# B. Franklin Pugh, Ph.D.

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### **Contact**

465 Biotechnology Bldg.

Department of Molecular Biology & Genetics

Cornell University Email: fp265@cornell.edu

Ithaca, NY 14853

## **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.
	Pennsylvania State University.
1998-2005	Associate Professor of Biochemistry & Molecular Biology.
	Pennsylvania State University.
2005- 2020	Professor of Biochemistry & Molecular Biology.
	Pennsylvania State University.
7/1/2020	Professor of Molecular Biology & Genetics.
	Cornell University.

# **Secondary Appointments**

2008-2017	Editor, Molecular and Cellular Biology
2004-2019	Director – Center for Eukaryotic Gene Regulation (11 faculty)
2007-2020	Willaman Professor of Molecular Biology (Endowed)
2014-2020	Evan Pugh University Professor (Highest academic honor at PSU)
2014-present	Fellow AAAS
2018-2020	Program Director – NIH T32 training grant in gene regulation
2020-present	Professor emeritus, Pennsylvania State University
2020-present	Greater Philadelphia Area Professorship
2020-present	Professor of Physiology and Biophysics, Cornell-Weill College of Medicine, NY, NY

### **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
Ad hoc	Member, NIH CDF-2, CDF-1, SEP, GCAT, MGB and Florida DoH 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

# **Thesis Research**

19 BS - Honors2 MS22 PhD18 Postdoc

# **Regular Classroom Teaching** (Enrollment - Limit/**Actual**/Dept. averages for student ratings)

1992-2000	BMMB 514 – Molecular Biology and Cellular Regulation (>40 - 7.0/6.2/5.3)
2003-2007, 18	BMB 251 – Molecular and Cellular Biology I (>200 – 7.0/ <b>5.2</b> /5.3)
2003-2008	BMB 252 – Molecular and Cellular Biology II (>100 – 7.0/5.8/4.7)
2011-2014	BMB 252H – Molecular and Cellular Biology II honors (11 – 7.0/ <b>5.0</b> /4.7)
2015-2017	BMB 547 – Advanced Topics in Gene Regulation
2016-2019	BMB 488 – Communities of Practice
2022-	BIOMG 3350 – Principles of Biochemistry

# <u>Historical Funding</u> (as PI, total = \$23M)

Years	Total	Agency	Project
1989-1991	\$71,000	Leuk. Lymph Soc.	Eukaryotic Transcription Initiation
1992-1996	\$158,000	Searle Found.	Searle Scholars Program
1994-1996	\$559,555	Natl. Inst. Health	Biochemistry of Eukaryotic Transcription Regulation
1998-2001	\$305,000	Am. Cancer Soc.	Cloning and Characterization of TBP-Associated Factors
1996-2001	\$225,075	Leuk. Lymph Soc.	Dimerization of TBP: Biochemical and Biological Consequences
1994-2013	\$1,485,205	Other	Various projects
1999-2001	\$208,000	Natl. Sci. Found.	Structure, Function, and Regulation of TATA Binding Protein Dimers
2005-2007	\$499,526	Natl. Sci. Found.	Computational Modeling of Genome-wide Transcriptional Regulation
2007-2020	\$4,899,053	Natl. Inst. Health	Promoter Regulation in Response to Environmental Stress
2000-2021	\$6,974,874	Natl. Inst. Health	Regulation of TBP Dimers
2007-2023	\$5,370,975	Natl. Inst. Health	High Resolution Mapping of Functional Elements in the Yeast Genome
2018-2021	\$1,344,086	Natl. Inst. Health	Genome-wide Structural Organization in Human Regulatory Complexes
2018-2022	\$970,345	Natl. Inst. Health	Eukaryotic Gene Regulation (EGR) Predoctoral Training Program
2022-2027	\$5,700,000	Natl. Inst. Health	MIRA and Epigenomic responses to environmental stress

## **Research Highlights** (Historical)

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

2021 Defined a nearly complete epigenomic architecture of yeast at single bp resolution.

### **Research Goals**

Our goal is to understand how all nuclear proteins work together to regulate genomes and to 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 yeast genome of nearly all mappable nuclear proteins (~500) 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. 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.

