BIOGRAPHICAL SKETCH

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NAME: Oakes, Christopher, C

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

POSITION TITLE Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Calgary, Calgary, Alberta, Canada	BSc.	04/1996	General Science
McGill University, Montreal, Quebec, Canada	BSc.	06/2000	Physiology
McGill University, Montreal, Quebec, Canada	MSc.	09/2001	Pharmacology
McGill University, Montreal, Quebec, Canada	Ph.D.	12/2007	Pharmacology
German Cancer Research Center, Heidelberg, Germany	Postdoctoral Fellowship	04/2015	Epigenomics and Cancer Risk Factors

A. Personal Statement

My research interests stem from a central tenet that epigenetic processes are essential to the regulation and the maintenance of cellular identity and function in health and disease. I began my scientific career investigating the role of epigenetics in the development of mammalian germ cells, stem cells and early embryonic lineages, and became fascinated by the extent and importance of epigenetic mechanisms in regulating germ line development. Through this experience, I learned the fundamentals of working within dynamic developmental systems while uncovering several novel aspects of germ line biology. Subsequently I applied this detailed knowledge to the investigation of the role of epigenetics in the development of cancer. With a focus on chronic lymphocytic leukemia (CLL) together with other tumor types, my research combined functional molecular approaches and profiling of leukemic patient samples, and integrated findings with developmental processes in founding normal cell populations. I have revealed that the pathogenesis of CLL stems from an imbalance of programming processes that otherwise occur normally. The success of this work lies with linking malignant cell states to the spectrum of normal development and maturation that is vital to properly interpret and identify disease-specific events. Further integration of epigenetic alterations with somatic mutations has revealed the role of genetic alterations in malignant reprogramming. These concepts derived from several years of dedicated research now underlies the basis of my new laboratory dedicated to exploring experimental epigenetics and hematology.

My laboratory is equipped with the capability of performing genome-wide and/or targeted evaluation of DNA methylation and other epigenetic modifications. I plan to build on our success in identifying and developing epigenetic biomarkers, some of which are in current clinical use, and plan to further develop my highly innovative productive research program and laboratory dedicated to the advancement of patient care through progressive understanding of the fundamental biology of leukemic and normal cells.

B. Positions and Honors

Positions and Employment

2015-present Tenure-track Assistant Professor, Division of Hematology, The Ohio State University, Columbus, OH

Honors and Awards:

1995 Heritage Fund Scholarship, Province of Alberta
1996 Dean's List for Academic Achievement, University of Calgary
2000 Graduate with Distinction, McGill University
2002 Maria Raiche Studentship Award, Montreal Children's Hospital
2003 Doctoral Research Award, Fonds de Recherche en Sante du Quebec (declined)
2003-2006 Doctoral Research Award, Canadian Institutes of Health Research
2006 McGill University Health Center Research Institute Studentship Award, (declined)

2006 Montreal Children's Hospital Research Institute Studentship Award
2008 Post-doctoral Fellowship Award, Canadian Institute of Health Research
2008 Post-Doctoral Fellowship Award, The Leukemia and Lymphoma Society (declined)
2014 Lymphoma Research Foundation-AACR Scholar-in-Training Award, AACRHematologic Malignancies: Translating Discoveries to Novel Therapies Conference.
2016 Young Investigator Award, Leukemia Research Foundation
2017 Medical Research Award, Gabrielle's Angel Foundation for Cancer Research

Other Experience and Professional Memberships

Memberships:
2015-present American Association of Cancer Research (AACR)
2015-present American Society of Hematology (ASH)

