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# Richard KP Benninger: Curriculum Vitae

Associate Professor of Bioengineering (primary)

Associate Professor of Pediatrics (secondary)

Member Barbara Davis center for childhood diabetes (division of research)

University of Colorado, Denver | Anschutz Medical campus

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## **Education**

### **Imperial College London:**

*Physics Department, Imperial College London (University of London), London, United Kingdom.*

#### **MSci in Physics:**

**October 1998 – June 2002**

First class honours

#### **PhD in Physics:**

**October 2002 – April 2006**

“Applications of Multi-focal Multi-photon Microscopy to Multi-dimensional Fluorescence Imaging”

Supervised by Paul M.W. French and Mark A.A. Neil.

Thesis viva performed by Tony Wilson and Robin W. Smith

### **Vanderbilt University:**

*Department of Molecular Physiology & Biophysics, Vanderbilt University Medical Center, Nashville, TN.*

#### **Post-doctoral Research Associate:**

**June 2006 – September 2009**

Initial research foci: Quantitative fluorescence Microscopy, Dynamics of pancreatic islet function

Primary Mentor: David W. Piston

## **Academic Appointments**

### **Vanderbilt University:**

*Department of Molecular Physiology & Biophysics, Vanderbilt University Medical Center, Nashville, TN.*

#### **Research Instructor:**

**October 2009 – June 2011**

### **University of Colorado:**

*Department of Bioengineering, University of Colorado Anschutz Medical campus, Aurora, CO.*

#### **Assistant Professor (tenure-track):**

**July 2011 – July 2017.**

#### **Associate Professor (with tenure)**

**July 2017 - present**

## **Honors and Awards**

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EPSRC PhD studentship with industrial CASE award (Kentech Ltd)	<b>2002- 2005</b>
Institute of Physics (Optics section) travel scholarship:	<b>2005</b>
European Physical Society travel grant:	<b>2005</b>
Burrough's Welcome Fund, Career Award at Scientific Interface (Finalist)	<b>2008</b>
NIDDK Imaging the islet workshop travel award:	<b>2009</b>
NIH K99/R00 Career development award, DK085145 (Awarded)	<b>2009-2014</b>
Vanderbilt 2009 Scholar in Diabetes	<b>2009</b>
JDRF Career development award (Awarded)	<b>2014-2019</b>
Biophysical Society Young Fluorescence Investigator award	<b>2015</b>

## **Memberships in Professional Societies**

Institute of Physics (UK)	<b>1998 – present</b>
Biophysical Society	<b>2004 – present</b>
Optical Society of America	<b>2005 – present</b>
American Diabetes Association	<b>2011 – present</b>
European Association for the Study of Diabetes	<b>2013 – present</b>
American Physiological Society	<b>2013 – present</b>

## **Service**

### **Institutional Service (University of Colorado):**

#### **Department of Bioengineering:**

Committee chair, Curriculum committee for Bioengineering program (undergraduate and graduate)  
**2012-present**

*Developing mission of committee; overseeing development, implementation and continued improvement of curriculum at graduate and undergraduate levels; interfacing with assessment and accreditation processes (ABET).*

Committee member, Admissions committee for Bioengineering program (graduate)  
**2012-2016**

Committee chair, Tenure-track faculty recruitment search committee  
**2015-2016**

Committee chair, Primary Unit committee for reappointment, tenure and promotion  
**2019-present**

#### **Barbara Davis Center for childhood diabetes:**

Organizer, Barbara Davis Center Research in Progress seminar series.  
**2012-2015**

Organizer, University of Colorado Diabetes seminar series.  
**2016-present**

#### **Advanced Light Microscopy Core:**

Committee member, Internal steering committee.  
**2011-present**

#### **Medical Scientist Training Program (MD-PhD):**

Committee member, Admissions committee for MSTP.  
**2013-2017**

#### **College of Engineering and Applied science (CEAS):**

Committee member, Scholarship committee.  
**2015-2017**

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Committee member, Dean of CEAS search committee

**2016-2017**

### **External Service:**

#### American Diabetes Association Scientific Sessions:

Oral session chair, "Metabolic and Molecular Mechanisms Regulating Insulin Secretion" (2015)

Ad hoc sub-committee for development of program in Islet biology/Insulin secretion (2015)

Oral session chair, "The Excited Beta cell" (2016)

Committee member, ADA Scientific sessions planning committee (2017-2019)

### **Peer Review and Referee work**

#### **Reviewer, journal publications:**

**2009-present**

American Journal of Physiology – Cell Phys.;  
American Journal of Physiology – Endo&Metab.;  
Analytical Chemistry;  
Australasian Physical & Engineering Sciences in Medicine;  
Biological Research;  
Biomedical Materials;  
Biophysical Journal;  
Cytometry partA;  
Diabetes.  
Federation of European Biochemical Societies Journal;  
Islets;  
Journal of Biomedical Optics;  
Journal Mathematical Biology;  
Journal of Optics;  
Mathematical Biosciences;  
Microfluidics and Nanofluidics;  
Molecular Metabolism;  
Nature Communications;  
Nature Metabolism;  
Nature Methods;  
New Journal of Physics;  
Photochemistry & Photobiology;  
PLoS Computational Biology;  
PLoS ONE;  
PNAS;  
Scientific Reports.