### **Publications**

- 1. Rojanaridpiched, C., Gracen, V. E., Everett, H. L., Coors, J. G., Pugh, B.F., and Boutyette, P. (1984). Multiple factor resistance in maize to European corn borer. *Maydica* 29, 305-315.
- 2. Cox, M. M., Pugh, B.F., Schutte, B. C., Lindsley, J. E., Lee, J. W., and Morrical, S. W. (1987). On the mechanism of recA protein-promoted DNA branch migration. *In DNA Replication and Recombination*, T. Kelly and R. McMacken, eds. (New York: Alan R. Liss, Inc.), pp. 597-607.
- 3. Pugh, B.F., and Cox, M. M. (1987). Stable binding of recA protein to duplex DNA. Unraveling a paradox. *J. Biol. Chem.* 262, 1326-36.
- 4. Pugh, B.F., and Cox, M. M. (1987). recA protein binding to the heteroduplex product of DNA strand exchange. *J. Biol. Chem.* 262, 1337-43.
- 5. Pugh, B.F., and Cox, M. M. (1987). Salt can functionally mimic DNA in activating the RecA protein ATPase. *In Protein structure, folding, and design*: Alan R. Liss, Inc.), pp. 275-82.
- 6. Pugh, B.F., and Cox, M. M. (1988). General mechanism for RecA protein binding to duplex DNA. *J. Mol. Biol.* 203, 479-93.
- 7. Pugh, B.F., and Cox, M. M. **(1988)**. High salt activation of recA protein ATPase in the absence of DNA. *J. Biol. Chem.* 263, 76-83.
- 8. Pugh, B.F., Schutte, B. C., and Cox, M. M. (1989). Extent of duplex DNA underwinding induced by RecA protein binding in the presence of ATP. *J. Mol. Biol.* 205, 487-92.
- 9. Hoey, T., Dynlacht, B. D., Peterson, M. G., Pugh, B.F., and Tjian, R. **(1990)**. Isolation and characterization of the Drosophila gene encoding the TATA box binding protein, TFIID. *Cell 61*, 1179-86.
- 10. Peterson, M. G., Tanese, N., Pugh, B.F., and Tjian, R. **(1990)**. Functional domains and upstream activation properties of cloned human TATA binding protein. *Science* 248, 1625-30.
- 11. Pugh, B.F., and Tjian, R. **(1990)**. Mechanism of transcriptional activation by Sp1: evidence for coactivators. *Cell 61*, 1187-97.
- 12. Pugh, B.F., and Tjian, R. **(1991)**. Transcription from a TATA-less promoter requires a multisubunit TFIID complex. *Genes Dev. 5*, 1935-45.
- 13. Pugh, B.F., and Tjian, R. (1991). Regulation of transcription in animal cells:

factors and mechanisms. *In Nuclear Processes and Oncogenes*, P. Sharp, ed. (New York: Academic Press, Inc.), pp. 201-210.

- 14. Tanese, N., Pugh, B.F., and Tjian, R. (1991). Coactivators for a proline-rich activator purified from the multisubunit human TFIID complex. *Genes Dev.* 5, 2212-24.
- 15. Pugh, B.F., and Tjian, R. **(1992)**. Diverse transcriptional functions of the multisubunit eukaryotic TFIID complex. *J. Biol. Chem. 267*, 679-82.
- 16. Taggart, A. K., Fisher, T. S., and Pugh, B.F. (1992). The TATA-binding protein and associated factors are components of pol III transcription factor TFIIIB. *Cell* 71, 1015-28.
- 17. Coleman, R. A., and Pugh, B.F. (1995). Evidence for functional binding and stable sliding of the TATA binding protein on nonspecific DNA. *J. Biol. Chem.* 270, 13850-9.
- 18. Coleman, R. A., Taggart, A. K., Benjamin, L. R., and Pugh, B.F. (1995). Dimerization of the TATA binding protein. *J. Biol. Chem.* 270, 13842-9.
- 19. Jackson, A. J., Ittmann, M., and Pugh, B.F. (1995). The BN51 protein is a polymerase (Pol)-specific subunit of RNA Pol III which reveals a link between Pol III transcription and pre-rRNA processing. *Mol. Cell. Biol.* 15, 94-101.
- 20. Pugh, B.F. (1995). Purification of the human TATA-binding protein, TBP. *In In Vitro Transcription and Translation Protocols*, M. J. Tymms, ed. (Totowa, N.J.: Humana Press, Inc.), pp. 359-67.
- 21. Pugh, B.F. (**1995**). Preparation of HeLa nuclear extracts. *In In Vitro Transcription and Translation Protocols*, M. J. Tymms, ed. (Totowa, N.J.: Humana Press, Inc.), pp. 349-358.
- 22. Pugh, B.F. (1996). Mechanisms of transcription complex assembly. Curr. Opin. Cell Biol. 8, 303-311.
- 23. Taggart, A. K., and Pugh, B.F. (1996). Dimerization of TFIID when not bound to DNA. Science 272, 1331-3.
- 24. Booth Jr., B. L., and Pugh, B.F. (1997). Identification and characterization of a nuclease specific for the 3' end of the U6 snRNA. *J. Biol. Chem.* 272, 984-991.
- 25. Coleman, R. A., and Pugh, B.F. (1997). Slow dimer dissociation of the TATA binding protein dictates the kinetics of DNA binding. *Proc. Natl. Acad. Sci. USA* 94, 7221-6.
- 26. Pugh, B.F. (1997). Dynamics of transcription complex assembly. *In Transcription Factors in Eukaryotes*, A. G. Papavassiliou, ed. (Austin, TX: R. G. Landes Co.).
- 27. Weideman, C. A., Netter, R. C., Benjamin, L. R., McAllister, J. J., Schmiedekamp, L. A., Coleman, R. A., and Pugh, B.F. (1997). Dynamic interplay of TFIIA, TBP and TATA DNA. *J Mol Biol* 271, 61-75.
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- 29. Jackson-Fisher, A. J., Chitikila, C., Mitra, M., and Pugh, B.F. (1999). A role for TBP dimerization in preventing unregulated gene expression. *Mol. Cell* 3, 717-727.
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- 31. Coleman, R. A., Taggart, A. K. P., Burma, S., Chicca II, J. J., and Pugh, B.F. (1999). TFIIA regulates TBP and TFIID dimers. *Mol. Cell* 4, 451-457.
- 32. Pugh, B.F. **(2000)**. Control of gene expression through regulation of the TATA binding protein. *Gene* 255, 1-14.
- 33. Pugh, B.F. (**2001**). The RNA polymerase II transcription machinery. *In Transcription Factors*, J. Locker, ed. (Oxford: BIOS Scientific Publishers), pp. 1-16

