Charlie Fehl, PhD

May 2023 August 2018

Chemical biology tools for glycoprotein function Machine-learning actionable target pathways Medicinal chemistry in sugar-linked disease risk 5101 Cass Avenue Chem 469 Detroit, MI 48202, USA (313) 577-5667 charlie.fehl@wayne.edu

Oct '14 – July '18 September 2014 May 2009	Postdoctoral research associate University of Oxford; UK PhD in medicinal chemistry University of Kansas; Lawrence; USA BS in biochemistry University of Michigan; Ann Arbor; USA
Research Aug 2018-present	Wayne State University Chemistry (Detroit, MI, USA) • Real-time chemical tools to track glycobiology processes in cells • Functional genomics to uncover sugar mechanisms in live cells • Treating metabolic diseases via sugar pathways Funded by an NIH R35 grant, July 2021–May 2026 Mizutani Foundation for Glycosciences Research Grant (2023-2025) NSF CAREER award, June 2023–June 2028
Oct. 2014-2018 Jan. 2016-2018	University of Oxford Chemistry (United Kingdom) Postdoctoral mentor: Benjamin G. Davis, FRS • High-throughput mass spectrometry and bioinformatic/machine learning methodology to predict glycosyltransferase enzyme functions Funded by a UK Catalysis Hub grant (UK EPSRC), Oct. 2014-Nov. 2018 • Visible light photoredox-catalyzed protein chemical ligation methods to install pure synthetic post-translational modifications on histone proteins
2011-2014 2010-2011 2009	University of Kansas Medicinal Chemistry (USA) Graduate mentors: Jeffrey Aubé & Emily E. Scott • Target-based, rational design of highly selective cytochrome P450 17A1 (CYP17A1) inhibitors (synthesis, assay devel., structural biology) Funded by an ACS Medicinal Chemistry Pre-doctoral Fellowship • Overcoming product inhibition to yield a catalytic Schmidt reaction – efficient and green access to amide and lactam bonds • Development of conditions for a tandem Prins/Friedel-Crafts reaction
Summer 2012	Universität Regensburg Chemistry (Germany) Mentor: Burkhard König • Visible-light control of reactivity encoded onto carbohydrate surfaces – organic photochemistry on cellulose sheets for biological applications Funded by a NIH Training Grant in Dynamic Aspects of Chemical Biology
2007-2009 2006-2007	University of Michigan Biological Chemistry (USA) Undergraduate mentor: Bruce Palfey • Biochemical mechanisms of flavin-dependent enzymes by kinetics study Mentor: Ruthann Nichols • Pharmacology of neuroactive peptides on fruit flies (animal studies)

Secondary appointment: Molecular Therapeutics, Karmanos Cancer Institute

Assistant Professor in Chemistry Wayne State University; Detroit; USA

Publications

- "Hyperglycemia and O-GlcNAc transferase activity drives cancer stem cell induction in triplenegative breast cancer." Saheed Ayodeji, Bin Bao, Emily A. Teslow, Lisa A. Polin, Greg Dyson, Aliccia Bollig-Fischer, **Charlie Fehl**. *Cancer Cell International* (2023) 23: article 102.
- "Synthesis and mammalian cell compatibility of light-released glycan precursors." Courtney A. Kondor†, Jaggaiah N. Gorantla† (†co-first authors), Garry D. Leonard, and **Charlie Fehl**. *Bioorganic and Medicinal Chemistry* (**2022**), *70*, 116918.
- "Spatiotemporal proximity labeling tools to track GlcNAc sugar-modified functional protein hubs during cellular signaling." Yimin Liu, Zachary Nelson, Saheed Ayodeji, Ali Reda, **Charlie Fehl**." *ACS Chem. Biol.*, **2022** *17*, 2153-2164.
- "Tools, tactics, and objectives to interrogate cellular roles of O-GlcNAc in disease." **Charlie Fehl*** and John A. Hanover* [*both corresponding]. *Nature Chemical Biology* (2022) *18*, 8-17.
- "Chemical synthesis and biological applications of O-GlcNAcylated peptides and proteins." Jessica M Groenevelt, Daniel J Corey, **Charlie Fehl**. *ChemBioChem* (2021) 22, 1854-1870.

