BIOGRAPHICAL SKETCH

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NAME: Pattenden, Samantha

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

POSITION TITLE: Director of Applied Epigenetic Screening Technologies, Associate 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)	END DATE MM/YYYY	FIELD OF STUDY
University of Toronto, Toronto, Ontario	Hon. BSc.	06/1997	Microbiology
University of Toronto, Toronto, Ontario	Ph.D.	06/2003	Molecular Biology
Stowers Institute for Medical Research, Kansas City, MO	Postdoctoral	05/2010	Chromatin Biology
University of North Carolina at Chapel Hill, Chapel Hill, NC	Postdoctoral	08/2015	Chromatin Biology

A. Personal Statement

The Pattenden lab is focused on the development of innovative techniques in chromatin-based therapeutic target discovery and cancer diagnostics. As Director of Applied Epigenetic Screening Technologies at the Center for Integrative Chemical Biology and Drug Discovery, my goal is to enable collaborators to apply chemical biology to the discovery of novel molecular targets, pathways and mechanisms. Our central strategy exploits tumor-specific changes in chromatin accessibility, a universal feature that is directly linked with transcriptional activation, DNA damage repair, replication, RNA processing, and nuclear organization. Since chromatin accessibility offers a comprehensive overview of the rewiring of transcriptional networks that accompanies processes such as cellular differentiation, tumor growth, metastasis, and therapeutic resistance, it is frequently more reliable in predicting cell behavior than gene expression profiles alone. This strategy has played a critical role in advancing several collaborative projects. We developed a chemical biology screening platform for Ewing sarcoma with Dr. Ian Davis (UNC, Genetics), based on chromatin accessibility to gain both mechanistic and therapeutic insight into tumor growth and development. This screening technique represents a promising new paradigm in oncology drug discovery since it is broadly applicable to other cancers and will potentially expand the repertoire of druggable chromatin-focused targets. Along with Dr. Paul Dayton (UNC, Biomedical Engineering), we patented and published a new method for fragmentation of DNA using a patented cavitation enhancement reagent, and founded Triangle Biotechnology, Inc., a company focused on the development of new sonication technologies. We have expanded the application of our technology to include extraction of chromatin from fixed cells and archived tissues to study changes in chromatin architecture.

1. Chiarella AM*, Quimby AL*, Mehrab-Mohseni M, Velasco B, Kasoji SK, Davis IJ, Dayton PA, Hathaway NA, Pattenden SG. Cavitation Enhancement Increases the Efficiency and Consistency of Chromatin Fragmentation from Fixed Cells for Downstream Quantitative Applications. Biochemistry. 2018 May 15;57(19):2756-2761. PubMed PMID: 29658277; PubMed Central PMCID: PMC5962036. *These authors contributed equally to this work.
2. Pattenden SG*, Simon JM*, Wali A*, Jayakody CN, Troutman J, McFadden AW, Wooten J, Wood CC, Frye SV, Janzen WP, Davis IJ. High-throughput small molecule screen identifies inhibitors of aberrant chromatin accessibility. Proc Natl Acad Sci U S A. 2016 Mar 15;113(11):3018-23. PubMed PMID: 26929321; PubMed Central PMCID: PMC4801272. *These authors contributed equally to this work.
3. Simon JM, Parker JS, Liu F, Rothbart SB, Ait-Si-Ali S, Strahl BD, Jin J, Davis IJ, Mosley AL, Pattenden SG. A Role for Widely Interspaced Zinc Finger (WIZ) in Retention of the G9a Methyltransferase on Chromatin. J Biol Chem. 2015 Oct 23;290(43):26088-102. PubMed PMID: 26338712; PubMed Central PMCID: PMC4646261.
4. Kasoji SK*, Pattenden SG*, Malc EP, Jayakody CN, Tsuruta JK, Mieczkowski PA, Janzen WP, Dayton PA. Cavitation Enhancing Nanodroplets Mediate Efficient DNA Fragmentation in a Bench Top Ultrasonic Water

Bath. PLoS One. 2015;10(7):e0133014. PubMed PMID: 26186461; PubMed Central PMCID: PMC4505845. *These authors contributed equally to this work.

