-Chek Network Meeting, Riga, Latvia (Roche)

2013 Clinical Experience with a Bihormonal Bionic Endocrine Pancreas / invited lecture
Diabetes and Technology Meeting (Danish Diabetes Academy), Copenhagen, Denmark

2013 Accuracy, Precision, and Reliability of Continuous glucose Monitors / invited lecture
Diabetes and Technology Meeting (Danish Diabetes Academy), Copenhagen, Denmark

2013 Challenges in the Development and Testing of Bihormonal Bionic Pancreas / invited lecture
Danish Diabetes Academy Workshop, Hvidovre Hospital, Copenhagen, Denmark

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|---|---|
| 2014 | Automated Control of Blood Glucose with a Bionic Pancreas / invited lecture JDRF Canada 2014 Diabetes Research Infosium, Toronto, Canada |
| 2014 | The Bionic Endocrine Pancreas: Automated Management of Glycemia / invited lecture to Clinical Endocrinology 2014, Boston, MA (ACCME accredited CME course by MGH/HMS; participants were from US, Europe, Asia, and Latin America) |
| 2014 | The Artificial and Bionic Pancreas: Update On Where We Are Today / invited lecture to the International Forum for the Advancement of Diabetes Research and Care, Berlin, Germany (Sanofi Aventis) |

Report of Clinical Activities and Innovations
Current Licensure and Certification

| Year | Type of License or Certification |
|---|---|
| 2004- | Massachusetts Medical License |
| 2004 | Diplomate, American Board of Internal Medicine – Internal Medicine |
| 2006 | Diplomate, American Board of Internal Medicine – Endocrinology, Diabetes, and Metabolism |

Practice Activities
List all clinical activities, both those at Harvard and its affiliates and those outside Harvard, and for each indicate:

| Year(s) | Type of activity | Name and location of practice | Level of activity |
|---|---|---|---|
| 2006-2007 | Ambulatory care | Neuroendocrinology, Massachusetts General Hospital | 2 sessions per month |
| 2006-present | Ambulatory care | Diabetes, Massachusetts General Hospital | 2 session per month |
| 2006-present | Inpatient consults | Diabetes, Massachusetts General Hospital | 1 weekend per 1-2 months |

Clinical Innovations

| Name of clinical innovation | Describe the influence or potential influence of the innovation on clinical care or practice management, including how the innovation is used or has been implemented locally (at HMS), regionally, nationally or internationally; if developed as a member of a committee, describe your contribution (1-2 sentences) |
|---|---|
| Data driven choice of CGM technology. | Did first head-head-head comparative effectiveness of all commercially available continuous glucose monitor (CGM) devices, allowing data driven recommendations to patients based on accuracy and reliability performance. This has changed practice in our MGH diabetes units (adult and pediatric) when prescribing CGM monitoring and when interpreting data collected by patients. These data have also been presented widely and have helped to motivate more work on improved glucose sensors by medical device companies. We have now tested three generations of sensors, reported in two publications, and continue to test new technologies as they near clinical use. |

Report of Technological and Other Scientific Innovations

| Innovation (date if applicable) | Patent, if any, pending or awarded /If described in print/on web, provide citation<br><br>Describe the influence or potential influence of the innovation on research or clinical care, including how the material is used locally (at HMS), regionally, nationally or internationally; if developed as a member of a committee, describe your contribution (1-2 sentences) |
|---|---|

Bi-hormonal closed-loop BG control in type 1 diabetes. I am collaborating with engineering colleagues on development, optimization, and clinical testing of closed-loop blood glucose (BG) technology utilizing both insulin and glucagon. This bi-hormonal closed-loop glucose control approach has the potential to provide much more effective BG control than is possible with insulin-only approaches. We have now completed the first outpatient trials in adults and adolescents, and will soon complete home use trials in adults and outpatient trials in pre-adolescent children. We hope such a device can be commercialized by 2017, which will dramatically change the way type 1 diabetes is managed.

