Nicole A. J. Krentz, PhD

Education

Ph.D. Cell and Developmental Biology
University of British Columbia

B.Sc. Cell Biology and Genetics (Co-operative Education)

2018
2019

University of British Columbia

Research Experience & Accomplishments

Assistant Professor 2023 – present

University of British Columbia, Faculty of Pharmaceutical Sciences

Postdoctoral Fellow 2020 – 2023

Stanford University, Department of Pediatrics – Endocrinology Supervisor: Dr. Anna L Glovn

- Discovered that RREB1 is required for cell fate determination of mesenchymal progenitor cells to adipocytes and osteoblast cells.
- Identified that RREB1 controls beta cell function and whole-body glucose homeostasis by transcriptionally regulating the development and function of pancreatic beta cells (<u>Mattis*</u>, <u>Krentz*</u>, et al. 2022).
- Included COVID-19 related research disruptions: laboratory shutdown from March July 2020; reduced density and shift-work from July 2020 June 2021.

Postdoctoral Fellow 2018 – 2020

University of Oxford, Wellcome Centre for Human Genetics Supervisor: Dr. Anna L Gloyn

- Demonstrated how coding variants in PAX4 influence diabetes risk by altering endocrine cell
 development and impacts the formation of alpha and beta cells (Lau*, Krentz*, et al. 2022).
- Identified that coding variants in *SLC30A8* undergo nonsense-mediated decay and result in haploinsufficiency (Dwivedi*, Lehtovirta*, Hastoy*, et al. 2019).

Graduate Student 2011 – 2018

University of British Columbia, BC Children's Research Hospital Institute Supervisor: Dr. Francis C Lynn

Thesis Title: Cell cycle regulates mouse and human pancreas development.

- Discovered a mechanistic link between G1 lengthening and endocrine cell formation through cyclin-dependent kinase phosphorylation of NEUROG3 (Krentz*, van Hoof*, et al. 2017).
- Established scRNA-seq in the lab and characterized single cell transcriptomes of developing mouse and human stem cell-derived endocrine progenitor cells (Krentz, et al. 2018).
- Generated knock-in reporter human embryonic stem cell lines using TALENs and CRISPR-Cas9 genome editing (Krentz, et al. 2014).

Research Assistant (co-op student and directed studies)

2010 - 2011

University of British Columbia, BC Children's Research Hospital Institute

Supervisor: Dr. Francis C Lynn

• Became competent in human embryonic stem cell culture and differentiation to pancreatic lineages.

Research Assistant (co-op student) 2009

University of British Columbia, BC Cancer Research Centre

Supervisor: Dr. Pamela A Hoodless

• Characterized how retinoic acid signalling regulates *Nepn* gene expression during embryonic midgut patterning (<u>Hou, et al. 2014</u>).

Fellowships & Studentships

Stanford Maternal & Child Health Research Institute Postdoctoral Fellowship	2021 – 2023
(\$120,000 USD)	
Natural Sciences and Engineering Research Council (NSERC) Postgraduate	2015 – 2017
Scholarship (\$42,000 CAD)	
Four Year Doctoral Fellowship University of British Columbia (\$72,000 CAD)	2014 – 2018
Sue Carruther's Graduate Studentship BC Children's Hospital Research Institute	2014 – 2016
(\$40,000 CAD)	
Canadian Institutes of Health Research (CIHR) funded Transplant Training	2011 – 2013
Research Program (\$22,000 CAD)	
BC Children's Hospital Research Institute Summer Studentship (\$2,500 CAD)	2010
University of British Columbia Faculty of Medicine Summer Studentship (\$3,000	2009
CAD)	

Honours and Awards

Robert Turner Research Associate, Green Templeton College, University of Oxford	2019
Travel Award for Till and McCulloch Meeting (funded by Stem Cell Network)	2017
Travel Award for 52 nd Annual European Association for the Study of Diabetes	2016
(EASD) meeting (funded by EASD)	
Bursary for RNA-sequencing Workshop (funded by Stem Cell Network)	2016
Travel Award for Till and McCulloch Meeting (funded by Stem Cell Network)	2015
Travel Award for Till and McCulloch Meeting (funded by Stem Cell Network)	2014
Travel Award for 50 th Annual EASD meeting (funded by EASD)	2014