B. Positions and Honors

Positions and Employment

1997 - 2003	Ph.D. Student, University of Toronto, Toronto
2003 - 2010	Senior Research Associate, Stowers Institute for Medical Research, Kansas City, MO
2010 - 2015	Postdoctoral Research Associate, University of North Carolina at Chapel Hill, Chapel Hill, NC
2015 - 2019	Assistant Professor, Center for Integrative Chemical Biology and Drug Discovery, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC
2017 -	Co-Founder, Triangle Biotechnology, Inc., Chapel Hill, NC
2017 -	Director of Applied Epigenetic Screening Technologies, Center for Integrative Chemical Biology and Drug Discovery, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC
2017 -	Member, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC
2019 -	Associate Professor, Center for Integrative Chemical Biology and Drug Discovery, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC

Other Experience and Professional Memberships

2002 -	Member, American Association for the Advancement of Science
2015 -	Member, American Society for Biochemistry and Molecular Biology

Honors

1998 - 1999	University of Toronto Open Fellowship, University of Toronto
1999 - 2001	Frank Fletcher Memorial Fund, Ontario Student Opportunity Trust Fund Fellowship, University of Toronto
2000	Research Day Prize, Student Oral Competition, Dept. of Ophthalmology, University of Toronto
2000	Nadler Family Prize, Student Oral Competition, Toronto Western Hospital Research Institute
2000 - 2003	KM Hunter/MRC Doctoral Research Fellowship, Canadian Institutes for Health Research
2002 - 2003	Vision Science Research Program Fellowship, Ontario Student Opportunity Trust Fund, University of Toronto
2004	Professional Development Award, Stowers Institute for Medical Research
2004 - 2006	NSERC Postdoctoral Fellowship, Natural Sciences and Engineering Research Council of Canada
2009	Best Oral Presentation by a Postdoctoral Researcher, Stowers Institute for Medical Research
2016	IBM Junior Faculty Development Award, University of North Carolina at Chapel Hill

C. Contribution to Science

1. Interrogating the role of chromatin and transcription in disease. My initial publications looked at how the retinoblastoma protein and the SWI/SNF chromatin remodeling complex modulated immune response to cancer. My findings were significant because they were among the first to demonstrate a role for SWI/SNF in immune surveillance and provided novel insight into its function as a tumor suppressor. In addition to studies in higher eukaryotes, I used *Saccharomyces cerevisiae* to understand how disruptions in chromatin signaling pathways affect gene transcription. The yeast Set2-Rpd3S pathway is important for the control of transcription memory. Mutations of components of this pathway result in cryptic transcription initiation within the coding region of approximately 30% of yeast genes. My work confirmed that promoters for cryptic transcription initiation sites with gene coding regions are independently regulated, and that their activation is dependent on factors that govern gene activation at canonical promoters.

a. Pattenden SG, Klose R, Karaskov E, Bremner R. Interferon-gamma-induced chromatin remodeling at the CIITA locus is BRG1 dependent. EMBO J. 2002 Apr 15;21(8):1978-86. PubMed PMID: 11953317; PubMed Central PMCID: PMC125964.

b. Ni Z, Karaskov E, Yu T, Callaghan SM, Der S, Park DS, Xu Z, Pattenden SG, Bremner R. Apical role for BRG1 in cytokine-induced promoter assembly. Proc Natl Acad Sci U S A. 2005 Oct 11;102(41):14611-6. PubMed PMID: 16195385; PubMed Central PMCID: PMC1253546.

c. Li B, Gogol M, Carey M, Pattenden SG, Seidel C, Workman JL. Infrequently transcribed long genes depend on the Set2/Rpd3S pathway for accurate transcription. Genes Dev. 2007 Jun 1;21(11):1422-30. PubMed PMID: 17545470; PubMed Central PMCID: PMC1877753.

d. Pattenden SG, Gogol MM, Workman JL. Features of cryptic promoters and their varied reliance on bromodomain-containing factors. PLoS One. 2010 Sep 23;5(9):e12927. PubMed PMID: 20886085; PubMed Central PMCID: PMC2944879.