34. Pugh, B.F. and D. Gilmour (**2001**) Genome-wide analysis of protein-DNA interactions in living cells. *Genome Biol.* 2, 1013.1-1013.3.

- 35. Chitikila, C., K. L. Huisinga, J. D. Irvin, M. Mitra, and B. F. Pugh (**2002**) Interplay of TBP inhibitors in global transcriptional control. *Mol. Cell* 10, 871-882.
- 36. Kou, H., Irvin, J. D., Huisinga, K. L., and Pugh, B.F. (**2003**). Structural and functional analysis of mutations along the crystallographic dimer interface of the yeast TATA binding protein. *Mol. Cell. Biol.* 23, 3186-3201.
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- 38. Basehoar, A. D., Zanton, S. J., and Pugh, B.F. (2004). Identification and distinct regulation of yeast TATA boxcontaining genes. *Cell* 116, 699-709.
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- 41. Zanton, S. J., and Pugh, B.F. (**2004**). Changes in genome-wide occupancy of core transcriptional regulators during heat stress. *Proc. Natl Acad. Sci. 101*, 16843-16848.
- 42. Alexander, D. E., Kaczorowski, D., Lowry, D. M., Jackson-Fisher, A. J., Zanton, S. J. and Pugh, B.F. (**2004**). The Brf1 subunit of RNA polymerase III transcription factor TFIIIB induces TBP dimers to dissociate. *J. Biol. Chem. 279*, 32401-32406.
- 43. Irvin, J. D., and Pugh, B.F. (2006). Genome-wide transcriptional dependence on TAF1 functional domains. *J. Biol. Chem.* 281, 6404-6412.
- 44. Durant, M., and Pugh, B.F. (**2006**). Genome-wide relationships between TAF1 and histone acetyltransferases in Saccharomyces cerevisiae. *Mol. Cell. Biol*. 26, 2791-2802.
- 45. Zanton, S. J., and Pugh, B.F. (**2006**). Full and partial genome-wide assembly and disassembly of the yeast transcription machinery in response to heat shock. *Genes Devel*. 20, 2250-2265. PMID: 16912275
- 46. Ioshikhes, I., Albert, I., Zanton, S. J., and Pugh, B.F. (2006). Nucleosome positions predicted through comparative genomics. *Nature Genetics*. 38, 1210-1215. PMID: 16964265
- 47. Pugh, B.F. (2006). HATs off to PIC assembly. *Mol Cell* 23, 776-777.
- 48. Albert, I., Mavrich, T. N., Tomsho, L. P, Qi, J., Zanton, S. J., Schuster, S. C., and Pugh, B.F. (**2007**) Translational and rotational settings of H2A.Z nucleosomes across the S. cerevisiae genome. *Nature* 446, 572-576. PMID: 17392789
- 49. Huisinga, K.L. and Pugh, B.F. (**2007**) A TATA Binding Protein regulatory network that governs transcription complex assembly. *Genome Biol* 8(4): R46. PMID: 17407552
- 50. Durant, M. and Pugh, B.F. (**2007**) NuA4-directed chromatin transactions throughout the *S. cerevisiae* genome. *Mol. Cell. Biol*. 15, 5327-35.
- 51. Venters, B. J., and Pugh, B.F. (2007). Chromatin meets RNA polymerase II. *Genome Biol* 8, 319.
- 52. Lee, C., Li, X., Hechmer, A., Eisen, M., Biggin, M.D., Venters, B.J., Jiang, C., Li, J., Pugh, B.F., and Gilmour, D.S. (2008). NELF and GAGA factor are linked to promoter proximal pausing at many genes in Drosophila. *Mol. Cell. Biol.* 28, 3290-3300. PMID: 18332113
- 53. Albert, I., Wachi, S., Jiang, C., and Pugh, B.F. (2008). GeneTrack a genomic data processing and visualization framework. *Bioinformatics*. 24, 1305-1306. PMID: 18388141