#### **Reviewer, grants and fellowships:**

**2011-present**

Diabetes UK (ad hoc)  
(UK) Medical Research Council (ad hoc)  
EU Horizon 2020 'Personalizing health and care' (first-stage reviewer)  
Czech Health Research Council (ad hoc)  
Washington University St. Louis DRTC P&Fs (ad hoc)  
Juvenile Diabetes Research Foundation ('FY16 Islet Immune SRA' Review Panel)  
NIH Cellular Aspects of Diabetes and Obesity study section (ad hoc member Feb, 2016)  
Juvenile Diabetes Research Foundation ('FY17 Beta Cell Regeneration Training Awards Panel)  
Juvenile Diabetes Research Foundation ('FY18 Restoring pancreatic alpha cell function to

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improve metabolic control in type 1 diabetes)

NIH Molecular and Cellular endocrinology study section (ad hoc member June, 2018)

Juvenile Diabetes Research Foundation ('FY18 Beta Cell Regeneration Training Awards Panel)

Juvenile Diabetes Research Foundation ('FY19 Beta Cell Regeneration Training Awards Panel)

NIH Molecular and Cellular endocrinology study section (ad hoc member June, 2019)

### **Editorial work:**

Guest Editor, PLoS Computational Biology

**2014-present**

### **Reviewer, Conference abstracts:**

**2015-present**

American Diabetes Association Scientific Sessions, program in Islet biology/Insulin secretion (2015)

## **Invited external seminars, symposia and workshops**

### **Institutional seminars:**

Invited seminar at Department of Cell Biology, University of North Carolina, Chapel Hill NC. (2010).

*"Live cell imaging of cell-cell communication in the islet of Langerhans"*

Invited seminar at Department of Bioengineering, Vanderbilt University, Nashville TN. (2011).

*"Live cell imaging of the islet of Langerhans and the regulation of insulin secretion"*

Invited seminar at Department of Biological Sciences, University of Denver, Denver, CO. (2013).

*"Gap junction channels in pancreatic islet function and diabetes"*

Visiting seminar at Oxford Center for Diabetes, Endocrinology and Metabolism (OCDEM), Oxford University, Oxford UK. (2015).

*"Dynamics of pancreatic islet function and dysfunction in diabetes"*

Invited seminar at the Institute of Molecular Biophysics, Florida State University, Tallahassee FL. (2018).

*"Imaging and modelling cellular cross-talk and heterogeneity in the islet of Langerhans"*

Invited seminar at Department of Molecular Physiology and Biophysics, Vanderbilt University, Nashville TN. (2019).

*"Dissecting the electrical connectivity within pancreatic islets"*

### **Invited symposia/workshop speaker:**

Invited speaker at South-East Two-photon Microscopy Workshop, Atlanta, GA. (2008)

*"An introduction to multi-photon FRET"*

Invited speaker at Biophysical Society Annual Meeting, Biological Fluorescence Subgroup, Boston MA. (2009). *"Quantitative multi-probe fluorescence microscopy of multi-cellular system dynamics"*

Invited speaker (Future approaches in life microscopy), EMBL, Heidelberg, Germany (2011).

*"Quantifying cellular signaling in the islet of Langerhans with pcFRET and live-cell imaging"*

Invited symposium speaker (Insulin pulsatility matters) at Endocrine Society Annual Meeting, San Francisco, CA. (2013)

*"Gap junction communication and coordination of pulsatile activity"*

Award speaker (Young Fluorescence Investigator) at Biophysical Society Annual Meeting, Biological Fluorescence Subgroup, Baltimore, MD. (2015).

*"Probing the coordinated dynamics of insulin secretion with fluorescence microscopy"*

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Invited symposium speaker (New Imaging Approaches to Assess Functional Beta-Cell Characteristics) at American Diabetes Association Scientific Sessions, New Orleans, LA. (2016)  
*"Characterizing beta cell heterogeneity and dysfunction using optogenetics"*

Invited symposium speaker (Emerging Diabetes Technologies & Beta Cell Biology) at The Carousel of Hope Symposium, Beverly Hills, CA. (2016)  
*"Intra-islet Regulation of Insulin Secretion"*

Invited symposium speaker at The Islet Society 2019, Maribor, Slovenia. (2019)  
*"Functional Roles for Islet Heterogeneity and Electrical Communication"*  
(note: a postdoc in my lab, Vira Kravets, spoke in my place)

Invited symposium speaker (From Gene to Cell to Micro-Organ) at The Keystone Symposia: Islet Biology, Sante Fe, NM. (2020)  
*"Imaging Islet Heterogeneity and Connectivity"*

Invited symposium speaker (Imaging the Pancreas in Diabetes, Cancer and Pancreas Disease Research) at NIH: NIDDK, Bethesda, MD. (2020)  
*"Cell-cell communication-channels in islet cell interactions"*

## **Teaching record**

### **Graduate Teaching (Vanderbilt University, 2009-2011):**

#### Department of Chemistry:

2 lectures in spectroscopy class: "Two photon fluorescence microscopy" and "Optical probes and fluorescent proteins" (2009).

#### Interdisciplinary graduate program:

Literature discussion group leader (2009-2010).

1 lecture in Molecular Endocrinology class: "Regulation of insulin secretion" (2011).

2 lectures in Program in Cell Biology imaging methods class: "Optical sectioning microscopy" and "Fluorescence biosensors" (2011).

#### Chemical and Physical Biology program:

Literature discussion group leader (2010-2011).

### **Graduate Teaching (University of Colorado, 2011-present):**

#### Department of Bioengineering:

Course instructor for BIOE5420 "Special topics in Bioengineering: Advanced Optical Imaging" 3 credit elective class, newly offered, (Spring 2012, 2013).

Course instructor for BIOE5053 "Optics and Microscopy in Biomedical Research" 3 credit elective class, converted from BIOE5420, (Spring 2014, 2015, 2017, 2018).

Course co-instructor for BIOE5030 "Technology for Bioengineers core" 3 credit core class, (Fall 2012, 2013, 2014).

Course co-instructor for BIOE5011 "Systems Physiology for Bioengineers" 3 credit core class, (Spring 2014, 2015, 2016).

#### Biomedical Sciences Program:

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Literature discussion group leader, (Fall 2012-2014, 2016-present).

## **Undergraduate Teaching (University of Colorado, 2015-present):**

### Department of Bioengineering:

Course instructor for BIOE3040 "Physiology for Bioengineers" 3 credit core class, newly offered, (Fall 2015, 2016, 2017, 2019).

### **Courses developed:**

BIOE5420 "Special topics in Bioengineering: Advanced Optical Imaging" 3 credit elective class.

