

Curriculum Vitae

Julia M. Shifman

Associate Professor

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Education

- 1993-1998 **University of Pennsylvania**, Ph. D. in Biophysics
Thesis: "Heme-Heme and Heme-Protein Interactions Inside De Novo Design Four Helix Bundles." Advisor: Prof. P. Leslie Dutton
- 1990-1993 **University of Minnesota**, Minneapolis, MN, B. Sc. in Physics summa cum laude
- 1989-1990 **Moscow Institute of Physics and Technology**, Department of General and Applied Physics

Academic positions

- 2018- present Chair, Department of Biological Chemistry
- 2012-present Associate Professor with tenure, **Hebrew University of Jerusalem**, Jerusalem, Israel
- 2004-2012* Assistant Professor, **Hebrew University of Jerusalem**, Jerusalem, Israel
- 1998-2004 Postdoctoral Associate, **California Institute of Technology**, Pasadena, CA
Advisor: Prof. S. L. Mayo

*Maternity leaves were taken in 2006, 2008, and 2012.

Visiting positions

- 2021-2022 Visiting faculty, **UCSF, San Francisco**, USA
- 2013-2014 Visiting Faculty, **EMBL, Hamburg**, Germany
- 2011-2012 Visiting Faculty, the Donnelly Center for Cellular and Biomolecular Research, **University of Toronto**. Associated with labs of Sachdev Sidhu and Philip Kim.
- 2003 Visiting Scientist, **Weizmann Institute of Science**

Teaching Experience

- 2016-2017, 2019 mini course for M. Sc. and Ph. D. students "Protein Design and Evolution" was taught at University of Granada (2016) and University of Vienna (2017) through the Erasmus staff motility program
- 2006-present "Protein Design and Evolution", graduate course
- 2007-present "Principles of Protein Folding"- graduate course
- 2018- present Biochemistry of the Cell, - 2nd year undergraduate course
- 2010-2011 "The Art of Scientific Presentation"- graduate course
- 2005-2006 "Introduction to Protein World: Sequence, Structure, Function"-undergraduate course

Editorial Activities

- 2020-present Editorial Board, Protein Engineering, Design, and Selection (PEDS)

2016 Section Editor in *Current Opinions in Structural Biology* for the August 2017 issue
"Protein Engineering and Design"

Services at Hebrew University

2018-present Chair, Department of Biological Chemistry
2005-2015 Organizer of all-Israeli forum in Protein Engineering
2005-2007 Organizer of a departmental seminar in Biochemistry
2005-present Served as a member at various Ph. D. and M. Sc. thesis committees in Hebrew University and other Israeli Universities

Organization of international meetings

2021-2022 Organizer of the ISF workshop: Advances in Protein design: from therapeutic proteins to synthetic biology, Oct. 23-27, 2022, Upper Galilee, Israel

2018 Scientific Advisor, Protein Design and Engineering meeting, Frankfurt, Germany, October 2018

2016-2017 Co-chair of the 4th International Conference on Protein-Protein Interactions, December 3-7th, 2017. Eilat, Israel;

2015 Organizer of International Advanced School in Computational and Structural Biology for graduate students and postdocs, Israel Institute of Advanced Studies, Jerusalem, January 10-14, 2016. *Among our lecturers were three Nobel Laureates: Roger Kornberg, Michael Levitt, and Ada Yonath. More than 100 students attended including more than 30 from abroad.*

2013-2015 Advisory Committee, GCTBio annual conference on Protein-Protein interactions (San Diego/Boston)

Peer Reviewed Publications

1. **Shifman, J. M.**, Moser, C. C., Kalsbeck, W. A., Bocian, D. F., and Dutton, P.L. (1998) Functionalized de novo designed proteins: mechanism of proton coupling to heme oxidation/reduction in heme protein maquettes. *Biochemistry* 37, 16815-16829.
2. **Shifman, J. M.**, Gibney, B. R., Sharp, R. E., and Dutton, P. L. (2000) Heme redox potential control in de novo designed 4-helix bundle proteins. *Biochemistry* 39, 14813-14821.
3. Shimaoka, M., **Shifman, J. M.**, Takagi, J., Mayo, S. L., Springer, T. A. (2000) Computational design of an integrin I domain stabilized in the high affinity conformation. *Nature Struc. Biol.* 7(8), 674-678.
4. **Shifman J. M.** and S. L. Mayo (2002) Modulating calmodulin specificity through computational protein design. *J. Mol. Biol.* 323, 417-423.
5. **Shifman J. M.** and S. L. Mayo (2003) Exploring the origins of binding specificity through computational redesign of calmodulin. *Proc. Nat. Acad. Sci. USA* 100(23) 13274-13279.