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- 58. Venters, B., and Pugh, B.F. (**2009**). A canonical promoter organization of the transcription machinery and its regulators in the Saccharomyces genome. *Genome Res.* 19, 360-371. PMID: 19124666
- 59. Jiang, C., and Pugh, B.F. (**2009**). Nucleosome positioning and gene regulation: advances through genomics. *Nature Rev. Genet. 10*, 161-172. PMID: 19204718
- 60. Venters, B., and Pugh, B.F. (2009). How eukaryotic genes are transcribed. *Crit. Rev. Bioch. Mol. Biol.* 44, 117-141. PMID: 19514890
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- 62. Jiang, C., and Pugh, B.F. (**2009**). A compiled and systematic reference map of nucleosome positions across the Saccharomyces genome. *Genome Biol.* 10, R109. PMID: 19814794
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- 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

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- 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 K., 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
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- 103. Lai, W. K. & Pugh, B. F. (**2017**). Genome-wide uniformity of human 'open' pre-initiation complexes. **Genome Res** 27, 15-26 PMID: 27927716.
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- 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
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- 110. Rossi MJ, Lai WKM, Pugh BF. (2018) Simplified ChIP-exo assays. Nat Commun. 9:2842-54. PMID: 30030442
- 111. 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
- 112. Yamada N, Lai WKM, Farrell N, Pugh BF, Mahony S (**2019**) Characterizing protein-DNA binding event subtypes in ChIP-exo data. *Bioinformatics* 35, 903-913. PMID: 30165373
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- 114. Yamada N, Kuntala PK, Pugh BF, Mahony S (2020) ChExMix: A Method for Identifying and Classifying Protein-DNA Interaction Subtypes. *Comput Biol*. 27, 429-435. PMID: 32023130
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- 116. Yamada N, Rossi MJ, Farrell N, Pugh BF, Mahony S. (**2020**) Alignment and quantification of ChIP-exo crosslinking patterns reveal the spatial organization of protein-DNA complexes. *Nucleic Acids Res.* 48, 11215-11226. PMC7672471
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- 119. Badjatia, N., Rossi, M.J., Bataille, A.R., Mittal, C., Lai, W.K.M., and Pugh, B.F. (**2021**). Acute stress drives global repression through two independent RNA polymerase II stalling events in Saccharomyces. *Cell Rep* 34, 108640.
- 120. Rossi, M.J., Kuntala, P.K., Lai, W.K.M., Yamada, N., Badjatia, N., Mittal, C., Kuzu, G., Bocklund, K., Farrell, N., Blanda, T.R., Mairose, J.D., Basting, A.V., Mistretta, K.S., Rocco, D.J., Perkinson, E.S., Kellogg, G.D., Mahony, S., and Pugh, B.F. (2021). A high-resolution protein architecture of the budding yeast genome. *Nature*, 592, 309-314.
- 121. Lai, W.K.M., Mariani, L., Rothschild, G., Smith, E.R., Venters, B.J., Blanda, T.R., Kuntala, P.K., Bocklund, K., Mairose, J., Dweikat, S.N., Mistretta, K., Rossi, M.J., James, D., Anderson, J.T., Phanor, S.K., Zhang, W., Shaw, A.P., Novitzky, K., McAnarney, E., Keogh, M.-C., Shilatifard, A., Basu, U., Bulyk, M.L., and Pugh, B.F. (2021). Screening of PCRP transcription factor antibodies in biochemical assays. *Genome Res*, 31, 1663-1679.

