BIOGRAPHICAL SKETCH

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

NAME: William Rowland Goodyer, MD, PhD

eRA COMMONS USER NAME (credential, e.g., agency login): wgoodyer

POSITION TITLE: Assistant Professor (Pediatric Cardiology – Electrophysiology)

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
McGill University, Montreal, Quebec, Canada	BS	05/1999	07/2004	Honors in Biology/ Classical Music
Stanford University School of Medicine, Stanford, CA	MD/PhD	08/2005	06/2013	Medicine/ Developmental Biology
Boston Combined Residency Program, Boston, MA	Residency	06/2013	06/2015	Pediatrics (Accelerated Research Program)
Lucile Packard Children's Hospital (LPCH), Stanford, CA	Pediatric Cardiology Fellowship	06/2015	07/2019	Pediatric Cardiology (Accelerated Research Track)
Cardiovascular Institute (CVI), Stanford, CA	Postdoctoral Research Fellowship	07/2017	07/2019	Cardiac Conduction System Development
Lucile Packard Children's Hospital (LPCH), Stanford, CA	Electrophysiology Fellowship	07/2019	07/2020	Pediatric Electrophysiology

A. Personal Statement

My overarching goal as a physician-scientist is to leverage molecular biology and translational medicine to improve the diagnosis, prevention and treatment of cardiac rhythm disorders. This passion has been cultivated from my experiences as a pediatric cardiologist, witnessing the morbidity and mortality associated with arrhythmias in children. These exposures have not only raised my awareness of the many unmet medical needs in the field of cardiology, but have also illustrated the numerous opportunities for how we can improve our current management of cardiac arrhythmias.

My earliest experiences in basic science came as an undergraduate, discovering a novel protein integral to the process of meiosis using *C. elegans* as a model system (**Goodyer et al. 2008, *Developmental Cell***). After graduating from McGill University (Montreal, Canada) with a BSc in Biology, I completed my graduate studies at Stanford University in the NIH-funded Medical Scientist Training Program (MSTP), with a PhD in Developmental Biology in the Seung Kim lab. By unveiling a novel molecular pathway underlying the proliferation and maturation of β-cells in both mice and humans (**Goodyer et al. 2012, *Developmental Cell***), I made my first successful foray into translational medicine with the discovery of a targetable pathway for possible disease modification, resulting in my first patent application. I subsequently completed residency training in Pediatrics at Boston Children's Hospital before returning to Stanford to complete a fellowship in Pediatric Cardiology and advanced fellowship in Pediatric Electrophysiology. Following my clinical training, I performed a postdoctoral fellowship in the Sean Wu laboratory where I researched the molecular regulators mediating cardiac conduction system (CCS) development by generating the first, comprehensive single cell atlas of the murine conduction system (**Goodyer et al. 2019, *Circulation Research***). I subsequently leveraged these findings to molecularly target the CCS *in vivo* using an antibody-dye conjugate, thereby

providing a first-in-kind method for preventing accidental damage to the CCS during cardiac surgeries (**Goodyer et al. 2022, *JCI***). For this and subsequent work, I have received numerous translational grants (Stanford SPARK Translational grant, Stanford Innovative Medicines Accelerator, and Stanford Maternal and Child Health Research Institute Transdisciplinary Award); a NIH K08 Career Development Award; an American Heart Association Transformational grant; two additional patents relating to the molecular targeting of the heart for diagnostic and therapeutic purposes; and was selected to attend the Eureka Monsoon School of Translational Medicine International Program in Singapore. Most recently, I was selected as the Associate Director of the internationally recognized SPARK Stanford translational research program, an incubator for launching promising new pre-clinical research into clinical practice.

In 2023, I was appointed as an Assistant Professor in Pediatric Cardiology and Electrophysiology at Stanford University, where my lab is dedicated to the improved diagnosis, prevention and treatment of cardiac arrhythmias.

