Daniel A. Bachovchin, Ph.D.

Memorial Sloan Kettering Cancer Center
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Professional Appointments:

- **Associate Member**, Chemical Biology Program, Sloan Kettering Institute, Memorial Sloan Kettering Cancer Center (MSKCC), June 2021 – present
- **Assistant Member**, Chemical Biology Program, Sloan Kettering Institute, MSKCC, September 2015 – June 2021
- **Faculty Member**, Tri-Institutional PhD Program in Chemical Biology of MSKCC, The Rockefeller University, and Weill Cornell Medical College, September 2015 – present
- **Faculty Member**, Gerstner Sloan-Kettering Graduate School of Biomedical Sciences, MSKCC, September 2015 – present
- **Faculty Member**, Pharmacology Program, Weill Graduate School of Medical Sciences, Cornell University, September 2015 – present

Education:

- **The Broad Institute of MIT and Harvard**, Cambridge, MA
  Postdoctoral Research Fellow, June 2011- August 2015
  Research Advisor: Professor Todd R. Golub
- **The Scripps Research Institute**, La Jolla, CA
  Ph.D. in Chemistry, May 2011
  Research Advisor: Professor Benjamin F. Cravatt
- **Harvard College**, Cambridge, MA
  A.B. in Chemistry, June 2005
  Magna Cum Laude, High Honors in Field
  Research Advisor: Professor M.-Christina White

Honors and Awards:

- Anna Fuller Fund Award, March 2021-February 2022
- Gabrielle's Angel Foundation Fellowship, July 2018-June 2021
- Pershing Square Sohn Prize for Young Investigators in Cancer Research, July 2018-June 2021
- Sloan Research Fellow in Chemistry, 2018

- Pew-Stewart Scholar Award for Cancer Research, July 2017-June 2021
- Stand Up to Cancer (SU2C) Innovative Research Grant, July 2017-June 2020
- Josie Robertson Investigator (MSKCC), September 2015 – August 2020
- California Breast Cancer Research Program Graduate Fellowship, July 2010-May 2011
- National Science Foundation Predoctoral Fellowship, September 2006-September 2009
- The Scripps Research Institute Dean's Fellowship, January 2005-January 2006
- John Harvard Scholar, 2003-2004 (Top 5% of Class GPA)
- Harvard College Research Program Fellowship, June 2003-August 2003
- Harvard College Scholar, 2001-2002, 2002-2003, 2004-2005

Publications:

40. Sharif, H.*; Hollingsworth, R.L. *; Griswold, A.R.*; Hsiao, J.C.; Wang, Q.; **Bachovchin, D.A.** [#] ; Wu, H. [#] "Structural mechanism of CARD8 regulation by DPP9." *Immunity,* 2021, *in press*.

39. Hollingsworth, R.L. *; Sharif, H. *; Griswold, A.R. *; Fontana, P.; Mintseris, J.; Dagbay, K.B.; Paulo, J.A.; Gygi, S.P.; **Bachovchin, D.A.** [#]; Wu, H. [#] "DPP9 sequesters the NLRP1 C-terminus to repress inflammasome activation." *Nature*, 2021, 592, 778-783.

38. **Bachovchin, D.A.** [#] "NLRP1: A jack of all trades, or a master of one?" *Mol. Cell*, 2021, 81, 423-425.

37. Hollingsworth, R.L. *; David, L.*; Li, Y.*; Griswold, A.R.; Ruan, J.; Sharif, H.; Fontana, P.; Orth-He, E.L.; Fu, T.M.; **Bachovchin, D.A.**; Wu, H. "Mechanism of filament formation in UPA-promoted CARD8 and NLRP1 inflammasomes" *Nature Commun*. 2021, 12, 189.

36. Chui, A.C.; Griswold, A.R.; Taabazuing, C.Y.; Orth, E.L.; Gai, K.; Rao, S.D.; Ball, D.P.; Hsiao, J.C.; **Bachovchin, D.A.** [#] "Activation of the CARD8 inflammasome requires a disordered region." *Cell Reports*. 2020, 33, 108264.