Characterized rapid-acting insulin pharmacokinetics. In the course of closed-loop BG control studies we found that the pharmacokinetic (PK) behavior of insulin lispro varied much more between individuals, and across a wider range, than expected based on published data describing populations of patients. In some patients, insulin lispro was absorbed even more slowly than regular human insulin. This has led to modification of insulin-on-board parameters programmed into patient pumps and an increased awareness of the potential role of insulin PK in failure to achieve glycemic goals and development of hypoglycemia among patients in the adult and pediatric diabetes practices at MGH. In addition, it motivated a study now underway to test whether there are differences between the PK characteristics of different rapid-acting insulin analogs within single individuals.

Validation of CGM technology for the ICU environment. We have performed a clinical trial demonstrating that a continuous glucose monitor is as accurate in the ICU as in the outpatient environment when calibrated more frequently than in the outpatient environment (e.g. every 6 hours). Although this finding has not, as yet, led to usage of CGM in MGH ICUs, this finding will pave the way to improved safety and efficacy of tight glycemic control in the ICU, in particular through the use of CGM as the input limb to a closed-loop BG control device.

Closed-loop blood glucose control in critical illness. I have guided adaption by engineering collaborators of closed-loop technology developed for use in type 1 diabetes to use in the critical care setting and designed clinical trial of closed-loop device using CGM sensing and automated IV insulin and dextrose dosing that were completed in October of 2013. A validated device for automated BG control in the ICU will be critical for finally performing a definitive test of the hypothesis that tight glycemic control can reduce mortality and morbidity in critically ill patients, which has been the subject of much controversy.

Closed-loop glucagon delivery for the prevention and treatment of hypoglycemia. Automated closed-loop insulin delivery is considered a high risk intervention owing to the risk for hypoglycemia. We are testing the portion of the bionic pancreas that delivers glucagon in the context of open-loop insulin delivery to see if it can reduce hypoglycemia in a double-blind, placebo controlled randomized controlled trial. This study can be done in an unsupervised outpatient setting because the delivery of glucagon will not increase the risk of hypoglycemia. This will allow us to get valuable insight into how partial automation of blood glucose control can improve care and provide real-world data on the interaction of patients with the bionic pancreas.

Evaluation of intradermal insulin delivery for improvement of insulin and glucagon pharmacokinetics. Preliminary studies have suggested that intradermal delivery of insulin can dramatically improve its

pharmacokinetics. These studies have been done in patients who already have relatively fast insulin pharmacokinetics. We have now completed and are analyzing a study to evaluate the impact of intradermal insulin on the PK of rapid-acting insulins and glucagon in patients with very slow absorption of insulin from the subcutaneous tissues.

Continuous insulin monitoring. The pharmacokinetics of insulin is an important determinant of success for closed-loop control. Unfortunately, the PK characteristics of rapid acting insulins vary greatly between individuals and to a lesser degree within an individual from infusion site to infusion site. Setting the parameters of a closed-loop bionic pancreas such that slow insulin absorption is assumed avoids insulin stacking but leads to loss of peak performance. In collaboration with engineering colleagues I am developing a device that assays the levels of insulin in microdialysis fluid obtained continuously from the subcutaneous space. We have now proven the feasibility of the device in vitro and are moving on to animal studies. After human studies are completed, we will feed the information back to the closed-loop algorithm and test the effect on quality of glycemic control.

Validation of stable glucagon formulations. I will be performing a hyperinsulinemic normoglycemic clamp study to compare the pharmacodynamics and pharmacokinetic properties of a stable formulation of glucagon (Xeris Pharmaceuticals) with freshly reconstituted glucagon (Eli Lilly) that is known to be unstable after reconstitution. A stable formulation of glucagon is critical to the development of a bionic pancreas. This study is investigator initiated, foundation funded, and I am the sponsor of the IND.