7. Yanover C., Fromer M., and **Shifman J. M.** (2007) Dead-End Elimination for Multi-state Protein Design, *J. Comp. Chem.*, 28 (13) 2122-2129.
8. **Shifman J. M.** (2008) Intricacies of beta-sheet protein design, *Structure* 16, 1751-1752, Impact factor 6.79;
9. Yosef E., Politi R., Choi M. H., and **Shifman, J. M.** Computational design of calmodulin mutants with up to 900-fold increase in binding specificity (2009), *J. Mol. Biol.*, 385, 1470-1480.

10. Sharabi O. , Peleg Y. , Mashiach E. , Vardy E., Ashani Y, Silman I., Sussman J. L., and **Shifman J. M.** (2009) Design, expression, and characterization of mutants of fasciculin optimized for interaction with its target acetylcholinesterase, *Prot. Eng. Des. Sel.*, 22, 641-648.
11. Fromer M. and **Shifman J. M.** (2009) Tradeoff between stability and multispecificity in design of promiscuous proteins, *PLoS Comp. Biol.*, 5(12) e1000627.
12. Sharabi O., Yanover C., Dekel A. and **Shifman J. M.** (2011) Optimizing energy functions for design of protein-protein interfaces, *J. Comp. Chem.*, 32(1), 23-32.
13. Filchinski D., Sharabi O., Rueppel A., Vetter I. R., Herrmann, C., and **Shifman J. M.** (2010) What makes Ras an efficient molecular switch: A biophysical and structural study of Ras-GDP interactions with mutants of Raf, *J. Mol. Biol.*, 399 (3), 422-435.
14. Sharabi O., Dekel A. and **Shifman J. M.** (2011) Triathlon for energy functions: is there a winner for the design of protein-protein interactions? *Prot Struct Funct Bioinf*, 79(5): 1487-98.
15. Erijman A, Aizner Y and **Shifman J. M.** (2011) Multispecific recognition: mechanisms, evolution, and design, *Biochemistry*, 50 (5), 602-611. **reviewed by Faculty 1000.**
16. Erijman A., Dantes A, Bernehim R, **Shifman J. M.**^Pand Peleg Y. (2011) Transfer PCR (TPCR) - a highway for cloning and protein engineering, *J Struct Biol*, 175(2), 171-177.
17. Sharabi O., Erijman A., and **Shifman J. M.** (2013) Computational methods for controlling binding specificity. *Meth Enzym*, 523, 41-59.
18. Sharabi, O., Shirian, J., and **Shifman, J. M.** (2013) Predicting affinity- and specificity-enhancing mutations at protein-protein interfaces, *Biochem Soc Trans* 41, 1166-1169.
19. Erijman A., **Shifman J. M.** , Peleg Y. (2014) A single-tube assembly of DNA using the Transfer-PCR(TPCR) platform, *Meth Mol Biol*, 1116, 89-101. Impact factor 1.24; the journal placed 277 out of 364, cited by others 22 times;
20. Aizner Y., Sharabi O., Shirian J., Dakwar. G., Risman M., Avraham O. and **Shifman J. M.** (2014) Mapping the binding landscape of a picomolar protein-protein complex through computation and experiment, *Structure*, 22(4), 636-645. Impact factor 6.79; the journal placed 5 out of 45, cited 24 times
21. Sharabi O., Shirian J., Grossman M., Lebedinker, M., Sagi I., & **Shifman J. M.** (2014) Affinity- and specificity-enhancing mutations are frequent in multistpecific interaction between MMP14 and its inhibitor TIMP2. *PLoS ONE*, 9(4): e93712.
22. Murciano-Calles J., McLaughlin, M. E., Erijman A.; Hooda Y., Chakravorty N., Martinez J. C.; **Shifman J. M.**, and Sidhu S. (2014), Alteration of the C-terminal ligand specificity of the Erbin PDZ domain by allosteric mutational effects, *J. Mol. Biol.*, 426(21), 3500–3508.
23. Erijman A., Rosenthal E., and **Shifman J. M.** (2014), How structure defines affinity, *PLoS ONE*, 9(10): e110085.
24. Kafurke U., Erijman A., Aizner Y., **Shifman J. M.**, Eichler J. (2015), Synthetic peptides mimicking the binding site of human acetylcholinesterase for its inhibitor fasciculin 2, *J. Pept. Sci.* 21(9), 723-730.
25. Rosenfeld L., Shirian J., Zur Y., Levaot N., **Shifman J. M.**, and Papo N. (2015), Combinatorial and computational approaches to identify important interactions in the macrophage colony stimulating factor (M-CSF)/c-fms complex, *J. Biol. Chem.* 290 (43), 26180–26193.
26. Erijman A., **Shifman J. M.** (2016) Ras effectors from biophysical and structural perspective, *Mini Rev Med Chem*, 16(5):370-5.