35. Johnson, D.C.; Okondo, M.C.; Orth, E.L.; Rao, S.D.; Huang, H.C.; Ball, D.P.; **Bachovchin, D.A.** [#] "DPP8/9 inhibitors activate the CARD8 inflammasome in resting lymphocytes." *Cell Death Dis*. 2020, 11, 628.

34. Taabazuing, C.Y.; Griswold, A.R.; **Bachovchin, D.A.** [#] "The NLRP1 and CARD8 inflammasomes." *Immunological Reviews*. 2020, doi: 10.1111/imr.12884.

33. Ball, D.P.*; Taabazuing, C.Y.*; Griswold, A.R.; Orth, E.L.; Rao, S.D.; Kotliar, I.B.; Vostal, L.E.; Johnson, D.C.; **Bachovchin, D.A.** [#] "Caspase-1 interdomain linker cleavage is required for pyroptosis." *Life Sci Alliance*. 2020, 3, e202000664.

32. Griswold, A.R.; Ball, D.P.; Bhattacharjee, A.; Chui, A.J.; Rao, S.D.; Taabazuing, C.Y.; **Bachovchin, D.A.** [#] "DPP9's enzymatic activity and not its binding to CARD8 inhibits inflammasome activation." *ACS Chem Biol*. 2019, 14, 2424-2429.

31. Gai, K.*; Okondo, M.C.*; Rao, S.D.; Chui, A.J.; Ball, D.P.; Johnson, D.C.; **Bachovchin, D.A.** [#] "DPP8/9 Inhibitors are universal activators of functional NLRP1 alleles." *Cell Death Dis*. 2019, 10, 587.

30. Griswold, A.R.; Cifani, P.; Rao, S.D.; Axelrod, A.J.; Miele, M.M.; Hendrickson, R.C.; Kensis, A.; **Bachovchin, D.A.**[#] "A chemical strategy for protease substrate profiling." *Cell Chem Biol*. 2019, 26, 901-907.

29. Chui, A.J*; Okondo, M.C.*; Rao, S.D.*; Gai, K.; Griswold, A.R.; Johnson, D.C.; Ball, D.P.; Taabazuing, C.Y.; Orth, E.L.; Vittimberga, B.A.; **Bachovchin, D.A.**[#] "N-terminal degradation activates the Nlrp1b inflammasome." *Science*. 2019, 365, 82-85.

28. Buckley B.J.; Aboelela, A.; Minaei, E.; Jiang, L.X.; Xu, Z.; Ali, U; Fildes, K; Cheung, C.Y.; Cook, S.M.; Johnson, D.C.; **Bachovchin, D.A.**; Cook, G.M.; Apte, M.; Huang, M.; Ranson, M.; Kelso, M.J. "6-Substituted Hexamethylene Amiloride (HMA) Derivatives as Potent and Selective Inhibitors of the Human Urokinase Plasminogen Activator for Use in Cancer." *J Med Chem*. 2018, 61, 8299-8320.

27. Johnson, D. C. *; Taabazuing, C. Y. *; Okondo, M. C.; Chui, A. J.; Rao, S. D.; Brown, F. C; Reed, C.; Peguero, E.; de Stanchina, E.; Kentsis, A.; **Bachovchin, D. A.**[#] "DPP8/9 inhibitor-induced pyroptosis for treatment of acute myeloid leukemia." *Nat Med*. 2018, 24, 1151-1156.

26. Okondo, M. C.*; Rao, S. D.*; Taabazuing, C. Y.*; Chui, A. J.; Poplawski, S. E.; Johnson, D. C.; **Bachovchin, D. A.**[#] "Inhibition of Dpp8/9 Activates the Nlrp1b Inflammasome." *Cell Chem Biol*. 2018, 25, 262-267.

