

JAMES KENNETH CHEN

Assistant Professor

Department of Chemical and Systems Biology, Stanford University School of Medicine
269 Campus Drive, CCSR 3155, Stanford, CA 94305-5174

Tel: (650) 725-3582; Fax: (650) 723-2253

Email: jameschen@stanford.edu; Website: <http://chen.stanford.edu>

EDUCATION

Harvard College , Cambridge, MA	1987 – 1991
A. B. degree in Chemistry, <i>Summa cum laude</i>	
Research Advisor: George M. Whitesides	
Harvard University , Cambridge, MA	1991 – 1998
Ph.D. degree in Chemistry and Chemical Biology	
Research Advisor: Stuart L. Schreiber	
Marine Biological Laboratory , Woods Hole, MA	Summer 1998
<i>Embryology: Concepts and Techniques in Modern Developmental Biology</i>	
Johns Hopkins School of Medicine , Baltimore, MD	1999 – 2003
Postdoctoral Fellow, Department of Molecular Biology and Genetics	
Research Advisor: Philip A. Beachy	

PROFESSIONAL EXPERIENCE

Assistant Professor , Department of Molecular Pharmacology, Stanford University School of Medicine, Stanford, CA	2003 – 2006
Assistant Professor , by courtesy, Department of Chemistry, Stanford University, Stanford, CA	2003 – present
Executive Director , High-Throughput Bioscience Center, Stanford University, Stanford, CA	2003 – present
Assistant Professor , Department of Chemical and Systems Biology, Stanford University School of Medicine, Stanford, CA	2006 – present

HONORS AND AWARDS

Harvard University Certification of Distinction in Teaching	1991
National Science Foundation Predoctoral Fellowship	1991 – 1994
American Chemical Society Organic Chemistry Predoctoral Fellowship	1994 – 1995
Damon Runyon-Walter Winchell Postdoctoral Fellowship	1999 – 2002
American Cancer Society Postdoctoral Fellowship	2002 – 2003
W. Barry Wood, Jr. Research Award, Johns Hopkins School of Medicine	2003
Kimmel Scholar Award, Sidney Kimmel Foundation for Cancer Research	2004 – 2006
Basil O'Connor Starter Scholar Research Award, March of Dimes Foundation	2005 – 2007
Terman Fellow, Stanford University	2005 – 2008
Astellas USA Foundation Award	2005
Faculty Fellow, Stanford University School of Medicine	2006
Brain Tumor Society/Rachel Molly Markoff Research Chair	2006 – 2008
American Cancer Society Research Scholar Award	2008 – 2011
NIH Director's Pioneer Award	2008 – 2013

PROFESSIONAL SERVICE AND MEMBERSHIPS

Member , American Chemical Society	1989 – present
Member , Bio-X, Stanford University	2003 – present
Consultant , Infinity Pharmaceuticals	2004
Member , Stanford University School of Medicine Faculty Diversity Committee	2004 – 2005
Member , Quantitative Chemical Biology Program Steering Committee, Stanford University School of Medicine	2004 – 2009
Member , Medical Scientist Training Program Admissions Committee, Stanford University School of Medicine	2004 – present
Departmental Representative , Stanford University School of Medicine Faculty Senate	2005 – 2006
Member , Stanford Comprehensive Cancer Center	2005 – present
Adhoc Reviewer , NIH Study Section (Innovative Molecular Analysis Technologies)	2005 – 2006
Member , Advisory Committee for the Scholarly Concentrations Program in the Molecular Basis of Medicine, Stanford University School of Medicine	2006 – present
Discussion Leader , Bioorganic Gordon Research Conference	2007
Consultant , Fate Therapeutics	2008 – present
Editorial Board Member , <i>Zebrafish</i>	2008 – present
Workshop Co-Chair , 8 th International Conference on Zebrafish Development and Genetics	2008
Departmental Representative , Stanford University School of Medicine Faculty Senate	2009 – present
Associate Member , Stanford Digestive Disease Center	2009 – present
Member , Society for Developmental Biology	2009 – present
Editorial Board Member , <i>Chemistry & Biology</i>	2009 – present

