

## B. Franklin Pugh, Ph.D.

### Contact

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### Education

Cornell University, Ithaca NY	B.S.	1983	Biology
University of Wisconsin-Madison	Ph.D.	1987	Molecular Biology

### Professional Employment

1987-1988 Postdoctoral Research Associate.  
*Michael Cox, Dept. of Biochemistry, University of Wisconsin-Madison.*

1988-1991 Postdoctoral Research Associate.  
*Robert Tjian, Dept. of Molecular & Cellular Biology, University of California-Berkeley.*

1992-1998 Assistant Professor of Biochemistry & Molecular Biology.  
*The Pennsylvania State University.*

1998-2005 Associate Professor of Biochemistry & Molecular Biology.  
*The Pennsylvania State University.*

2005- present Professor of Biochemistry & Molecular Biology.  
*The Pennsylvania State University.*

### Secondary Titles

2008-2017 Editor, *Molecular and Cellular Biology*

2004-present Director – Center for Eukaryotic Gene Regulation (11 faculty)

2007-present Willaman Professor of Molecular Biology (Endowed)

2014-present Evan Pugh University Professor (Highest academic honor at PSU)

2014-present Fellow AAAS

### Awards and Service

1988-91 Leukemia Society of America Postdoctoral Fellow

1992-95 Searle Scholar

1996-01 Leukemia & Lymphoma Society Scholar

1996 Daniel Tershak Faculty Teaching Award

1999-03 Member, American Cancer Society Peer Review Committee on Genetic Mechanisms

2001-03 Member, Peer Review Panel – Florida Department of Health

2002-present Member (ad hoc), NIH CDF-2, CDF-1, SEP, GCAT, MGB Study Sections

2001-05 Senator, Penn State Faculty Senate

2004-06 Chair - Penn State University Genomics Futures Committee

2006 Penn State University Faculty Scholars Medal

2006-2007 Chair – Eberly College of Science Committee – Dept Head search

2010 Designed the Center for Eukaryotic Gene Regulation, Penn State University

## **Research Highlights** (Historical)

- 1987 Deciphered biochemical mechanisms of homologous recombination (*graduate student*)
- 1991 Discovered transcriptional co-activators (*postdoc*)
- 1992 Identified subunits of TFIIB as TBP and TAFs (*assistant professor*)
- 1996 Discovered autoregulation of TFIID through dimerization (*assistant professor*)
- 2004 Identified genome regulation as TATA/SAGA/stress and TATA-less/TFIID/housekeeping (*assoc. professor*)
- 2007 Developed first ChIP-seq assay (*associate professor*)
- 2008 First high-resolution genome-wide map of Drosophila nucleosome organization (*professor*)
- 2011 Mapped binding locations of >200 transcription factors across the yeast genome (*professor*)
- 2011 First genome-wide biochemical reconstitution of chromosome nucleosome organization (*professor*)
- 2011 Invented the ChIP-exo assay (*professor*)
- 2012 Defined genomic structure of transcription machinery and chromatin remodelers at single bp resolution.
- 2014 Identified alternative nucleosome structures and asymmetry in composition on a genomic scale.
- 2015 Define nucleosome-specific chromatin remodeler organization on a genomic scale in mouse ES cells
- 2016 Reconstituted nucleosome organization on a genomic scale with purified histones and remodelers.

## **Research Goals**

Our goal is to understand how all nuclear proteins work together to regulate genomes, and apply this knowledge towards better diagnosis and management of human diseases. We use the well-known budding yeast as both a technological and conceptual model. To date, we have defined the positional organization along the genome of nearly all mappable nuclear proteins (>400) at near single-bp resolution using the ChIP-exo assay that we developed. This provides an understanding of the structural organization of protein complexes along the genome *in vivo*. Assembly dynamics are next monitored through rapid reprogramming of the genome (e.g., 5 min. of acute heat shock). Function is then assessed through CRISPR/Cas9-engineered depletion of factors, and through biochemical reconstitution of protein/DNA complexes on a genomic scale. Parallel strategies are being conducted in model human cell lines and clinical samples. We intend to identify the mappable protein/DNA interactions that correlate best with disease states and their treatment outcomes so as to develop improved medical diagnostics.

## **Commercial activity**

- 2012** Founded Peconic, LLC – a service-based epigenome mapping company.
- 2013** Rhee, H. S. and Pugh, B. F., Methods, Systems and Kits for Detecting Protein-Nucleic Acid Interactions. U.S. Patent No. 8,367,334 to Penn State. Commercially licensed.
- 2018** Rossi, M. J. and Pugh, B. F., Improved DNA Library Construction of Immobilized Chromatin immunoprecipitated DNA. U.S. Provisional Patent Application No. 62/636,229 to Penn State.