Report of Education of Patients and Service to the Community

Activities
May include a brief, one-sentence description of each role if needed (optional)

| Year(s) | Organization or institution / Role (Sponsor, if any)<br>One sentence description (optional) |
|---|---|
| 1990-1991 | Spartanburg Day School / Teacher<br>Taught 7th grade Biology, Sophomore Chemistry, and Junior Physicas |
| 1996-1999 | Dallas Morning News-Toyota Regional Science & Engineering Fair, Dallas, TX<br>Grand Awards Judge 1998, Judge 1996-1999 |
| 2011-present | Speaker at Type 1 Diabetes education course run by MGH Diabetes Center several times each year. |
| 2013 | Panelist for Type 1 Diabetes Exchange Glu online community Bionic Pancreas Open House (took questions submitted online by members of Glu and live questions from attendees) |

Educational Material for Patients and the Lay Community

| Group materials (in print or other media) into three categories |
|---|

Patient educational material

| Year | Title | Type of contribution (Sponsor, if any) | Citation, if any |
|---|---|---|---|
| 2005 | Guide to potassium in foods for patients with diabetes | Patient handout (adapted from handout for non-diabetic patients) | MGH Primary Care Office InSight, Patient Information |

Report of Scholarship
Publications

| Include only manuscripts that are published or accepted for publication (forthcoming) in print or other |
|---|

media; do not include manuscripts that have been submitted but not accepted for publication or those that are in preparation; Please use bold-faced type for your name in the authorship list. Numbering of contributions should start with "1" in each new section.

Peer reviewed publications in print or other media

Group peer reviewed publications in three categories under the following headings:
-Research investigations
-Other peer-reviewed publications (e.g., case reports, proceedings of meetings which are full-length manuscripts)
-Research publications without named authorship

Research Investigations:


1. Plummer BF, **Russell SJ**, Reese WG, Watson WH, Krawiec M. Sterically Congested Polycyclic Aromatic Hydrocarbons with Nonoptimal Geometries. 4,5-Didehydroacenapthene as a Precursor for the Synthesis of 7,14 Diphenyl-8,9-(1',8'-naphthenylene)acephenanthrene. Journal of Organic Chemistry 1991; 56:3219-23.
2. Plummer BF, Currey JA, **Russell SJ**, Steffen LK, Watson WH, Bourne SA. The Synthesis and X-ray Crystallographic Analysis of a Stable Norbornadienone: 17-oxo-7,16-methano-7,16-diphenylcyclopenta[d,e] tribenzo[a,h,j]antharacene. Structural Chemistry 1995; 6: 167-73.
3. **Russell SJ**, Sathyanarayana UG, Johnston SA. Isolation and Characterization of SUG2: A Novel ATPase Family Component of the Yeast 26S Proteasome. Journal of Biological Chemistry 1996; 271:32810-7.
4. **Russell SJ**, Steger KA, Johnston SA. Sub-cellular Localization, Stoichiometry, and Protein Levels of 26S Proteasome Subunits in Yeast. Journal of Biological Chemistry 1999; 274:21943-52.
5. **Russell SJ**, Reed SH, Huang W, Friedberg EC, Johnston SA. The 19S Regulatory Complex of the Proteasome Functions Independently of Proteolysis in Nucleotide Excision Repair. Molecular Cell 1999; 3:687-95.
6. **Russell SJ**, Johnston SA. Evidence that Proteolysis of Gal4 Can Not Explain the Transcriptional Effects of Proteasome ATPase Mutations. Journal of Biological Chemistry 2001; 276:9825-31.
7. **Russell SJ**, Gonzalez F, Joshua-Tor L, Johnston SA. Selective Chemical Inactivation of AAA Proteins Reveals Distinct Functions of Proteasomal ATPases. Chemistry & Biology 2001; 8:941-50.
8. Gillete TG, Huang W, **Russell SJ**, Reed SH, Johnston SA, Friedberg EC. The 19S Complex of the Proteasome Regulates Nucleotide Excision Repair in Yeast. Genes and Development 2001; 15:1528-39.
9. Laustsen PG, **Russell SJ**, Cui L, Entingh-Pearsall A, Holzenberger M, Liao R, Kahn CR. Essential Role of Insulin and IGF-1 Receptor Signaling in Cardiac Development and Function. Molecular and Cellular Biology 2007; 27:1649-1664.
10. Katic M, Kennedy AR, Leykin I, Norris A, McGettrick A, Gesta S, **Russell SJ**, Bluher M, Maratos-Flier E, Kahn CR. Mitochondrial Gene Expression and Increased Oxidative Metabolism: Role in Increased Lifespan of Fat-Specific Insulin Receptor Knockout Mice. Aging Cell 2007; 6:827-839.
11. El-Khatib FH*, **Russell SJ*#**, Nathan DM, Sutherlin RG, Damiano ER. A Bi-Hormonal Closed-Loop Blood Glucose Control Device for Type 1 Diabetes. Science Translational Medicine 2010; 2:27 27ra27. (*Co-first authors; #, Corresponding author)
12. **Russell SJ**, El-Khatib FH, Nathan DM, Damiano ER. Efficacy Determinants of Subcutaneous Micro-Dose Glucagon during Closed-Loop Control. Journal of Diabetes Science and Technology 2010; 4:1288-1304.
13. Boucher J, Mori MA, Lee K, Liew CW, Macotela Y, Smyth G, Rourk M, **Russell SJ**, Bluher M, Kahn CR. Impaired Thermogenesis and Adipose Development in Mice with Fat-Specific Disruption of Insulin and IGF-1 Signaling. Nature Communications 2012; 3:302.
14. **Russell SJ**, El-Khatib FH, Nathan DM, Magyar KL, Jiang J, Damiano ER. Blood glucose control in type 1 diabetes with a bihormonal bionic endocrine pancreas. Diabetes Care 2012; 11:2148-55.
15. Mori MA, Raghavan P, Thomou T, Boucher J, Robida-Stubbs S, Macotela Y, **Russell SJ**, Kirkland JL, Blackwell TK, Kahn CR. Role of microRNA Processing in Adipose Tissue in Stress Defense and