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122. Zhao, T., Vvedenskaya, I.O., Lai, W.K., Basu, S., Pugh, B.F., Nickels, B.E., and Kaplan, C.D. (2021). Ssl2/TFIIH function in transcription start site scanning by RNA polymerase II in Saccharomyces cerevisiae. *Elife* 10:e71013

- 123. Sun Q., Nematbakhsh, A., Kuntala, P.K., Kellogg, G., Pugh, B.F., Lai, W.K.M (**2022**) STENCIL: A web templating engine for visualizing and sharing life science datasets. *PLoS Comput Biol* 18: e1009859.
- 124. John J, Jabbar J, Badjatia N, Rossi MJ, Lai WKM, Pugh BF. (2022). Genome-wide promoter assembly in E. coli measured at single-base resolution. *Genome Res.* 2022;32(5):878-92.
- 125. Shao D, Kellogg GD, Nematbakhsh A, Kuntala PK, Mahony S, Pugh BF, Lai WKM. (2022). PEGR: a flexible management platform for reproducible epigenomic and genomic research. *Genome Biol.* 2022;23(1):99.
- 126. Mittal C, Lang O, Lai WKM, Pugh BF. (2022). An integrated SAGA and TFIID PIC assembly pathway selective for poised and induced promoters. *Genes Dev* 36: 985-1001.

#### Significance of selected publications -

- 11. Pugh, B.F., and Tjian, R. (1990). Mechanism of transcriptional activation by Sp1: evidence for coactivators. Cell 61, 1187-97. This paper reports the initial discovery of a class of human proteins, termed "coactivators", that connect transcriptional activators to the transcription machinery, thereby biochemically-defining gene regulatory circuit.
- 23. Taggart, A. K., and Pugh, B.F. (1996). Dimerization of TFIID when not bound to DNA. Science 272, 1331-3. TFIID promotes gene transcription by assembling the transcription machinery via stable interactions with promoters. This paper describes the a mechanism by which human TFIID auto-regulates its own assembly, and suggesgts a novel mechanism by which genes are kept quiescent.
- 38. Basehoar, A. D., Zanton, S. J., and Pugh, B.F. (2004). Identification and distinct regulation of yeast TATA box-containing genes. Cell 116, 699-709. The TATA box DNA element resides at the core of eukaryotic gene regulation, but it was unknown which genes contained a TATA box. This paper describes the first assignment of TATA boxes to genes on a genomic scale. This identification also precipitated the discovery of a deep dichotomy in the regulatory mechanism of eukaryotic genes. It defined stress-induced genes as having a distinct core transcription initiation complex and distinct mechanism of regulation compared to "housekeeping" genes. This discovery allowed scientists to infer how any gene of interest was likely to be regulated.
- 48. Albert, I., Mavrich, T. N., Tomsho, L. P, Qi, J., Zanton, S. J., Schuster, S. C., and Pugh, B.F. (2007) Translational and rotational settings of H2A.Z nucleosomes across the S. cerevisiae genome. Nature 446, 572-576. Whether the nucleosomes that package eukaryotic chromosomes are randomly distributed across a genome or organized into specific patterns was unknown. This paper reports the first-ever ChIP-seq experiment, a technology that now dominates the field of functional genomics. Equally important, it demonstrated that every eukaryotic gene is packaged into an array of nucleosomes, all essentially organized in the same way (except for the TATA-class).
- 54. Mavrich, T.N., Jiang, C., Ioshikhes, I.P., Li, X., Venters, B.J., Zanton, S.J., Tomsho, L.P., Qi, J., Glaser, R., Schuster, S.C., Gilmour, D.S., Albert, I., and Pugh, B.F. (2008). Nucleosome organization in the Drosophila genome. Nature. 453, 358-362. It was not known whether higher eukaryotes packaged their chromosomes as in yeast. This paper describes the first genome-wide map of individual nucleosome positions in flies. It also revealed the organization of the transcription machinery and DNA regulatory elements around nucleosomes on a genomic scale.
- 71. Zhang, Z., Wippo, C.J., Wal, M. Ward, E., Korber, P., Puqh, B.F. (2011) A packing mechanism for nucleosome organization rReconstituted across a eukaryotic genome. Science. 332, 977-980. How nucleosomes become organized on genes was unclear. This manuscript reports the astonishing feat of biochemical reconstitution of proper nucleosome organization on a genomic scale using pure DNA, pure histones, ATP and a cell-free extract. It revealed the chromatin remodelers are responsible for organizing nucleosomes on a genomic scale. This opens the door to creating synthetic chromosomes that can be studied in vitro as enzymological substrates (see pub. 100).
- 75. Rhee, H-S., and Pugh, B.F. (2011) Comprehensive genome-wide protein-DNA interactions detected at single nucleotide resolution. Cell. 147, 1408-19. Technologies for determining where proteins bind along a genome had been rather low resolution, thereby limiting our understanding of chromosome regulation. This paper reports the

development of the ChIP-exo assay. Its single-nucleotide resolution allows the structural organization of protein-DNA interactions to be defined on a genome scale.