Ongoing and recently completed projects that I would like to highlight include:

American Heart Association Transformational Project Grant **Goodyer (PI)**
07/01/24-06/31/27
Novel Imaging of the CCS to Reduce Surgical Complications
The goal of this research is to create a novel method for the advanced imaging of the cardiac conduction system to help in preoperative planning of cardiac surgeries.

NIH R01 (NHLBI) (1R01HL1738451) (Marsden PI, Ellis Co-PI) **Goodyer (Co-I)**
05/03/24–04/30/29
A Multi-Physics Simulator for Pediatric Cardiac Surgical Planning
The research goals are to employ computer modeling and advanced imaging modalities to generate a first-in-kind multi-physics model simulators of complex congenital heart disease for improved surgical planning.

Stanford Transdisciplinary Initiatives Program Grant (Engreitz PI) **Goodyer (PI)**
06/01/23-05/31/25
Precision Treatment of Pediatric Cardiac Arrhythmias
The goal is to validate a novel antibody-drug conjugate for the treatment of atrial arrhythmias in children.

Additional Ventures Single Ventricle Research Fund Award **Goodyer (Co-I)**
07/01/22–06/31/25
A Reference Map of Enhancers During Human Fetal Heart Development to Understand the Genetic Etiology of Single Ventricle Diseases.
The goals of this project are to build a comprehensive resource guide of enhancers and their target genes during normal human heart development and hypoplastic left heart syndrome.

NIH Mentored Clinical Scientist Research CDA (K08HL153785) (NHLBI) **Goodyer (PI)**
09/01/20–08/31/25
Elucidation of the Development and Function of the Cardiac Conduction System
The goal is to better understand CCS development and disease through the characterization of *Cpne5*.

Stanford Child Health Research Institute K-awards Support Grant **Goodyer (PI)**
11/01/20-12/31/22
Elucidation of the Development and Function of the Cardiac Conduction System
Supplemental support for instructors on K-awards funds innovative translational research.

Citations:

a. **Goodyer WR,** Beyersdorf BM, Duan L, van den Berg NS, Mantri S, Galdos FX, Puluca N, Buikema JW, Lee S, Salmi D, Robinson ER, Rogalla S, Cogan DP, Khosla C, Rosenthal EL, Wu SM. In vivo visualization and molecular targeting of the cardiac conduction system. *Journal of Clinical Investigation.* 2022. PMCID: PMC9566899.
b. **Goodyer WR**, Beyersdorf B, Paik DT, Tian L, Li G, Buikema JW, Chirikian O, Choi S, Venkatraman S, Adams EL, Tessier-Lavigne M, Wu JC, Wu SM. Transcriptomic Profiling of the Developing Cardiac Conduction System at Single-Cell Resolution. *Circulation Research*. 2019. PMCID: PMC6675655.
c. **Goodyer WR**, Dunn K, Caleshu C, Jackson M, Wylie J, Moscarello T, Platt J, Reuter C, Smith A, Trela A, Ceresnak SR, Motonaga KS, Ashley E, Yang P, Dubin AM, Perez, M. Broad Genetic Testing in a Clinical Setting Uncovers a High Prevalence of Titin Loss-of-Function Variants in Very Early-Onset Atrial Fibrillation. *Circulation: Genomic and Precision Medicine*. 2019. PMCID: PMC10626994.
d. **Goodyer WR**, Gu X, Liu Y, Bottino R, Crabtree GR, Kim SK. Neonatal β cell development in mice and humans is regulated by calcineurin/NFAT. *Developmental Cell*. 2012. PMCID: PMC3587727.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