C. Contribution to Science

1. My current research focuses on investigating the role of epigenetics in B cell malignancy, with a primary focus on understanding the evolution and impact of epigenetic programming on the cancer cell phenotype. Epigenetic alterations are pervasive in cancer and continually develop during disease progression, however the mechanisms that promote changes to the tumor epigenome are undefined. My work in CLL was the first to uncover the coevolution of genetic (somatic) aberrations and highlights a prominent role of genetic aberrations in the selection of novel methylation patterns in cancer. These results establish that genetic alterations have a powerful impact on the coevolution and selection of novel epigenetic patterns and have been followed by other studies, confirming that this finding is likely to be a consistent and broad feature of cancer. Further work published in *Nature Genetics* dissects the origins of epigenetic programming in CLL by situating CLL epigenomic states within the range of programming that occurs during normal B cell maturation. This work uncovers that CLL development is linked to an imbalance of transcription factor programming activity and demonstrates the impact of epigenetics on the malignant phenotype. Furthermore the degree of epigenetic programming achieved by the tumor cell-of-origin shows a universal and robust impact on clinical outcomes in the disease.
    a. **Oakes CC**, Seifert M, Assenov Y, Gu L, Przekopowitz M, Ruppert AS, Serva A, Koser S, Brocks D, Lipka D, Bogatyrova O, Mertens D, Zapatka M, Lichter P, Döhner H, Küppers R, Zenz T, Stilgenbauer S, Byrd JC and Plass C. DNA methylation dynamics during B cell maturation underlie a continuum of disease phenotypes in chronic lymphocytic leukemia. Nat Genet. 2016 Mar;48(3):253-64. PMCID: PMC4963005.
    b. **Oakes CC**, Claus R, Gu L, Assenov Y, Hüllein J, Zucknick M, Bieg M, Brocks D, Bogatyrova O, Schmidt CR, Rassenti L, Kipps TJ, Mertens D, Lichter P, Döhner H, Stilgenbauer S, Byrd JC, Zenz T, Plass C. Evolution of DNA methylation is linked to genetic aberrations in chronic lymphocytic leukemia. Cancer Discovery. 2014 Mar;4(3):348-61 PMCID: PMC4134522
    c. Giacopelli B, Zhao Q, Ruppert AS, Agyeman A, Weigel C, Wu YZ, Gerber MM, Rabe KG, Larson MC, Lu J, Blachly JS, Rogers KA, Wierda WG, Brown JR, Rai KR, Keating M, Rassenti LZ, Kipps TJ, Zenz T, Shanafelt TD, Kay NE, Abruzzo LV, Coombes KR, Woyach JA, Byrd JC, **Oakes CC**. Developmental subtypes assessed by DNA methylation-iPLEX forecast the natural history of chronic lymphocytic leukemia. Blood. 2019 Aug 22;134(8):688-698. PMCID: PMC6706807.

2. In parallel to my work in hematological cancer, I have investigated epigenetic mechanisms in controlling gene expression programs in other normal cell lineages and tumors types. Recent work explores how epigenetic therapies reprogram the epigenome on a genome-wide scale, revealing fundamental aspects of resistance and sensitivity to specific epigenetic drugs. This work promises to help guide how to predict and assess responses use these therapies and how best to combine with other treatment modalities, including immunotherapy. I have also examined how epigenetic mechanisms control key genes in the development and licensing of NK cells, specifically focusing on how duplicated genes with nearly identical genetic sequences establish differential functional epigenetic states and regulation. Furthermore, my work in prostate cancer mirrors my efforts in B cell malignancies to unravel how aberrant epigenetic signatures are established. Here we have uncovered that an epigenetic regulator, termed BAZ2A, is involved in epigenetic remodeling and promotion of prostate cancer cell growth. We show that BAZ2A interacts with other key epigenetic regulators to maintain aberrant epigenetic silencing of tumor-suppressor genes frequently repressed in metastasis.

a. Brocks D, Schmidt CR, Daskalakis M, Li D, Li J, Jang HS, Zhang B, Lipka DB, Schott J, Bierhoff H, Assenov Y, Helf M, Ressnerova A, Lindroth A, Haas S, Essers M, Imbusch CD, Brors B, Oehme I, Witt O, Lübbert M, Stoecklin G, Gerhäuser C, Wang T, **Oakes CC***, Plass C*. DNMT and HDAC inhibitors induce cryptic transcription start sites encoded in long terminal repeats.. Nat Genet. 2017 Jul;49(7):1052-1060. PMCID: PMC6005702. (*equal contribution)
b. Victor AR, Weigel C, Scoville SD, Chan WK, Chatman K, Nemer MM, Mao C, Young KA, Zhang J, Yu J, Freud AG, **Oakes CC***, Caligiuri MA*. Epigenetic and Posttranscriptional Regulation of CD16 Expression during Human NK Cell Development. J Immunol. 2018 Jan 15;200(2):565-572 PMCID: PMC5881939. (*equal contribution)
c. Gu L*, Frommel SC*, **Oakes CC***, Simon R, Grupp K, Gerig KY, Bär D, Robinson MD, Baer C, Weiss M, Gu Z, Kuner R, Sültmann H, Provenzano M, Yaspo M-L, Brors B, Korbel J, Schlomm T, Sauter G, Eils R, Plass C and Santoro R. BAZ2A (TIP5) is involved in epigenetic alterations in prostate cancer and its overexpression predicts disease recurrence. Nat Genet. 2015 Jan;47(1):22-30. (*equal contribution)
d. Roos-Weil D, Giacopelli B, Armand M, Della-Valle V, Ghamlouch H, Decaudin C, Metzner M, Lu J, Le Garff-Tavernier M, Leblond V, Vyas P, Zenz T, Nguyen-Khac F, Bernard O, **Oakes CC**. Identification of two DNA methylation subtypes of Waldenström's macroglobulinemia with plasma and memory B cell features. Blood. 2020 Jul 30;136(5):585-595.