- 76. Rhee, H-S., and Pugh, B.F. (2012) Genome-wide structure and organization of eukaryotic pre-initiation complexes. Nature. 483, 295-301. Here, the ChIP-exo assay was applied to define the first structure of transcription pre-initiation complexes located at core promoters across a genome.
- 81. Yen, K., Vinayachandran, V., Batta, K., Koerber, R.T., and Pugh, B.F. (2012). Genome-wide nucleosome specificity and directionality of chromatin remodelers. Cell. 149, 1461-1473. How chromatin remodelers organize nucleosomes on chromosomes was unknown. High-resolution mapping was used to show that remodelers use a "division-of-labor" approach to bind specific nucleosome positions on genes and slide them into an organized state.
- 89. 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. This work reports on the widespread subnucleosomal structures in dynamic chromatin, including novel half-nucleosomes, regulated interactions of H3 tails with linker DNA and asymmetric placement of histone variants and modifications on nucleosomes in relation to the direction of transcription.
- 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. \*co-corresponding author. This work was performed equally between the two labs, and reports on the genome-wide reconstitution of promoter nucleosome organization with purified proteins. This represents the first-ever biochemical reconstitution of an entire epigenome (chromatin on a genomic scale) using only pure components: histones, DNA, six remodelers, and two sequence-specific DNA binding proteins. From this, a four-stage genome-wide assembly mechanism was deduced, that now paves the way for detailed mechanistic studies.
- 120. Rossi, M.J., Kuntala, P.K., Lai, W.K.M., Yamada, N., Badjatia, N., Mittal, C., Kuzu, G., Bocklund, K., Farrell, N., Blanda, T.R., Mairose, J.D., Basting, A.V., Mistretta, K.S., Rocco, D.J., Perkinson, E.S., Kellogg, G.D., Mahony, S., and Pugh, B.F. (2021). A high-resolution protein architecture of the budding yeast genome. Nature, 592, 309-314. This is the first report of a nearly complete epigenome map in any organisms. It was performed at single bp resolution. It examines >800 different chromatin proteins of which >400 revealed insight into the regulation of genes, enhancers, replication origins, centromeres, heterochromatin and transposons. A clear picture of promoter architecture at constitutive vs inducible gene expression emerged.

### **Invited Lectures** (accepted)

- 1987 University of California Berkeley
- 1988 Rockefeller University
- 1990 European Molecular Biology Laboratory (EMBL), Heidelberg, Germany

University of Lausanne, Switzerland

Institut de Chimie Biologique, Strasbourg, France

University of Chicago

University of Wisconsin-Madison

1991 Albert Einstein College of Medicine

Rutgers University

Harvard University Medical School

The Pennsylvania State University

Johns Hopkins University

- 1992 Keystone meeting on Molecular and Cellular Biology, Fundamental Mechanisms of Transcription. The Pennsylvania State University, Hershey Medical Center.
- 1993 15th International tRNA Workshop (Cap d'Agde, France).

Wistar Institute, Philadelphia.

University of Medicine and Dentistry of New Jersey.

Biochimie et Génétique Moléculaire, Centre d'Estude de Saclay, France.

Bowling Green State University, OH.