07/2024-Present - Associate Director of Stanford SPARK Translational Research Program
01/2023-Present - Assistant Professor, Pediatric Cardiology/Electrophysiology, LPCH
11/2020-Present - Pediatric Cardiology Board Certification
07/2020-01/2023 - Instructor, Pediatric Cardiology (Electrophysiology), LPCH, Stanford University
07/2019-07/2020 - Pediatric Electrophysiology Advanced Fellow, LPCH, Stanford University
07/2018 - Eureka Monsoon School of Translational Medicine Certificate Program (Singapore)
2017-Present - Stanford Pediatric Cardiology Boot Camp Simulation Faculty
2017-Present - Member of American College of Cardiology (ACC)
2017-Present - Member of Heart Rhythm Society (HRS)
2017-Present - Pediatric & Congenital Electrophysiology Society Education Committee Member
2017-2019 - Postdoctoral Fellow, P.I.: Dr. Sean Wu, Stanford University
2017-2019 - Intern Selection Committee Member for Lucile Packard Children's Hospital
2017-2018 - Fellows Council Representative for Pediatric Cardiology, LPCH
2016-Present - General Pediatrician Board Certification
2015-Present - Member of American Heart Association (AHA)
2015-Present - Member of the Stanford Society for Physician Scientists (SSPS)
06/2015-07/2019 - Pediatric Cardiology Fellow (Accelerated Research Track), LPCH, Stanford University
2013-2014 - Executive Committee Member of Residency Program Training Committee, Stanford Pediatrics
06/2013-06/2015 - Pediatric Resident (Accelerated Research Program), Boston Children's Hospital
2010-2011 - Stanford Partners for Academic Excellence Student Athlete Mentor, Stanford
2010 - Teacher Assist. for "'Intro to Academic Medicine" Grant Writing Course (INDE 232), Stanford University
08/2005-05/2013 - Medical Scientist Training Program (MSTP) (MD/PhD), Stanford University

Other Experience

2018 - ACC ACCEL (ACC Extended Learning)/FIT (Fellows in Training) Research Program member
2018 - Duke Heart Center/Duke Clinical Research Institute Fellows' Presentation Skills Course
2016 - Stanford Spectrum Intensive Course in Clinical Research: Study Design and Performance

Honors

2024 - American Society for Clinical Investigation (ASCI) Young Physician-Scientist Award (YPSA)
2023 - Stanford Department of Pediatrics Faculty Award – Basic Science Research Award
2022-2023 - Stanford Department of Pediatrics Fellowship Honor Roll for Teaching
2020 - Eli Gang Heart Rhythm Society 2020 - Most Innovative Abstract Award
2020 - Selected Finalist for the Katz Basic Science Research Prize for Early Career Investigators at the American Heart Association Scientific Sessions 2020
2020 - Medtronic Heart Rhythm Society Scholarship

2019 - Awarded Best Oral Presentation in the Faculty/Trainee Basic-Translational Science Section at the Stanford Heart Center Research Symposium
2018 - Maternal and Child Health Research Institute Eureka Translational Medicine Award to attend the Monsoon School of Translational Medicine International Certificate Program (Singapore)
2018 - Alpha Omega Alpha (AOA) Honor Medical Society Inductee
2018 - Stanford Cardiovascular Institute (CVI) Research Travel Award
2017-2018 - Pediatric Cardiology - Chief Fellow
2016-2017 - Fellow of the Year (Outpatient), Lucile Packard Children's Hospital
2009 - French-American Foundation for Medical Research and Education Scholarship
2005-2013 - National Institute of Health (NIH) Medical Scientist Training Program (MSTP)