Best Presentation Awards

Oral Presentation Award, Postdoc level: 13 th Annual Pediatrics Research Retreat	2022
Oral Presentation Award, Postdoc level: Stanford Diabetes Research Center	2020
(SDRC) Frontiers in Diabetes	
Oral Presentation Award, PhD level: Alberta-BC Islet Workshop	2017
Poster Presentation Award, PhD level: BC Regenerative Medicine Research Day	2017
Poster Presentation Award, PhD level: Vancouver Diabetes Research Day	2016
Oral Presentation Award, PhD level: Alberta-BC Islet Workshop	2015
Poster Presentation Award, PhD level: 21st Annual Chung Research Day	2015
Poster Presentation Award, PhD level: 20th Annual Chung Research Day	2014
Poster Presentation Award, PhD level: 15 th Annual Transplantation Research Day	2011

First-Author Original Research Publications

- 1. KK Mattis*, **NAJ Krentz***, C Metzendorf, F Abaitua, AF Spigelman, H Sun, JM Ike, S Thaman, AK Rottner, A Bautista, E Mazzaferro, M Perez-Alcantara, JE Manning Fox, JM Torres, A Weslowska-Andersen, GZ Yu, A Mahajan, A Larsson, PE MacDonald, B Davies, M den Hoed, AL Gloyn (2023). Loss of RREB1 in pancreatic beta cells reduces cellular insulin content and affects endocrine cell gene expression. *Diabetologia*. 66(4):674*-694. *Co-First Authors.
- 2. HH Lau*, **NAJ Krentz***, F Abaitua, M Perez-Alcantara, JW Chan, J Ajeian, S Ghosh, B Champon, H Sun, A Jha, S Hoon, NS Tan, D Gardner, SL Kao, ES Tai, AL Gloyn[#], AKK Teo[#] (2022). PAX4 loss of function alters human endocrine cell development and influences diabetes risk. *bioRxiv*. Version 1 posted: May 15, 2022. *Co-First Authors. *Co-Corresponding Authors.
 - Highlighted in: "May in preprints" by the Node
- 3. NAJ Krentz*, MYY Lee, EE Xu, SLJ Sproul, A Maslova, S Sasaki, FC Lynn* (2018). Single-cell transcriptome profiling of mouse and hESC-derived pancreatic progenitors. *Stem Cell Reports*. 11(6):1551-1564. *Co-Corresponding Authors. Citations: 68. Impact Factor: 5.5
- 4. NAJ Krentz*, D Van Hoof*, Z Li, A Watanabe, M Tang, C Nian, MS German*, FC Lynn* (2017). Phosphorylation of NEUROG3 Links Endocrine Differentiation to the Cell Cycle in Pancreatic Progenitors. *Developmental Cell*. 41(2):129-142. *Co-First Authors. *Co-Corresponding Authors. Citations: 68. Impact Factor: 7.1
 - Highlighted in: O Cleaver (2017). Beta Cell Renewal versus Differentiation: Slow and Steady. Wins the Race. *Developmental Cell*. 41(3):223-225 (Preview).
- <u>5.</u> **NAJ Krentz**, C Nian, FC Lynn (2014). TALEN/CRISPR-mediated eGFP knock-in at the OCT4 locus does not impact differentiation of human embryonic stem cells towards endoderm. *PLoS ONE*. 9(12):e114275. Citations: 31. Impact Factor 3.7

Co-Author Original Research Publications

- 1. TA Alghamdi, **NAJ Krentz**, N Smith, AF Spigelman, V Rajesh, A Jha, M Ferdaoussi, K Suzuki, J Yang, JE Manning Fox, H Sun, Z Sun, AL Gloyn[#], PE MacDonald[#] (2022). Zmiz1 is required for beta-cell maturation and mass expansion upon high fat feeding. *Molecular Metabolism*. 66;101621. *Co-Corresponding Authors.
- 2. CMJ Chu*, H Modi*, C Ellis, **NAJ Krentz,** S Skovsø, YB Zhao, H Cen, N Noursadeghi, E Panzhinskiy, X Hu, DA Dionne, YH Xia, S Xuan, MO Huising, TJ Kieffer, FC Lynn, JD Johnson (2021). Dynamic *Ins2* gene activity defines beta-cell maturity states. *Diabetes*. db211065. *Co-First Authors.
- 3. OP Dwivedi*, M Lehtovirta*, B Hastoy*, V Chandra, **NAJ Krentz**, S Kleiner, D Jain, A Richard, F Abaitua, NL Beer, A Grotz, RB Prasad, O Hansson, E Ahlqvist, U Krus, I Artner, A Suoranta, D Gomez, A Baras, B Champon, AJ Payne, D Moralli, SK Thomsen, P Kramer, I Spiliotis, R Ramracheya, P Chabosseau, A Theodoulou, R Cheung, M van de Bunt, J Flannick, M Trombetta, E Bonora, CB Wolheim, L Sarelin, RC Bonadonna, P Rorsman, B Davies, J Brosnan, MI McCarthy, T Otonkoski, JO Lagerstedt, GA Rutter, J Gromada, AL Gloyn*, T Tuomi*, L Groop* (2019). Loss of ZnT8 function protects against diabetes by enhanced insulin secretion. *Nature Genetics*. 51(11):1596-1606. *Co-First Authors. *Co-Corresponding Authors. Citations: 59. Impact Factor: 27.6
- <u>4.</u> SA Campbell, CL McDonald, **NAJ Krentz**, FC Lynn, BG Hoffman (2019). TrxG Complex Catalytic and Non-catalytic Activity Play Distinct Roles in Pancreas Progenitor Specification and Differentiation. *Cell Reports*. 28:1830-1844. Citations: 7. Impact Factor: 8.1