25. Goel, P.; Jumpertz, T.; Mikles, D.C.; Tichá, A.; Nguyen, M.T.N.; Verhelst, S.; Hubalek, M.; Johnson, D.C.; **Bachovchin, D.A.**; Ogorek, I.; Pietrzik, C.U.; Strisovsky, K.; Schmidt, B.; Weggen, S. "Discovery and Biological Evaluation of Potent and Selective N-Methylene Saccharin-Derived Inhibitors for Rhomboid Intramembrane Proteases." *Biochemistry*. 2017, 56, 6713-6725.

24. Tichá, A.; Stanchev, S.; Vinothkumar, K.R.; Mikles, D.C.; Pachl, P.; Began, J.; Škerle, J.; Švehlová, K.; Nguyen, M.T.N.; Verhelst, S.H.L.; Johnson, D.C.; **Bachovchin, D.A.**; Lepšík, M.; Majer, P.; Strisovsky, K. "General and Modular Strategy for Designing Potent, Selective, and Pharmacologically Compliant Inhibitors of Rhomboid Proteases." *Cell Chem Biol*. 2017, 24, 1523-1536.

23. Taabazuing, C. Y.; Okondo, M. C.; **Bachovchin, D. A.**[#] "Pyroptosis and apoptosis pathways engage in bidirectional crosstalk in monocytes and macrophages." *Cell Chem Biol*. 2017, 24, 507-514.

22. Keckesova, Z.; Donaher, J.; DeCock, J.; Freinkman, E.; Lingrell, S.; **Bachovchin, D. A**.; Bierie, B.; Tischler, V.; Noske, A.; Reinhardt, F.; Thiru, P.; Golub, T.R.; Vance, J., Okondo, M.; Weinberg, R. "LACTB, a tumor suppressor that modulates lipid metabolism and differentiation." *Nature.* 2017, 543, 681-686.

21. Okondo, M.C.; Johnson, D. C., Sridharan, R., Go, E. B., Chui, A. J., Wang, M. S., Poplawski, S. E., Wu, W., Liu, Y.; Lai, J. H.; Sanford, D. G.; Arciprete, M. O.; Golub, T. R.; Bachovchin, W. W.; **Bachovchin, D. A**.[#] "Inhibition of DPP8/9 induces pro-caspase-1-dependent pyroptosis in monocytes and macrophages." *Nat Chem Biol.* 2017, 13, 46-53.

20. Hatzios, S. K.; Abel, S.; Martell, J.; Hubbard, T.; Sasabe, J.; Munera, D.; Clark, L.; **Bachovchin, D. A.**; Qadri, F.; Ryan, E. T.; Davis , B. M.; Weerapana, E.; Waldor, M. K. "Chemoproteomic profiling of host and pathogen enzymes active in cholera." *Nat Chem Biol.* 2016*,* 12, 268-274.

19. Zhao, N.; Darby, C.; Small, J.; **Bachovchin, D. A.**; Jiang, X.; Burns-Huang, K.; Botella, H.;

Ehrt, S.; Boger, D.; Anderson, E.; Cravatt, B. F.; Speers, A.; Fernandez-Vega, V.; Rosen, H.; Spicer, T.; Nathan, C. "A target-based screen against mycobacterial acid resistance protease implicates an additional periplasmic serine protease in regulation of intrabacterial pH homeostasis in *Mycobacterium tuberculosis*." *ACS Chem Biol.* 2015, 10, 364-371.

18. **Bachovchin, D. A.**; Koblan, L. W.; Wu, W.; Liu, Y.; Li, Y.; Zhao, P.; Woznica, I.; Shu, Y.; Lai, J. H.; Poplawski, S. E.; Kiritsy, C. P.; Healey, S. E.; DiMare, M.; Sanford, D. G.; Munford, R. S.; Bachovchin, W. W.; Golub, T. R. "A high-throughput, multiplexed assay for superfamily-wide profiling of enzyme activity." *Nat Chem Biol.* 2014, 10, 656-663.