C. Contributions to Science

1. Profiled the Transcriptional Landscape of the Entire Cardiac Conduction System (CCS) at Single-Cell Resolution: Despite an essential role for the CCS in heart development and function, the CCS has remained challenging to interrogate due to inherent obstacles including small cell numbers, large cell type heterogeneity, complex anatomy, and difficulty of isolation. During my postdoctoral fellowship, I set out to overcome these longstanding limitations in the field by employing single-cell RNA-sequencing (scRNA-seq) on over 22,000 cells of the developing mouse heart. All major cell types of the murine heart were successfully captured, including bona fide clusters of cells consistent with each major component of the CCS. Unsupervised weighted gene co-expression network analysis led to the discovery of a host of novel CCS genes. Further, using whole mount immunolabelling with volume imaging (iDISCO+) in three dimensions on intact mouse hearts, I validated the expression of a subset of these candidates. Additionally, use of iDISCO+ allowed, for the first time, the 3D visualization of the entire, intact CCS and its subcomponents within the heart. Finally, subcluster analysis unveiled the successful isolation of distinct CCS cell subtypes, including the clinically relevant but previously poorly characterized "transitional cells" that bridge the CCS and surrounding myocardium. This work represented the first comprehensive assessment of the transcriptional profiles from the entire CCS at single-cell resolution and provided a gene atlas for facilitating future efforts in conduction cell identification, isolation and characterization in the context of development and disease. My work resulted in a first author manuscript in *Circulation Research* and last author review in *Current Cardiology Reports*, in addition to five other co-authored manuscripts.

a. Galdos FX, Xu S, **Goodyer WR,** Duan L, Huang YV, Lee S, Zhu H, Lee C, Wei N, Lee D, Wu SM. devCellPy is a machine learning-enabled pipeline for automated annotation of complex multilayered single-cell transcriptomic data. ***Nature Communications.*** 2022. PMCID: PMC9452519.
b. **Tabula Sapiens Consortium** et al. Wyss-Coray T. The Tabula Sapiens: A multiple-organ, single-cell transcriptomic atlas of humans. ***Science.*** 2022. PMCID: PMC9812260.
c. Mantri S, Wu SM, and **Goodyer WR**. Molecular Profiling of the Cardiac Conduction System: The Dawn of a New Era. ***Current Cardiology Reports***. 2021. PMID: 34196831. DOI: 10.1007/s11886-021-01536-w.
d. **Goodyer WR**, Beyersdorf B, Paik DT, Tian L, Li G, Buikema JW, Chirikian O, Choi S, Venkatraman S, Adams EL, Tessier-Lavigne M, Wu JC, Wu SM. Transcriptomic Profiling of the Developing CCS at Single-Cell Resolution. ***Circulation Research***. 2019. PMCID: PMC6675655.

2. Created Novel Optical Imaging Diagnostic Tools to Visualize the CCS in Mice: Accidental intraoperative injury to the CCS, from an inability to visualize the conduction system, remains a significant complication of both pediatric and adult cardiac surgeries. Damage to the CCS can result in a host of life-threatening arrhythmias and remains a significant cause of morbidity, increased cost, and decreased long-term survival. To date, there exists no *in vivo* method to detect the CCS. In order to address this unmet medical need, I developed a novel, fluorescent, antibody-based method for the real-time, intraoperative visualization of the CCS. I have demonstrated that this method demonstrates high sensitivity and specificity for labeling the entire CCS following systemic injection in mice. This tool provides a proof-of-principle for the *in vivo* labeling of cardiac substructures for the first time and lays the foundation for translational opportunities including real-time CCS visualization during cardiac interventions, as well as targeted delivery of therapeutics. I am currently finalizing a first author manuscript for submission on these proof-of-principle experiments and a provisional patent has already been filed. For my work, I received two different pilot translational grants (Spectrum SPARK and Stanford Predictives and Diagnostics Accelerator [SPADA]) for which I am the lead Principal Investigator.

Additionally, I received an award from the Stanford Maternal and Children Health Research Institute to attend the Monsoon School of Translational Medicine International Program in Singapore.

a. **Goodyer WR,** Beyersdorf BM, Duan L, van den Berg NS, Mantri S, Galdos FX, Puluca N, Buikema JW, Lee S, Salmi D, Robinson ER, Rogalla S, Cogan DP, Khosla C, Rosenthal EL, Wu SM. In vivo visualization and molecular targeting of the cardiac conduction system. ***Journal of Clinical Investigation.*** 2022. PMCID: PMC9566899.
b. **PCT International Patent (PCT/US2020/040965):** Novel Molecular Tools to Visualize and Target the CCS**.** Inventors: **Goodyer WR**, Beyersdorf B, Van Den Berg N, Rosenthal E, and Wu SM.
c. **PCT International Patent (PCT/US2023/015747)**: Monoclonal Antibodies for Targeting the Cardiac Conduction System. **Goodyer WR** and Wu SM.