2. The use of chemical biology to gain mechanistic insight into epigenetic pathways. As a Director within the Center for Integrative Chemical Biology and Drug Discovery at UNC, I have access to a large chemical biology toolbox that my laboratory can utilize for interrogation of transcription and epigenetic signaling networks. For example, I combined genomic and pharmacological methods to compare localization of the lysine methyltransferase, G9a, on chromatin to its enzymatic activity. I provided evidence that G9a and its protein-interacting partners have unique functions when bound to chromatin that are independent of G9a catalytic activity.

a. Simon JM, Parker JS, Liu F, Rothbart SB, Ait-Si-Ali S, Strahl BD, Jin J, Davis IJ, Mosley AL, Pattenden SG. A Role for Widely Interspaced Zinc Finger (WIZ) in Retention of the G9a Methyltransferase on Chromatin. J Biol Chem. 2015 Oct 23;290(43):26088-102. PubMed PMID: 26338712; PubMed Central PMCID: PMC4646261.

b. Xu B, On DM, Ma A, Parton T, Konze KD, Pattenden SG, Allison DF, Cai L, Rockowitz S, Liu S, Liu Y, Li F, Vedadi M, Frye SV, Garcia BA, Zheng D, Jin J, Wang GG. Selective inhibition of EZH2 and EZH1 enzymatic activity by a small molecule suppresses MLL-rearranged leukemia. Blood. 2015 Jan 8;125(2):346-57. PubMed PMID: 25395428; PubMed Central PMCID: PMC4287641.

c. Konze KD*, Pattenden SG*, Liu F, Barsyte-Lovejoy D, Li F, Simon JM, Davis IJ, Vedadi M, Jin J. A chemical tool for in vitro and in vivo precipitation of lysine methyltransferase G9a. ChemMedChem. 2014 Mar;9(3):549-53. PubMed PMID: 24443078; PubMed Central PMCID: PMC4005005. *These authors contributed equally to this work.

d. Konze KD, Ma A, Li F, Barsyte-Lovejoy D, Parton T, Macnevin CJ, Liu F, Gao C, Huang XP, Kuznetsova E, Rougie M, Jiang A, Pattenden SG, Norris JL, James LI, Roth BL, Brown PJ, Frye SV, Arrowsmith CH, Hahn KM, Wang GG, Vedadi M, Jin J. An orally bioavailable chemical probe of the Lysine Methyltransferases EZH2 and EZH1. ACS Chem Biol. 2013;8(6):1324-34. PubMed PMID: 23614352; PubMed Central PMCID: PMC3773059.

3. Chromatin accessibility as a platform for cancer diagnostics and therapeutic discovery. Chromatin-associated proteins frequently occur as modular subunits of various protein complexes with non-overlapping activities within the cell. For this reason, hit compounds derived from typical *in vitro* screens based on a single domain of a chromatin-associated protein are likely to have limited efficacy or significant off-target effects when tested *in vivo*. Currently, however, there are very few *in vivo* chromatin-based assays that are suitable for high throughput screening campaigns. We and others have demonstrated that characteristic chromatin accessibility patterns in tumors can change following treatment with small molecule inhibitors. Consequently, chromatin accessibility could serve as a strategy to screen for chemical inhibitors, to assess pharmacodynamics, and to establish biomarkers for preclinical and clinical trials. In collaboration with Dr. Ian Davis, we have developed a novel high throughput screen for small molecule inhibitors of aberrant chromatin accessibility in cancer. This approach enables discovery of compounds that affect an underlying chromatin defect without *a priori* target selection, which avoids the pitfalls associated with *in vitro* chromatin-associated protein screens. To assess the diagnostic potential of chromatin accessibility patterns in tumor cells, my laboratory has invented a method for extraction of chromatin from formalin fixed, paraffin embedded (FFPE) tissue, which incorporates a patented cavitation enhancement reagent from Dr. Paul Dayton. We demonstrated the utility of this cavitation enhancement reagent for chromatin extraction from cells for

