Isaac J. Krauss, Ph. D.

Curriculum Vitae

Department of Chemistry
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BIOGRAPHICAL INFORMATION

Born and raised in Fairbanks, Alaska, 12/21/75

DEGREES

Ph. D. 2003 (Chemistry, Columbia University, Advisor James Leighton)
M. Phil. 2002 (Chemistry, Columbia University, Advisor James Leighton)
M. A. 2000 (Chemistry, Columbia University, Advisor James Leighton)
B. A. 1998 (Chemistry, Stanford University, Advisor Barry M. Trost)

PROFESSIONAL EXPERIENCE

Brandeis University, Waltham, MA (July 2008–present)
Assistant Professor of Chemistry
Roche Bioscience, Palo Alto, CA (Summer 1996)
Summer intern in natural product synthesis

EDUCATION

Memorial Sloan–Kettering Cancer Center, New York, NY (January 2004 – June 2008)
NIH Postdoctoral Fellow working on carbohydrate vaccines and natural product synthesis
Advisor: Professor Samuel J. Danishefsky
Columbia University, New York, NY (August 1998 – September 2003)
Graduate work on diastereo- and enantioselective transition-metal-catalyzed reactions
Advisor: Professor James L. Leighton
Stanford University, Palo Alto, CA (September 1993 – June 1998)
Undergraduate research on pi-allyl substitutions
Advisor: Professor Barry M. Trost (September 1996 – June 1998)
Teaching assistant for 4 courses in organic and analytical chemistry, including one quarter as Head TA.
West Valley High School, Fairbanks, AK (September 1989-June 1993)
Graduated as valedictorian

INDEPENDENT RESEARCH

Project A: Chemical Biology My laboratory is involved in directed evolution of modified DNAs and peptides. In the DNA field, we have developed a system which allows selections of DNA aptamers decorated with large carbohydrates. We have applied this system to the directed evolution of DNA-scaffolded glycoclusters which bind to broadly-neutralizing anti-HIV antibody 2G12 with low nanomolar affinity. In a related project, we have modified the peptide directed evolution technique, mRNA display, to enable directed evolution of glycopeptides. We have used this technique to discover glycopeptides which

are very close mimics of HIV protein gp120, being recognized by antibody 2G12 with sub-nanomolar affinities. Both the glycoDNA and glycopeptide constructs are being investigated for their applications as HIV vaccines.

Project B: Organic Synthesis We are also interested in the development of synthetic methods and organic synthesis. Recently we have developed a method for homoallylation and homocrotylation of aldehydes using cyclopropanated allyl- and crotylboronates, allowing access to 1,3-syn or anti-substituted bishomoallylic alcohols, which are difficult to access by other methods. These compounds are important for the synthesis of numerous tetrahydrofuran and tetrahydropyran-containing natural products.

RESEARCH EXPERIENCE (Postdoctoral and Predoctoral)

Postdoc in Synthesis and Chemical Biology, Memorial Sloan–Kettering Cancer Center, New York, NY (January 2004 – June 2008)
In the laboratory of Samuel Danishefsky, developed a total synthesis of the unstable macrolide, isomigrastatin, a natural product which inhibits the migration of cancer cells and is part of a family of natural products with anti-metastatic properties.
Together with other post docs in the Danishefsky, Moore, and Massague groups at Sloan–Kettering, developed migrastatin analogs with improved anti-metastatic properties in *in vivo* metastasis models in mice.
Designed and synthesized multivalent cyclic glycopeptide mimics of an epitope on HIV glycoprotein gp120. In collaboration with Merck, these compounds were used to raise anti-carbohydrate antibodies in guinea pigs and rhesus macaques.

Ph. D. work in Transition-Metal-Catalyzed Reactions, Columbia University, New York, NY (January 1999 – September 2003)
In the laboratory of James Leighton, used a directing group strategy to develop branched selective rhodium-catalyzed hydroformylation, allowing a non-aldol route to anti-polypropionate motifs.
Developed easily-synthesized sulfonamide-phosphine hemi-labile ligands which induced unprecedentedly high ee's in asymmetric conjugate addition of organozinc reagents and proceeded under practical room-temperature conditions.

Undergraduate Research in Transition-Metal-Catalyzed Reactions, Stanford University, Palo, Alto, CA (September 1996 – June 1998)
In the laboratory of Barry Trost, Developed conditions for asymmetric alkylation of malonate and imide (C- and N-) nucleophiles with racemic gamma-hydroxybutenolide carbonates, using Pd-catalyzed pi-allyl substitution reactions. The observation that recovered butenolide ee was much less than product ee led to the development of a dynamic kinetic resolution process which was applied to the total synthesis of aflatoxin B.