Mentored publications:

- "Light-driven post-translational installation of reactive protein side chains." Josephson B*, **Fehl C***, Iseneggar P* [*co-first authors], Nadal S...Davis BG *et al. Nature* (**2020**) *585*, 530.
- "Functional and informatics analysis enables glycosyltransferase activity prediction." Yang, M* **Fehl C*** [*co-first], Lees KV...Davis BG *et al. Nature Chemical Biology* (**2018**) *14*, 1109.
- "Structure-based design of inhibitors with improved selectivity for steroidogenic cytochrome P450 17A1 over cytochrome P450 21A2." **Fehl C**, Vogt C, Yadav R, Li K, Scott EE, Aubé J. *Journal of Medicinal Chemistry* (2018) 61, 4946.
- "Proteins as templates for complex synthetic metalloclusters progress toward bio-inspired heterometallic systems." **Fehl C**, Davis BG. *Proc. of the Royal Society A* **(2016)** *472*, 20160078.
- Outperforming Nature's Catalysts: Designing Metalloenzymes for Chemical Synthesis. **Fehl C,** Jarvis AG, Palm-Espling M, Davis BG, Kamer PCJ. In *Modern Developments in Catalysis*; World Scientific Press: Singapore (**2016**) 89-122.
- "Temperature Dependence of Turnover in a Sc(OTf)₃-Catalyzed Intramolecular Schmidt Reaction." Fehl C, Hirt EE, Li SW, Aubé J. *Tetrahedron Letters* (2015) 56, 3137.
- "Overcoming Product Inhibition in Catalysis of the Intramolecular Schmidt Reaction." Motiwala H, **Fehl C**, Li SW, Hirt EE, Porubsky P, and Aubé J. *Journal of the American Chemical Society* (2013) *135*, 9000.
- "Photocatalytic Surface Patterning of Cellulose using Diazonium Salts and Visible Light." Schroll P, **Fehl C**, Dankesreiter S, König B. *Organic & Biomolecular Chemistry* (2013) 11, 6510.
- "Hofmann, Curtius, Schmidt, Lossen and Related Reactions." **Fehl C,** Liu R, McCleod M, Motiwala HM, Aubé J. In *Comprehensive Organic Synthesis*, 2nd Ed; Elsevier Limited: Amsterdam (**2014**) pp. 598-635.
- "Use of a Tandem Prins/Friedel—Crafts Reaction in the Construction of the Indeno-Tetrahydropyridine Core of the Haouamine Alkaloids: Formal Synthesis of (–)-Haouamine A." Fenster E, **Fehl C**, Aubé J. *Organic Letters* (**2011**) *13*, 2614-2617.

Patents

Inhibitors of CYP17A1. Fehl C, Scott EE, Aubé J. United States Patent 9,611,270 (2017).

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June 2023-2028	NSF CAREER, "Illuminating O-GlcNAc-driven functions of the human
	proteome (\$833,737 award)
Feb 2023-2025	Mizutani Foundation for Glycosciences – Research Grant (\$80k)
July 2022	Faculty competition for postdoctoral research fellow (Wayne State)
July 2021-2026	NIH R35 MIRA, "Spatiotemporal tools to interrogate O-GlcNAc
	functions in cellular signaling" (\$1.9 M)
	+ Administrative Supplement to Garry Leonard (2022-2024).
August 2021-22	NIH S10 grant: NMR spectrometer (minor contributor)
February 2021-22	WSU "Grants Boost" program (\$35k)
January 2021	Karmanos Cancer Institute Proteomics Award (\$3k)
August 2020	Faculty competition for postdoctoral research fellow (Wayne State)
April 2020	Ebbing Faculty Development Award. (\$2.4k)
Jan 2020	Initiative for Maximizing Student Diversity Fellowship-Zackary Nelson
March 2019	University Research Grant (Wayne State University) (\$10k)
July 2016	Competitive 2-year renewal of UK Catalysis Hub grant
September 2012	ACS Div. of Medicinal Chemistry predoctoral fellow
August 2011	NIH Training Grant in Dynamic Aspects of Chemical Biology

Awards

January 2021	Wayne State Grants Writing Workshop Selected Participant – Life Sciences
August 2020	American Chemical Society Outreach Training Program
October 2019	Advisor to WSU Chem. Club as they built "World's Largest Periodic Table"
March 2018	Best talk: Syngenta Postdoctoral Symposium (Oxford Chemistry Dept.)
November 2013	1st Place poster award – KU Cancer Center Symposium (\$1000 award)
November 2012	Les & Betty Mitscher Prize for Excellence in Medicinal Chemistry (KU)
April 2012	Poster competition winner – MIKI Graduate Research Symposium
May 2009	Merck Index Award (Undergraduate Research Award)

Mentoring

Graduate students

Class of 2022 Courtney Kondor, successfully defended Ph.D. thesis on May 20, 2022.