## **Publications** *since 2014*

- 89. Chang, G.S., Chen, X.A., Park, B., Rhee, H.S., Li, P., Han, K.H., Mishra, T., Chan-Salis, K.Y., Li, Y., Hardison, R.C., Wang Y., Pugh B.F. (2014) A comprehensive and high-resolution genome-wide response of p53 to stress. *Cell Rep.* 8, 514-27. PMID: 25043190
- 90. Rhee, H-S., Bataille, A. R., Zhang, L., and Pugh, B.F. (2014) Subnucleosomal Structures and Nucleosome Asymmetry Across a Genome. *Cell* 159, 1377-1388. PMID: 25480300
- 91. Wang S., Chen X.A., Hu J., Jiang J.K., Li Y., Chen-Salis K.Y., Gu Y., Chen G., Thomas C., Pugh B.F., Wang Y. (2015) ATF4 Gene Network Mediates Cellular Response to the Anticancer PAD Inhibitor YW3-56 in Triple Negative Breast Cancer Cells. *Mol Cancer Ther.* 14, 877-888. PMID: 25612620
- 92. Mahony S, Pugh BF (2015) Protein-DNA binding in high-resolution. *Crit Rev Biochem Mol Biol.* 3:1-15. PMID: 26038153

93. Han G.C., Vinayachandran V., Bataille A.R., Park B., Chan-Salis K.Y., Keller C.A., Long M., Mahony S., Hardison R.C., Pugh B.F. (2015) Genome-Wide Organization of GATA1 and TAL1 Determined at High Resolution. *Mol Cell Biol.* 36, 157-172. PMID: 26503782
94. Reja, R., Vinayachandran, V., Ghosh, S. & Pugh, B. F. (2015) Molecular mechanisms of ribosomal protein gene coregulation. *Genes & Devel.* 29, 1942-1954. PMID: 26385964
95. Schneider M., Hellerschmied D., Schubert T., Amlacher S., Vinayachandran V., Reja R., Pugh B.F., Clausen T., Köhler A. (2015) The Nuclear Pore-Associated TREX-2 Complex Employs Mediator to Regulate Gene Expression. *Cell* 162, 1016-1028. PMID: 26317468
96. de Dieuleveult M., Yen K.\*, Hmitou I., Depaux A., Boussouar F., Bou Dargham D., Jounier S., Humbertclaude H., Ribierre F., Baulard C., Farrell N.P., Park B., Keime C., Carrière L., Berlivet S., Gut M., Gut I., Werner M., Deleuze J.F., Olaso R., Aude J.C., Chantalat S., Pugh B.F.\*, Gérard M.\* (2016) Genome-wide nucleosome specificity and function of chromatin remodellers in ES cells. *Nature* 530, 113-116. PMID: 26814966 \*co-corresponding author.
97. Baranello L., Wojtowicz D., Cui K., Devaiah BN., Chung HJ., Chan-Salis KY., Guha R., Wilson K., Zhang X., Zhang H., Piotrowski J., Thomas C.J., Singer D.S., Pugh B.F., Pommier Y., Przytycka T.M., Kouzine F., Lewis B.A., Zhao K., Levens D. (2016). RNA Polymerase II Regulates Topoisomerase 1 Activity to Favor Efficient Transcription. *Cell* 165, 357–371. PMID: 27058666
98. Iwafuchi-Doi M., Donahue G., Kakumanu A., Watts J.A., Mahony S., Pugh B.F., Lee D., Kaestner K.H., Zaret K.S. (2016). The Pioneer Transcription Factor FoxA Maintains an Accessible Nucleosome Configuration at Enhancers for Tissue-Specific Gene Activation. *Mol Cell.* 62, 79-91. PMID: 27058788
99. Aguilar-Gurrieri, C., Larabi, A., Vinayachandran, V., Patel, N. A., Yen, K., Reja, R., Ebong, I. O., Schoehn, G., Robinson, C. V., Pugh, B. F. & Panne, D. (2016) Structural evidence for Nap1-dependent H2A-H2B deposition and nucleosome assembly. *EMBO J.* 35, 1465-1482. PMID: 27225933.
100. Krietenstein, N., Wal, M., Watanabe, S., Park, B., Peterson, C.L., Pugh\*, B.F., and Korber\*, P. (2016). Genomic nucleosome organization reconstituted with pure proteins. *Cell* 167, 709-721. PMID: 27768892 \*co-corresponding author.
101. Jeronimo, C., Langelier, M.F., Bataille, A.R., Pascal, J.M., Pugh, B.F., and Robert, F. (2016). Tail and Kinase Modules Differently Regulate Core Mediator Recruitment and Function In Vivo. *Mol Cell* 64, 455-466. PMID: 27773677
102. Van Oss, S. B., Shirra, M. K., Bataille, A. R., Wier, A. D., Yen, K., Vinayachandran, V., Byeon, I. L., Cucinotatta, C. E., Heroux, A., Jeon, J., Kim, J., VanDenmark, A. P., Pugh, B. F. & Arndt, K. M. (2016) The histone modification domain of paf1 complex subunit rtf1 directly stimulates h2b ubiquitylation through an interaction with rad6. *Mol Cell* 64, 815-825 PMID: 27840029.
103. Lai, W. K. & Pugh, B. F. (2017). Genome-wide uniformity of human 'open' pre-initiation complexes. *Genome Res* 27, 15-26 PMID: 27927716.
104. Lai WKM, Pugh BF. (2017) Understanding nucleosome dynamics and their links to gene expression and DNA replication. *Nat Rev Mol Cell Biol.* 18, 548-562. PMID: 28537572
105. Rossi MJ, Lai WKM, Pugh BF. (2017) Correspondence: DNA shape is insufficient to explain binding. *Nat Commun.* 8, 15643. PMID: 28580956
106. Vinayachandran V, Reja R, Rossi MJ, Park B, Rieber L, Mittal C, Mahony S, Pugh BF. (2018) Widespread and precise reprogramming of yeast protein-genome interactions in response to heat shock. *Genome Res.* 28, 357-366. PMID: 29444801
107. Miller JE, Zhang L, Jiang H, Li Y, Pugh BF, Reese JC. (2018) Genome-Wide Mapping of Decay Factor-mRNA Interactions in Yeast Identifies Nutrient-Responsive Transcripts as Targets of the Deadenyase Ccr4. *G3 (Bethesda)*. 8, 315-330. PMID: 29158339.

