

**BIOGRAPHICAL SKETCH**

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NAME R. Blake Hill		POSITION TITLE Associate Professor of Biology and Chemistry Johns Hopkins University	
eRA COMMONS USER NAME (credential, e.g., agency login) rhill5			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Kalamazoo College, Kalamazoo MI	BA	1984	Chemistry, Biology
Yale University, New Haven CT	PhD	1995	Biophysical Chemistry
University of Pennsylvania, Philadelphia PA	Postdoc	2000	Biochem. & Biophys.

**A. Personal Statement**

Dr. Hill is defining the chemical and biophysical basis, regulatory mechanisms, and biological consequences of reversible protein-membrane interactions, or protein amphitropism. His current research program focuses on understanding protein amphitropism in the context of two key cellular processes: mitochondrial fission and cellular apoptosis. This research builds on the previous training of Dr. Hill in Chemistry and Biophysics, but includes more recently acquired expertise in Cell Biology and Genetics. His lab has developed new genetic and cell biological tools and using this interdisciplinary approach, they have made significant advances in each area including the identification of two new types of amphitropism: (1) soluble domains of membrane proteins that can insert into membranes in monomeric form, and (2) soluble, cytosolic proteins that can insert into membranes upon oligomerization. He and his laboratory have also made fundamental advances in understanding the molecular basis of fission protein Fis1's regulation of mitochondrial fission. In the area of apoptosis, they have found that Bcl-2 proteins may be localized for a function in the regulation of mitochondrial morphology that is independent of apoptosis. Although Dr. Hill approaches the general problem of protein amphitropism in the context of mitochondrial morphology and function, members of his laboratory also apply their findings on amphitropism for beneficial purposes in drug discovery and delivery.

**B. Positions and Honors****Positions and Employment**

1981	Quality Control Lab Technician, L. Perrigo Co., Allegan, MI
1982	NMR Technician, Kalamazoo College, Kalamazoo, MI
1983	Research Intern, General Motors Institute, Flint, MI
1984	Research Intern, National Institute of Child Health and Human Development, NIH, Bethesda, MD
1984-1987	Chemist, Drug Delivery Research, The Upjohn Co., Kalamazoo, MI
1987-1994	Graduate Student, Dr. James H. Prestegard, Department of Chemistry, Yale University
1995-2000	Postdoctoral Fellow, Dr. William F. DeGrado, Biochem. & Biophysics, University of Pennsylvania
2000-2007	Assistant Professor, Departments of Biology (primary) & Chemistry (secondary). Krieger School of Arts and Sciences, Johns Hopkins University, Baltimore, MD
2007-	Associate Professor, Departments of Biology (primary) & Chemistry (secondary). Krieger School of Arts and Sciences, Johns Hopkins University, Baltimore, MD

## **Honors**

Kalamazoo College Honors Scholarship ('80-'84), Frederick S. Heyl Doctoral Fellowship ('87-'92), NIH NRSA Postdoctoral Fellowship ('96-'98), George W. Raiziss Postdoctoral Fellowship ('98-'00), Reviewer for articles submitted to *PNAS*, *Nature Structural & Molecular Biology*, *The Journal of American Chemical Society*, *The Journal of Biological Chemistry*, *Journal of Molecular Biology*, *Biochemistry*, *Biophysical Journal*, *Journal of Cell Science*, *Cell Death & Differentiation*, *Protein Science*, *Proteins*, *PLOS-1*, *European Biophysics Journal*, *Analytical Biochemistry*, *Chemical Reviews*, *European Journal of Biochemistry*, *FEBS Letters*, *Journal of Cellular Biochemistry*, *Journal of Cellular and Molecular Medicine*, *Protein & Peptide Letters*, *Protein Engineering, Design, and Selection*, 2000 to current; Ad hoc grant reviewer for International Science & Technology Center, 2003-2005; Ad hoc member, various NIH study sections, 2003-current; Member, Career and Networking Committee of The Protein Society, 2006-8, Member of the Membership Committee of The Protein Society, 2008-current, Chair, Mentoring Committee of the Protein Society, 2008-present.