chromatin immunoprecipitation assays and fragmentation of genomic DNA for high throughput sequencing applications. Intellectual property around our technique for extraction of chromatin from FFPE tissue includes an issued patent and a provisional patent filing.

a. Pattenden SG, Streeter JE, Jayakody CN, Wood CC, Shenoy SK, Janzen WO, Dayton PA., inventors. Methods and systems for using encapsulated microbubbles to process biological samples. United States 9,982,290. 2018 May 28.
b. Chiarella AM*, Quimby AL*, Mehrab-Mohseni M, Velasco B, Kasoji SK, Davis IJ, Dayton PA, Hathaway NA, Pattenden SG. Cavitation Enhancement Increases the Efficiency and Consistency of Chromatin Fragmentation from Fixed Cells for Downstream Quantitative Applications. Biochemistry. 2018 May 15;57(19):2756-2761. PubMed PMID: 29658277; PubMed Central PMCID: PMC5962036. *These authors contributed equally to this work.
c. Pattenden SG*, Simon JM*, Wali A*, Jayakody CN, Troutman J, McFadden AW, Wooten J, Wood CC, Frye SV, Janzen WP, Davis IJ. High-throughput small molecule screen identifies inhibitors of aberrant chromatin accessibility. Proc Natl Acad Sci U S A. 2016 Mar 15;113(11):3018-23. PubMed PMID: 26929321; PubMed Central PMCID: PMC4801272. *These authors contributed equally to this work.
d. Kasoji SK*, Pattenden SG*, Malc EP, Jayakody CN, Tsuruta JK, Mieczkowski PA, Janzen WP, Dayton PA. Cavitation Enhancing Nanodroplets Mediate Efficient DNA Fragmentation in a Bench Top Ultrasonic Water Bath. PLoS One. 2015;10(7):e0133014. PubMed PMID: 26186461; PubMed Central PMCID: PMC4505845. *These authors contributed equally to this work.

D. Additional Information: Research Support

Ongoing Research Support

Not Assigned, UNC Chancellor's Creativity Hub Pattenden, Strahl (MPI) 07/01/19-06/30/21
The Chemical Epigenomics Creativity Hubs: integrating scientific fields to enable grand discoveries
Multidisciplinary, multi-PI project to leverage chemical biology techniques to interrogate epigenetic processes.
Role: Planning, oversight

NCI (R33CA206939) Pattenden, Davis, Dayton (PI) 07/01/17-06/30/20
The application of Enhanced Cavitation to enable DNA and Chromatin Extraction from Archived Tissues
Investigation into the use of nanodroplets as a cavitation enhancement tool to improve biospecimen processing and extraction of chromatin from FFPE tumor tissue. Role: project lead, planning, analysis, oversight

NCI (R43CA236177) Kasoji, Pattenden (MPI) 04/09/19-04/08/20
Technology for Overcoming Bottlenecks in Chromatin Extraction from Challenging Biological Samples
Investigation into the use of nanodroplets as a cavitation enhancement tool to improve biospecimen processing. Role: UNC subcontract lead, planning, analysis, oversight

RX03812113, Eshelman Institute for Innovation Pattenden, Davis (PI) 06/01/18-02/28/20
Development of a First-in-Class High Throughput Assay Based on Chromatin Accessibility
Development of a 384-well screening platform based on the ATAC method. Role: Planning, analysis, oversight