BIOE5053 "Optics and Microscopy in Biomedical Research" 3 credit elective class (converted from 5420).

BIOE3040 "Physiology for Bioengineers" 3 credit core class

### **Courses significantly modified:**

BIOE5030 "Technology for Bioengineers core" 3 credit core class.

BIOE5011 "Systems Physiology for Bioengineers" 3 credit elective class.

BIOE4053 "Optics and Microscopy in Biomedical Research" 3 credit elective class (cross-listed with 5053).

## **Mentoring**

Member of the Bioengineering Graduate program; Biomedical Sciences graduate program (BSP); Medical Scientist Training program (MSTP); Integrated Physiology graduate program (IPHY); Cell biology, Stem cells and Development graduate program (CSD).

### **MS students:**

#### Bioengineering graduate program, University of Colorado.

Imane Oubou 2011-2012

*Currently regional director Gen Next.*

Thomas Hraha 2011-2013

*Recipient of NSF Teaching fellows award.*

*RACAS outstanding graduate research award.*

*Bioengineering graduate program outstanding achievement award 2013.*

*Author on 4 peer-reviewed publications (to date, 2 as first author)*

*Currently staff scientist at SomaLogic Inc*

Chris Wilson 2012-2014

*First author on 1 manuscript in preparation*

*Currently engineer at Avicenna (AMETEK EMC)*

Alireza Hemmati 2013-2016

*Author on 2 peer-reviewed publications (to date)*

Aleena Notary 2013-2015

*Author on 2 peer-reviewed publication (to date, 1 as first author),*

*Currently staff scientist at National Jewish Health*

Nurin Ludin 2015-2017

*Author on 2 peer-reviewed publication (to date),*

*First author on 1 manuscript submitted*

*Currently intern at Islet Sciences Inc.*

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Danny Enge	2017-present
Vinh Pham	2017-present
Anna Davis	2018-present
Dominic Isaacs	2018-present

### PhD students:

#### Bioengineering graduate program, University of Colorado.

Matthew Westacott	2012-2017
<i>Author on 5 peer-reviewed publications (to date, 3 as first author), First author on 1 manuscript in preparation Awarded an F31 from NIH/NIDDK (Score 10) Awarded 'Best thesis' 2017-2018, University of Colorado Denver   Anschutz medical campus Currently staff scientist/bioinformatician at SomaLogic Inc</i>	
David Ramirez	2015-present
<i>T32 trainee (Cardiovascular Biomechanics and Imaging) Author on 1 peer-reviewed publication (to date) First author on 1 manuscript in revision Awarded an F31 from NIH/NIDDK (Score 13)</i>	
JaeAnn Dwulet	2016-present
<i>First author on 1 manuscript in revision</i>	

### Postdoctoral fellows:

Nikki Farnsworth, PhD	2012-2017
<i>Recipient of Blum-Kovler scholarship Awarded an F32 from NIH/NIDDK (Score 10) Bioengineering department outstanding achievement award 2014. Author on 5 peer-reviewed publications (to date, 4 as first author) First author on 2 manuscripts in preparation Awarded an Advanced Postdoc Fellowship from JDRF Currently Assistant Professor (tenure track) Colorado School of Mines</i>	
Joshua St.Clair, PhD	2015-2017
<i>T32 trainee (Cardiovascular Biomechanics and Imaging) Author on 2 peer-reviewed publication (to date, 1 as first author) First author on 1 manuscript in preparation Awarded an F31 from NIH/NIDDK (Score 19) Currently medical science liaison at Astrazeneca/MedImmune</i>	
Jose Miranda, PhD	2016-present
<i>First author on 1 manuscript in preparation</i>	
Vira Kravets, PhD	2017-present
<i>Awarded a Postdoc Fellowship from JDRF</i>	

### Thesis committees (PhD candidates):

#### Bioengineering graduate program, University of Colorado.

Gregory Futia [PI: Emily Gibson]	2012-2017
<i>Committee chair</i>	
Tina Govindarajan [PI: Robin Shandas]	2012-2019
Hans Andersen [PI: Richard Weir]	2013-2017

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*Committee chair*

Arjun Fontaine [PI: Richard Weir] 2013-2017

*Committee chair*

Amin Famili [PI: Daewon Park] 2013-2014

*Committee chair*

Mason McClatchey [PI: Jane Reusch] 2013-2017

Baris Ozbay [PI: Diego Restrepo, Emily Gibson] 2014-2017

*Committee chair*

Jennifer Wagner [PI: Kendall Hunter] 2014-present

Chris Erickson [PI: Karin Payne] 2015-present

Laura Elson [PI: Richard Weir] 2015-2018

Robert Hefferen [PI: Diego Restrepo, Emily Gibson] 2016-2018

Chemical and Biological Engineering graduate program, University of Colorado.

Kelly Shekiri [PI: Kristi Anseth] 2013-present

Integrative Biology graduate program, University of Colorado.

Abena Watson-Siriboe [PI: Jefferson Knight] 2014-2015

Integrated Immunology graduate program, University of Colorado.

Braxton Jamison [PI: Katy Haskins] 2016-present

Neuroscience graduate program, University of Colorado.

Shelly Jones [PI: Nathan Schoppa, Joel Zylberberg] 2017-present

Michael Thornton [PI: Ethan Hughes] 2019-present

Cell Biology, Stem Cell and Development (CSD) graduate program, University of Colorado.

Alexandra Theis [PI: Lori Sussel] 2018-present

Ali Shilleh [PI: Holger Russ] 2019-present

*Committee chair*

Molecular Biology graduate program, University of Colorado.