## **C. Selected Peer-reviewed Publications**

1. M.G. VanderHeiden, X.X. Li, E. Gottlieb, **R.B. Hill**, C.B. Thompson, and M. Colombini, "Bcl-x<sub>L</sub> promotes both the open configuration of the VDAC and metabolite passage through the outer mitochondrial membrane", *J. Biol. Chem.* **276**, 19414-19419 (2001).
2. J.A. Dohm, S.J. Lee, J.M. Hardwick, **R.B. Hill\***, and A.G. Gittis\*, "The cytosolic domain of the human mitochondrial fission protein Fis1 adopts a TPR fold", *Proteins* **54**, 153-6 (2004). NIHMS#274167
3. G.R. Thuduppathy and **R.B. Hill**, "Applications of NMR Spin Relaxation Methods for Measuring Biological Motions", *Methods Enzymol.* **384**, 243-64(2004).
4. Y. Fannjiang, W.C. Cheng, S.J. Lee, B. Qi, J. Pevsner, J.M. McCaffery, **R.B. Hill**, G. Basañez, and J.M. Hardwick, "Mitochondrial fission proteins regulate programmed cell death in yeast.", *Genes Dev.*, **18**, 2785-97(2004). PMID: PMC528898
5. G.R. Thuduppathy and **R.B. Hill**, "Acid destabilization of the solution conformation of Bcl-x<sub>L</sub> does not drive its pH-dependent insertion into membranes", *Protein Sci*, **15**, 248-57(2006). PMID: PMC1752203
6. G.R. Thuduppathy, J. W. Craig, V. Kholodenko, A. Schon, and **R.B. Hill**, "Evidence that membrane insertion of the cytosolic domain of Bcl-x<sub>L</sub> might be governed by an electrostatic mechanism", *J. Mol. Biol.*, **359**, 1045-58(2006). PMID: PMC1785297
7. G.R. Thuduppathy, O. Terrones, J. W. Craig, G. Basañez, and **R.B. Hill**, "The N-terminal domain of Bcl-x<sub>L</sub> reversibly binds membranes in a pH-dependent manner", *Biochemistry* **45**, 14533-42(2006). PMID: PMC1764622
8. F.J. Tan, J.E. Zuckerman, A.Z. Fire, and **R.B. Hill**, "Regulation of apoptosis by *C. elegans* CED-9 in the absence of the C-terminal transmembrane domain", *Cell Death Differ.* **14**, 1925-35(2007). NIHMS# 274168.
9. R.C. Wells, L.K. Picton, S.C.P. Williams, F.J. Tan, and **R.B. Hill**, "Direct binding of the dynamin-like GTPase, Dnm1, to mitochondrial dynamics protein Fis1 is negatively regulated by the Fis1 N-terminal arm.", *J. Biol. Chem.* **282**, 33769-75(2007). NIHMS#274170.
10. L.J. Siskind, L. Feinstein, T. Yu, J.S. Davis, D. Jones, J. Choi, J.E. Zuckerman, W. Tan, **R. B. Hill**, J.M. Hardwick, and M. Colombini "Anti-apoptotic Bcl-2 family proteins disassemble ceramide channels", *J. Biol. Chem.* **283**, 6622-6630(2008). PMID: PMC2713582
11. D.A. De Cotiis, M.P. Woll, T.E. Fox, **R.B. Hill**, R. Levenson, J.M. Flanagan, "Optimized expression and purification of myristoylated human neuronal calcium sensor 1 in *E. coli*." *Protein Expr. Purif.* **61**, 103-12(2008).
12. F.J. Tan, M. Husain, C.M. Manlandro, M. Koppenol, A.Z. Fire, & **R.B. Hill**, "CED-9 and mitochondrial homeostasis in *C. elegans* muscle. *J. Cell Sci.* **102**, 3373-82(2008). PMID: PMC2785848
13. M.M. Parrott, S.A. Sitarski, R.J. Arnold, L.K. Picton, **R.B. Hill**, and S. Mukhopadhyay. "Role of conserved cysteines in the alphavirus E3 protein. *J Virol.* **83**, 2584-91(2009). PMID: PMC2648270
14. L.K. Picton†, S. Casares†, A.C. Monahan, A. Majumdar, & **R.B. Hill**, "Evidence for conformational heterogeneity of fission protein Fis1 from *S. cerevisiae*", *Biochemistry* **21**, 6598-609(2009). PMID: PMC2785846