'Metabolic labeling tools to study complex human glycoproteins'

Current students Saheed Ayodeji: 'Informatics to classify epigenetic sugar signaling'

Daniel Corey: 'Affinity labeling/enrichment of O-GlcNAc 'readers'' **Zachary Nelson**: 'Biocatalytic tools for in vivo glycoprotein labeling'

Garry Leonard: 'Controllable strategies to manipulate sugars in cells' Caleb Aboagye: 'Rational design of OGT inhibitors for chemotherapy'

Steven Balboa: 'Next-gen bioorthogonal sugar probes for cell activities'

Kadiri Oseni: 'Programmable tools for O-GlcNAc capture in signaling'

Postdoctoral fellows

Aug 2020—Jun 2022 Dr. Jess Stachowski, 'In vivo photoredox glycoprotein labeling'

accepted a tenure-track faculty position at Nazareth College, NY, USA!

Dec 2022—current Dr. Arun Thangarasu, 'Chemical control of O-GlcNAc in disease'

March 2023—current Dr. Jaggaiah Naidu, 'Photocaged tools to study O-GlcNAc proteins'

Undergraduate students

[underlining indicates student graduated]

Joined Fall 2018 Anthony Cicalo, Douglas Haslitt*, and Ali Reda* (*honors student)

Joined Summer 2019 <u>Laura Hanselman</u>**, visiting summer student from Kalamazoo College

(**Won a Sherman Fairchild Summer Research Stipend for support)

Fall 2019 <u>Mariem Abdullah, Charlie Trice, Logan Nguyen*, Vince Pallo</u>

Summer 2020 Sydni Alexis Elebra*** (on a ***ReBUILDetroit fellowship)

Summer 2021 Mariia Barttelt Winter 2022 Austin Agrusa

2023-current: Tristan Wrong, Fatima Bazzi, Christopher Hancock

Teaching

Winter 2023-current WSU: CHM6635/7635 Tools of Molecular Biology Fall 2022-current WSU: CHM6240/7240 Organic Spectroscopy Winter 2019-2021 WSU: CHM 1240 Organic Chemistry I

Fall 2018-2021 WSU: CHM 6270/7270 Advanced Bioorganic Chem. & Drug Design 2015-2018 Oxford teaching: Biological Chemistry, Organic chemistry (undergrad) 2015-2018 Oxford lecturing: "Synthesis for Biology & Medicine" graduate course

Service:

August 2022 – onward Graduate Studies Committee (WSU Chemistry Department)

Sept 30-Oct 1, 2022 Organized Midwest Carbohydrate & Glycobiology Symposium (MCGS)
September 2022August 2021-2022 Chair, WSU Chemistry "Diversity, Equity, and Inclusion" Committee
American Chemical Society CARB Division virtual webinar organizer.

Sept. 2019 – 2021 WSU Graduate Admissions

Sept 2019 – onward WSU Gopal Symposium Committee

Jan. 2019 WSU Paul A. Schaap Endowed Chair Search Committee

Jan 2019 – 2021 Faculty advisor to WSU Climbs Hard (grad/undergrad climbing club)
Jan 2019 – 2021 Faculty advisor to American Chemical Society Student Affiliates club

Sept. 2018–19 Undergraduate Research Advisor (Chemistry Department)

Outreach:

October 23, 2019 Built the 'World's Largest Periodic Table' with the WSU Chem Club

https://www.freep.com/story/news/local/michigan/detroit/2019/10/23/wa

yne-state-university-builds-worlds-largest-periodic-table/4078085002/ Organized WSU Chemistry AP Day program (high school outreach)

April 23, 2019 Organized WSU Chemistry AP Day program (high school outreach)
April, 15, 2019 Organized Madison Preparatory High School visit to Chemistry
Aug 2015–Aug 2017 Member, American Association of Pharmaceutical Sciences Blog

Committee [steered blog readership and policy]

• Emphasized outreach, scientific ethics, 'popular glycobiology,' important developments

• Facilitated Oxford student posts on entrepreneurship, gender issues in science

Selected Invited Talks and Conference Presentations

- 41. *invited conference talk:* UK Catalysis Hub Summer Conference 2023 (July 17-18, 2023, Harwell, UK) Real-time chemical tools to capture and control sugar signaling in cells
- 40. *invited conference talk:* Carbohydrates Gordon Research Conference (6/18-23, 2023, Plymouth, NH) Real-time chemical tools to capture and control sugar signaling in cells
- 39. University of Newcastle (Newcastle, United Kingdom) (May 19, 2023)