TEACHING EXPERIENCE

2008–present (Brandeis University): Chem 25b (Sophomore Organic lecture, 140-190 students) 135a (Advanced Organic Chemistry: Synthesis II, 8-17 students) 134b (Advanced Organic Chemistry: Synthesis I, 16 students)
1998–2000 (Columbia University): *as TA*, 3 semesters organic chemistry lecture
1997–1998 (Stanford University) : *as TA*, 2 quarters organic chemistry lecture (Chem 33 and 131), 1 quarter analytical chemistry lab (Chem 134)
1998 (Stanford University): *as Head TA*, 1 quarter organic chemistry lab (Chem 130/132)

HONORS AND AWARDS

Summer 1997: Pfizer Summer Undergraduate Research Fellowship

January 2005 – December 2007: NIH NRSA Postdoctoral Fellowship F32-AI063976
2013 Thieme Chemistry Journal Award
2013 NSF CAREER Award
2015 Strage Award for Aspiring Young Science Faculty
2015 Waltzer Award for Teaching

PROFESSIONAL SOCIETIES

09/2000 – 09/2004, 03/2010–present: Member, American Chemical Society
03/2010–present: Member, American Society for Biochemistry and Molecular Biology

PROFESSIONAL SERVICE

Review of Grant Proposals:
04/2009 – ACS Petroleum Research Fund DNI proposals
04/2012 – NIH ZAI1-JBS-A M1 Special Emphasis Panel ("CHAVI-ID" HIV vaccine program)
08/2012 – ACS Petroleum Research Fund DNI proposals
03/2013 – NSF electronic review for Macromolecular/Supramolecular/Nanochemistry program
03/2014 – NIH/CSR *ad hoc* member, VACC study section (HIV/AIDS Vaccines)
11/2014 – NIH ZAI1 DR-A (J2) 1 Special Emphasis Panel ("Innovation for HIV Vaccine Discovery" RFA)
03/2015 – NIH ZRG1 BCMB-R (50) R Special Emphasis Panel ("Facile Methods and Technologies for Synthesis of Biomedically Relevant Carbohydrates" RFA)
06/2015 – NIH/CSR *ad hoc* member, SBCA study section (Synthetic and Biological Chemistry)

referee work for journals: *Nat. Commun.; Nat. Chem.; Nat. Chem. Biol.; J. Am. Chem. Soc.; Angew. Chem.; Chem. Sci.; Retrovirology; Org. Lett.; Tetrahedron Lett.; Bioorg. Med. Chem. Lett.; ACS Catalysis; Eur. J. Med. Chem.*

RESEARCH SUPPORT

NIH R01-AI090745 (06/2010-05/2014, currently in no-cost extension) "Rational and Combinatorial Design of Immunogens to Elicit 2G12-like Antibodies" Award amount: $1,655,922

ACS Petroleum Research Fund Doctoral New Investigator Award 51975-DNI1 (01/2012-08/2015) "Stereoselective Homoallylation of Aldehydes and Related Compounds" $100,000 Total Costs

NSF CAREER CHE-1253363 (06/2013-05/2018) "Stereoselective Homoallylation and Homocrotylation" Award amount: $550,000

NIH R01-AI113737 (07/2014-06/2019) "Design of Immunogens to Elicit PGT122-Like Antibodies" PI: Krauss, I.J., co-PI: Nemazee, D. Award amount: $2,174,374 ($1,874,222 to Krauss)

POSTDOCTORAL AND GRADUATE PUBLICATIONS

1. "Highly Regioselective and Diastereoselective Directed Hydroformylation of Allylic Ethers: A New Approach to Propionate Aldol Synthesis" **Krauss, I. J.**; Wang, C. C. Y.; Leighton, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 11514–5.

2. “Highly Practical and Enantioselective Cu-Catalyzed Conjugate Addition of Alkylzinc Reagents to Cyclic Enones at Ambient Temperature” **Krauss, I. J.**; Leighton, J. L., *Org. Lett.* **2003**, *5*, 3201–3.

3. “Total Synthesis of Isomigrastatin” **Krauss, I. J.**; Mandal, M.; Danishefsky, S. J. *Angew. Chem. Int. Ed.* **2007**, *46*, 5576–9.

4. “Fully Synthetic Carbohydrate HIV Antigens Designed on the Logic of the 2G12 Antibody” **Krauss, I. J**; Joyce, J G.; Finnefrock, A. C.; Song, H. C.; Dudkin, V. Y.; Geng, X.; Warren, J. D.; Chastain, M.; Shiver, J. W.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2007**, *129*, 11042–4.

5. “Total Synthesis of Spirotenuipesines A and B” Dai, M.; **Krauss, I. J.**; Danishefsky, S. J. *J. Org. Chem.* **2008**, *73*, 9576–83.

