

David L. Zechel
Professor of Chemistry
Curriculum vitae

Department of Chemistry, Queen's University,
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Birthplace

Winnipeg, Manitoba, Canada, 1973

Research Interests

Enzyme mechanisms, organophosphonate degradation, enzymatic halogenation, natural product biosynthesis, plastic biodegradation.

Professional Experience and Service

2020-present	Co-lead of Open Plastic (www.openplastic.com)
2020-2021, 2023	Acting Head, Dept. of Chemistry, Queen's University
2019 - 2023	Associate Head, Dept. of Chemistry, Queen's University
2019 - 2023	Graduate Program Coordinator, Dept. of Chemistry, Queen's University
2019 - 2023	Member of the NSERC Discovery Grant review panel 1504 (Chemistry)
2017 to present	Full Professor, Dept. of Chemistry, Queen's University
2010 - 2017	Associate Professor, Dept. of Chemistry, Queen's University
2004 - 2010	Assistant Professor, Dept. of Chemistry, Queen's University

Research Experience

2017-2018 and 2010–2011	Sabbatical stays with Professor Andreas Bechthold, Institut für Pharmazeutische Wissenschaften, Albert-Ludwigs-Universität, Freiburg, Germany. Identification and genetic manipulation of natural product biosynthetic pathways in <i>Streptomyces</i> sp.
2002 - 2004	Post-doctoral fellow with Prof. Andreas Plückthun, Biochemisches Institut, Universität Zürich, Switzerland. Development of ribosome display for evolution of proteins. Selection of novel protein folds from random secondary-structure protein libraries.
2001 - 2002	Post-doctoral fellow with Prof. Gideon Davies, York Structural Biology Laboratory, University of York, UK. Study of glycosidase mechanism through X-ray crystallography, transition state analogue inhibitors, isothermal titration calorimetry and kinetic analysis.
1996 - 2001	Ph.D. student with Prof. Stephen Withers, Department of Chemistry, University of British Columbia. Study of glycosidase mechanism. Engineering mutant glycosidases (glycosynthases) for the synthesis of oligosaccharides and carbon fluorine bonds. Development of ESI-MS for the analysis of enzyme kinetics.
1995	Summer student with Hemosol (Toronto), development of cross-linked hemoglobin as a blood substitute. NSERC USRA funded.
1994	Summer student with Ian Manners, U of T Chemistry. Synthesis of organometallic polymers. NSERC USRA funded.
1992, 1993	Summer student with Ronald Kluger, U of T Chemistry. Studies on cross-linked hemoglobin as a blood substitute. NSERC USRA funded.

Education and Training

2013, 2016, 2019, 2022	Whitewater Rescue Technician, Level III certification
2021, 2024	Wilderness First Responder and Wilderness Advanced First Aid certification
1996 - 2001	Ph.D. in chemistry and enzymology, Department of Chemistry, University of British Columbia
1991 - 1995	B.Sc. in chemistry and biochemistry, University of Toronto. Summer research experiences with Ronald Kluger (1992, 1993) and Ian Manners (1994)

Awards, Fellowships, Distinctions

2021	Distinguished Organic Lecture, Dept. of Chemistry, University of British Columbia
2016	NSERC Directed Accelerator Supplement, \$120,000, awarded to the top 10% of NSERC DG grants in the competition.
2011	Ontario / Baden-Württemberg Faculty Exchange Award (held in Bechthold lab, Albert-Ludwigs Universität Freiburg).
2007	Ontario Early Researcher Award
2006	<i>Synlett</i> and <i>Synthesis</i> Journal Award
2004	Boehringer Ingelheim Award for Organic or Bioorganic Chemistry (Ph.D thesis)
2002-2004	Human Frontier Science Program Postdoctoral Fellow (Plückthun Lab)
2001	Arthur S. Hawkes Fellowship (UBC)
2000-2001	University of British Columbia Graduate Fellowship
1998-2000	Izaak Walton Killam Predoctoral Fellowship
1992-2000	Natural Sciences and Engineering Research Council of Canada (NSERC) scholar (undergraduate and graduate)
1991-1995	University of Toronto Arbor Scholar
1991-1995	Canada Science Scholar