3. My early work addressed the role of epigenetics in the field of germ cell biology and embryology. At the time of this work, a role for DNA methylation was known in controlling the function of a limited set of genes, however a genome-wide view of DNA methylation in the germ line and early embryonic development was lacking. As I was the first to employ a genome-wide approach to explore DNA methylation configurations in germ stem cells, I pioneered several discoveries surrounding highly dynamic and unique programming throughout the process of germ and embryonic stem cell development, as well as in early embryonic and placental tissues. I revealed that the integrity of these patterns is compromised during aging and that treatment with epigenetic therapies impacts on germ cell quality and embryogenesis, which was used, in part, to issue a warning for use of these therapeutics in people of reproductive age. I served as the lead author of the following studies:

   a. **Oakes CC**, Smiraglia DJ, Plass C, Trasler JM, Robaire B. Aging results in hypermethylation of ribosomal DNA in sperm and liver of male rats. Proc Natl Acad Sci U S A. 2003 Feb 18;100(4):1775-80. PMCID: PMC149909
   b. **Oakes CC**, La Salle S, Smiraglia DJ, Robaire B, Trasler JM. A Unique Configuration of Genome-Wide DNA Methylation Patterns in the Testis. Proc Natl Acad Sci U S A. 2007 Jan 2;104(1):228-33. PMCID: PMC1765440
   c. **Oakes CC**, Kelly TL, Robaire B, Trasler JM. Adverse effects of 5-aza-2'-deoxycytidine on spermatogenesis include reduced sperm function and selective inhibition of de novo DNA methylation. J Pharmacol Exp Ther. 2007 Sep;322(3):1171-80.
   d. McGraw S*, **Oakes CC***, Martel J, Cirio MC, de Zeeuw P, Mak W, Plass C, Bartolomei MS, Chaillet JR, Trasler JM. Loss of DNMT1o disrupts imprinted X chromosome inactivation and accentuates placental defects in females. PLoS Genetics. 2013 Nov;9(11) PMCID: PMC3836718 (*equal contribution)

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1vS5Bg0RhCg5B/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Pelotonia Idea Award — Oakes/Mundy-Bosse/Freud (MPI) — 07/01/2019 – 06/30/2021
James Comprehensive Cancer Center, OSU
"Discovery and therapeutic targeting of the epigenetic developmental blockade in extranodal natural killer/T cell lymphoma"

Pelotonia Idea Award — Oakes/Blachly/Baiocchi (MPI) — 07/01/2019 – 06/30/2021
James Comprehensive Cancer Center, OSU

"Rapid assessment of the origin and significance of Epstein-Barr virus in patients using DNA methylation and nanopore sequencing"

HCLF Research Grant Oakes (PI) 07/01/2020 – 06/30/2021
"Identification of novel molecular subtypes of the hairy cell leukemia variant using epigenetics"

New Laboratory Start-up Oakes (PI) 03/23/2015 – 03/22/2022
The Ohio State University Comprehensive Cancer Center

Completed Research Support

Medical Research Award Oakes (PI) 03/01/2017 – 02/28/2020
Gabrielle's Angel Foundation for Cancer Research
The Role of EGR in establishing a malignant epigenetic program of therapy resistance in CLL

Industry-Sponsored Research Grant Oakes (PI) 04/2018 - 09/2019
"DNA methylation epityping of the Epstein-Barr Virus genome as a novel biomarker for patient stratification in virus-associated lymphomas."

Division-Sponsored Research Grant Oakes/Blachly (MPI) 06/01/2018 – 05/30/2019
Division of Hematology, OSU
"Discerning the origin of EBV in patients using DNA methylation"

Young Investigator Award Oakes (PI) 07/01/2016 – 06/30/2017
Leukemia Research Foundation
The Role of Early Growth Response (EGR) in Establishing a Malignant Epigenetic Program in CLL.

SFMR/HCLF Research Grant Oakes (PI) 12/01/2016 – 11/30/2017
The Sass Foundation for Medical Research and the Hairy Cell Leukemia Foundation.
Using epigenetics for novel classification and discovery of pathogenic mechanisms and therapeutic targets in HCL.