Roberto Castro-Gutierrez [PI: Holger Russ] 2019-present

**Undergraduate students:**

Amy Nguyen (2012)

*Participating in NIDDK summer internship in diabetes research*

Rachelle Walter (2014-present)

*Recipient of American Physiological society summer research fellowship*

*Second author on 1 peer-reviewed publication (to date)*

Dan Pham (2015)

*Recipient of Children's Hospital Colorado Summer Child Health Research Internship*

Kelly Stanik (2016)

*Recipient of Children's Hospital Colorado Summer Child Health Research Internship*

Samantha Passman (2016-2018)

*Author on 2 peer-reviewed publications (to date)*

*Recipient of UROP grant award*

*Outstanding graduate student award*

Michaela Pott (2017-2018)

*Recipient of UROP mini-grant award*

*Outstanding graduate student award*

Manal Yunes (2019)



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*Recipient of Biological Sciences Initiative award*

## **Grant support**

### **Active Research Funding:**

**R01 DK106412**

(07/01/2015– 05/31/2020)

NIH/NIDDK

*“Emergent multi-cellular properties regulating pancreatic islet function”*

- Research project grant to understand how sub-populations of cells can exhibit disproportionate control through electrical coupling of the cellular signaling mechanism underling the regulation of insulin secretion.

Role: Principal Investigator

225,000 USD/year direct costs

**R01 DK102950**

(07/01/2015– 04/30/2020)

NIH/NIDDK

*“Multicellular interactions and dynamics of pancreatic islet function in diabetes”*

- Research project grant to understand how gap junction channels are disrupted during the early development of type2 diabetes and how modulating gap junction function can recover disruptions to insulin secretion and protect against beta cell decline.

Role: Principal Investigator

225,000 USD/year direct costs

**JDRF 1-INO-2019-783-S-B**

(06/01/2019-05/31/2020)

Juvenile Diabetes Research Foundation

*“Image-guided therapeutic targeting the islet microenvironment”*

- Innovation award to examine biodistribution of sub-micron sized ultrasound contrast agents, and test whether local immunomodulation can be achieved within the islet microenvironment through targeted delivery of peptide mimotopes to impact diabetes progression.

Role: Principal Investigator

150,000 USD/year direct costs

### **Completed Research Funding:**

**JDRF 5-CDA-2014-198-A-N**

(06/01/2014– 05/31/2019)

Juvenile Diabetes Research Foundation

*“Interactions between islet function and beta cell autoimmunity during the pathogenesis of type1 diabetes”*

- Career development award to examine pancreatic islet dysfunction during the asymptomatic phase of type1 diabetes, and testing whether pancreatic islet function can be modulated to protect against immune-mediated cell death and delay the onset of the disease.

Role: Principal Investigator

136,363 USD/year direct costs

**JDRF 1-INO-2017-435-A-N**

(06/01/2017-03/31/2019)

Juvenile Diabetes Research Foundation

*“Non-invasive imaging of pancreas blood flow redistribution to assess insulinitis and islet decline in type1 diabetes”*

- Innovation award to validate whether contrast enhance ultrasound measurements of islet blood flow can be used to predict therapeutic disease prevention and disease reversal in animal models of type1 diabetes.

Role: Principal Investigator

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100,000 USD/year direct costs

**OT2 OD023852**

(09/24/2016– 07/31/2018)

NIH/OD (SPARC)

*“Development of a Bidirectional Optogenetic Minimally Invasive Peripheral Nerve Interface with Single Axon Read-in & Read-out Specificity”*

- SPARC program project to develop an Optical Probe capable of activating and reporting on axon activity in nerves of parasympathetic nervous system that control endocrine pancreas function.

Role: Co Investigator

328,802 USD/year direct costs {*subject to increase or decrease with milestones*}

**U01 AI101990 subaward**

(04/01/2015– 10/30/2016)

Cooperative Study Group for Autoimmune Disease Prevention (Benaroya Research Institute)

*“Non-invasive imaging of islet vascular dysfunction associated with the progression of type 1 diabetes”*

- Pilot project to develop and apply non-linear ultrasound contrast imaging to determine altered islet blood flow linked with insulinitis and the development of type1 diabetes

Role: Principal Investigator (subaward)

72,495 USD/year direct costs

**JDRF 47-2014-1**

(11/01/2013– 04/30/2015)

Juvenile Diabetes Research Foundation

*“Mapping the histopathological landscape of type 1 diabetes: a pilot study”*

- Innovation award to apply novel optical imaging and immunofluorescence to perform large scale mapping of immune cell and islet cell distribution in intact pancreata of healthy individuals and those with type1 diabetes. Role: Co-Principal Investigator

136,113 USD/year direct costs (between 3 investigators)

**R00 DK085145**

(09/01/2011– 08/31/2014)

NIH/NIDDK

*“Multi-cellular interactions and dynamics underlying islet function”*

- Career development award to to establish an independent research program to study inter-cellular signaling in the islet of Langerhans which underlies the regulation of insulin secretion.

Role: Principal Investigator

233,189 USD/year direct costs

**S10 OD016257**

(07/10/2013– 07/09/2014)

NIH/NIDDK

*“Zeiss 2-photon (2P) LSM780 laser scanning confocal microscope”*

- Shared instrumentation grant to procure a new confocal / 2-photon laser scanning microscope with additional; fluorescence lifetime imaging capability.

Role: Co-Principal Investigator / Principal Investigator

594,525 USD/year direct costs

**U24 DK076169 subaward**

(10/01/2010– 09/30/2011)

MMPC MicroMouse program (Georgia Health Science University)

*“ $\beta$ -cell gap-junctional coupling effects on plasma insulin oscillations”*

- Pilot and Feasibility grant to understand how islet gap junctions affect in-vivo plasma insulin dynamics and glucose tolerance

Role: Principal Investigator (subaward)

35,528 USD/year direct costs

**K99 DK085145**

(09/25/2009– 08/31/2011)

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NIH/NIDDK

*"Multi-cellular interactions and dynamics underlying islet function"*

- Career development award to establish an independent research program to study inter-cellular signaling in the islet of Langerhans which underlies the regulation of insulin secretion.

Role: Principal Investigator

88,776 USD/year direct costs

### **Active and completed Mentoring grants:**

**JDRF 3-APF-2019-749-A-N**

(03/01/2019-02/28/2022)

Juvenile Diabetes Research Foundation

*"The Role of Protein Kinase C delta and Extracellular Matrix Interactions in Mediating Beta Cell Decline in Type 1 Diabetes"*

- Mentored Advanced Postdoc fellowship award to investigate how PKCdelta and matrix interactions modulate beta cell death by apoptosis in the progression of type1 diabetes.