15. **R.B. Hill** and L. Pellegrini "The PARL family of mitochondrial rhomboid proteases." *Semin Cell Dev Biol.* **21**,582-92(2010). PMID: PMC2908206
16. C.R. Chang†, C.M. Manlandro†, D. Arnoult, J. Stadler, A.E. Posey, **R.B. Hill**\*, and C. Blackstone\*, "A lethal *de novo* mutation in the middle domain of the dynamin-related GTPase Drp1 impairs higher-order assembly and mitochondrial division", *J. Biol. Chem.* **285**, 32494-503(2010). PMID: PMC2952251
17. F.J. Tan, F.J., J.E. Zuckerman, R.C. Wells, **R.B. Hill**, "The *C. elegans* B-cell lymphoma 2 (bcl-2) homolog Cell death abnormal 9 (CED-9) associates with and remodels lipid membranes", *Protein Sci.* **20**,62-74(2011). NIHMS# 274294.
18. D.V. Jeyaraju, H.M. McBride, **R.B. Hill**\*, L. Pellegrini\*, "Structural and mechanistic basis of Parl activity and regulation", *Cell Death Differ.*, (in press).NIHMS# 274432.
19. R.C. Wells and **R.B. Hill**, "The Fis1 cytosolic domain binds and reversibly clusters lipid vesicles", *PLoS-1*, (in press).

†co-first authors \*co-corresponding authors

## D. Research Support

### ONGOING

R01 GM067180-6 Hill (PI) 01/01/04-03/31/14

NIH / NIGMS

Fis1 Regulation of Mitochondrial Fission

The specific aims of this proposal are to determine the molecular basis of Fis1-mediated assembly of the mitochondrial fission complex.

NIH / NIGMS Hill (PI) 06/01/11-06/31/13

Research Supplements to Promote Diversity in Health-Related Research

This supplement funds salary and supplies for a Hopkins sophomore that aspires to earn a PhD and become a professor at a top-tier institution.

### COMPLETED

2009 National Institutes of Health ARRA Award

3R01 GM067180-05S1, "Multiangle Laser Light Scattering and Refractive Index Detectors for Measuring Protein-Protein and Protein-Lipid Interactions"

Total Award: \$64,000

Role: Principal Investigator

2005 National Institutes of Health Shared Instrumentation Grant

S10-RR020922, "600 MHz NMR Spectrometer for Shared Use"

Total Award: \$500,000

Role: Principal Investigator

2005 National Science Foundation Major Research Instrumentation Grant

DBI-0500580, "Peptide Synthesis System to Probe Protein Structure and Interactions with other Biological Macromolecules and Ions"

Total Award: \$85,858

Role: Contributor

2004 National Institutes of Health Shared Instrumentation Grant

S10-RR017850, "400 MHz NMR Spectrometer for Shared Use"

Total Award: \$360,000

Role: Contributor

2002 American Cancer Society Institutional Research Grant

IRG-58-005-41, "Uncovering the Molecular Details of Inhibiting Bcl-x<sub>L</sub>"

Total Award: \$20,000

Role: Principal Investigator

Program Director/Principal Investigator (Last, First, Middle):

2002 National Science Foundation Major Research Instrumentation Grant  
DBI-0216077, "Acquisition of a 750 MHz NMR Spectrometer/Cryoprobe  
System and High Field NMR Console/Probe Upgrades for Biomolecular  
NMR Spectroscopy"  
Total Award: \$1,178,025  
Role: co-Principal Investigator