PUBLICATIONS (PEER-REVIEWED)

1. Chu, Y.-H., **Chen, J. K.**, and Whitesides, G. M. (1993) Affinity electrophoresis in multisectional polyacrylamide slab gels is a useful and convenient technique for measuring binding constants of aryl sulfonamides to bovine carbonic anhydrase B. *Anal. Chem.* 65: 1314-1322.
2. **Chen, J. K.**, Lane, W. S., Brauer, A. W., Tanaka, A., and Schreiber, S. L. (1993) Biased combinatorial libraries: novel ligands for the SH3 domain of phosphatidylinositol 3-kinase. *J. Am. Chem. Soc.* 115: 12591-12592.
3. Yu, H., **Chen, J. K.**, Feng, S., Dalgarno, D., Brauer, A. W., and Schreiber, S. L. (1994) Structural basis for the binding of proline-rich peptides to SH3 domains. *Cell* 76: 933-945.
4. Gomez, F. A., **Chen, J. K.**, Tanaka, A., Schreiber, S. L., and Whitesides, G. M. (1994) Affinity capillary electrophoresis: insights into the binding of SH3 domains by peptides derived from an SH3-binding protein. *J. Org. Chem.* 59: 2885-2886.
5. **Chen, J. K.** and Schreiber, S. L. (1994) SH3 domain-mediated dimerization of an N-terminal fragment of the phosphatidylinositol 3-kinase p85 subunit. *Bioorg. Med. Chem. Lett.* 4: 1755-1760.
6. Feng, S., **Chen, J. K.**, Yu, H., Simon, J. A., and Schreiber, S. L. (1994) Two binding orientations for peptides to the Src SH3 domain: development of a general model for SH3-ligand interactions. *Science* 266: 1241-1247.