Role: Primary Mentor (Nikki Farnsworth PI)

284,308 USD/year direct costs

**JDRF 3-PDF-2019-741-A-N**

(03/01/2019-02/28/2022)

Juvenile Diabetes Research Foundation

*"Beta cell heterogeneity under diabetic conditions in human islets in situ"*

- Mentored Postdoc fellowship award to identify beta cell sub-populations within the intact human islet and their changes in the progression of type1 diabetes.

Role: Primary Mentor (Vira Kravets PI)

177,876 USD/year direct costs

**F31 DK121488**

(07/01/2019– 06/30/2021)

NIH/NIDDK

*"Contrast Enhanced Ultrasound with Submicron Nanobubble Contrast Agent Detects Diabetes Progression in Mouse Models of Type 1 Diabetes"*

- Mentored Predoctoral fellowship to characterize how a novel sub-micron sized ultrasound contrast agent can track type1 diabetes progression and therapeutic reversal.

Role: Primary Mentor (David Ramirez PI)

38,016 USD/year direct costs

**F32 DK102276**

(09/01/2014– 08/31/2017)

NIH/NIDDK

*"Regulation of islet gap junction coupling and function under inflammatory conditions"*

- Mentored Postdoctoral fellowship to investigate how inflammatory conditions disrupt gap junction channel function and the regulation of electrical activity, such as during the progression of type1 diabetes

Role: Primary Mentor (Nikki Farnsworth PI)

53,282 USD/year direct costs

**F31 DK107043**

(08/01/2016– 07/31/2017)

NIH/NIDDK

*"Examination of Functional Subpopulations in the Islet of Langerhans Using Optogenetics"*

- Mentored Predoctoral fellowship to apply optogenetics to discover functional sub-populations of cells within the islet and understand how they exert control over other cells to impact islet function.

Role: Primary Mentor (Matthew Westacott PI)

34,776 USD/year direct costs

**F32 DK112525**

(12/01/2016– 05/31/2018, finished 06/30/2017)

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NIH/NIDDK

*"The role of gap junction coupling in regulating islet dysfunction in type2 diabetes"*

- Mentored Postdoctoral fellowship to understand how gap junction coupling is disrupted during the progression of type2 diabetes and to modulate this disruption to preserve insulin secretion.

Role: Primary Mentor (Josh St Clair PI)

54,294 USD/year direct costs

### **Internal competitive funding:**

**Novel Clinical-Translational Methods**

(05/01/2013-04/30/2014)

NIH CTSA (CCTSI)

*"Multi-parameter quantitative analysis of cellular populations in-situ"*

- Pilot grant as part of the CCTSI's novel methods program to develop a method to quantify immune cell populations in-situ, combining the powers of confocal microscopy and flow cytometry.

Role: Principal Investigator

25,000 USD/year direct costs

## **Bibliography**

### **Peer-Reviewed Research Articles:**

1. Richard K.P. Benninger, Björn Önfelt, Mark A.A. Neil, Daniel M. Davis, Paul M.W. French. "Fluorescence Imaging of Two-Photon Linear Dichroism: Cholesterol Depletion disrupts Molecular Orientation in Cell Membranes." *Biophysical Journal* (2005) **88**: pp609-622.
2. Richard K.P. Benninger, Oliver Hoffman, James McGinty, Jose Requejo-Isidro, Ian Munro, Mark A.A. Neil, Andrew J. deMello, Paul M.W. French. "Time-resolved fluorescence imaging of solvent interactions in microfluidic devices" *Optics Express*. (2006) **13**: pp6275-6285.
3. Richard K.P. Benninger, Yasemin Koç, Oliver Hoffman, Jose Requejo-Isidro, Mark A.A. Neil, Paul M.W. French, Andrew J. deMello. "Quantitative 3D Mapping of Fluidic Temperatures within Microchannel Networks Using Fluorescence Lifetime Imaging" *Analytical Chemistry* (2006) **78**: pp2272-2278.
4. Björn Önfelt, Shlomo Nedvetski, Richard K.P. Benninger, Mark A Perbhoo, Stefanie Sowinski, Alistair N. Hume, Miguel C. Seabra, Mark A.A. Neil, Paul M.W. French, Daniel M. Davis. "Structurally Distinct Membrane Nanotubes between Human Macrophages Support Long-Distance Vesicular Traffic or Surfing of Bacteria" *Journal Immunology* (2006) **177**: pp8476-83.
5. Pieter DeBeule, Dylan M. Owen, Hugh B. Manning, Clifford B. Talbot, Jose Requejo-Isidro, Christopher Dunsby, James McGinty, Richard K.P. Benninger, Daniel Elson, Ian Munro, M. John Lever, Praveen Anand, Mark A.A. Neil, Paul M.W. French. "Rapid Hyperspectral Fluorescence Lifetime Imaging" *Microscopy Research Techniques* (2007) **70**: pp481-484
6. Richard K.P. Benninger, Oliver Hoffman, Björn Önfelt, Ian Munro, Christopher Dunsby, Daniel M. Davis, Mark A.A. Neil, Paul M.W. French, Andrew J. deMello. "Fluorescence Lifetime Imaging of Dye: DNA Interactions within Continuous Flow Microfluidic Systems" *Angewandte Chemie International Edition (English)*. (2007) **46**: pp2228-2231
7. Sunil Kumar, Christopher Dunsby, Pieter A.A. DeBeule, Dylan M. Owen, U Anand, Peter M.P. Lanigan, Richard K.P. Benninger, Daniel M. Davis, Mark A.A. Neil, Praveen Anand, Christopher Benham, Alan Naylor, Paul M.W. French. "Multifocal multiphoton excitation and time correlated single photon counting detection for 3-D fluorescence lifetime imaging" *Optics Express*. (2007) **15**: pp12548-12561