3. Elucidated the Coordinated Regulation of Postnatal Pancreatic β-Cell Development in Mice and Humans by Calcineurin/NFAT Signaling: Defects in pancreatic β-cell function and number underlie many human diseases, most notably diabetes mellitus. Emerging strategies to achieve replacement or regeneration of β-cells rely on knowledge about β-cell formation and growth; however, much remains unknown of the molecular mechanisms underlying their development and maturation. For my graduate studies, I worked in the Seung Kim laboratory, and honed my skills in Genetics and Molecular Biology, investigating the role of calcineurin/NFAT signaling in the development of pancreatic β-cells. Specifically, I demonstrated that the calcineurin/NFAT pathway coordinately regulates the *in vivo* maturation and proliferation of β-cells in mice and humans, findings germane to the pathogenesis and/or possible treatment of multiple pancreatic diseases. For these research efforts, I was granted an American Diabetes Association Clinical Scholars Fellowship as well as a French-American Foundation for Medical Research and Education Scholarship. My work led to a first-author publication in ***Developmental Cell*** and a co-first author book chapter on pancreas development. Finally, my work also led to a patent filing relating to the methods and compositions for modulating pancreatic β-cell proliferation and maturation.

a. **Goodyer WR**, Gu X, Liu Y, Bottino R, Crabtree GR, Kim SK. Neonatal β cell development in mice and humans is regulated by calcineurin/NFAT. ***Dev. Cell***. 2012. PMCID: PMC3587727.
b. *Benitez CM, ****Goodyer WR**, Kim SK. Deconstructing pancreas developmental biology. ***Cold Spring Harb Perspect Biol***. 2012. PMCID: PMC3367550. ****Co-first authors**
c. **Patent (Application #: US20140030234A1):** Methods and compositions for modulating islet β-cell development. Inventors: **Goodyer, WR**; Crabtree, GR, Wang, P and Kim, SK.

4. Uncovered a Key Molecular Regulator in the Pairing and Recombination of Chromosomes During Meiosis: All sexually reproducing organisms rely on meiosis, a specialized type of cell division that results in the creation of haploid gametes with which sexual reproduction may occur. Disruptions to the meiotic process can result in inappropriate segregation of chromosomes leading to developmental disabilities such as Trisomy 21. My research career began as an undergraduate in the Monique Zetka laboratory, using *C. elegans* to investigate the mechanisms underlying meiosis, resulting in an Honors Thesis. I uncovered a novel protein essential for several key steps in meiosis and, in doing so, I discovered a new biologic mechanism for coupling meiotic double strand break formation with homolog pairing, disruption of which leads to chromosome mis-segregation. For this work, I was awarded two sequential Natural Sciences and Engineering Council of Canada (NSERC) National Undergraduate Summer Research Scholarships as well as a Canadian National Graduate Scholarship. My work culminated in multiple national and international conference oral presentations as well as another first author article in ***Developmental Cell*** and a second author review article.

a. **Goodyer W**, Kaitna S, Couteau F, Ward JD, Boulton SJ, Zetka M. HTP-3 links DSB formation with homolog pairing and crossing over during *C. elegans* meiosis. ***Dev. Cell***. 2008. PMID: 18267094.
b. Couteau F, **Goodyer W**, Zetka M. Finding and keeping your partner during meiosis. ***Cell Cycle***. 2004. PMID: 15280669.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1DelhzcrH155p/bibliography/50929194/public/?sort=date&direction=ascending.