Longevity. Cell Metabolism 2012; 16:336-47.
16. Larkin ME, Beauharnais CC,Magyar K, Macey L, Grennan K, Boykin E, **Russell SJ**. Obtaining surrogate consent for a minimal-risk research study in the ICU setting. Clinical Trials 2012; 10:93-6.
17. Damiano ER, El-Khatib FH, Zheng H, Nathan DM, **Russell SJ**. A Comparative Effectiveness Analysis of Three Continuous Glucose Monitors. Diabetes Care 2012; 36:251-9.
18. Lee K, **Russell SJ**, Ussar S, Boucher J, Vernochet C, Mori M, Smyth G, Rourk M, Cederquist C, Rosen E, Kahn B, Kahn CR. Lessons on Conditional Gene Targeting in Mouse Adipose Tissue. Diabetes 2013; 62:864-74.
19. El-Khatib FH*, **Russell SJ*#**, Magyar KL, Sinha M, McKeon, K, Nathan DM, Damiano ER. Autonomous and continuous adaptation of a bihormonal bionic pancreas in adults and adolescents with type 1 diabetes. Journal of Clinical Endocrinology and Metabolism 2014; 99:101-1711. (*Co-first authors; #, Corresponding author)
20.Damiano ER, McKeon, K, El-Khatib FH, Zheng H, Nathan DM, **Russell SJ**. A Comparative Effectiveness Analysis of Three Continuous Glucose Monitors: The Navigator, G4 Platinum, and Enlite. In press, Journal of Diabetes Science and Technology 2014; 99 (5), 1701-1711.
21. **Russell SJ**, El-Khatib FH, Sinha M, Magyar KL, McKeon, K, Goergen L, Balliro C, Hillard M, Nathan DM, Damiano ER. Outpatient Glycemic Control with a Bionic Pancreas in Type 1 Diabetes. New England Journal of Medicine 2014; 371 (4), 313-325.

Other Peer-Reviewed Publications:
1. **Russell SJ**, Kahn CR. Endocrine Regulation of Aging. Nature Reviews Molecular Cell Biology 2007; 8:681-691.