 Seminar: Chemical tools to capture and control hexosamine sugars in hyperglycemic disease
- 38. University of York (York, United Kingdom) (May 17, 2023)

 Seminar: Chemical tools to capture and control hexosamine sugars in hyperglycemic disease
- 37. Leiden University Medical Center (Newcastle, Netherlands) (April 24, 2023)

 Seminar: Chemical tools to capture and control hexosamine sugars in hyperglycemic disease
- 36. University of California San Diego (San Diego, CA, USA) (Feb 27, 2023)

 Seminar: Spatiotemporal chemical tools to functionally probe sugar signaling in cells & disease
- 35. Ohio State University (Columbus, OH, USA) (Feb 21, 2023)

 Seminar: Chemical tools to functionally probe sugar signaling in cells and disease
- 34. Michigan State University (East Lansing, MI, USA) (Feb 15, 2023) Seminar: Real-time chemical tools to capture and control sugar signaling in cells
- 33. Ole Miss University (Oxford, MS, USA) (Dec14, 2022)

 Seminar: Chemical tools to functionally probe sugar signaling in cells and disease
- 32. Xavier University of Louisiana (New Orleans, LA, USA) (Nov 10, 2022)

 Seminar: "Chemical Systems to Capture Functions of Sugar Modifications in Disease"
- 31. Medical College of Wisconsin (Milwaukee, WI, USA) (Oct 19, 2022)

 Seminar: Chemical strategies for capturing dynamic cellular glycosylation events
- 30. *invited conference talk:* Midwest Carbohydrate and Glycobiology Symposium (Detroit, MI) Oct 1, 2022 Chemical strategies for capturing dynamic O-GlcNAc protein glycosylation events in cells
- 29. *invited conference talk:* ASBMB meeting "O-GlcNAc Regulation of Cellular Physiology and Pathology" (Athens, GA), July 8, 2022
 - Title: "Real-time chemical tools to capture and control sugar signaling in cells"
- 28. *invited conference talk:* Bioorganic Gordon Research Conference: June 13, 2022 (Andover, NH) "Spatiotemporal strategies for tracking glycoprotein functions in cells"
- 27. *Invited conference talk:* ACS Central Regional Meeting (CERM): June 7-10, 2022 (Ypsilanti, MI) **Intracellular tools to study protein assemblies regulated by O-GlcNAc sugar modifications in signaling**
- 26. CIC BioGUNE (Centro de Investigación Cooperativa en Biociencias) (Bilbao, Spain) (May 3, 2022) In-person seminar: "Real-time chemical tools to capture and control sugar signaling in cells"

- 25. Leiden Institute of Chemistry (Leiden, Netherlands) (April 26, 2022)

 In-person seminar: "Real-time chemical tools to capture and control sugar signaling in cells"
- 24. *invited conference talk:* ACS Spring 2022 National Meeting (San Diego, CA) (March 21st, 2022) "In situ methods for capturing dynamic O-GlcNAc protein glycosylation events"
- 23. University of Illinois Chicago: Pharmaceutical Sciences (Chicago, IL) (March 16, 2022) Seminar: "Real-time tools to capture and control O-GlcNAc signaling in cells"
- 22. WSU Pharmaceutical Sciences (Detroit, MI) (March 9, 2022)

 Seminar: "Real-time chemical tools to capture and control sugar signaling in cells"
- 21. The Queen's University Belfast (Virtual; Northern Ireland, UK) (Feb 2nd, 2022) Seminar: "Real-time chemical tools to capture and control sugar signaling in cells"
- 20. *invited conference talk:* Pacifichem Conference (Virtual; Honolulu, HI) (Dec 21st, 2021)

 Chemical tools for tracking O-GlcNAc glycoprotein dynamics in real-time couple cellular glucose metabolism with signaling
- 19. Central Michigan University (Mount Pleasant, MI) (Nov 22, 2021)

 Seminar: Real-time chemical tools to modulate sugar signaling in cells
- 18. *invited conference talk:* Society for Glycobiology Annual Meeting (San Diego, CA) (Nov 5th, 2021) Real-time chemical tools to capture and control sugar signaling in cells
- 17. WSU Chemistry-Biology Interface Training Grant seminar (Detroit, MI) (Nov 2, 2021) Seminar: Real-time chemical tools to capture and control sugar signaling in cells
- 16. Morgan State University (Baltimore, MD) (Oct 5th, 2021)

