

# Amy E. Keating

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## Professional Positions

Jay A. Stein Professor of Biology	2022 – 2027
Member, Koch Institute for Integrative Cancer Research	July 1, 2018 – present
Professor of Biology and Biological Engineering, MIT	July 1, 2015 – present
Associate Professor of Biological Engineering, MIT	July 1, 2014
Associate Professor of Biology, MIT	July 1, 2007
Assistant Professor of Biology, MIT	January 1, 2002

## Education

Ph.D. Organic Chemistry	February 1998
University of California, Los Angeles	
Thesis: <i>Molecular Mechanics, Quantum Mechanics and Direct Dynamics Applied to the Study of Organic Carbene Reactivity</i>	
Advisors: Kendall N. Houk & Miguel Garcia-Garibay	
Special Student, Chemistry	September 1992 - June 1993
Harvard University, Cambridge, MA	
A.B. Physics	June 1992
Harvard University, Cambridge, MA	

## Teaching at MIT

Research Experiences in BioPharma  
Principles of Biochemical Analysis  
Topics in Protein Biochemistry  
Topics in Chemical Biology  
Foundations of Computational and Systems Biology

## Professional Activities & Leadership Positions

President-past of The Protein Society	2021 – 2022
Associate Department Head	2020 – present
President of The Protein Society (elected)	2019 – 2021
Alfred P. Sloan Foundation Computational and Evolutionary Molecular Biology fellowship selection committee	2018 – 2021
President-elect of The Protein Society (elected)	2018 – 2019
Member, Editorial Board of <i>Protein Science</i>	2016 – present
Member, External Advisory Committee for the Dartmouth Institute for Biomolecular Targeting	2016 – 2021
Co-chair, Proteins Gordon Conference (elected)	2013
Director or Co-Director and NIH T32 co-PI, MIT Biology graduate program	2012 – present
Member, Executive Council of the Protein Society (elected)	2012 – 2015
Chair, Publications Committee of the Protein Society	2012 – 2015
Member, Editorial Board of <i>Journal of Molecular Biology</i>	2011 – present
Member, Scientific Advisory Board, Protabit LLC	2011 – 2014
Vice-chair, Proteins Gordon Conference	2011

**Awards and Honors (since 2000)**

Georgina Sweet Award for Women in Quantitative Biomedical Science  
 Director's Transformative R01 award  
 Irwin and Helen Sizer Career Development Chair  
 Surdna Foundation Scholar Award  
 Robert A. Swanson Career Development Chair  
 Outstanding UROP Mentor Award  
 Merck /MIT Collaboration Program Postdoctoral Fellowship  
 Helen Hay Whitney Postdoctoral Fellowship  
 Program in Mathematics and Molecular Biology Fellowship