Google Scholar metrics: Citations = 1,331 / h-index = 15 / i10-index = 16 (10/1/2014)

Non-peer reviewed scientific or medical publications/materials in print or other media

| Group materials into the following categories:<br>-Proceedings of meetings or other non-peer reviewed research publications<br>-Reviews, chapters, monographs and editorials<br>-Books/Textbooks for the medical or scientific community<br>-Case reports<br>-Letters to the Editor |
|---|

Book Chapters:
1. **Russell SJ**, Miller KK. Pituitary Apoplexy. Diagnosis and Management of Pituitary Disorders. Swearingen B, Biller BMK (Eds). Humana Press, 2008.
2. **Russell SJ**, Miller KK. Pituitary Apoplexy. A Case-Based Guide to Clinical Endocrinology. Terry Davies (Ed). Springer, 2008.
3. **Russell SJ**, Thompson T. Endocrine Disorders and Glucose Management. Critical Care Handbook of the Massachusetts General Hospital. Luca M. Bigatello (Ed). Lippincott Williams and Wilkins 2009.

Editorials:
1. **Russell SJ**. Continuous Glucose Monitoring Awaits Its "Killer App". Journal of Diabetes Science and Technology 2008; 2:490-494.
2. Nathan DM, **Russell SJ**. The Future of Care for Type 1 Diabetes. Canadian Medical Association Journal 2013; published ahead of print January 28, 2013, doi:10.1503/cmaj.130011

Professional educational materials or reports, in print or other media

| For each item indicate:<br>-Type of material (e.g., syllabus, teaching case) |
|---|

-If published in print or on the web, provide citation
-Intended audience (including course number if applicable) and brief description of how the material is used locally (at HMS), regionally, nationally or internationally; if developed as a member of a committee, describe your contribution (1-2 sentences)

1. Pituitary Apoplexy (review), MGH Neuroendocrine Clinical Center Newsletter, 2008 (intended for continuing medical education of referring physicians)

Clinical Guidelines and Reports

For each item indicate:
-Type of material (e.g., clinical protocol or standard of care)
-If published in print or on the web, provide citation
-Description of the how the material is used locally (at HMS), regionally, nationally or internationally; if developed as a member of a committee, describe your contribution (1-2 sentences)

1. Diabetic Ketoacidosis (review and clinical protocol), MGH Department of Medicine Teaching Handout, 2003 (intended for use by medical residents while managing diabetic ketoacidos)

Thesis

Provide full citation for doctoral thesis

Studies of SUG1 and SUG2, ATPases of the 26S Proteasome and Their Contributions to Proteolylsis, Nucleotide Excision Repair, and Gene Transcription. Dallas (TX): University of Texas Southwestern Medical Center; 1999

Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings

List abstracts published and exhibits presented at meetings during the last 3 years which have not already been published as full length manuscripts. May also list all abstracts or exhibits, regardless of date or publication as full-length manuscript, which received special recognition at a meeting (e.g., juried poster presentation, meeting commendation).