 Seminar: Chemical tools to track cellular hyperglycemia and investigate molecular mechanisms of breast cancer risk
- 15. Western Illinois University (Macomb, IL) (Sept 13, 2021)

 Seminar: Real-time chemical tools to modulate sugar signaling in cells
- 14. *invited conference talk:* Mid-South Glycoscience Meeting @ Ole Miss University, (Oxford, MS)(July 2021) Real-time chemical tools to modulate dynamic sugar signaling in cells
- 13. WSU C.S. Mott Center for Human Development (Detroit, MI) (June 2nd, 2021) *Seminar:* Real-time chemical tools to modulate sugar signaling in cells
- 12. GlycoNET Seminar Series (virtual @ University of Alberta, Canada) (March,15 2021) "Real-time chemical tools to assess dynamic O-GlcNAc glycoprotein functions"
- 11. WSU Pharmacology (Detroit, MI) (April 3rd, 2021)

 Seminar: Real-time chemical tools to modulate dynamic sugar signaling in cells
- 10. Wayne State University, Biological Sciences Dept. Seminar (Detroit, MI) (Mar 30, 2021) Seminar: "Real-time chemical tools to modulate dynamic sugar signaling in cells"
- 9. Creighton University, Chemistry Dept. Seminar (Nebraska, USA, 2021) (Jan 28, 2021)

- Seminar: "Real-time chemical tools to modulate sugar signaling in cells"
- 8. *invited conference talk:* Amer. Chem. Soc. CARB Division Young Investigator Symposium (Jan, 2021) "Real-time chemical tools to assess dynamic O-GlcNAc glycoprotein functions"
- 7. Karmanos Cancer Institute (WSU) Molecular Therapeutics Seminar (Detroit MI, 2020) Seminar: "Real-Time Chemical Tools to Target Tumor Metabolic Reprogramming"
- 6. California State University, East Bay Chemistry Dept. Seminar (California, 2020) Seminar: "Dynamic Sugar Signaling and Tool Development"
- invited conference talk: ACS Fall 2020 National Meeting talk (2020)
 "Chemical tools for tracking O-GlcNAc glycoprotein dynamics in real time"
- 4. Youngstown State University, Chemistry Dept. Seminar (Ohio, USA, 2019)

 Seminar: "Chemical Control of Glycoprotein Signaling in Metabolic Disease"
- 3. High Throughput Chemistry & Chemical Biology Gordon Research Conf. (New London, NH) (June, 2019) *Poster:* "Chemical tools to determine therapeutic sugar signaling pathways in disease"
- 2. Carbohydrates Gordon Research Conference, Hong Kong, China, June 2019

 Poster: "Chemical tools to determine therapeutic sugar signaling pathways in disease"
- 1. *invited conference talk:* ACS Detroit Local Section "Chemistry in the Motor City" Symposium (Oct, 2018) "Chemical tools to track protein modification signaling" (*Keynote Seminar*)

Selected trainee talks:

invited conference talk: Bioorganic Gordon Research Seminar Invited Talk (Andover, NH); June, 2018 "Metallaphotoredox-catalyzed protein functionalization enables the synthesis of pure epigenetic species for defined biophysical interaction studies"

invited conference talk: Syngenta Inc. (Jealott's Hill campus, UK); May, 2018 "In situ boronate activation for metallaphotoredox-initiated protein functionalization"

Oxford Chemical Biology Departmental Seminar (Oxford, UK); September 2017 "Functional Screening and Chemical-Bioinformatics Enables Family-Wide Prediction of Sugar Biocatalysis Networks"

invited conference talk: American Chemical Society Spring National Meeting (San Francisco, CA, April 2017) "Structural insight from activity: Functional screening of the entire *Arabidopsis* GT1 family enables cheminformatic-bioinformatic predictions of glycosyltransferase reactions and protein features"

Oxford Chemical Biology Departmental Meeting (Oxford, UK)(September, 2017)

Talk: "Functional Screening and Chemical-Bioinformatics Enables Family-Wide Prediction of Sugar Biocatalysis Networks"

Capitol Research Summit (Topeka, KS) – presented to state legislators (February, 2013)

Poster: "Targeting Sex Hormone Production at the Source – Next-Generation Therapeutics for Prostate and Breast Cancers"