7. Combs, A. P., Kapoor, T. M., Feng, S., **Chen, J. K.**, Daude-Snow, L. F., Schreiber, S. L. (1996) Protein structure-based design of combinatorial libraries: discovery of non-peptide binding elements to the Src SH3 domain. *J. Am. Chem. Soc.* 118: 287-288.
8. Liang, J., **Chen, J. K.**, Schreiber, S. L., and Clardy, J. (1996) Crystal structure of PI3K SH3 domain at 2.0 Å resolution. *J. Mol. Biol.* 257: 632-643.
9. **Chen, J. K.**, Lane, W. S., and Schreiber, S. L. (1999) The identification of myriocin-binding proteins. *Chem. Biol.* 6: 221-235.
10. Taipale, J., **Chen, J. K.**, Cooper, M. K., Wang, B., Mann, R. K., Milenkovic, L., Scott, M. P., and Beachy, P. A. (2000) The effects of oncogenic mutations in Smoothed and Patched can be reversed by cyclopamine. *Nature* 406: 1005-1009.
11. Berman, D. M., Karhadkar, S. S., Hallahan, A. R. Pritchard, J. I., Eberhart, C. G., Watkins, D. N., **Chen, J. K.**, Cooper, M. K., Taipale, J., Olson, J. M., and Beachy, P. A. (2002) Medulloblastoma growth inhibition by Hedgehog pathway blockade. *Science* 297: 1559-1561.
12. **Chen, J. K.**, Taipale, J., Cooper, M. K., and Beachy, P. A. (2002) Inhibition of Hedgehog signaling by direct binding of cyclopamine to Smoothed. *Genes Dev.* 16: 2743-2748.
13. **Chen, J. K.**, Taipale, J., Young, K. E., Maiti, T., and Beachy, P. A. (2002) Small molecule modulation of Smoothed activity. *Proc. Natl. Acad. Sci. U. S. A.* 99: 14071-14076.
14. Chen, W., Ren, X., Nelson, C. D., Barak, L. S., **Chen, J. K.**, Beachy, P. A., de Sauvage, F., and Lefkowitz, R. J. (2004) Activity-dependent internalization of Smoothed mediated by beta-Arrestin 2 and GRK2. *Science* 306: 2257-2260.
15. Sinha, S. and **Chen, J. K.** (2006) Purmorphamine activates the Hedgehog pathway by targeting Smoothed. *Nat. Chem. Biol.* 2: 29-30.
16. Meloni, A. R., Fralish, G. B., Kelly, P., Salahpour, A., **Chen, J. K.**, Wechsler-Reya, R. J., Lefkowitz, R. J. and Caron, M. G. (2006) Smoothed signal transduction is promoted by G-protein coupled receptor kinase 2. *Mol. Cell. Biol.* 26: 7550-7560.
17. Esengil, H., Chang, V., Mich, J. K., and **Chen, J. K.** (2007) Small-molecule regulation of zebrafish gene expression. *Nat. Chem. Biol.* 3: 154-155.
18. Shestopalov, I. A., Sinha, S., and **Chen, J. K.** (2007) Light-controlled gene silencing in zebrafish embryos. *Nat. Chem. Biol.* 3: 650-651.
19. Esengil, H. and **Chen, J. K.** (2008) Gene regulation technologies for zebrafish. *Mol. BioSystems* 4: 300-308.
20. Shestopalov, I. A. and **Chen, J. K.** (2008) Chemical technologies for probing embryonic development. *Chem. Soc. Rev.* 37: 1294-1307.
21. Low, W.-C., Wang, C., Pan, Y., Huang, X.-Y., **Chen, J. K.**, and Wang, B. (2008) The decoupling of Smoothed from G-alpha-i proteins has little effect on Gli3 protein processing and Hedgehog-regulated chick neural tube patterning. *Dev. Biol.* 321: 188-196.
22. Stanton, B. Z., Peng, L. F., Maloof, N., Nakai, K., Wang, X., Herlihy, K. M., Duffner, J. L., Taveras, K. M., Hyman, J. M., Lee, S. W., Koehler, A. N., **Chen, J. K.**, Fox, J. L., Mandinova, A., and Schreiber, S. L. (2009) A small molecule that binds Hedgehog and blocks its signaling in human cells. *Nat. Chem. Biol.* 5: 154-156.
23. Cupido, T., Rack, P. G., Firestone, A. J., Hyman, J. M., Han, K., Sinha, S., Ocasio, C. A., and **Chen, J. K.** (2009) The imidazopyridine derivative JK184 reveals dual roles for microtubules in Hedgehog signaling. *Angew. Chem. Intl. Ed. Engl.* 48: 2321-2324.
24. Mich, J.K., Blaser, H., Thomas, N. A., Firestone, A. J., Yelon, D., Raz, E., and **Chen, J. K.** (2009) Germ cell migration in zebrafish is cyclopamine-sensitive but Smoothed-independent. *Dev. Biol.* 328:342-354.

25. Yang, H., Xiang, J., Wang, N., Zhao, Y., Hyman, J., Jiang, J., **Chen, J. K.**, Yang, Z., and Lin, S. (2009) Converse conformational control of Smoothed activity by structurally related small molecules. *J. Biol. Chem.* 284: 20876-20884.
26. Hyman, J. M., Firestone, A. J., Heine, V. M., Zhao, Y., Ocasio, C. A., Han, K., Sun, M., Rack, P. G., Sinha, S., Wu, J. J., Solow-Cordero, D. E., Jiang, J., Rowitch, D. H., and **Chen, J. K.** (2009) Small-molecule inhibitors reveal multiple strategies for Hedgehog pathway blockade. *Proc. Natl. Acad. Sci. U. S. A.* 106: 14132-14137.
27. Ouyang, X., Shestopalov, I. A., Sinha, S., Zheng, G., Pitt, C. L. W., Li, W.-H., Olson, A. J., and **Chen, J. K.** (2009) Versatile synthesis and rational design of caged morpholinos. *J. Am. Chem. Soc.* 131: 13255-13269.