8. Richard K.P. Benninger\*, Shu Mao\*, Yuling Yan, Chutima Petchprayoon, David Jackson, Christopher J. Easley, David W. Piston, Gerard Marriott "Optical lock-in detection of fluorescence resonance energy transfer using synthetic and genetically-encoded optical switches" *Biophysical Journal* (2008) **94**: pp4515-24. (\* Equal contributors)
9. Richard K.P. Benninger, Min Zhang, W. Steven Head, Leslie S. Satin, David W. Piston "Gap Junction Coupling and Calcium Waves in the Pancreatic Islet" *Biophysical Journal* (2008) **95**: pp5048-5061.
10. Richard K.P. Benninger, William J. Ashby, Elisabeth A. Ring, David W. Piston "A single-photon counting detector for increased sensitivity in two-photon laser scanning microscopy" *Optics Letters* (2008) **33**: pp2895-7.
11. Richard K.P. Benninger, Bruno Vanherberghen, Stephen Young, Sabrina Tanner, Fiona F. Culley, Tim Schnyder, Mark A.A. Neil, Daniel Wüstner, Paul M.W. French, Daniel M. Davis, Björn Önfelt "Live cell linear dichroism imaging reveals extensive membrane ruffling within the docking structure of Natural Killer cell immune synapses" *Biophysical Journal- Biophysical Letters* (2009) **96** L13-15.
12. Subhadra C. Gunawardana, Richard K.P. Benninger, David W. Piston "Subcutaneous transplantation of embryonic pancreas for correction of type 1 diabetes" *American Journal of Physiology- Endocrinology and Metabolism* (2009) **296** E323-332.
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### **Manuscripts in Revision, Submitted, or in Preparation:**

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- .. JaeAnn Dwulet\*, Nurin F.W. Ludin\*, Robert Piscopio, Wolf Schleicher Ong Moua, Matthew J. Westacott, Richard KP Benninger. "How gap junction electrical coupling regulates the electrical response of  $\beta$ -cells that are heterogeneous in glucokinase activity." *Manuscript in Revision* (\* Equal contributors)
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- .. Nikki L. Farnsworth, Jose Miranda, Robert Piscopio, Audrey Heintz, Richard KP Benninger. "Connexin36 gap junction coupling protects against cytokine-induced apoptosis via reducing  $[Ca^{2+}]$  and calcineurin activation". *Manuscript in Preparation*.
- .. Jose Miranda, Wolfgang Schleicher, David Ramirez, Samantha Payne-Landgrave, Richard KP Benninger. "The dynamics of Beta-cell electrical activity regulates NFAT activity". *Manuscript in Preparation*
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- .. Nikki L. Farnsworth, Robert Piscopio, Wolfgang Schleicher, Richard KP Benninger. "Protein Kinase C delta activation, translocation and cleavage mediates beta cell apoptosis in response to proinflammatory cytokines". *Manuscript in Preparation*.



## **Published/Presented Conference Abstracts:**

*posters and oral presentations, presenting author in bold*

**2005:** "Imaging Lipid Structure with Fluorescence-detected 2-photon Linear Dichroism" **R.K.P.Benninger**, B.Önfelt, M.A.A.Neil, D.M.Davis, P.M.W.French. *Poster Presentation at Biophysical Society Meeting*: Long Beach, CA.

"Imaging Lipid Structure with Fluorescence-detected 2-photon Linear Dichroism" **R.K.P.Benninger**, B.Önfelt, M.A.A.Neil, D.M.Davis, P.M.W.French. *Oral Communication at Focus on Microscopy*: Jena, Germany.

"Application of Multi-photon Multi-focal Microscopy for Biological Imaging" **R.K.P.Benninger**, B.Önfelt, C.B.Talbot, O.Hofmann, J.Requejo-Isidro, P.M.W.French. *Oral Communication at PREP 2005*: Lancaster, UK.

"Application of Time-resolved Fluorescence Imaging for Microfluidic Technology" **R.K.P.Benninger**, O.Hofmann, Y.Koç, B.Önfelt, J.McGinty, J.Requejo-Isidoro, I.Munro, M.A.A.Neil, A.J.deMello, P.M.W.French. *Oral Communication at IoP meeting on Optics and Microfluidics*: Edinburgh, UK.

"Application of Multi-dimensional Fluorescence Imaging to Microfluidic Devices" **R.K.P.Benninger**, J.McGinty, O.Hofmann, J.Requejo-Isidro, I.Munro, D.S.Elson, C.Dunsby, B.Önfelt, D.M.Davis, M.A.A.Neil, A.J.deMello, P.M.W.French. *Oral Communication at CLEO-Europe, Biophotonics*: Munich, Germany.

"3D High-speed Time-resolved Fluorescence Imaging of Solvent Interactions in Microfluidic Devices" **R.K.P.Benninger**, O.Hofmann, J.McGinty, J.Requejo-Isidro, I.Munro, M.A.A.Neil, **A.J.deMello** and P.M.W.French. *Oral Communication at Micro-TAS*: Boston, MA (2005)

**2007:** "Methods to Study Gap Junction Conductance in Pancreatic Islets" **R.K.P.Benninger**, S.J.LeMarchand, J.V.Rocheleau, M.Zhang, L.S.Satin, D.W.Piston. *Poster Presentation at Biophysical Society Meeting*: Baltimore, MD.

"Imaging and Modeling of Gap Junction Connectivity in the Islets of Langerhans" **R.K.P.Benninger**, S.J.LeMarchand, J.V.Rocheleau, M.Zhang, L.S.Satin, A.Sherman, D.W.Piston. *Oral Communication at MBI Workshop on Insulin Secretion, Insulin Action and Type II Diabetes*: Columbus, OH.

"Imaging inter-cellular communication in the Pancreatic Islet" **R.K.P.Benninger**, S.J.LeMarchand, J.V.Rocheleau, M.Zhang, L.S.Satin, D.W.Piston. *Oral Communication & Poster Presentation at European Biophysics Congress*: London, UK.