108. Rossi MJ, Lai WKM, Pugh BF. (2018) Genome-wide determinants of sequence-specific DNA binding of general regulatory factors. *Genome Res.* 28, 497-508. PMID: 29563167
109. García-Molinero V, García-Martínez J, Reja R, Furió-Tarí P, Antúnez O, Vinayachandran V, Conesa A, Pugh BF, Pérez-Ortín JE, Rodríguez-Navarro S. (2018) The SAGA/TREX-2 subunit Sus1 binds widely to transcribed genes and affects mRNA turnover globally. *Epigenetics Chromatin* 11, 13. PMID: 29598828
110. Rossi MJ, Lai WKM, Pugh BF. (2018) Simplified ChIP-exo assays. *Nat Commun.* 9:2842-54. PMID: 30030442
111. Yamada N, Lai WKM, Farrell N, Pugh BF, Mahony (2018) Characterizing protein-DNA binding event subtypes in ChIP-exo data. *Bioinformatics* (in press) PMID: 30165373
112. Niu B, Coslo DM, Bataille AR, Albert I, Pugh BF, Omiecinski CJ. (2018) In vivo genome-wide binding interactions of mouse and human constitutive androstane receptors reveal novel gene targets. *Nucleic Acids Res.* 46, 8385-8403. PMID: 30102401

### Invited Lectures (accepted, since 2015)

- 2015  
 Tongji University, Shanghai, China  
 Southern Medical University, Guangzhou, China  
 Genomics Meeting, Lorne, Australia  
 Pennsylvania State University (*Huck Distinguished Lecture series*)  
 Vanderbilt University, Nashville, TN  
 ENCODE Workshop, Bethesda, MD  
 Indiana University, Indianapolis, IN  
 Keystone Meeting on DNA Methylation/Epigenomics, Keystone, CO  
 Genomic Symposium, Northwestern University, Chicago, IL (*Keynote Lecture*)  
 Cold Spring Harbor Meeting on Eukaryotic Transcription, CSHL, NY  
 Chromatin Structure Course, Wellcome Trust Genome Campus, Hinxton (*Keynote Lecture*)  
 Transcription Symposium, Strasbourg, France  
 Symposium on Chromatin in Development and Disease, Marburg, Germany  
 AACR Conference on Chromatin and Cancer, Atlanta, GA  
 Conference on noncoding RNA, Gainesville, FL  
 Virginia Tech, Blacksburg, VA
- 2016  
 Gordon Research Conference, Les Diablerets, Switzerland  
 EMBO Conference on Gene Transcription in Yeast, San Felieu, Spain  
 Netherlands Cancer Institute, Amsterdam, Netherlands  
 Jackson labs, Bar Harbor, ME  
 ASBMB meeting on Transcription, Snowbird, UT  
 Duquesne University, Pittsburgh, PA
- 2017  
 University of Rochester, Rochester, NY  
 National Institutes of Health, Bethesda, MD  
 University of Texas, San Antonio, TX  
 Cold Spring Harbor Meeting on Eukaryotic Transcription, CSHL, NY  
 Geisinger Medical Center, Danville, PA  
 Ludwig-Maximillian University, Munich, Germany
- 2018  
 Cornell University, Ithaca, NY  
 Conference on RNA polymerase II, Hong Kong  
 Academia Sinica, Tapei, Taiwan  
 University of Oregon, Eugene, OR  
 Washington State University, Pullman, WA  
 Thomas Jefferson University, Philadelphia, PA  
 National Institutes of Health, Bethesda, MD  
 EMBO Conference on Gene Transcription in Yeast, San Felieu, Spain  
 Weill/Cornell Medicine, New York, NY  
 Gordon Conference on Chromatin Structure, Newry, ME  
 University of Wisconsin, Madison, WI  
 ASBMB meeting on transcription regulation, Snowbird, UT  
 Oklahoma Medical Research Foundation, Oklahoma City, OK