**Publications**

1. Houk KN, Nakamura K, Sheu C, Keating AE. (1996) *Gating as a control element in constrictive binding and guest release by hemicarcerands*. Science 273, 627-9. PMID: 8662548.
2. Shin SH, Keating AE, Garcia-Garibay MA. (1996) *Transforming a nonselective carbene rearrangement into a highly selective process by using crystalline media*. J Am Chem Soc. 118, 7626-7.
3. Keating AE, Shin SH, Houk KN, Garcia-Garibay MA. (1997) *Combining quantum mechanical reaction pathways with force field lattice interactions to model a solid-state phototransformation*. J Am Chem Soc. 119, 1474-5.
4. Shin SH, Cizmeciyan D, Keating AE, Khan SI, Garcia-Garibay MA. (1997) *Control of carbene reactivity by crystals. A highly selective 1,2-H shift in the solid-to-solid reaction of 1-(4'-biphenyl)-2-phenyldiazopropane to (Z)-1-(4'-biphenyl)-2-phenylpropene*. J Am Chem Soc. 119, 1859-68.
5. Nakamura K, Sheu C, Keating AE, Houk KN, Chapman RG, Sherman JC, Jorgensen WL. (1997) *Self-assembling ternary complex stabilities and template ratios in carceplex formation*. J Am Chem Soc. 119, 4321-2.
6. Keating AE, Garcia-Garibay MA, Houk KN. (1997) *Origins of stereoselective carbene 1,2-shifts and cycloadditions of 1,2-dichloroethylidene: a theoretical model based on CBS-Q and B3LYP calculations*. J Am Chem Soc. 119, 10805-09.
7. Keating AE, Garcia-Garibay MA, Houk KN. (1998) *Influence of bystander substituents on the fates of 1,2-H and 1,2-Ph shifts in singlet and triplet carbenes*. J Phys Chem A 102, 8467-76.
8. Keating AE, Shin SH, Huang FK, Garrell RL, Garcia-Garibay MA. (1999) *Experimental and computational modeling of biphenyl twisting in a solid-to-solid carbene reaction*. Tetrahedron Lett. 40, 261-4.
9. Keating AE, Merrigan SR, Singleton DA, Houk KN. (1999) *Experimental proof of the non-least-motion cycloadditions of dichlorocarbene to alkenes: kinetic isotope effects and quantum mechanical transition states*. J Am Chem Soc. 121, 3933-8.
10. Garcia-Garibay MA, Houk KN, Keating AE, Cheer CJ, Leibovitch M, Scheffer JR, Wu LC. (1999) *Computational prediction of the enantioselectivity of a solid-state photoreaction*. Org Lett. 1, 279-81.
11. Keating AE, Malashkevich VN, Tidor B, Kim PS. (2001) *Side-chain repacking calculations for predicting structures and stabilities of heterodimeric coiled coils*. Proc Natl Acad Sci USA. 98, 14825-30. PMID: PMC64943.
12. Keating TA, Marshall CG, Walsh CT, Keating AE. (2002) *The structure of VibH represents nonribosomal peptide synthetase condensation, cyclization and epimerization domains*. Nat Struct Biol. 9, 522-6. PMID: 12055621.
13. Newman JR, Keating AE. (2003) *Comprehensive identification of human bZIP interactions with coiled-coil arrays*. Science 300, 2097-2101. PMID: 12805554.
14. Fong JH, Keating AE, Singh M. (2004) *Predicting specificity in bZIP coiled-coil protein interactions*. Genome Biol. 5: R11. PMID: PMC395749.