1. Oxidative Stress Resistance in FIRKO Mice Cannot Be Explained by Constitutive Activation of ROS Detoxifying Enzymes. Steven J. Russell, Carly Cederquist, C. Ronald Kahn. The Paul B. Beeson Career Development Awards in Aging Research Program Annual Meeting, Lake Geneva, WI (2009)
1. Tissue-specific, Cell Non-autonomous Regulator of Aging in the Fat-specific Insulin Receptor Knockout (FIRKO) Mouse. Steven J. Russell, Carly Cederquist , Marcelo Mori, Ji-Sun Park, C. Ronald Kahn, Keystone Symposium: Healthspan and Diseases of Aging, Tahoe City, CA (2010).
2. Regulation of Aging and Mitochondrial Energetics by Insulin Signaling in Fat. Steven J. Russell, Carly Cederquist, Ji Sun Park, Marcelo Mori, Stephane Gesta, Ryo Suzuki and C. Ronald Kahn, The Paul B. Beeson Career Development Awards in Aging Research Program Annual Meeting, Asheville, NC (2010)
3. Cell Non−Autonomous Regulation of Aging by the Insulin Receptor in Adipose Tissue: Studies in the FIRKO Mouse. Steven J. Russell, Carly Cederquist , Marcelo Mori, Ji-Sun Park, C. Ronald Kahn, American Diabetes Association 70th Annual Scientific Sessions, Orlando, FL (2010).
4. Accuracy of the Abbott Freestyle Navigator in ICU Patients, Steven J. Russell, Catherine C. Beauharnais, Hui Zheng, David M. Nathan, International Hospital Diabetes Meeting, Barcelona, Spain (2011)
5. Pre-clinical Studies of an Automated Closed-loop Blood-Glucose Control System for the Hospital Setting Using Interstitial Continuous Glucose Monitoring and Intravenous Insulin and Dextrose, John Jiang, Firas H. El-Khatib, Steven J. Russell, Edward R. Damiano, International Hospital Diabetes Meeting, Barcelona, Spain (2011)
6. A Comparative Analysis of Three Continuous Glucose Monitors: Not All Are Created Equal, Edward R. Damiano, Firas H. El-Khatib, Kendra L. Magyar, David M. Nathan, Steven J. Russell, Advanced

Technology & Treatment of Diabetes Meeting, Barcelona, Spain (2012)
7. Accuracy of the Abbott Freestyle Navigator in ICU Patients, Steven J. Russell, Catherine C. Beauharnais, Hui Zheng, David M. Nathan, Advanced Technology & Treatment of Diabetes Meeting, Barcelona, Spain (2012)
8. Pre-clinical Studies of an Automated Closed-loop Blood-Glucose Control System for the Hospital Setting Using Interstitial Continuous Glucose Monitoring and Intravenous Insulin and Dextrose, John Jiang, Firas H. El-Khatib, Steven J. Russell, Edward R. Damiano, Advanced Technology & Treatment of Diabetes Meeting, Barcelona, Spain (2012)
9. Pre-clinical Studies of an Automated Closed-loop Blood-Glucose Control System for the Hospital Setting Using Interstitial Continuous Glucose Monitoring and Intravenous Insulin and Dextrose, John Jiang, Firas H. El-Khatib, Steven J. Russell, Edward R. Damiano, American Diabetes Association Annual Scientific Session, Philadelphia, PA (2012)
10. The Abbott Freestyle Navigator Continuous Glucose Monitor Achieves
Accuracy in ICU Patients Comparable to Healthy Subjects When Calibrated at 6 Hour Intervals, Catherine C. Beauharnais, Hui Zheng, David M. Nathan, Steven J. Russell, American Diabetes Association Annual Scientific Session, Philadelphia, PA (2012)
11. The Abbott Freestyle Navigator Continuous Glucose Monitor Achieves Accuracy in ICU Patients Comparable to that in Healthy Subjects When Calibrated at 6 Hour Intervals, Steven J. Russell, Catherine C. Beauharnais, David M. Nathan, Hui Zheng, Hospital Diabetes Meeting, Cambridge, MA (2012)
12. A Robustly Adaptive Bi-Hormonal Bionic Pancreas for Automated Glucose Control in Children and Adults, Steven J. Russell, Firas H. El-Khatib, Hui Zheng, David M. Nathan, Edward R. Damiano, American Diabetes Association Annual Scientific Session, Chicago, IL (2013)
13. A Comparative Effectiveness Analysis of Three Continuous Glucose Monitors. Edward R. Damiano, Firas H. El-Khatib, Hui Zheng, David M. Nathan, Steven J. Russell, American Diabetes Association Annual Scientific Session, Chicago, IL (2013)
14. Optimizing Insulin PK to Improve Glucose Control with a Bionic Pancreas, Manasi Sinha, Firas H. El-Khatib, Edward R. Damiano, Steven J. Russell, American Diabetes Association Annual Scientific Session, Chicago, IL (2013)
15. Pharmacokinetics and Pharmacodynamics of a Chemically Stable Micro-Dosed Glucagon in a Diabetic Swine Model of Type 1 Diabetes, John Jiang, Katherine M. McKeon, Firas H. El-Khatib, Steven J. Prestrelski, Nancy L. Scott, Brett Newswanger, Patrick Sluss, Steven J. Russell, Edward R. Damiano, American Diabetes Association Annual Scientific Session, Chicago, IL (2013)
16. Optimizing Insulin Pharmacokinetics to Improve Glucose Control with a Bionic Pancreas (Adult Cohort), Manasi Sinha, Firas H. El-Khatib, Edward R. Damiano, Steven J. Russell, American Diabetes Association Annual Scientific Session, Chicago, IL (2013)
17. Optimizing Insulin Pharmacokinetics to Improve Glucose Control with a Bionic Pancreas (Adult and Pediatric Cohort), Manasi Sinha, Firas H. El-Khatib, Edward R. Damiano, Steven J. Russell, Pediatric Academic Societies/ Pediatric Endocrine Society Annual Meeting, Washington D.C. (2013)
Multiday Outpatient Glycemic Control in Adults with Type 1 Diabetes Using a Bihormonal Bionic Pancreas: The Beacon Hill Study, Steven Jon Russell, Firas H. El-Khatib, Kendra L Magyar, Manasi Sinha, Laura G Goergen, Courtney Balliro, Katherine McKeon, David M. Nathan and Edward R Damiano, Endocrine Society's 96th Annual Meeting and Expo, Chicago, IL (2014)