PUBLICATIONS (NON-PEER-REVIEWED)

28. Prime, K. L., Chu, Y.-H., Schmid, W., Seto, C. T., **Chen, J. K.**, Spaltenstein, A., Zerkowski, J., and Whitesides, G. M. (1992) Molecular recognition in gels, monolayers, and solids. In P. Stroeve, A. C. Balazs, eds, *Macromolecular Assemblies in Polymeric Systems*. ACS Symposium Series 493. American Chemical Society, Washington, DC, pp 228-239.
29. **Chen, J. K.** and Schreiber, S. L. (1995) Combinatorial synthesis and multidimensional NMR: an approach to understanding protein-ligand interactions. *Angew. Chem. Int. Ed. Engl.* 34: 953-969.
30. Shestopalov, I. A. and **Chen, J. K.** (2008) Chemical developments. *Chemical Biology*. Issue 7, Research News.
31. **Chen, J.K.** (2008) Fish 'n clicks. *Nat. Chem. Biol.* 4: 391-392.
32. **Chen, J.K.** and Hurlstone, A. F. (2008) Targeted and conditional gene expression workshop, 8th International Conference on Zebrafish Development and Genetics. *Zebrafish* 5: 193-195.

INVITED LECTURES

1. "Molecular studies of embryonic signal transduction." Symposium on Drug Discovery through Chemical Genomics, Reverse Proteomics Research Institute (Tokyo, Japan). September 30, 2003.
2. "Molecular studies of embryonic signal transduction." Exploratory Research Laboratories, Fujisawa Pharmaceuticals Co., Ltd. (Tsukuba City, Japan). October 1, 2003.
3. "Molecular studies of embryonic signal transduction." Developmental Biology Seminar Series, Center for Developmental Biology, RIKEN (Kobe, Japan). October 3, 2003.
4. "Chemical probes of embryonic signal transduction." Organic Chemistry Seminar, Department of Chemistry, Stanford University (Stanford, CA). October 15, 2003.
5. "Chemical probes of embryonic signal transduction." Cardiovascular Research Center Seminar Series, Massachusetts General Hospital (Charlestown, MA). November 25, 2003.
6. "Targeting the Hedgehog signaling pathway with small molecules." Beyond Genome 2005 Conference: Future of Medicine (San Francisco, CA). June 16, 2005.
7. "Chemically inducible gene expression in zebrafish." 1st Annual Strategic Conference of Zebrafish Investigators (Mount Desert Island Biological Laboratory, Salisbury Cove, ME), September 17, 2005.
8. "Chemical regulation of zebrafish gene expression." Pacificchem 2005 Congress (Honolulu, HI). December 16, 2005.
9. "Small molecule regulation of the Hedgehog signaling pathway." Discovery on Target 2006 Conference: Chemogenomics (Boston, MA). October 24, 2006.