15. Ali MH, Taylor CM, Grigoryan G, Allen KN, Imperiali B, Keating AE. (2005) *Design of a heterospecific, tetrameric, 21-residue miniprotein with mixed alpha/beta structure*. Structure 13, 225-34. PMID: 15698566.
16. Jiang T, Keating AE. (2005) *AVID: an integrative framework for discovering functional relationships among proteins*. BMC Bioinformatics 6, 136. PMCID: PMC1177925.
17. Zhou F, Grigoryan G, Lustig SR, Keating AE, Ceder G, Morgan D. (2005) *Coarse-graining protein energetics in sequence variables*. Phys Rev Lett. 95, 148103. PMID: 16241695.
18. Taylor CM, Keating AE. (2005) *Orientation and oligomerization specificity of the Bcr coiled-coil oligomerization domain*. Biochemistry 44, 16246-56. PMCID: PMC2526250.
19. McDonnell AV, Jiang T, Keating AE, Berger B. (2006) *Paircoil2: improved prediction of coiled coils from sequence*. Bioinformatics 22, 356-8. PMID: 16317077.
20. Grigoryan G, Keating AE. (2006) *Structure-based prediction of bZIP partnering specificity*. J Mol Biol. 355, 1125-42. PMID: 16359704.
21. Grigoryan G, Zhou F, Lustig SR, Ceder G, Morgan D, Keating AE. (2006) *Ultra-fast evaluation of protein energies directly from sequence*. PLoS Comput Biol. 2, e63. PMCID: PMC1479088.
22. Keating AE. (2007) *A rational route to probing membrane proteins*. Genome Biol. 8, 214. PMCID: PMC1929131.
23. Fu X, Apgar JR, Keating AE. (2007) *Modeling backbone flexibility to achieve sequence diversity: the design of novel alpha-helical ligands for Bcl-x<sub>L</sub>*. J Mol Biol. 371,1099-117. PMCID: PMC1994813.
24. Grigoryan G, Ochoa A, Keating AE. (2007) *Computing van der Waals energies in the context of the rotamer approximation*. Proteins 68, 863-78. PMID: 17554777.
25. Grigoryan G, Keating AE. (2008) *Structural specificity in coiled-coil interactions*. Curr Opin Struct Biol. 18, 477-83. PMCID: PMC2567808.
26. Apgar JR, Gutwin KN, Keating AE. (2008) *Predicting helix orientation for coiled-coil dimers*. Proteins 72, 1048-65. PMCID: PMC2562949.
27. Zizlsperger N, Malashkevich VN, Pillay S, Keating AE. (2008) *Analysis of coiled-coil interactions between core proteins of the spindle pole body*. Biochemistry 147, 11858-68. PMID: 18850724.
28. Grigoryan G, Reinke AW, Keating AE. (2009) *Design of protein-interaction specificity gives selective bZIP-binding peptides*. Nature 458, 859-64. PMCID: PMC2748673.
29. Zhang H, Chen J, Wang Y, Peng L, Dong X, Lu Y, Keating AE, Jiang T. (2009) *A computationally guided protein-interaction screen uncovers coiled-coil interactions involved in vesicular trafficking*. J Mol Biol. 392, 228-41. PMID: 19591838.
30. Schneider M, Fu X, Keating AE. (2009) *X-ray vs. NMR structures as templates for computational protein design*. Proteins 77, 97-110. PMCID: PMC2732408.
31. Apgar JR, Hahn S, Grigoryan G, Keating AE. (2009) *Cluster expansion models for flexible-backbone protein energetics*. J Comput Chem. 30, 2402-13. PMID: 19360809.
32. Fire E, Gullá SV, Grant RA, Keating AE. (2010) *Mcl-1-Bim complexes accommodate surprising point mutations via minor structural changes*. Protein Sci. 19, 507-19. PMCID: PMC2866276.
33. Reinke AW, Grigoryan G, Keating AE. (2010) *Identification of bZIP interaction partners of viral proteins HBZ, MEQ, BZLF1, and K-bZIP using coiled-coil arrays*. Biochemistry 49,1985-97. PMCID: PMC2841013.
34. Zizlsperger N, Keating AE. (2010) *Specific coiled-coil interactions contribute to a global model of the structure of the spindle pole body*. J Struct Biol. 170, 246-56. PMID: 20139001.
35. Reinke AW, Grant RA, Keating AE. (2010) *A synthetic coiled-coil interactome provides heterospecific modules for molecular engineering*. J Am Chem Soc. 132, 6025-31. PMCID: PMC2940225.