27. Rosenfield L., Heyne M., **Shifman J. M.** and Papo, N. (2016) Protein engineering by combined computational and in vitro evolution approaches, *Trends in Biochem Sciences*, 41(5), 421-33.
28. Leung I., Dekel A., **Shifman J.M.**, and Sidhu S. S. (2016), Saturation scanning of ubiquitin variants reveals a common hot spot for binding to USP2 and USP21, *Proc. Nat. Acad. Sci. USA*, 113(31):8705-10.
29. Shirian J., Sharabi O., **Shifman J. M.** Cold spots in protein binding (2016), *Trends in Biochem Sciences*, 41(9):739-45. Opinion article.
30. Rabinovich E., Heyne M., Bakhman, A., Kosloff, M., **Shifman, J. M.** and Papo, N. (2017) Identifying residues that determine SCF molecular-level interactions through a combination of experimental and *in silico* analyses, *J. Mol. Biol.*, 429(1):97-114
31. Arkadash V., Yosef, G., Shirian, J., Cohen, I., Horev, Y. Grossman, M., Sagi, I., Radisky, E. S., **Shifman J. M.**, and Papo, N^{PM}. (2017) Development of high-affinity and high-specificity inhibitors of MMP-14 through computational design and directed evolution, *J. Biol. Chem.*, 292 (8), 3481-3495;
32. **Shifman J. M.** and Papo N. (2017) Editorial overview: Engineering and Design: New trends in designer proteins, *Curr. Opin. Struct. Biol.*, 45, IV-VI.
33. Cohen A., Rosenthal E. and **Shifman, J. M.** (2017) Analysis of Structural Features Contributing to Weak Affinities of Ubiquitin/Protein Interactions, *J. Mol. Biol.*, 429(22), 3353-3362.
34. Shirian J., Arkadash V., Cohen I., Sapir T., Radisky E. S., Papo N. and **Shifman J. M.** (2018) Converting a broad matrix metalloproteinase family inhibitor into a specific inhibitor of MMP-9 and MMP-14, *FEBS lett*, 592(7):1122-1134.
35. Moshe Ben-David, Haiming Huang, Mark GF Sun^s Carles Corbi-Verge, Evangelia Petsalaki, Ke Liu, David Gfeller, Pankaj Garg, Wolfram Tempel, Irina Sochirca, **Julia M Shifman**, Alan Davidson, Jinrong Min, Philip M Kim, Sachdev S Sidhu (2019), Allosteric Modulation of Binding Specificity by Alternative Packing of Protein Cores, *J. Mol. Biol.*, 431(2), 336-350.
36. M Heyne, N Papo, **J. M. Shifman** (2020) Generating quantitative binding landscapes through fractional binding selections combined with deep sequencing and data normalization, *Nature Commun.*, 11 (1), 1-7, Impact factor 13.6, cited 11 times
Press release about the article: <https://new.huji.ac.il/news/השיטה-החדשה-מאפשרת-פיתוחן-של-תרופות-ספציפיות-עבור-כל-חלבון-מטרה-ועבור-מחלות-רבות>
The article is highlighted in Bissette AJ, (2021) Comm. Chemistry 4, 166
37. Thillaivillalan D., Singh S., Killoran R. C., Singh A., Xu X., **Shifman J. M.**, Smith M. J. (2020) RASSF effectors couple diverse Ras subfamily GTPases to the Hippo pathway. *Science Signal.*, 13(653), eabb4778.
38. Heyne M., Shirian J., Cohen I., Peleg, Y., Radisky, E. R., Papo N., **Shifman J. M.** (2021) Climbing up and down binding landscapes through deep mutational scanning of three homologous protein-protein complexes. *JACS*, 143, 41, 17261-17275,
The article is highlighted in Bissette AJ, (2021) Comm. Chemistry 4, 166
39. Bonnadio A. and **Shifman J. M.** (2021) Computational design and experimental optimization of protein binders for biomedical applications, *Prot. Eng. Des. Sel.*, 34, gzab020
40. Singh A., Erijman A., Noronha A., Kumar H., Peleg Y., Yarden Y., **Shifman J. M.** (2021) RASSF5 (NORE1A) variants engineered for high-affinity Ras binding promote anti-cancer activities in lung adenocarcinoma, *J. Biol. Chem.*, 297(6), 101353.