6. “An Oligosaccharide-based HIV-1 2G12 Mimotope Vaccine Induces Carbohydrate-specific Antibodies that Fail to Neutralize HIV-1 Virions” Joyce, J. G.; **Krauss, I. J.**; Song, H. C.; Opalka, D. W.; Grimm, K. M.; Nahas, D. D.; Esser, M. T.; Hrin, R.; Feng, M.; Dudkin, V.; Chastain, M. C.; Shiver, J. W.; Danishefsky, S. J. *Proc. Natl. Acad. Sci. USA*, **2008** *105*, 15684–9.

7. “A New Model for the Presentation of Tumor–Associated Antigens and the Quest for an Anticancer Vaccine: A Solution to the Synthesis Challenge via RCM” Jeon, I.; Lee, D.; **Krauss, I. J.**; Danishefsky, S. J. *J. Am. Chem. Soc.* **2009**, *131*, 14337–44.

8. “Diverted Total Synthesis Leads to the Generation of Promising Cell-Migration Inhibitors for Treatment of Tumor Metastasis: In vivo and Mechanistic Studies on the Migrastatin Core Ether Analog” Oskarsson, T.; Nagorny, P.; **Krauss, I. J.**; Perez, L.; Mandal, M.; Yang, G.; Ouerfelli, O.; Xiao, D.; Moore, M. A. S.; Massague, J.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2010**, *132*, 3224–8.

9. “Confirmation of the Structures of Synthetic Derivatives of Migrastatin in the Light of Recently Disclosed Crystallographically Based Claims” Nagorny, P. **Krauss, I.**; Njardarson, J. T.; Perez, L. Gaul, C.; Yang, G.; Ouerfelli, O.; Danishefsky, S. J. *Tetrahedron Lett.* **2010**, *51*, 3873–5.

PUBLICATIONS AT BRANDEIS

10. “Enzyme-Instructed Molecular Self Assembly Confers Nanofibers and A Supramolecular Hydrogel of Taxol” Gao, Y.; Kuang, Y.; Guo, Z.-F.; Guo, Z.; **Krauss, I. J.**; Xu, B. *J. Am. Chem. Soc.* **2009**, *131*, 13576–7.

11. “A Concise Asymmetric Synthesis of the Bromophycolide A and D Skeleton” Lin, Hongkun; Pochapsky, Susan, S.; **Krauss, Isaac J.** *Organic Lett.* **2011**, *13*, 1222–5.

12. “Multivalent Glycocluster Design Through Directed Evolution” MacPherson, I. S.; Temme, J. S.; Habeshian, S. M.; Felczak, K.; Pankiewicz, K.; Hedstrom, L.; **Krauss, I. J.** *Angew. Chem. Int. Ed.* **2011**, *50*, 11238–11242. (***Selected as a “Hot Paper”***)

13. “Homoallylboration and Homocrotylboration of Aldehydes” Pei, W.; Krauss, I. J. *J. Am. Chem. Soc.* **2011** ,*133*, 18514–18517. (***Highlighted in*** **Synfacts 2012**, *8*, 203).

14. "Enantioselective Homocrotylboration of Aliphatic Aldehydes" Lin, H.; Pei, W.; Wang, H.; Houk, K. N.; **Krauss, I. J.** *J. Am. Chem. Soc.* **2013**, *135*, 82–5. (***Highlighted in Synfacts*** **2013**, *9*, 315, and in ***Organic Synthesis Highlights***, http://www.organic-chemistry.org/Highlights/2014/24February.shtm).

15. "Directed Evolution of 2G12-Targeted Nonamannose Glycoclusters by SELMA" Temme, J. S.; Drzyzga, M. G.; MacPherson, I. S.; **Krauss, I. J**. *Chem. - Eur. J.* **2013**, *19*, 17291-5.

16. "High Temperature SELMA: Evolution of DNA-Supported Oligomannose Clusters Which Are Tightly Recognized by HIV bnAb 2G12" Temme, J. S.; MacPherson, I. S.; Decourcey, J. F.; **Krauss, I. J.** *J. Am. Chem. Soc.* **2014**, *136*, 1726-9 (***reviewed in F1000 Prime***).

17. "Directed Evolution of Multivalent Glycopeptides Which Are Tightly Recognized by HIV Antibody 2G12" Horiya, S.; Bailey, J.; Guillen-Schlippe, Y. V.; Temme, J. S.; **Krauss, I. J.** *J. Am. Chem. Soc.*, **2014**, *136*, 5407-15 (***Highlighted in C&E News***, 3/31/2014, ***reviewed in F1000 Prime***).

18. "Boron Carboxylate Catalysis of Homoallylboration" Dugas, G. J.; Lam, Y.; Houk, K. N.; **Krauss, I. J.**, *J. Org. Chem.* **2014**, *79*, 4277-84 (***Selected as Featured Article***).