LCCC 1729, Syndax Pharmaceuticals, Lineberger Moschos (Pattenden co-I) 10/01/18-09/30/20
Breaking Innate PD-1 Inhibitor (PD1i) Resistance Using Epigenetic Modifiers; Antitumor Efficacy and Correlative Analyses of Entinostat plus Pembrolizumab in Non-Inflamed Metastatic Melanoma (MM)
Clinical trial to assess the utility of HDAC inhibitors in preventing PD-1 inhibitor resistance in metastatic melanoma treatment. Role: Analysis of chromatin accessibility changes in biopsy samples.

Completed Research Support

NCI (R43CA232902) Kasoji, Dayton (Pattenden co-I) 07/05/18-11/30/19
Towards commercialization of cavitation-enhancing nanodroplets for DNA sample fragmentation in NGS applications
Role: Provide support for testing of nanodroplets and use of sonication devices for DNA fragmentation.

2017-TEG-1505, North Carolina Biotechnology Pattenden, Kline (MPI) 07/01/17-12/31/18

Advancement of Cavitation-Enhancing Perfluorocarbon Nanodroplets for DNA Sample Fragmentation in NGS Applications
Technology enhancement grant to prepare nanodroplet technology for licensing. Role: Planning, analysis, oversight

2KR951706, NC TraCS Pattenden, Davis (PI) 10/01/17-09/30/18
I*nvestigation of a novel compound which can alter aberrant chromatin accessibility in Ewing sarcoma*
Characterization of the effects of a chemical probe on chromatin accessibility in Ewing sarcoma cells. Role: planning, analysis, oversight.

RX03712106, Eshelman Institute for Innovation Pattenden, Calabrese (PI) 06/01/17-05/31/18
Developing Small Molecule Probes to Inhibit the Regulatory Capacity of Long Noncoding RNAs
High throughput screen to identify compounds that inhibit the gene regulatory activity of long noncoding RNAs. Role: planning, analysis, oversight

2017-IDG-1005, North Carolina Biotechnology Pattenden (PI) 03/28/17-03/27/18
Advanced acoustic sonication for high throughput nucleic acid fragmentation, biospecimen processing, and drug discovery
Funds for purchase of a common multi-user piece of equipment, the Covaris LE220 Focused Ultrasonicator. Role: planning, oversight

550KR151619, NC TraCS $5-50K Pattenden, Davis, Dayton (PI) 01/01/17-12/31/17
The Application of Enhanced Cavitation to Enable Chromatin Extraction from Archived Tissues
Investigation into the use of cavitation enhancement to improve biospecimen processing. Role: planning, analysis, oversight

2KR861603, NC TraCS Calabrese, Pattenden (MPI) 01/01/17-12/31/17
Developing small molecule probes to inhibit the regulatory capacity of long noncoding RNAs
High throughput screen to identify compounds that inhibit the gene regulatory activity of long noncoding RNAs. Role: planning, analysis, oversight

A16-0277-001, Hyundai Hope on Wheels Davis (Pattenden, co-I) 10/01/15-09/30/17
Chromatin-based strategies to target Ewing Sarcoma
Understanding mechanism and novel treatment strategies for Ewing sarcoma and other similar diseases. Role: Assistance with chemoproteomics and chromatin accessibility screening.

UNC Lineberger Innovation/UCRF Davis, Pattenden, Johnson, Frye (MPI) 09/01/16-08/31/17
Chromatin Architecture as a Platform for Drug Development.
Changes in chromatin organization in tumors as a platform for therapeutic discovery and cancer diagnostics.

R21CA173124, NCI/NIH Pattenden, Dayton (MPI) 09/12/12-08/31/16
Cavitation Enhancement of Biospecimen Processing for Improved DNA Fragmentation
Investigation into the use of microbubbles as a cavitation enhancement tool to improve biospecimen processing and DNA fragmentation. Role: planning, analysis, oversight.