36. Dutta S, Gullá S, Chen TS, Fire E, Grant RA, Keating AE. (2010) *Determinants of BH3 binding specificity for Mcl-1 versus Bcl-x<sub>L</sub>*. J Mol Biol. 398, 747-62. PMCID: PMC2896288.
37. Stewart ML, Fire E, Keating AE, Walensky LD. (2010) *The MCL-1 BH3 helix is an exclusive MCL-1 inhibitor and apoptosis sensitizer*. Nat Chem Biol. 6, 595-601. PMCID: PMC3033224.
38. Hahn S, Ashenberg O, Grigoryan G, Keating AE. (2010) *Identifying and reducing error in cluster-expansion approximations of protein energies*. J Comput Chem. 31, 2900-14. PMID: 20602445.
39. Trigg J, Gutwin K, Keating AE, Berger B. (2011) *Multicoil2: predicting coiled coils and their oligomerization states from sequence in the twilight zone*. PLoS One, 6(8):e23519. PMCID: PMC3162000.
40. Schreiber G, Keating AE. *Protein binding specificity versus promiscuity*. (2011) Curr Opin Struct Biol. 21, 50-61. PMCID: PMC3053118.
41. Chen TS, Reinke AW, Keating AE. (2011) *Design of peptide inhibitors that bind the bZIP domain of Epstein-Barr virus protein BZLF1*. J Mol Biol. 408, 304-20. PMCID: PMC3087387.
42. Ashenberg O, Rozen-Gagnon K, Laub MT, Keating AE. (2011) *Determinants of homodimerization specificity in histidine kinases*. J Mol Biol. 413, 222-35. PMCID: PMC3210482.
43. Thompson KE, Bashor CJ, Lim WA, Keating AE. (2012) *SYNZIP protein interaction toolbox: in vitro and in vivo specifications of heterospecific coiled-coil interaction domains*. ACS Synth Biol. 1, 118-29. PMCID: PMC3339576.
44. Chen TS, Keating AE. (2012) *Designing specific protein-protein interactions using computation, experimental library screening, or integrated methods*. Protein Sci. 21, 949-63. PMCID: PMC3403433.
45. London N, Gullá S, Keating AE, Schueler-Furman O. (2012) *In silico and in vitro elucidation of BH3 binding specificity toward Bcl-2*. Biochemistry 51, 5841-50. PMCID: PMC3711574.
46. DeBartolo J, Dutta S, Reich L, Keating AE. (2012) *Predictive Bcl-2 family binding models rooted in experiment or structure*. J Mol Biol. 422, 124-44. PMCID: PMC3600422.
47. Yin WB, Reinke AW, Szilágyi M, Emri T, Chiang YM, Keating AE, Pócsi I, Wang CC, Keller NP. (2013) *bZIP transcription factors affecting secondary metabolism, sexual development and stress responses in Aspergillus nidulans*. Microbiology 159 (Pt 1), 77-88. PMCID: PMC3542729.
48. Negron C, Keating AE. (2013) *Multistate protein design using CLEVER and CLASSY*. Methods Enzymol. 523, 171-90. PMID: 23422430.
49. Chen TS, Palacios H, Keating AE. (2013) *Structure-based redesign of the binding specificity of anti-apoptotic Bcl-x(L)*. J Mol Biol. 425, 171-85. PMCID: PMC3557458.
50. Ashenberg O, Keating AE, Laub MT. (2013) *Helix bundle loops determine whether histidine kinases autophosphorylate in cis or in trans*. J Mol Biol. 425, 1198-209. PMCID: PMC3636764.
51. Dutta S, Chen TS, Keating AE. (2013) *Peptide ligands for pro-survival protein Bfl-1 from computationally guided library screening*. ACS Chem Biol. 8, 778-88. PMCID: PMC3631442.
52. Reinke AW, Baek J, Ashenberg O, Keating AE. (2013) *Networks of bZIP protein-protein interactions diversified over a billion years of evolution*. Science 340, 730-4. PMCID: PMC4115154.
53. Kaplan JB, Reinke AW, Keating AE. (2014) *Increasing the affinity of selective bZIP-binding peptides through surface residue redesign*. Protein Sci. 23, 940-53. PMCID: PMC4088978.
54. DeBartolo J, Taipale M, Keating AE. (2014) *Genome-wide prediction and validation of peptides that bind human pro-survival Bcl-2 proteins*. PLoS Computational Biology 10, e1003693. PMCID: PMC4072508.
55. Foight GW, Ryan JA, Gullá SV, Letai A, Keating AE. (2014) *Designed BH3 Peptides with High Affinity and Specificity for Targeting Mcl-1 in Cells*. ACS Chem Biol. 9, 1962-8. PMCID: PMC4168798.