- <u>5.</u> EE Xu, **NAJ Krentz**, S Tan, S Chow, M Tang, C Nian, FC Lynn (2015). SOX4 cooperates with neurogenin 3 to regulate endocrine pancreas formation in mouse models. *Diabetologia*. 58(5):1013-23. Citations: 23. Impact Factor: 6.2
- <u>6.</u> J Hou, W Wei, RS Saund, P Xiang, TJ Cunningham, Y Yi, O Alder, DYD Lu, JGA Savory, **NAJ Krentz**, R Montpetit, R Cullum, N Hofs, D Lohnes, RK Humphries, Y Yamanaka, G Duester, Y Saijoh, PA Hoodless (2014). A regulatory network controls Nephrocan expression and midgut patterning. *Development*. 141(19):3772-81. Citations: 4. Impact Factor: 3.7
- 7. PV Sabatini, **NAJ Krentz**, B Zarrouki, CY Westwell-Roper, C Nian, RA Uy, AMJ Shapiro, V Poitout, FC Lynn (2013). Npas4 is a novel activity-regulated cytoprotective factor in pancreatic β-cells. *Diabetes*. 62(8): 2808-20. Citations: 34. Impact Factor: 8.8

Reviews

- 1. **NAJ Krentz**, LD Shea, MO Huising, JAM Shaw (2021). Restoring normal islet mass and function in type 1 diabetes through regenerative medicine and tissue engineering. *Lancet Diabetes & Endocrinology*. 9(10):708-724. Citations: 5. Impact Factor: 32.1
- **2. NAJ Krentz** (2021). Improvements in stem cell to beta-cell differentiation for the treatment of diabetes. *Journal of Immunology and Regenerative Medicine*. 12:100043.
 - Invited sole author review for Article collection "Restoring pancreatic beta-cell function in type 1 diabetes – the twin challenges of regenerative medicine and host immunity"
- 3. NAJ Krentz*, AL Gloyn* (2020). Insights into pancreatic islet cell dysfunction from type 2 diabetes mellitus genetics. *Nature Reviews Endocrinology*. 16(4):202-212. *Co-Corresponding Authors. Citations: 61. Impact Factor 43.4
 - Named a 'Highly Cited Paper' by Web of Science (top 1% of papers of a similar age)

Book Chapters

1. **NAJ Krentz**, FC Lynn (2016). Using CRISPR-Cas9 genome editing to enhance cell-based therapies for the treatment of diabetes mellitus. Kurstad Turksen (ed). *Genome Editing*. Springer. Chapter 8, p 127-147.

Invited Talks

External Meetings:

- Cell Fate Decisions in Diabetes Risk. *University of British Columbia, Faculty of Pharmaceutical Sciences (job talk)*. November 2022, Vancouver, BC.
- Exploring pleiotropic effects of T2D-risk alleles in *RREB1* using *in vitro* and *in vivo* models. *Australasian Diabetes Congress 2022.* August 2022, Virtual.
- Investigating the role of type 2 diabetes-associated genes in pancreatic islet cell dysfunction. San Jose State University Biology 201. September 2020, Virtual.
- Using pluripotent stem cells to study the genetics of diabetes. *Bay Area Islet Biology Meeting*. July 2020, Virtual.
- Identifying mechanisms for T2D GWAS variants in iPSCs. *EASD Islet Study Group and Beta-Cell Workshop*. March 2019, Oxford, UK.

