BIOGRAPHICAL SKETCH

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NAME: Stephen Kevin Burley

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POSITION TITLE: University Professor and Henry Rutgers Chair; RCSB PDB Director; Institute Director

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Western Ontario, London, Canada	B.Sc.	06/1980	Physics
University of Oxford, Oxford, UK	D.Phil.	11/1983	Structural Biology
Harvard Medical School, Boston, MA	M.D.	06/1987	Medicine

A. Personal Statement

Stephen Burley is an expert in structural biology, proteomics, bioinformatics, structure/fragment-based drug discovery, and clinical medicine/oncology. Burley currently serves as a University Professor and Henry Rutgers Chair, Founding Director of the Institute for Quantitative Biomedicine, and Director of the RCSB Protein Data Bank at Rutgers, The State University of New Jersey. He is also a Member of the Rutgers Cancer Institute of New Jersey, where he serves as Co-Leader of the Cancer Pharmacology Research Program working to carefully select and mentor Program Members, and foster an interactive and cancer-focused environment that leads to impactful science. From 2008 to 2012, Burley was a Distinguished Lilly Research Scholar in Lilly Research Laboratories. Prior to joining Lilly, Burley served as the Chief Scientific Officer and Senior Vice President of SGX Pharmaceuticals, Inc., a publicly traded biotechnology company that was acquired by Lilly in 2008. Until 2002, Burley was the Richard M. and Isabel P. Furlaud Professor at The Rockefeller University, and an Investigator in the Howard Hughes Medical Institute. He has authored/coauthored more than 250 scholarly scientific articles. Burley received an M.D. degree from Harvard Medical School in the joint Harvard-MIT Health Sciences and Technology program and, as a Rhodes Scholar, received a D.Phil. in Molecular Biophysics (structural biology) from Oxford University. He trained in internal medicine at the Brigham and Women's Hospital and did post-doctoral work with Gregory A. Petsko at the Massachusetts Institute of Technology and William N. Lipscomb, Jr. at Harvard University. With William J. Rutter and others at the University of California at San Francisco and Rockefeller, Burley co-founded Prospect Genomics, Inc. (acquired by SGX in 2001). He is a Fellow of the Royal Society of Canada and the New York Academy of Sciences, and recipient of a Doctor of Science (*Honoris causa*) from his alma mater the University of Western Ontario, from which he received a B.Sc. in Physics in 1980.

Ongoing and recently completed projects that I would like to highlight include:

NSF DBI 1832184 (S.K. Burley) 03/01/2019-02/29/2024
NIH R01GM133198 (S.K. Burley) 08/01/2019-07/31/2024
DOE DE-SC0019749 (S.K. Burley) 04/01/2019-03/31/2024
PDB Management by the Research Collaboratory for Structural Bioinformatics

NIH P30CA072720
S.K. Libutti (PI); Role: Member and Cancer Pharmacology Program Co-Lead
03/01/97-02/28/24
Cancer Center Support Grant

CINJ Seed Funding
S.K. Burley (PI)
04/01/2021-03/31/2023

3D-Cancer Structuralyzer: Informatics Technology Platform for Enhancing the Impact of 3D Structure Information on Cancer Research

NSF 2019297
S.K. Burley (PI)
07/01/2020-06/30/2023
CIBR: BBSRC-NSF/BIO: Next generation Protein Data Bank - FACT infrastructure with value added FAIR data supporting diverse research and education user communities

NSF 2129634
S.K. Burley (PI)
12/01/2021-11/30/2024
BBSRC-NSF/BIO: From atoms to molecules to cells - Multi-scale tools and infrastructure for visualization of annotated 3D structure data

NSF DBI 1338415
S.K. Burley (PI)
04/01/2014-03/31/2019
PDB Management by the Research Collaboratory for Structural Bioinformatics

NIH U01GM111528
M.K. Gilson (PI); Role: Co-PI
9/15/2014-08/31/2019
An Open Resource to Advance Computer-Aided Drug Design

NIH R01GM122845
L. Xie (PI); Role: Co-PI
08/15/2017-06/30/2022
Omics Data Integration and Analysis for Structure-based Multi-target Drug Design

B. Positions, Scientific Appointments and Honors

Positions and Employment

2018- Executive Vice Chancellor, Rutgers University
2017- Henry Rutgers Chair, Rutgers University
2017- University Professor, Rutgers University
2016- Co-Lead, Cancer Pharmacology Research Program, Rutgers Cancer Institute of New Jersey
2016- Research Scientist, Step IX, San Diego Supercomputer Center, UC San Diego
2015- Founding Director, Institute for Quantitative Biomedicine at Rutgers
2014- Director, RCSB Protein Data Bank
2013- Member, Rutgers Cancer Institute of New Jersey

Other Experience and Professional Memberships - (* No longer active)

American Association for the Advancement of Science
American Chemical Society
American Crystallographic Association
American Society for Biochemistry and Molecular Biology
Biophysical Society
New York Academy of Sciences
Protein Society
International Structural Genomics Organization*
American Society of Hematology*
American Association of Cancer Research*