1994 Keystone meeting on Molecular and Cellular Biology, Fundamental Mechanisms of Transcription.

	FASEB Meeting, Santa Cruz, CA
	University of Vermont.
1995	Searle/Chicago Community Trust.
	Penn State Summer Symposium in Molecular Biology on Chromosomal Controls of Gene Expression.
	Cold Spring Harbor Meeting on Cancer Cells Cold Spring Harbor Laboratory.
	Pennsylvania State University, Dept. of Chemistry.
1996	Symposium on Protein-Protein Interactions, Penn State University
	University of Texas - Austin.
	University of North Carolina - Chapel Hill.
1997	The Pennsylvania State University, Hershey Medical Center.
	Cold Spring Harbor Gene Regulation Course.
1998	Keystone meeting on Transcriptional Mechanisms, Taos, NM
1999	Penn State University, Summer Symposium,
	ASBMB Fall Symposium, Lake Tahoe, CA
	Towsen University, MD
2001	Penn State University, Hershey, PA
	Eukaryotic Transcription Meeting, Cold Spring Harbor Laboratory, NY
2002	Integrated Bioinformatics Meeting, Zurich, Switzerland
	Mid-Atlantic Yeast Conference, Cornell University, NY
	New York University, School of Medicine, NY
2003	Keystone Meeting on Transcription, Santa Fe, NM
	Summer Symposium, Penn State University
	Michigan State University, East Lansing, MI
	Ohio State University - OARDC, Wooster, OH
2004	University of California, Davis, CA
	Systems Biology Meeting, Cold Spring Harbor Laboratory, NY
	University of South Carolina – Columbia, SC
	Center for Cellular & Molecular Biology, Hyderabad, India
	Department of Biotechnology, New Delhi, India
	Indian Transcription Assembly Meeting, Pune, India
2005	Michigan State University, East Lansing, MI
	Systems Biology Meeting, Cold Spring Harbor Laboratory, NY
	Summer Symposium, Penn State University
2006	MD Anderson Cancer Center, Houston, TX
	University of Rochester, Rochester, NY
	ASBMB Meeting on Chromatin, Kiawah, SC
2007	Eukaryotic Transcription Meeting, Cold Spring Harbor Laboratory, NY
	Center for Cell and Molecular Biology, Hyderabad, India
	Indian Institute of Sciences, Bangalore, India
	Bioconvene Conference on Bioinformatics, Hyderabad, India
	Vimta Labs, Hyderabad, India
	University of Southern Illinois, Carbondale, IL
	University of Missouri, Kansas City, MO
	Stowers Institute, Kansas City, MO
2008	State University of New York, Stony Brook, NY
	EMBO Yeast transcription meeting, St. Feliu de Guixol, Spain
	BioMaPS Summer School in Chromatin, Rutgers University, NJ
	Transcription Regulation by Chromatin meeting, Michigan State University, MI
	EMBL Transcription meeting, Heidelberg, Germany
	Scottish Chromatin Group meeting, Dundee, Scotland

ASBMB meeting on Transcriptin Regulation, Granlibakken, Lake Tahoe, NV

Chromatin and Transcription Regulation meeting, Weizmann Institute, Israel

Pittsburgh Area Chromatin Meeting, University of Pittsburgh, PA

Dept. of Biology, Duquesne University, Pittsburgh, PA

Dept. of Biochemistry, State University of New York, Buffalo, NY

2009 CEA Genomics Institute, Paris, France

ASMBMB meeting on Gene Regulation, New Orleans, La (Venters)

24th International Conference on Yeast Genetics & Molecular Biology, Manchester, UK (Yen)

16<sup>th</sup> Conversation on nucleosome positioning, Albany, NY

Cold Spring Harbor Course on Eukaryotic Gene Regulation, CSHL, NY

Mechanisms of Eukaryotic Transcription Meeting, Cold Spring Harbor Laboratory, NY