17. Liu, X.; Dix, M.; Speers, A.; **Bachovchin, D. A**.; Zuhl, A. M.; Cravatt, B. F.; Kodadek, T. "Rapid development of a potent photo-triggered inhibitor of the serine hydrolase RBBP9." *ChemBioChem.* 2012, 13, 2082-2093.

16. Adibekian, A.; Martin, B.; Chang, J. W.; Hsu, K. L.; Tsuboi, K.; **Bachovchin, D. A**.; Speers, A. E.; Brown, S. J.; Spicer, T.; Fernandez-Vega, V.; Rosen, H.; Cravatt, B. F. "Confirming target engagement of reversible inhibitors in vivo by kinetically tuned activity-based probes." *J Am Chem Soc.* 2012, 134, 10345-10348.

15. Dillon, M. B.; **Bachovchin, D. A**.; Brown, S. J.; Finn, M. J.; Rosen, H.; Cravatt, B. F.; Mowen, K. A. "Novel inhibitors for PRMT1 discovered by high-throughput screening using activity-based fluorescence polarization." *ACS Chem Biol.* 2012, 7, 1198-1204.

14. Zuhl, A. M.; Mohr, J. T.; **Bachovchin, D. A.**; Niessen, S.; Hsu, K. L.; Berlin, J. M.; Dochnahl, M.; Lopez-Alberca, M. P.; Fu, G. C.; Cravatt, B. F. "Competitive activity-based protein profiling identifies aza-β-lactams as a versatile chemotype for serine hydrolase inhibition." *J Am Chem Soc.* 2012, 134, 5068-5071.

13. **Bachovchin, D. A**.; Cravatt, B. F. "The pharmacological landscape and therapeutic potential of serine hydrolases." *Nat Rev Drug Discov.* 2012, 11, 52-68.

12. Tsuboi, K.; **Bachovchin, D. A.**; Speers, A. E.; Spicer, T. P.; Fernandez-Vega, V.; Hodder, P.; Rosen, H.; Cravatt, B. F. "Potent and selective inhibitors of glutathione *S*-transferase omega 1 that impair cancer drug resistance." *J Am Chem Soc.* 2011, 133, 16605-16616.

11. Lone, A. M.; **Bachovchin, D. A.**; Westwood, D.; Speers, A. E.; Spicer, T. P.; Fernandez-Vega, V.; Chase, P.; Hodder, P. S.; Rosen, H.; Cravatt, B. F.; Saghatelian, A. "A substrate-free activity-based protein profiling screen for the discovery of selective PREPL inhibitors." *J Am Chem Soc*. 2011, 133, 11665-11674.

10. **Bachovchin, D. A**.*; Zuhl, A. M.*; Speers, A. E.; Wolfe, M. R.; Weerapana, E.; Brown, S. J.; Rosen, H.; Cravatt, B. F. "Discovery and optimization of sulfonyl acrylonitriles as selective, covalent inhibitors of protein phosphatase methylesterase-1." *J Med Chem*. 2011, 54, 5229-5226.

9. Adibekian, A.; Martin, B. R.; Wang, C.; Hsu, K.; **Bachovchin, D. A.**; Niessen, S.; Hoover, H.; Cravatt, B. F. "Click-generated triazole ureas as a versatile scaffold for ultrapotent in vivo-active serine hydrolase inhibitors." *Nat Chem Biol.* 2011, 7, 469-478.

8. **Bachovchin, D. A.**; Mohr, J. T.; Speers, A. E.; Wang, C.; Berlin, J. M.; Spicer, T. P.; Fernandez-Vega, V.; Chase, P.; Hodder, P. S.; Schürer, S. C.; Nomura, D. K.; Rosen, H.; Fu, G. C.; Cravatt, B. F. "Academic cross-fertilization by public screening yields a remarkable class of protein phosphatase methylesterase-1 inhibitors." *Proc Natl Acad Sci.* 2011, 108, 6811-6816.