56. Reich LL, Dutta S, Keating AE. (2014) *SORTCERY - a high-throughput method to affinity rank peptide ligands*. J Mol Biol. 427:2135-50. PMID: PMC4394037.
57. Dutta S, Ryan J, Chen TS, Kougentakis C, Letai A, Keating AE. (2014) *Potent and specific peptide inhibitors of human pro-survival protein Bcl-x<sub>L</sub>*. J Mol Biol. 427, 1241-53. PMID: PMC4357494.
58. Negron C, Keating AE. (2014) *A Set of computationally designed orthogonal antiparallel homodimers that expands the synthetic coiled-coil toolkit*. J Am Chem Soc. 136, 16544-56. PMID: PMC4277747.
59. Potapov V, Kaplan JB, Keating AE. (2015) *Data-driven prediction and design of bZIP coiled-coil interactions*. PLoS Comput Biol. 11: e1004046. PMID: PMC4335062.
60. Foight GW, Keating AE. (2015) *Locating Herpesvirus Bcl-2 Homologs in the Specificity Landscape of Anti-Apoptotic Bcl-2 Proteins*. J Mol Biol. 427, 2468-90. PMID: PMC4520770.
61. Chen R, Rishi HS, Potapov V, Yamada MR, Yeh VJ, Chow T, Cheung CL, Jones AT, Johnson TD, Keating AE, DeLoache WC, Dueber JE. (2015) *A Barcoding Strategy Enabling Higher-Throughput Library Screening by Microscopy*. ACS Synth Biol. 4, 1205-1216. PMID: PMC4654675.
62. Burrer CM, Foight GW, Keating AE, Chan GC. (2015) *Selective peptide inhibitors of antiapoptotic cellular and viral Bcl-2 proteins lead to cytochrome c release during latent Kaposi's sarcoma-associated herpesvirus infection*. Virus Res. 211, 86-88. PMID: PMC4792251.
63. Riquelme DN, Meyer AS, Barzik M, Keating A, Gertler FB. (2015) *Selectivity in subunit composition of Ena/VASP tetramers*. Biosci Rep. 35: e00246. PMID: PMC4520770
64. Sirin S, Apgar JR, Bennett EM, Keating AE. (2016) *AB-Bind: Antibody Binding Mutational Database for Computational Affinity Predictions*. Protein Sci. 25, 393-409. PMID: PMC4815335.
65. Foight GW, Keating AE. (2016) *Comparison of the peptide binding preferences of three closely related TRAF paralogs: TRAF2, TRAF3, and TRAF5*. Protein Sci. 25, 1273-1289. PMID: PMC4918428.
66. Chang JB, Kim YH, Thompson E, No YH, Kim NH, Arrieta J, Manfrinato VR, Keating AE, Berggren KK. (2016) *The Orientations of Large Aspect-Ratio Coiled-Coil Proteins Attached to Gold Nanostructures*. Small 12, 1498-1505. PMID: 26799936.
67. Rezaei Araghi R, Ryan JA, Letai A, Keating AE. (2016) *Rapid Optimization of Mcl-1 Inhibitors using Stapled Peptide Libraries Including Non-Natural Side Chains*. ACS Chem Biol. 11, 1238-1244. PMID: PMC4874891.
68. Reich LL, Dutta S, Keating AE. (2016) *Generating High-Accuracy Peptide-Binding Data in High Throughput with Yeast Surface Display and SORTCERY*. Methods Mol Biol. 1414: 233-47. PMID: PMC4912380.
69. Rezaei Araghi R, Keating AE. (2016) *Designing helical peptide inhibitors of protein-protein interactions*. Curr Opin Struct Biol. 39: 27-38. PMID: PMC5282971.
70. Foight GW, Chen TS, Richman D, Keating AE. (2017) *Enriching Peptide Libraries for Binding Affinity and Specificity Through Computationally Directed Library Design*. Methods Mol Biol. 1561:213-232 PMID: PMC5553629.
71. Rodríguez-Martínez JA, Reinke AW, Bhimsaria D, Keating AE, Ansari AZ. (2017) *Combinatorial bZIP dimers display complex DNA-binding specificity landscapes*. Elife. pii: e19272. PMID: PMC5349851.
72. Jenson JM, Ryan JA, Grant RA, Letai A, Keating AE. (2017) *Epistatic mutations in PUMA BH3 drive an alternate binding mode to potently and selectively inhibit anti-apoptotic Bfl-1*. Elife. pii: e25541. PMID: PMC5464773.
73. Park WM, Bedewy M, Berggren KK, Keating AE. (2017) *Modular assembly of a protein nanotriangle using orthogonally interacting coiled coils*. Sci Rep. 7, 10577. PMID: PMC5585338.
74. Frappier V, Duran M, Keating AE. (2017) *PixelDB: Protein-peptide complexes annotated with structural conservation of the peptide binding mode*. Protein Sci. 27: 276-285. PMID: PMC5734312.