Honors

University of Western Ontario (1976-1980)
- Gold Medal in Physics
- VEECO Instruments Incorporated Prize for Physics

University of Western Ontario Faculty Association Award
University of Western Ontario Undergraduate Scholarship (Full)
Rhodes Scholar (elected 1980)
Harvard Medical School (1983-1987)
Magna Cum Laude
Leon Reznick Memorial Prize for Excellence and Accomplishment in Research
Fellow, Royal Society of Canada (elected 1995)
Fellow, New York Academy of Sciences (elected 1997)
Richard M. and Isabel P. Furlaud Chair (The Rockefeller University, 1999)
Doctor of Science (*Honoris Causa*) Western University (2016)
Henry Rutgers Chair (Rutgers University, 2017)

C. Contribution to Science

1. Eukaryotic RNA Polymerase II Transcription Initiation - Burley determined a series of high resolution X-ray crystal structures that revealed the structural bases for the first two steps in assembly of the eukaryotic RNA polymerase II transcription initiation complex, including the TATA-box Binding Protein (TBP), complexes of TBP recognizing double stranded DNA TATA-boxes found in nature, a complex of transcription factor IIB recognizing the preformed TBP-DNA complex, and a complex of Negative Cofactor 2 poisoning assembly of the RNA polymerase II pre-initiation complex by recognizing a TBP-DNA complex and blocking recruitment of TFIIB.
    a. D.B. Nikolov, S.-H. Hu, J.P. Lin, A. Gasch, A. Hoffmann, M. Horikoshi, N.-H. Chua, R.G. Roeder, and **S. K. Burley** (1992) Crystal structure of TFIID TATA-box binding protein. *Nature 360*, 40-46. PMID: 1436073
    b. J.L. Kim, D.B. Nikolov, and **S.K. Burley** (1993) Co-crystal structure of TBP recognizing the minor groove of a TATA element. *Nature 365,* 520-527. PMID: 8413605
    c. D.B. Nikolov, H. Chen, E.D. Halay, A. Usheva, K. Hisatake, D.K. Lee, R.G. Roeder, and **S. K. Burley** (1995) Crystal structure of a TFIIB-TBP-TATA element ternary complex. *Nature 377*, 119-128. PMID: 7675079
    d. K. Kamada, F. Shu, H. Chen, S. Malik, M. Meisterernst, R.G. Roeder, and **S.K. Burley** (2001) Crystal structure of negative cofactor 2 recognizing the TBP-DNA transcription complex. *Cell 106*, 71-81. PMID: 11461703

2. Eukaryotic Gene Regulation and DNA Sequence Recognition - Burley determined a series of high resolution X-ray crystal structures that revealed the structural bases for DNA recognition by transcription factors responsible for regulating pre-mRNA transcription in eukaryotes, including complexes of the Myc-Max and Mad-Max heterodimers recognizing the 5'-CACGTG-3' duplex, Sterol Response Element Binding Protein recognizing the 5'-CACGTG-3' duplex and the Sterol Response Element, Hepatocyte Nuclear Factor 3/*forkhead* recognizing its cognate DNA duplex.
    a. S.K. Nair and **S.K. Burley** (2003) X-ray structures of Myc-Max and Mad-Max recognizing DNA: Molecular bases of regulation by proto-oncogenic transcription factors. *Cell 112*, 193-205. PMID: 12553908
    b. Parraga, L. Bellsolell, A.R. Ferre-D'Amare, and **S.K. Burley** (1998) Co-crystal structure of SREBP-1 recognizing a sterol regulatory element. *Structure 6*, 661-672. PMID: 9634703
    c. K.L. Clark, E.D. Halay, E. Lai, and **S.K. Burley** (1993) Co-crystal structure of the HNF-3/*fork head* DNA-recognition motif resembles histone H5. *Nature 364*, 412-420. PMID: 8332212
    d. K.S. Gajiwala, H. Chen, F. Cornille, B.P. Roques, W. Reith, B. Mach, and **S.K. Burley** (2000) Structure of a winged-helix protein reveals a new mode of DNA binding. *Nature 403,* 916-921. PMID: 10706293

3. RNA-binding Proteins and Pre-mRNA Splicing - Burley determined a series of high-resolution X-ray crystal structures that revealed the structural bases of RNA recognition and aspects of pre-mRNA splicing, including a complex of Poly-A Binding Protein recognizing the mRNA poly-A tail, a complex of a Nova KH domain recognizing an RNA hairpin, a complex of She2P recognizing an RNA hairpin, and a heterodimeric complex of two pre-mRNA splicing factors.
    a. R.C. Deo, J. Bonanno, N. Sonenberg, and **S.K. Burley** (1999) Recognition of polyadenylate RNA by the poly (A)-binding protein. *Cell 98,* 835-845. PMID: 10499800

b. H.A. Lewis, K. Musunuru, K.B. Jensen, C. Edo, R.B. Darnell, and **S.K. Burley** (2000) Sequence specific RNA binding by a Nova KH domain: Implications for paraneoplastic disease and fragile X syndrome. *Cell 100*, 323-332. PMID: 10676814
c. Niessing, S. Hüttelmaier, D. Zenklusen, Robert H. Singer, and **Stephen K. Burley** (2004) She2p is a novel RNA-binding protein with a Basic Helical Hairpin Motif. *Cell 119*, 491-502. PMID: 15537539