**2008:** "In vivo imaging of Ca activity in pancreatic islets" **R.K.P.Benninger**, L.R.Nyman, M.Shiota, D.W.Piston. *Poster Presentation at Biophysical Society Meeting*: Long Beach, CA.

"Gap junction communication in the pancreatic islet" **R.K.P.Benninger**, M.Zhang, W.S.Head, L.S.Satin, D.W.Piston. *Oral Communication at (Upper-) Midwest Islet Club*: Nashville TN.

"High sensitivity photochromic-FRET using multi-photon excitation" **R.K.P.Benninger**, S.Mao, G.Marriott, D.W.Piston. *Oral Communication at South-East two-photon microscopy user meeting*: Atlanta GA.

**2009:** "Quantitative experimental measurements and mathematical modeling of multi-cellular dynamics in the islet of Langerhans" **R.K.P.Benninger**, M.Zhang, W.S.Head, L.S.Satin, D.W.Piston. *Poster Presentation at Biophysical Society Meeting*: Boston, MA.

"Quantitative imaging and modeling of multi-cellular interactions and dynamics in the islet" **R.K.P. Benninger**, M.Zhang, W.S.Head, L.S.Satin, D.W.Piston. *Oral Communication at NIDDK Imaging the Islet workshop*: Washington, DC.

"Loss of  $\beta$ -cell Ca triggering as the primary mechanism underlying secretory failure in KATP-induced Neonatal Diabetes Mellitus" **R.K.P.Benninger**, M.S.Remedi, A.Ustione, W.S.Head, D.W.Piston, C.G.Nichols. *Oral presentation at American Diabetes Association annual scientific sessions*: New Orleans, LA.

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- 2010:** "Metabolism-excitation coupling in a model of  $K_{ATP}$  channel neonatal diabetes mellitus" **R.K.P.Benninger**, M.S.Remedi, A.Ustione, W.S.Head, D.W.Piston, C.G.Nichols. *Poster Presentation at Biophysical Society Meeting*: San Francisco, CA.  
"Gap junction coupling and insulin secretion" **R.K.P.Benninger**, W.S. Head, D.W.Piston. *Poster Presentation at Keystone Conference on Islet Biology*: Whistler, BC, Canada.  
"Islet Gap Junction Coupling and the Regulation Insulin Secretion" **R.K.P.Benninger**, W.S. Head, D.W.Piston. *Oral Presentation at Midwest Islet club*: Indianapolis IN.
- 2011:** "Origin and Dynamics of Calcium Waves in the Islet of Langerhans" **R.K.P.Benninger**, T.Hutchens, W.S.Head, D.W.Piston. *Poster Presentation at Biophysical Society Meeting*: Baltimore, MD.  
"Multiple mechanisms of cell-cell communication regulate islet function and insulin secretion" **R.K.P.Benninger**, W.S.Head, L.S.Satin, D.W.Piston. *Oral presentation at American Diabetes Association annual scientific sessions*: San Diego, CA.
- 2013:** "Gap-junction suppression of electrical activity in normal and diabetic pancreatic islets" L.M.Nguyen, M.Pozzoli, **R.K.P.Benninger** *Poster Presentation at Biophysical Society Meeting*: Philadelphia, PA.  
"Dimensionality and Calcium Dynamics in Pancreatic  $\beta$ -Cell Clusters" **T.H.Hraha**, A.B.Bernard, K.S.Anseth, **R.K.P.Benninger** *Poster Presentation at Biophysical Society Meeting*: Philadelphia, PA.  
"Effects of low level inflammation on beta cell coupling in isolated mouse islets" **N.L.Farnsworth**, **R.K.P.Benninger** *Oral presentation at Western Regional Islet Study Group*: Los Angeles, CA.  
"Modulating islet gap junction coupling enhances insulin release and normalizes glycemia in a mouse model of neonatal diabetes mellitus" L.M.Nguyen, M.Pozzoli, **R.K.P.Benninger** *Poster Presentation at American Diabetes Association annual scientific sessions*: Chicago, IL. \*Poster selected for guided audio tour.  
"Pancreatic Primary Cell Aggregates are Functionally Superior to Age-Matched Islets" **T.H.Hraha**, K.Shekiro, A.B.Bernard, K.S.Anseth, **R.K.P.Benninger** *Poster Presentation at American Diabetes Association annual scientific sessions*: Chicago, IL.  
"Modulating Connexin36 gap junctions in the pancreatic islet normalizes glycemic control in a mouse model of neonatal diabetes" L.M.Nguyen, M.Pozzoli, **R.K.P.Benninger** *Oral presentation at International gap junction conference*: Charleston, SC.  
"Low Level Inflammation Affects  $\beta$ -Cell Gap Junction Coupling and Insulin Dynamics in Pancreatic Islets" **N.L.Farnsworth**, A.Hemmati, M.Pozzoli, **R.K.P.Benninger** *Poster presentation at International gap junction conference*: Charleston, SC.
- 2014:** "Optogenetic excitation of the pancreatic  $\beta$ -cell" **M.J.Westacott**, M.Pozzoli, **R.K.P.Benninger** *Poster Presentation at Biophysical Society Meeting*: San Francisco, CA.  
"Critical behavior in the pancreatic islet depends on the balance between cellular excitability and electrical coupling" **T.H.Hraha**, M.J.Westacott, L.M.Nguyen, M.Pozzoli, **R.K.P.Benninger** *Poster Presentation at Biophysical Society Meeting*: San Francisco, CA.  
"Disrupted Electrical Regulation in Islet Dysfunction and the Implications in Diabetes" **N.L.Farnsworth**, A.Hemmati, T.H.Hraha, **R.K.P.Benninger** *Poster Presentations at Keystone Conference on Islet Biology*: Keystone, CO.  
"A critical balance between  $K_{ATP}$  activity and gap junction coupling determines islet dysfunction and diabetes" **T.H.Hraha**, M.J.Westacott, M.Pozzoli, **R.K.P.Benninger** *Oral and Poster Presentations at Keystone Conference on Islet Biology*: Keystone, CO.
- 2015:** "Regulation of coupled  $\beta$ -cell cAMP dynamics" C.L.Wilson, M.Westacott, **R.K.P.Benninger** *Poster Presentations at Biophysical Society Meeting*: Baltimore, MD.  
"Stimulated Insulin Secretion in the Pancreatic  $\beta$ -Cell by Channelrhodopsin-2" **M.J.Westacott**, M.Pozzoli, **R.K.P.Benninger**. *Poster Presentations at Keystone Conference on Optogenetics*: Denver, CO.