19. "Recent Strategies Targeting HIV Carbohydrates in Vaccine Design" Horiya, S.; MacPherson. I. S.; **Krauss, I. J.** *Nat. Chem. Biol.* **2014**, *10*, 990-999.

20. "Glycocluster ligand selection using SELMA - SELection with Modified Aptamers" Temme, J. S.; **Krauss, I. J.** *Curr. Protoc. Chem. Biol.* **2015**, *7*, 73-92.

21. "Enantioselective *syn* and *anti* Homocrotylation of Aldehydes: Application to Formal Synthesis of Spongidepsin" Lin, H.; Tian, L.; **Krauss, I. J.** *J. Am. Chem. Soc. in press.*

INVITED LECTURES (as faculty)

1. Stonehill College (October 2008)
2. University of Southern Maine (November 2008)
3. Merrimack College (October 2010)
4. Carbohydrates Gordon Research Conference (June 2011)
5. Colgate University (Novermber 2011)
6. Dartmouth College (January 2012)
7. ACS Symposium on Host-Pathogen Interactions, Carbohydrate Section (March 2012, 243rd ACS meeting)
8. Brown University (April 2012)
9. Hobart William and Smith College (April 2012)
10. ACS Organic Division "Young Academic Investigators Symposium" (August 2012, 244th ACS meeting)
11. Tufts University (October 2012)
12. University of Massachusetts, Dartmouth (November 2012)
13. Rhode Island College (November 2012)
14. University of Rhode Island (February 2012)
15. Hokkaido University, Sapporo, Japan (February 2012)
16. Bioorganic Chemistry Gordon Research Conference (June 2013)
17. Carbohydrates Gordon Research Conference (June 2013)
18. Organic Reactions and Processes Gordon Research Conference (July 2013)
19. Ra Pharma (July 2013)
20. Emmanuel College Merck Lecture (September 2013)
21. Clark University (October 2013)

22. Merrimack College (October 2013)
23. MRSEC Seminar, Brandeis University (November 2013)
24. Northeastern University (Dec 2013)
25. University of Pittsburgh (February 2014)
26. University of Pennsylvania (February 2014)
27. Temple University (February 2014)
28. University of Delaware (February 2014)
29. Texas A&M University (February 2014)
30. Bridgewater State University (February 2014)
31. Young Investigators in Glycoscience Symposium (March 2014, 247th ACS meeting)
32. Columbia University (April 2014)
33. University of North Carolina, Chapel Hill (April 2014)
34. University of California, Irvine (April 2014)
35. University of Texas, Austin (April 2014)
36. University of Colorado, Boulder (April 2014)
37. Colorado State University (April 2014)
38. University of California, Davis (April 2014)
39. University of California, Santa Barbara (April 2014)
40. University of California, Berkeley (April 2014)
41. Memorial Sloan-Kettering Cancer Center (May 2014)
42. The Scripps Research Institute, La Jolla (May 2014)
43. Bowdoin College (May 2014)
44. Brandeis University, Chemistry Department (September 2014)
45. St. Anselm College (October 2014)
46. University of Georgia / Complex Carbohydrate Research Center (October 2014)
47. University of Michigan, Midwest Carbohydrate Symposium (October 2014)
48. PerkinElmer (scheduled for October 2014)
49. Middlebury College (November 2014)
50. Biochemistry/Biophysics Friday Seminar, Brandeis University (March 2015)
51. "Frontiers in Glycoscience" Symposium (March 2015, 249th ACS Meeting, Denver, CO)
52. "Carbohydrate Synthesis for Medicinal Chemistry and Biology" Symposium (August 2015, 20th ACS Meeting, Boston, MA)
53. SUNY Albany (October 2015)
53. "Carbohydrate Recognition in Health and Disease" Symposium #342 (Pacifichem 2015, Scheduled for December 2015)

PATENTS

Danishefsky, S. J.; Dudkin, V. Y.; Geng, X.; Mandal M.; **Krauss, I. J**. (2004) *GP120 Specific Antigens and Uses Thereof.* Application No.: PCT/US03/39471

Krauss, I. J.; Hedstrom, L;. MacPherson, I. *Methods for the Development of Vaccines Based on Oligosaccharide-Oligonucleotide Conjugates.* US Provisional Patent # 61/353857, filed 6/11/2010 (Allowance granted 3/20/2015)

Krauss, I. J. *High-Temperature Selection of Nucleotide-Supported Carbohydrate Vaccines* US Provisional Patent BUG04360, filed 12/5/2013

Krauss, I. J.; Guillen Y. V. G. *Directed Evolution of Glycopeptides* US Provisional Patent BUG04460, filed 12/5/2013