Internal Meetings:

• Insights into metabolic tissue development & function from human genetics. Stanford *Maternal Child Health Research Institute Seminar Series*. June 2022, Virtual.

- Exploring pleiotropic effects of T2D-risk alleles in *RREB1* using *in vitro* and *in vivo* models. 6th Annual Frontiers in Diabetes Research Symposium. April 2022, Stanford, CA.
- The Translational Genomics of Diabetes group: who are we and what do we do? *Stanford Diabetes Research Group Seminar Series*. June 2020, Virtual.
- Identifying mechanisms for T2D GWAS variants in hiPSCs. *Wellcome Centre for Human Genetics Seminar Series*. October 2018, Oxford, UK.
- Using CRISPR-Cas9 to study pancreas development and diabetes. *Genome Editing Workshop*. July 2018, Oxford, UK.
- Loss of ZnT8 function protects against diabetes by enhanced insulin secretion. *Wellcome Centre for Human Genetics Diabetes Disease Day*. October 2018, Oxford, UK.
- Using CRISPR to enhance cell based therapies for the treatment of diabetes. *BC Cancer Research Centre CRISPR Mini Symposium*. November 2016, Vancouver, BC.

International Consortia:

- An introduction to cellular models deployed in the Translational Genomics of Diabetes lab. *AMP-CMD Model Systems Seminar Series*. October 2021, Virtual.
- Genetics and diabetes. Canadian Islet Research and Training Network. October 2020, Virtual.
- Insights into type 2 diabetes from integrating human genetics and genome editing in hiPSCs. FUSION-Oxford-Broad T2D Genetics Summit. July 2018, Boston, MA.

Panels:

• Stem Cell-Derived Islet Replacement: Promise and Challenges. 6th Annual Frontiers in Diabetes Research Symposium. April 2022, Stanford, CA.

Public Engagement:

- Using CRISPR to study diabetes. Pint of Science UK. May 2019, Oxford, UK.
- Using CRISPR to study diabetes. *St. Anne's College, University of Oxford, Biomedical Applications of CRISPR*. February 2019, Oxford, UK.
- From birth to death: improving the life of a beta cell for diabetes treatment. Canadian Diabetes Innovations: From the lab to the patient. November 2015, Vancouver, BC.

Select Oral & Poster Presentations (First-Author Only)

- NAJ Krentz*, HH Lau*, F Abaitua, M Perez-Alcantara, JW Chan, J Ajeian, B Champon, H Sun, A Jha, S Hoon, NS Tan, D Gardner, SL Kao, ES Tai, AL Gloyn*, AKK Teo* (2022). PAX4 loss of function alters human endocrine cell development and influences diabetes risk. 82nd Scientific Sessions American Diabetes Association, New Orleans, LA. (Poster). *Co-First Authors. *Co-Corresponding Authors.
- 2. **NAJ Krentz**, GZ Yu, J Li, V Rajesh, KK Mattis, RD Cox, JW Knowles, JY Wu, AL Gloyn (2022). Type 2 diabetes-risk alleles in the transcription factor *RREB1* alter bone and fat development. 13th Annual Pediatrics Research Retreat, Stanford, CA. (**Oral; Award Recipient**).
- 3. **NAJ Krentz**, M Perez-Alcantara, F Abaitua, J Ajeian, V Rajesh, A Jha, H Sun, B Champon, CE Duff, D Moralli, B Davies, AL Gloyn (2021). Type 2 diabetes-associated gene *PAX4* is required for human endocrine cell development. *Western Regional Islet Study Group Meeting*, Stevenson, WA. (Oral).
- 4. **NAJ Krentz**, V Rajesh, GZ Yu, J Li, KK Mattis, JW Knowles, JY Wu, RD Cox, AL Gloyn (2021). Ras Responsive Element Binding Protein 1 (RREB1) influences cell fate from mesenchymal stem cells. 4th Annual Stanford Maternal & Child Health Research Institute Symposium, online. (Poster).