"GLP1R Regulation of Gap Junction Coupling in the Islet of Langerhans" **R.Walter**, N.L.Farnsworth, R.K.P.Benninger *Poster Presentations at Experimental Biology*: Boston, MA.

"Pro-inflammatory cytokines disrupt islet gap junctions early in the development of type 1 diabetes in NOD mice via PKC $\delta$ - phosphorylation of connexin36" **N.L.Farnsworth**, A.Hemmati, R.K.P.Benninger *Poster Presentations at American Diabetes Association annual scientific sessions*: Boston, MA.

"Proinflammatory Cytokines Disrupt Islet Gap Junction Channels and Ca<sup>2+</sup> Homeostasis early in the Development of Type1 Diabetes in NOD Mice" **R.K.P.Benninger**, N.L.Farnsworth, J. StClair, *Poster Presentations at European Association for the Study of Diabetes annual meeting*: Stockholm, Sweden.

**2016:** "Spatial Homogeneities in Metabolic Activity Control Electrical Activity in Pancreatic Islets" **M.J.Westacott**, R.K.P.Benninger *Poster Presentations at Biophysical Society Meeting*: Los Angeles, CA.

"Ageing disrupts human islet electrical activity" M.J.Westacott, N.L.Farnsworth, J.R.St.Clair, **R.K.P.Benninger** *Poster Presentations at Keystone Conference on Islet Biology*: Keystone, CO.

"Connexin36 Gap Junction Coupling Protects Against Cytokine-Induced  $\beta$ -Cell Death and Dysfunction with Ca<sup>2+</sup> Dependence" **N.L.Farnsworth**, A.Heintz, R.K.P.Benninger *Poster Presentations at American Diabetes Association annual scientific sessions*: New Orleans, LA. \*Poster selected for guided audio tour.

"Age/BMI Predict Electrical Activity and Coordination in Human Pancreatic Islets" **M.J.Westacott**, N.L.Farnsworth, J.R.StClair, A.Heintz, R.K.P.Benninger *Poster Presentations at American Diabetes Association annual scientific sessions*: New Orleans, LA. \*Poster selected for guided audio tour.

"Serine-293 on Connexin-36 Regulates  $\beta$ -cell Dysfunction in the Pre-Diabetic Islet of Langerhans" **J.R.StClair**, N.L.Farnsworth, A.Heintz, R.K.P.Benninger *Poster Presentations at American Diabetes Association annual scientific sessions*: New Orleans, LA. \*Poster selected for guided audio tour.

**2017:** "Disrupted Cx36 Gap Junction Coupling Contributes to the Progression of Type 1 Diabetes in NOD Mice" **N.L.Farnsworth**, A.Heintz, R.K.P.Benninger. *Oral Presentations at American Diabetes Association annual scientific sessions*: San Diego, CA.

"Contrast enhanced ultrasound non-invasively measures changes in islet blood flow distribution associated with type1 diabetes progression" J.R.St.Clair, D.Ramirez, S.Passman, D.Henderson, **R.K.P.Benninger**. *Oral Presentation at American Diabetes Association annual scientific sessions*: San Diego, CA.

"Maintaining Connexin-36 Function in a Diabetogenic Environment Precludes Islet Dysfunction and Beta-Cell Death" J.R. St.Clair, N.L. Farnsworth, A. Heintz, N. Ludin. **R.K.P. Benninger**. *Oral Presentations at International gap junction conference*: Glasgow, UK.

**2018:** "Electrical activity disruption associated with diabetes is recovered by Modafinil" V.Kravets, M.J.Westacott, O.Moua, **R.K.P.Benninger** *Poster Presentations at Keystone Conference on Islet Biology*: Keystone, CO.

"NFAT regulation in  $\beta$ -cell dysfunction" J.Miranda, **R.K.P.Benninger** *Poster Presentations at Keystone Conference on Islet Biology*: Keystone, CO.

"Subpopulations of  $\beta$ -cells play a Disproportionate Role in Multicellular Islet Dynamics" J.Dwulet, **R.K.P.Benninger** *Oral and Poster Presentations at Keystone Conference on Islet Biology*: Keystone, CO.

"Contrast-Enhanced Ultrasound with Sub-Micron Sized Contrast Agents Detects Diabetes Progression in Mouse Models of Type 1 Diabetes" D.Ramirez, C.Hernandez, L.Papazian, A.Exner, R.K.P.Benninger. *Oral Presentations at American Diabetes Association annual scientific sessions*: Orlando, FL.

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**2019:** "Detecting pancreatic islet immune infiltration in pre-symptomatic type1 diabetes using sub-micron scale ultrasound contrast agents" **R.K.P. Benninger**, D.Ramirez, A.Exner, M.Borden. *Oral Presentations at European symposium on Ultrasound Contrast Imaging*: Rotterdam, Netherlands.

"Protein kinase C delta mediates cytokine-induced apoptosis in the pancreatic beta-cell" N.L.Farnsworth, R.Piscopio, and **R.K.P. Benninger**. *Poster presentation at American Diabetes Association annual scientific sessions*: San Francisco, CA.

"Distinct functional beta cell subpopulations in intact islets of Langerhans" V.Kravets, W.Schleicher, **R.K.P.Benninger**. *Oral Presentations at American Diabetes Association annual scientific sessions*: San Francisco, CA.