7. Weerapana, E.*; Wang, C.*; Simon, G. M.; Khare, S.; Richter, F.; Dillon, M. B.; **Bachovchin, D. A.**; Mowen, K.; Baker, D.; Cravatt, B. F. "Quantitative reactivity profiling predicts functional cysteines in native and designed proteins." *Nature.* 2010, *468*, 790-795.

6. **Bachovchin, D. A.***; Ji, T.*; Li, W.*; Simon, G. M.; Hoover, H.; Niessen, S.; Cravatt, B. F. "A superfamily-wide portrait of serine hydrolase inhibition achieved by library-versus-library screening." *Proc Natl Acad Sci.* 2010, *107*, 20941-20946.

5. Knuckley, B.; Jones, J. E.; **Bachovchin, D. A.**; Slack, J.; Causey, C. P.; Brown, S. J.; Rosen, H.; Cravatt, B. F.; Thompson, P. R. "A Fluopol-ABPP HTS Assay to Identify PAD Inhibitors." *Chem Comm.* 2010, *46,* 7175-7177.

4. **Bachovchin, D. A.**; Wolfe, M. R.; Masuda, K.; Brown, S. J.; Spicer, T. P.; Fernandez-Vega, V.; Chase, P.; Hodder, P.S.; Rosen, H.; Cravatt, B. F. "Oxime esters as selective, covalent inhibitors of the serine hydrolase retinoblastoma-binding protein 9 (RBBP9)." *Bioorg Med Chem Lett*. 2010, *20*, 2254-2258.

3. **Bachovchin, D. A.;** Brown, S. J.; Rosen, H.; Cravatt, B. F.; "Identification of selective inhibitors of uncharacterized enzymes by high-throughput screening with fluorescent activity-based probes." *Nat. Biotechnol.* 2009, *27*, 387-394.

2. Fraunhoffer, K. J.; **Bachovchin, D. A.;** White, M.C. "Hydrocarbon oxidation *vs.* C-C Bond forming approaches for efficient syntheses of oxygenated molecules." *Org Lett.* 2005, *7,* 223-226.

1. Haddad, K. C.; Sudmeier, J. L.; **Bachovchin, D. A.**; Bachovchin, W.W.; "α-lytic protease can exist in two separately stable conformations with different His57 mobilities and catalytic activities." *Proc Natl Acad Sci.* 2005, *102*, 1006-1011.

*Equal contribution
Corresponding author

Invited Seminars:

- "Activation of the NLRP1 Inflammasome" March 23, 2021, EPFL Seminar Series (virtual), Lausanne, Switzerland, 2021
- "Activation of the NLRP1 Inflammasome" February 8, 2021, Gene Center, Ludwig-Maximilians Universitat (virtual), Munich, Germany, 2021
- "Activation of the NLRP1 Inflammasome" November 6, 2020, Inflammasome Therapeutics Summit (virtual), Boston, MA, 2020
- "Activation of the NLRP1 Inflammasome" November 3, 2020, Department of Pharmacology, Weill Cornell Medicine, New York, NY.
- "Recent insights into CARD8 activation" October 26, 2020, InflammaZoom Webinar Series, Cambridge Immunology Network, University of Cambridge, UK.
- "Activation of the NLRP1 Inflammasome" February 4, 2020, Oregon Health Sciences University,

Portland, OR.