- 5. **NAJ Krentz**, M Perez-Alcantara, F Abaitua, J Ajeian, A Jha, H Sun, B Champon, CE Duff, D Moralli, B Davies, AL Gloyn (202). Investigating the role of the type 2 diabetes-associated gene *PAX4* in human endocrine cell development. *Stanford Diabetes Research Center Frontiers of Diabetes Meeting*, online. (**Oral; Award Recipient**).
- 6. **NAJ Krentz**, F Abaitua, KK Mattis, M Perez-Alcantara, CE Duff, B Davies, A Weslowska-Andersen, MI McCarthy, A Mahajan, AL Gloyn (202). Using human induced pluripotent stem cell differentiation to model tissue-specific mechanisms of type 2 diabetes. *11th Annual Pediatrics Research Retreat*, online. (Poster).
- 7. **NAJ Krentz**, EE Xu, FC Lynn (2018). Single Cell Transcriptome Profiling of the Mouse and Human Endocrine Pancreas Lineages. *Keystone Frontiers in Islet Biology and Diabetes*, Keystone, CO. (Oral).
- 8. **NAJ Krentz***, D van Hoof*, Z Li, A Watanabe, M Tang, C Nian, MS German*, FC Lynn* (2017). Phosphorylation of NEUROG3 Links Endocrine Differentiation to the Cell Cycle in Pancreatic Progenitors. *BC Regenerative Medicine Research Day*, Vancouver, BC. *Co-First Authors. #Co-Corresponding Authors. (**Poster; Award Recipient**).
- NAJ Krentz, M Tang, A Watanabe, FC Lynn (2017). Increasing pancreatic progenitor cell cycle length drives endocrine differentiation in vivo, Alberta-BC Islet Meeting, Silverstar, BC. (Oral; Award Recipient).
- 10. **NAJ Krentz**, A Watanabe, M Tang, FC Lynn (2015). Pancreatic progenitor cell G1 lengthening is required for endocrine cell differentiation. *Vancouver Diabetes Research Day*, Vancouver, BC. (**Poster; Award Recipient**). 21st Annual W.B. & M.H. Chung Research Day, Vancouver, BC. (**Poster; Award Recipient**). Alberta-BC Islet Meeting, Silverstar, BC. (**Oral; Award Recipient**).
- 11. **NAJ Krentz**, M Tang, A Watanabe, FC Lynn (2014). Increasing G1 length during pancreatic progenitor cell differentiation. 20th Annual W.B. & M.H. Chung Research Day, Vancouver, BC. (**Poster; Award Recipient**).
- 12. **NAJ Krentz**, A Watanabe, M Tang, FC Lynn (2014). G1 lengthening promotes pancreatic progenitor cell differentiation in mouse embryonic development. *50th EASD Annual Meeting*, Vienna, Austria. (Oral).
- 13. **NAJ Krentz**, FC Lynn (2014). TALEN Mediated Knock-in of eGFP into OCT4 Locus of Human Embryonic Stem Cells Does Not Affect Differentiation Potential: A Promising Strategy For Generating Cell Specific Reporter Lines. *12th Annual International Society for Stem Cell Research*, Vancouver, BC. (Poster).
- 14. **NAJ Krentz**, FC Lynn (2011). Lengthening G1 during stem cell differentiation improves endocrine cell formation. *15th Annual Transplantation Research Day*, Vancouver, BC. (**Poster; Award Recipient**).

Leadership & Service

We Ask Because We Care Steering Committee, Stanford, CA	2022
Science fair judge, STEAM Fair La Entrada School, Menlo Park, CA	2020
Volunteer, Pint of Science, UK	2019
Volunteer, In2ScienceUK, University of Oxford	2018
Organizing committee, 5 th Annual Transplant Trot, Vancouver, BC	2015 – 2016

Organizing committee, Vancouver Diabetes Research Day, Vancouver, BC Organizing committee, Stem Cell Talks, Vancouver, BC Organizing committee, Research Education Outreach, BCCHRI, Vancouver, BC	2014 - 2017 2014 - 2015 2013 - 2014
Membership in Professional Organizations	
Member, American Diabetes Association Member, Green Templeton College, University of Oxford	2021 – 2022 2018 – 2022
Member, European Association for the Study of Diabetes	2014 – 2016
Member, Stem Cell Network	2011 – 2017

Professional Development

- 1. Attendee: 4th DZD Diabetes Research School. Freising, Germany, September 2016.
- 2. Attendee: Stem Cell Network RNA-sequencing Workshop. Ottawa, ON, March 2016.
- 3. Attendee: UBC Multi-colour Flow Cytometry Course. Vancouver, BC, September 2011.

Peer Review

Reviewer for Circulation: Genomic and Precisions Medicine, JCI Insight, Molecular Metabolism, Journal of Immunology and Regenerative Medicine, BMC Biology, Diabetologia, Endocrine Reviews, Islets, PLoS One, Scientific Reports.

Abstract reviewer for American Diabetes Association and Islet Study Group Meetings (2023).

Abstract reviewer for 2nd Annual Vancouver Diabetes Research Day (2015).