75. Rezaei Araghi R, Bird GH, Ryan JA, Jenson JM, Godes M, Pritz JR, Grant RA, Letai A, Walensky LD, Keating AE. (2018) *Iterative optimization yields Mcl-1-targeting stapled peptides with selective cytotoxicity to Mcl-1-dependent cancer cells*. Proc Natl Acad Sci USA 115:E886-E895. PMID: PMC5798337.
76. Jenson JM, Xue V, Stretz L, Mandal T, Reich LL, Keating AE. (2018) *Peptide design by optimization on a data-parameterized protein interaction landscape*. Proc Natl Acad Sci U S A. 115(44):E10342-E10351. PMID: PMC6217393.
77. Frappier V, Jenson JM, Zhou J, Grigoryan G, Keating AE. (2019) *Tertiary structural motif sequence statistics enable facile prediction and design of peptides that bind anti-apoptotic Bfl-1 and Mcl-1*. Structure 27(4):606-617. PMID: PMC6447450.
78. Shemesh OA, Linghu C, Piatkevich KD, Goodwin D, Celiker OT, Gritton H, Romano M, Gao R, Yu CC, Tseng HA, Bensussen S, Narayan S, Yang CT, Freifeld L, Siciliano C, Gupta I, Wang J, Pak N, Yoon YG, Ullmann JFP, Guner-Ataman B, Noamany H, Sheinkopf ZR, Park WM, Asano S, Keating AE, Trimmer JS, Reimer J, Tolias A, Bear MF, Tye KM, Han X, Ahrens MB, Boyden ES. (2020) *Precision Calcium Imaging of Dense Neural Populations via a Cell-Body-Targeted Calcium Indicator*. Neuron S0896-6273(20)30398-6. PMID: PMC7415598
79. Linghu C, Johnson SL, Valdes PA, Shemesh OA, Park WM, Park D, Piatkevich KD, Wassie AT, Liu Y, An B, Barnes SA, Celiker OT, Yao CC, Yu CJ, Wang R, Adamala KP, Bear MF, Keating AE, Boyden ES. (2020) *Spatial Multiplexing of Fluorescent Reporters for Imaging Signaling Network Dynamics*. Cell. 183(6):1682-1698.e24. PMID: PMC7771521
80. Frappier V, Keating AE. (2021) *Data-driven computational protein design*. Curr Opin Struct Biol. 69: 63-69. PMID: PMC8405559.
81. Hwang T, Parker S, Hill SM, Ilunga MW, Grant RA, Mouneimne G, Keating AE. (2021) *A distributed residue network permits conformational binding specificity in a conserved family of actin remodelers*. eLife 10:e70601 DOI: [10.7554/eLife.70601](https://doi.org/10.7554/eLife.70601). PMID: PMC8639148.
82. Hwang T, Grant RA, Ilunga MW, Sivaraman V, Keating AE. (2021) *Native proline-rich motifs exploit sequence context to target actin-remodeling Ena/VASP proteins*. eLife 11:e70680 DOI: [0.7554/eLife.70680](https://doi.org/10.7554/eLife.70680) PMID: [PMC8789275](https://pubmed.ncbi.nlm.nih.gov/38789275/)
83. Swanson S, Sivarama V, Grigoryan G, Keating AE. (2022) *Tertiary motifs as building blocks for the design of protein-binding peptides*. Protein Science, in press. <http://dx.doi.org/10.1002/pro.4322>

### Preprints

- Li A, Sundar V, Grigoryan G, Keating AE. (2022) *TERMinator: A Neural Framework for Structure-Based Protein Design using Tertiary Repeating Motifs*. arXiv doi 10.48550/arXiv.2204.13048
- Aguilar F, Yu S, Grant R, Swanson S, Ghose D, Su BG, Sarosiek K, Keating AE. (2022) *Discovery of diverse human BH3-only and non-native peptide binders of pro-apoptotic BAK indicate that activators and inhibitors use a similar binding mode and are not distinguished by binding affinity or kinetics*. BioRxiv doi 10.1101/2022.05.07.491048
- Halpin J, Whitney D, Rigoldi F, Sivaraman V, Singer A, Keating AE. (2022) *High-throughput discovery of TRAF6-interacting peptides identifies determinants of positive and negative design and shows known and candidate human interaction partner motifs are not optimized for affinity*. BioRxiv doi 10.1101/2022.05.08.491058

### Book

Keating A.E., ed. *Methods in Protein Design*, Elsevier, 2013.