10. "Hedgehog pathway-dependent cell migration in zebrafish." 2nd Annual Strategic Conference of Zebrafish Investigators (Asilomar, CA). February 3, 2007.
11. "Chemical biology of embryonic development." China-USA Early Career Workshop on Chemical Biology (Shanghai, China). May 22, 2007.
12. "Light-controlled gene silencing in zebrafish embryos." Bio-organic Gordon Conference (Andover, NH). June 11, 2007.
13. "Chemical probes of embryonic signaling and patterning." Chemistry and Biochemistry Seminar Series, Department of Chemistry and Biochemistry, University of Delaware (Newark, DE). February 13, 2008.
14. "Chemical probes of embryonic signaling and patterning." Biochemistry and Molecular Biology Seminar Series, Department of Biochemistry and Molecular Biology, Mayo Clinic (Rochester, MN). March 4, 2008.
15. "Chemical probes of embryonic signaling and patterning." Medicinal Chemistry Seminar Series. Department of Medicinal Chemistry, University of Michigan (Ann Arbor, MI). March 13, 2008.
16. "Chemical probes of embryonic signaling and patterning." Pharmacology and Molecular Sciences Seminar Series. Department of Pharmacology and Molecular Sciences, Johns Hopkins University School of Medicine (Baltimore, MD). March 19, 2008.
17. "Small-molecule antagonists of the Hedgehog pathway." Hedgehog Signaling in Development and Disease, Stanford University School of Medicine (Stanford, CA). June 22, 2008.
18. "Light-controlled gene silencing using caged morpholinos." 8th International Conference on Zebrafish Development and Genetics, University of Wisconsin-Madison (Madison, WI). June 26, 2008.
19. "Spatiotemporal control of embryonic gene expression through synthetic chemistry." Neuroscience Consortium Cutting Edge Seminar, National Institute on Drug Abuse, National Institutes of Health (Bethesda, MD). August 14, 2008.
20. "Chemical probes of embryonic signaling and patterning." Department of Biology Seminar Series, Department of Biology, Indiana University (Bloomington, IN). October 2, 2008.
21. "Chemical probes of embryonic signaling and patterning." Technogeek Seminar Series, Division of Translational Research, University of Texas-Southwestern Medical Center (Dallas, TX). November 4, 2008.
22. "Chemical probes of embryonic signaling and patterning." 2008 RIKEN Conference on Chemical Biology (Narita, Japan). November 13, 2008.
23. "Caged morpholinos: Design, synthesis, and application." Gene Inactivation Workshop, 3rd Annual Strategic Conference of Zebrafish Investigators (Asilomar, CA). January 27, 2009.
24. "Chemical probes of embryonic signaling and patterning." Chemical Biology Seminar Series. Department of Chemistry, University of Illinois at Urbana-Champaign (Urbana, IL). February 5, 2009.
25. "Chemical probes of embryonic signaling and patterning." MCDB Seminar Series. Department of Molecular, Cell, and Developmental Biology, University of California-Los Angeles (Los Angeles, CA). February 26, 2009.
26. "Chemical probes of embryonic signaling and patterning." Lectures in the Chemical Sciences, Organic Chemistry Seminar, Department of Chemistry and Chemical Biology, Harvard University (Cambridge, MA). March 10, 2009.
27. "Chemical probes of embryonic signaling and patterning." Biophysics/Chemistry and Chemical Biology Seminar Series, University of California-San Francisco (San Francisco, CA). March 20, 2009.

28. "Hedgehog pathway antagonists: New mechanisms and targets." 237th American Chemical Society National Meeting (Salt Lake City, UT). March 25, 2009.
29. "Chemical probes of embryonic signaling and patterning." MCDB Seminar Series, Department of Molecular, Cellular, and Developmental Biology, Yale University (New Haven, CT). April 8, 2009.
30. "Hedgehog pathway antagonists: New mechanisms and targets." 100th Annual American Association for Cancer Research Meeting (Denver, CO). April 18, 2009.
31. "Hedgehog pathway antagonists: New mechanisms and targets. San Francisco Nature SciCafe, Gladstone Institute, University of California-San Francisco (San Francisco, CA). April 24, 2009.
32. "Chemical probes of embryonic signaling and patterning." Chemical Biology Seminar Series, Rockefeller University (New York City, NY). May 6, 2009.
33. "Chemical probes of embryonic signaling and patterning." Genentech (South San Francisco, CA). June 16, 2009.
34. "Chemical probes of embryonic signaling and patterning." Exelixis (South San Francisco, CA). June 26, 2009.
35. "Transcriptional target discovery through caged morpholino technologies." 6th European Zebrafish Genetics and Development Meeting (Rome, Italy). July 17, 2009.
36. "Small-molecule modulation of the Hedgehog pathway." Pfizer (La Jolla, CA). July 29, 2009.
37. "A caged morpholino-based strategy for transcriptional target discovery." 10th International Conference on Systems Biology, Stanford University (Stanford, CA). September 1, 2009.
38. "Chemical probes of embryonic signaling and patterning." Center for Biosciences Seminar, Karolinska Institutet (Stockholm, Sweden). October 6, 2009.
39. "Chemical probes of embryonic signaling and patterning." Genes and Development Seminar Series. National Institute for Medical Research-Mill Hill (London, United Kingdom). October 8, 2009.