Narrative Report (limit to 500 words)

In general, we suggest the following structure for the narrative:
An opening paragraph that provides an overall summary of your major activities and achievements. Include an estimate of the proportion of your effort dedicated to teaching, research, clinical service, administrative activities and other relevant professional roles
Description of achievements in your Area of Excellence (Investigation, Teaching and Educational Leadership, or Clinical Expertise and Innovation); may include a description of work in progress such as

pending grants or manuscripts in preparation
Description of contributions to Teaching and Education (if not your area of excellence). This may include a description of mentorship activities not discussed elsewhere in the CV
Description of contributions in Significant Supporting Activities, if any
A final paragraph that integrates and summarizes the contributions described above

My research effort is divided into translational and basic science. In the translational arena, I am working to develop technologies to improve the care of people with type 1 diabetes and hyperglycemia of critical illness. In the basic science arena, I am investigating how insulin signaling in fat regulates metabolism, energy utilization, and longevity. My teaching activities are focused on education of Endocrine fellows, Medicine resident physicians, and occasionally medical students rotating on the Endocrine Consult Service. I spend 80% of my time on research, 10% of my time on clinical care, and 10% on teaching.

I am collaborating with Dr. Edward Damiano in the Department of Biomedical Engineering at Boston University on the development and clinical testing of a closed loop glucose control system (artificial endocrine pancreas) for type 1 diabetes. The system is unique in utilizing micro-doses of glucagon as well as insulin, both administered subcutaneously. Our first-in-humans study in adults with type 1 diabetes demonstrated the feasibility of safe blood glucose control by a bi-hormonal artificial pancreas. Our second phase study included children, incorporates structured exercise, and increases the duration of closed-loop control to two days. A third phase examined the effectiveness of adaptive meal priming boluses vs. no meal priming bolus in both adults and children. We have recently completed two fourth phase study including experiments ten days in length (five days of closed-loop and five days of usual care) using a full wearable system during which subjects have no restrictions on their food intake or activity. In one study, subjects were able to roam freely within the downtown area of Boston and slept in a hotel at night. The study involved adolescents 12-20 year of age and was conducted in diabetes camp setting. A report on these outpatient studies appeared in the New England Journal of Medicine in June, 2014. We completed another camp study in pre-adolescent children 6-11 in summer 2014. The results are currently being analyzed, but top level results are very similar to those in adults and adolescent children. These bridge studies prepared us for outpatient studies to come. We began a multicenter home study in 2014 that I am coordinating from MGH.