- "Activation of the CARD8 Inflammasome" November 14, 2019, Gabrielle's Angel Foundation Symposium, Miami, FL.
- "Activation of the NLRP1 Inflammasome" October 31, 2019, Inflammasome Therapeutics Summit, Boston, MA.
- "Activation of the NLRP1 Inflammasome" October 1, 2019, Merck/NYC Symposium, New York, New York.
- "Activation of the NLRP1 Inflammasome" July 23, 2019, FASEB Microbial Pathogenesis, Aspen Snowmass, Colorado.
- "A Chemical Strategy for Protease Substrate Profiling" June 6, 2019, Pfizer Pershing Square Sohn Retreat, Pearl River, New York.
- "DPP8/9 inhibitor-induced pyroptosis." March 27, 2019, Immunology and Microbiology Program, University of Massachusetts Medical School, Worcester, Massachusetts.
- "DPP8/9 inhibitor-induced pyroptosis." September 26, 2018, EMBO Workshop – The Inflammasomes, Martinsried, Germany.
- "Small molecule inducers of pyroptosis." June 5, 2018, Gordon Research Conference – Proteolytic enzymes and their inhibitors, Lucca, Italy.
- "Mechanism and therapeutic potential of small molecule inducers of pyroptosis." April 12, 2018, Center for Experimental Therapeutics Retreat, New York, NY.
- "Mechanism and therapeutic potential of small molecule inducers of pyroptosis." March 18, 2018, Pew Annual Meeting, Marana, AZ.
- "Inhibition of DPP8/9 induces pyroptosis in monocytes and macrophages." March 10, 2017, Department of Chemical and Biomolecular Engineering, New York University Tandon School of Engineering, New York, New York.
- "Inhibition of DPP8/9 induces pyroptosis in monocytes and macrophages." February 8, 2017, GTCBio 3rd Protease Inhibitors in Drug Discovery Conference, San Diego, California.
- "Inhibition of DPP8/9 induces pyroptosis in monocytes and macrophages." February 6, 2017, Department of Chemistry and Biochemistry, Queens College, New York, New York.
- "Mechanism and therapeutic potential of small molecule pyroptosis inducers." January 12, 2017, Pediatric Grand Rounds, Memorial Sloan Kettering Cancer Center, New York, New York.
- "Small molecule inducers of pyroptotic cell death." October 25, 2016, New York Academy of Sciences – Emerging Paradigms in Drug Discovery & Chemical Biology, New York, New York.
- "Inhibition of DPP8/9 induces pro-caspase-1-dependent pyroptosis in monocytes and macrophages." September 15, 2016, Baruch College, New York, New York.

- "EnPlex: High-throughput, family-wide profiling of enzyme activity." March 2, 2016, GTCBio 2nd Protease Inhibitors in Drug Discovery Conference, San Diego, California.

- "EnPlex: High-throughput, family-wide profiling of enzyme activity." October 7, 2015, International Proteolysis Society Annual Meeting, Penang, Malaysia.

- "A High-Throughput Multiplexed Assay for Superfamily-wide Profiling of Enzyme Activity." November 5, 2014, Cambridge Biomedical and Luminex Technical Seminar, Cambridge, MA.

- "High-throughput, family-wide profiling of serine hydrolase inhibitors." November 13, 2013, Broad Institute Retreat, Boston, MA.

- "Multiplexed, high-throughput activity-based protein profiling of serine hydrolases." February 19, 2013, Broad Cancer Program Meeting, Cambridge, MA.

- "Aza-β-lactams as selective, covalent inhibitors of serine hydrolases." September 14, 2011, Applied Pharmaceutical Analysis Conference, Boston, MA.

- "Discovery of a remarkable class of protein phosphatase methylesterase-1 (PME-1) inhibitors." May 1, 2011, World Molecular Engineering Network Meeting, San Jose del Cabo, Mexico.

- "Discovery and characterization of a aza-β-lactam inhibitor of protein phosphatase methylesterase-1 (PME-1)." May 2, 2010, World Molecular Engineering Network Meeting, San Jose del Cabo, Mexico.

- "Identification of selective inhibitors of uncharacterized enzymes by high-throughput screening with fluorescent activity-based probes." September 11, 2009, TSRI Graduate Student Retreat, San Diego, CA.