41. Rabinovitch E., Mihara K., Sananes A. Zaretsky M., Heyne M. **Shifman J. M.**, Aharoni A., Hollenberg M. D., Papo N. (2021), Inhibition of the PAR1 canonical cleavage and activation sequence: applying a KLK4 proteinase substrate capture approach as an antagonist strategy, *Sci. Rep.* 11(1), 1-13.

42. Gurusinghe, S., Oppenheimer, B. and **Shifman J. M.** (2022), Cold spots are universal in protein-protein interactions, *Prot. Sci.*, 31 (10), e4435, Impact factor 6.7.

43. Bonadio, A., B Wenig, A Hockla, ES Radisky^r, **JM Shifman^r** (2022) A broad matrix metalloproteinase inhibitor with designed loop extension exhibits ultrahigh specificity for MMP-14 bioRxiv, 2022.12. 29.522231, *J. Mol. Biol.*, in press.

44. Tomazini A., **Shifman J. M.** (2023) Targeting Ras by Protein Engineering, submitted to Oncotarget

45. Bonadio A., Oguche S., Lavy, T., Kleinfeld O. and **Shifman J. M.** (2023) Computational design of Matrix Metalloproteinase-9 (MMP-9) resistant to auto-cleavage, bioRxiv 10.1101/2023.04.11.536383 submitted to *Biochem. J.*

Book Chapters

Kumar H & **Shifman JM** (2020) Predicting mutational effects. Chapter 6, *In Protein interactions: computational methods, analysis and applications*, ed Gromiha MM (World Scientific Publishing Singapore), 145

Shifman J. M. and Singh A. (2018) Computational Protein Design, Encyclopaedia of Biophysics, Ed. Gordon C. K. Roberts and Anthony Watts, DOI: 10.1007/978-3-642-35943-9_10084-1

Shifman J. M. and M. Fromer (2009) Search algorithms in *Protein Engineering and Design*, (S. Park and J. Cochran, Eds), Taylor & Francis. Boca Raton, 293-312

Shifman J. M. (2009) Computational design of protein-protein interactions in *Computational Protein-Protein interactions*, ed. Gideon Schreiber and Ruth Nussinov. Taylor & Francis, CRC press, 129-144.

Patents

Patent # 6,951,927, October 4, 2005; “Proteins With Integrin-Like Activity”, together with Timothy A. Springer, Stephen L. Mayo, and Motomu Shimaoka

US Provisional patent # 62/419.497 filed 2016: “Peptide Inhibitors Against MMP-14 and MMP-9 ” together with Niv Papo, Jason Shirian, and Valeria Arkadash