PATENTS

1. Beachy, P.A., **Chen, J. K.**, and Taipale, J. Regulators of the Hedgehog pathway. Compositions and uses related thereto. PCT Int. Pub. WO 01/27135. April 19, 2001.
2. **Chen, J. K.**, Hyman, J. M., and Ocasio, C. A. Hedgehog pathway antagonists and methods of use. Patent pending, PCT/US09/33913. February 12, 2009.
3. **Chen, J. K.**, Sinha, S., Shestopalov, I. A., and Ouyang, X. Photocleavable linker methods and compositions. Patent pending. U. S. patent application number 12/485,774. June 16, 2009.

FUNDING (ACTIVE)

R01 GM072600 07/2005 – 06/2010
NIH/NIGMS
 PI: Chen, J. K.
 "Chemical regulation of zebrafish gene expression"

RSG-08-041-01-DDC (ACS Research Scholar Award) 01/2008 – 12/2011
American Cancer Society
 PI: Chen, J. K.
 "Hedgehog signaling and vertebrate germ cell migration"

1-FY-08-433	06/2008 – 05/2011
March of Dimes Foundation	
PI: Chen, J. K.	
“No-tail patterning of the zebrafish midline”	
DP1 OD003792	09/2008 – 09/2013
NIH Director’s Pioneer Award	
PI: Chen, J. K.	
“Chemical embryology: Technologies for manipulating and visualizing development”	
R01 CA136574	12/2008 – 11/2013
NIH/NCI	
PI: Chen, J. K.	
“Hedgehog pathway blockade by Gli antagonists”	
<u>FUNDING (COMPLETED)</u>	
Beckman-Ludwig Translational Program in Cancer Research	01/2004 – 12/2005
Stanford University	
Co-PIs: Kuo, C. J. and Chen, J. K.	
“Isolation and characterization of novel Hedgehog antagonists for therapy of gastrointestinal malignancies”	
OTL Research Incentive Award	06/2004 – 08/2006
Stanford University	
PI: Chen, J. K.	
“Constitutive and conditional gene silencing in zebrafish”	
Kimmel Scholar Award	07/2004 – 06/2006
Sidney Kimmel Foundation for Cancer Research	
PI: Chen, J. K.	
“Chemical and genetic studies of the Hedgehog pathway”	
Basil O’Connor Starter Scholar Research Award	02/2005 – 01/2007
March of Dimes Foundation	
PI: Chen, J. K.	
“Photochemical regulation of zebrafish gene expression for embryological studies”	
Gift Funds to the Stanford High-Throughput Bioscience Center	08/2005
Anonymous Donor	
PI: Chen, J. K.	
“Stanford High-Throughput Bioscience Center”	
Terman Fellow Award	09/2005 – 08/2008
Stanford University	
PI: Chen, J. K.	
“Spatiotemporal control of zebrafish gene expression”	
Astellas USA Foundation Award	11/2005 – 10/2006
Astellas USA Foundation	
PI: Chen, J. K.	

Brain Tumor Society Award

09/2006 – 08/2008

Brain Tumor Society/Rachel Molly Markoff Foundation

PI: Chen, J. K.

“Novel Hedgehog pathway antagonists as potential medulloblastoma therapeutics”