4. High-throughput X-ray Crystallography/Fragment-based Drug Discovery - Burley led development of an industry-leading platform for high-throughput X-ray structure determination and fragment-based drug discovery at SGX Pharmaceuticals, Inc., a NASDAQ-traded biotechnology company, which was subsequently acquired by Eli Lilly and Company. At SGX and Lilly, Burley oversaw discovery of highly selective, drug-like protein kinase inhibitors, two of which were the focus of successful US FDA Investigational New Drug Applications.

    a. J. Blaney, V. Nienaber, and **S.K. Burley** (2006) Fragment-based Lead Discovery and Optimization Using X-ray Crystallography, Computational Chemistry, and High-Throughput Organic Synthesis. In *Fragment-based Approaches in Drug Discovery*, edited by W. Jahnke and D.A. Erlanson (WILEY-VCH Verlag GmbH and Co., KGaA, Weinheim) pp. 215-248.
    b. T. O'Hare, C.A. Eide, J.W. Tyner, A.S. Corbin, M.J. Wong, S. Buchanan, K. Holme, K.A. Jessen, C. Tang, H.A. Lewis, R.D. Romero, **S.K. Burley**, and M.W. Deininger (2008) SGX393 inhibits the CML mutant Bcr-AblT315I and preempts *in vitro* resistance when combined with nilotinib or dasatinib. *Proceedings of the National Academy of Sciences USA 105*, 5507-5512. PMCID: PMC2291110
    c. S.G. Buchanan, J. Hendle, P.S. Lee, C.R. Smith, P.Y. Bounaud, K.A. Jessen, C.M. Tang, N.H. Huser, J.D. Felce, K.J. Froning, M.C. Peterman, B.E. Aubol, S.F. Gessert, J.M. Sauder, K.D. Schwinn, M. Russell, I.A. Rooney, J. Adams, B.C. Leon, T.H. Do, J.M. Blaney, P.A. Sprengeler, D.A. Thompson, L. Smyth, L.A. Pelletier, S. Atwell, K. Holme, S.R. Wasserman, S. Emtage, **S.K. Burley,** and S.H. Reich (2009) SGX523 is an exquisitely selective, ATP-competitive inhibitor of the MET receptor tyrosine kinase with antitumor activity *in vivo*. *Molecular Cancer Therapeutics 8*, 3181-3190. PMID: 19934279

5. Eukaryotic RNA Polymerase II Transcription Initiation - Burley currently leads the RCSB Protein Data Bank (PDB), which is headquartered at Rutgers, The State University of New Jersey with additional performance sites at University of California San Diego and University of California San Francisco. The RCSB PDB is jointly funded by the National Science Foundation, the National Institutes of Health, and the US Department of Energy. As a founding member of the Worldwide Protein Data Bank (wwPDB) partnership, the RCSB PDB supports more than 50,000 structural biologist data depositors around the globe and serves as the wwPDB Archive Keeper for the PDB archive. Now in its 51st year of continuous operation, the PDB archive houses more than 185,000 experimentally determined, three-dimensional structures of biological macromolecules. It is a core global biodata resource central to research and education in fundamental biology, biomedicine, bioenergy, and bioengineering/biotechnology. During 2021, the RCSB PDB enabled more than two billion PDB data file downloads and delivered PDB data *via* its research-focused web portal RCSB.org to more than five million unique users worldwide at no charge with no limitations on data usage, and the RCSB PDB outreach/educational web portal PDB101.RCSB.org supported more than 800,000 educators and students.

    a. **S.K. Burley** *et al*. (2022) RCSB Protein Data Bank: Celebrating 50 years of the PDB with new tools for understanding and visualizing biological macromolecules in 3D. *Protein Science 31*, 187-202. PMID: 34676613
    b. D.S. Goodsell and **S.K. Burley** (2022) RCSB Protein Data Bank Resources for Structure-facilitated Design of mRNA Vaccines for Existing and Emerging Viral Pathogens. *Structure 30*, 55-68. PMCID: PMC8567414
    c. **S.K. Burley** *et al*. (2021) RCSB Protein Data Bank: Powerful new tools for exploring 3D structures of biological macromolecules for basic and applied research and education in fundamental biology, biomedicine, biotechnology, bioengineering, and energy sciences. *Nucleic Acids Research 49*, D437-D451. PMCID: PMC7779003
    d. **S.K. Burley** (2021) Impact of structural biologists and the Protein Data Bank on small-molecule drug discovery and development. *Journal of Biological Chemistry Reviews 296*, 100559. PMCID: PMC8059052

List of Published Work: https://pubmed.ncbi.nlm.nih.gov/?term=burley+sk