Some subjects in the closed-loop study absorbed the rapid-acting insulin lispro (Humalog) much more slowly than expected. Preliminary data suggested that this might be due to lispro-specific anti-insulin antibodies in some subjects. I have developed antibody reagents to perform comparative pharmacokinetic studies of all commercially available rapid-acting insulin analogs in individual subject using a novel approach called multiplex pharmacokinetic profiling, in which all analogs are injected simultaneously and then measured individually in plasma with analog-specific immunoassays. We have developed assays using these reagents in collaboration with Pat Sluss in the MGH Immunoassay Core. We have recently completed a study comparing the pharmacokinetics of intradermal vs. subcutaneous delivery of rapid-acting insulin analogs. The overall goal of both of these studies is to find ways of improving the effectiveness of closed-loop blood glucose control. To improve the ability of closed-loop systems I have begun a project in collaboration with Lindy Kahanovitz and Tania Konry to develop a microfluidic lab-on-a-chip continuous glucose monitor. The goal is to develop a wearable device that will sample interstitial fluid using microdialysis and continuously assay insulin levels. This data can be fed back to the bionic pancreas device which can integrate it with dosing information to calculate the speed of insulin absorption in real-time. This can be used to further refine dosing. We have succeeded in producing a sensitive assay on beads and are now integrating this into a microfluidic platform.

We are also investigating new, more stable glucagon formulations for use in the bihormonal bionic pancreas. We have recently completed a study comparing the pharmacokinetics and pharmacodynamics of stable glucagon formulations after aging with freshly prepared Lilly glucagon. This study used the hyperinsulinemic normoglycemic clamp technique and was be performed in the MGH Clinical Research

Center in 2014. Data analysis is underway and final results will available in 2014.

I have also investigating the accuracy of a continuous glucose monitor in critically ill patients receiving insulin therapy and to drive automated blood glucose control in this setting. A trial of the Abbott Navigator enrolling subjects from all MGH ICUs is now completed with data on more than 70 subjects, making it the largest study of a continuous glucose monitoring device in the ICU setting. The study found that the accuracy of the Navigator in this setting was comparable to that in the outpatient setting if calibrations are performed every six hours. This clears the way to using the CGM sensor to drive closed-loop control. I cooperation with Ed Damiano I have develop a closed-loop blood glucose control system for management of hyperglycemia in critical illness using an automated control of insulin and dextrose infusions. Pre-clinical studies have demonstrated tight control in a porcine model of rapidly fluctuating insulin resistance. We have recently completed a first-in-human study of this device and are preparing the results for publication.

In the basic arena, I worked in the laboratory of C. Ronald Kahn at the Joslin Diabetes Center through early 2012 investigating the regulation of longevity by insulin signaling in fat. We have shown that deletion of the insulin receptor in fat decreases the levels of multiple biomarkers of aging and senescence in the solid organs, including non-adipose tissues with normal insulin receptor expression, and that this correlates with reduced production of reactive oxygen species (ROS) in the same tissues. This suggests that both the lean and long-lived phenotypes of FIRKO mice may be explained by an adipose derived factor that controls the degree of mitochondrial uncoupling, and thus energy expenditure and ROS production, systemically. We are currently working to identify this factor. We have also found that there is dramatic pancreatic islet hypertrophy and preservation of islet function in old age in this animal model, which is being investigated in collaboration with the Bonner-Weir lab at Joslin. Recently we discovered that the levels of most serum immunoglobulins increase with age in multiple strains of mice and are reduced by interventions that prolong lifespan. These project are now winding down as I devote all of my research effort to translational projects related to diabetes care.

In addition to research activities, I see patients 4 half-days a month in the MGH Diabetes Center and provide occasional weekend coverage for the practice. I teach endocrine fellows, medical residents, and medical students while attending on the Inpatient Endocrine Consult Service for 3 weeks of each year. I also do some teaching of my research assistants in the laboratory, one of whom has gone on to graduate school after working with me.