SKMB Gene Regulation workshop, Lausanne, Switzerland

Dept of Biochemistry, UCLA, CA

Dept of Biological Science, Columbia U., New York

Kansas University Medical Center, Kansas City, KS

Ohio Plant Biotechnology Consortium

2010 Dept. Biochemisty and Molecular Biology, University of Florida, Gainesville, FL

University of Sherbrooke, Sherbrooke, Canada

Albert Einstein University, New York

EMBO Yeast transcription meeting, St. Feliu de Guixol, Spain

IRCB, Montreal, Canada

Emory University, Atlanta, GA

NIEHS, NIH, Chapel Hill, NC

U. Pennsylvania, Philadelphia, PA

Chromatin and epigenetics meeting, Munich, Germany

ASBMB meeting on transcription, Granlibakken, NV

Gordon Conference on chromatin, NH

Keystone meeting on transcription, Big Sky, MT

Intelligent Systems and Molecular Biology, Boston, MA

2011 EMBL meeting on chromatin, Heidelberg, Germany

Fred Hutchinson Cancer Research Center, Seattle, WA

Keystone Symposium Histone Code: Fact or Fiction?, Midway, UT

NIH Workshop: NCI Center of Excellence in Chromatin Biology, Bethesda, MD

University of Texas Southwestern, Dallas, TX

NIH Symposium: Chromosome Structure and Function Symposium, Bethesda, MD

Northwestern University, Evanston, IL

Cold Spring Harbor Course on Eukaryotic Gene Regulation, CSHL, NY

Cold Spring Harbor meeting on Eukaryotic Gene Regulation, CSHL, NY

Chromatin and Systems Biology Meeting, Spetses, Greece

High Throughput Approaches to Epigenomics Meeting, Bordeaux, France

2012 Memorial Sloan Kettering Cancer Research, NY, NY

U. Virginia, Charlottesville, VA

Cold Spring Harbor meeting on Systems Biology, CSHL, NY

Cold Spring Harbor course on Eukaryotic Gene Regulation, CSHL, NY

Gordon Research Conference on Chromatin Structure and Function, Il Ciocco, Italy

Rafael University, Milan, Italy

Genomic Symposium, New York University, NY

U. Utrecht, Netherlands

EMBO Yeast transcription meeting, St. Feliu de Guixol, Spain

Beyond the Genome, Harvard Medical School, Boston

Cornell University, Ithaca, NY

10<sup>th</sup> EMBL meeting "Transcription and Chromatin", Heidelberg, Germany

Yeast Genetics Meeting, Princeton, NJ

MD Anderson Cancer Center, Houston, TX

Conference on Gene Regulation, Athens, Greece (Keynote speaker)

EMBL meeting "From Functional Genomics to Systems Biology", Heidelberg, Germany

Meeting on Genetics Symposium, U. Pennsylvania, Philadelphia, PA (Keynote speaker)

Temple University, Philadelphia, PA

University of Michigan, Ann Arbor, MI

Harvard Medical School, Boston, MA (invited by students)

2013 Pacific Symposium on Biocomputing, Kona, HI

Epigenitic and Chromatin meeting, Harvard Medical School, MA

Keystone meeting on Epigenetic Marks and Cancer Drugs, Santa Fe, NM

University of Colorado, Boulder, CO

Meeting on high-throughput DNA sequencing and the central dogma, Insitut Curie, Paris, France

Meeting on Chromatin and Epigenetics, Heidelberg, Germany

FASEB meeting on transcription, chromatin and epigenetics, Nassau, Bahamas

Cold Spring Harbor course on Eukaryotic Gene Regulation, CSHL, NY

Stonybrook University, Stonybrook, NY (invited by students)

Cold Spring Harbor meeting on Eukaryotic Gene Regulation, CSHL, NY

Ludwig-Maximillian University, Munich, Germany (Octoberfest lecture)

Meeting on chromatin and the DNA damage response, Boston, MA (Keynote speaker)

EMBO meeting on nuclear structure and dynamics, Avignon, France

Vienna Biocenter, Vienna, Austria

Meeting on chromatin structure and function, Grand Cayman Islands

Stanford University, Palo Alto, Ca

University of California, San Francisco, CA

2014 Keystone meeting on nuclear receptors and biological networks, Taos, NM (Keynote speaker)

Keystone meeting on transcription regulation, Santa Fe, NM

ASBMB Annual Meeting, San Diego, CA

Meeting on Nucleosomes and Chromatin, Hinxton, UK

Gordon Conference on Chromatin Structure and Function, Waltham, MA

EMBO Conference on Gene Transcription in Yeast, San Felieu, Spain

FASEB Meeting on Yeast Chromatin Structure, Steamboat Springs, CO

EMBL Conference on Transcription and Chromatin, Heidelberg, Germany

Meeting on Total Transcription, Hinxton, UK

Cold Spring Harbor Meeting on Chromatin and Epigenetics, CSHL, NY

Stowers Institute, Kansas City, MO

Symposium on Epigenetics, University of Chicago, IL

ASBMB meeting on Transcription, Snowbird, UT

Nobel Conference on Systems Biology, Karolinska, Sweden

MD Anderson Cancer Center, Houston, TX

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
2010	EMBO Conference on Gene Transcription in Yeast, San Felieu, Spain
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	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
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	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
	University of Pennsylvania, Philadelphia, PA
2019	Dept. of Biology, University of Pittsburgh, Pittsburgh, PA
	Penn State Cancer Institute, Penn State University, University Park, PA
	NIH workshop on Renewable Antibodies, Rockville, MD
2020	Cornell University, Ithaca, NY
	Cold Spring Harbor Meeting on Eukaryotic Transcription, CSHL, NY
2021	University of California, San Diego
2022	EMBO Conference on Gene Transcription in Yeast, San Felieu, Spain
	ASBMB meeting on transcription regulation, Snowbird, UT
	Keynote speaker Yeast Biology meeting, Munich, Germany
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