Undergraduate Course Instruction

2018 to present	Chem 282 Organic Chemistry (400-500 students each year)
2013 - 2018	Chem 311 Physical Organic Chemistry (50-70 students per year)
2009, 2011 - 2017	Chem 281 Organic Chemistry (500 students each year)
2005 - 2008	Chem 212 Principles of Chemical Reactivity (250 to 300 students each year)
2007 – 2011, 2013	Chem 323 Biological Chemistry (course developer , 35-50 students per year)
2004 - present	Chem 417 Research Project (1 to 2 4 th year students each year)
2004 - present	BCHM 422 Advanced Biochemistry Laboratory II (supervised several students from this program in my lab since 2004)

Graduate Course Instruction

2013, 2015	Chem 915, Biosynthesis of Natural Products (course developer)
2005, 2008	Chem 814, Carbohydrate Chemistry
2006	Chem 983, Solving Reaction Mechanisms
2010	Chem 915, Protein Engineering
2005 to 2018 09/12/2024	Chem 883, Bioorganic Chemistry

RESEARCH FUNDING (2015 – present)

- 2022-2024, NSERC Alliance – Missions Grant, \$991,200 (**\$203,200 to DLZ**). Circular economy for vinyl plastics.
- 2020-2025, Genome Canada Large Scale Applied Research Program (LSARP), **\$7.9 million CAD (\$435,635 to DLZ)**, Open Plastic: optimizing a microbial platform to break down and valorize waste plastic. Role: co-lead with George diCenzo, Laurence Yang, and James McLellan.
- 2017-2022, NSERC Strategic Grant, \$851,400 (**\$179,100 to DLZ**), Biodegradation of the most commonly used herbicide on earth. Trevor Charles (PI, U. Waterloo), Geoff Horsman (Wilfrid Laurier U.), Ze-Chun Yuan (U. Western Ontario), Keri Wang (A&L Canada Labs)
- 2016-2019, NSERC Directed Accelerator Supplement, **\$120,000**, From Genes to Molecules: Mining Bacterial Genomes for New Enzyme Reactions. Zechel (PI).
- 2016-2025, NSERC Discovery Grant, **\$550,000**, From Genes to Molecules: Mining Bacterial Genomes for New Enzyme Reactions. Zechel (PI).
- 2015-2016, NSERC RT11, **\$99,274**, Shaker incubators for cultivation of bacteria, Zechel DL (PI), Jia Z, Ross A, Smith S.
- 2011-2016, NSERC Discovery Grant, **\$150,000**, From Genes to Molecules: Mining Bacterial Genomes for New Enzyme Reactions. Zechel (PI).

Publications (2010-present)

59. Hollands S; Tasch J, Simon DJ, Wassouf D, Barber I, Gessner A, Bechthold A, Zechel DL*. Analysis of the cryptic biosynthetic gene cluster encoding the RiPP curacozole reveals a phenylalanine-specific peptide hydroxylase. *Chem. Sci.* **2024**, 15, 19858. DOI: 10.1039/D4SC02262A.
58. Katharina Pallitsch*, David L. Zechel*. The functional importance of bacterial oxidative phosphonate pathways. *Biochem. Soc. Trans.*, **2023**, 51, 487-499. *Invited review*.
57. Pasternak, ARO; Balanus, MJ; Zechel DL*. Discovery of 3'-O- β -Glucosyltubercidin and the Nucleoside Specific Glycosyltransferase AvpGT through Genome Mining. *ACS Chemical Biology*, **2022**, 17, 3507-3514. *Highlighted as a supplementary cover*.
56. Pasternak, ARO; Bechthold, A; Zechel, DL*. Identification of Genes Essential for Sulfamate and Fluorine Incorporation During Nucleocidin Biosynthesis. *ChemBioChem* **2022**, 23, e202200140. <https://doi.org/10.1002/cbic.202200140>. *Featured on the cover and as a "Very Important Paper"*.
55. Gama SR, Stankovic T, Hupp K, Hejami AA, McClean M, Evans A, Beauchemin D, Hammerschmidt F, Pallitsch K*, Zechel DL*, Biosynthesis of the Fungal Organophosphonate Fosfonochlorin Involves an Iron(II) and 2-(Oxo)glutarate Dependent Oxacyclase. *ChemBioChem*, **2022**, 23, e202100352. <https://doi.org/10.1002/cbic.202100352>. *Featured on cover*.
54. Bernhardt, M., Berman, S., Zechel, D. L., and Bechthold, A*. Role of Two Exceptional trans Adenylation Domains and MbtH-like Proteins in the Biosynthesis of the Nonribosomal Peptide WS9324A from *Streptomyces calvus* ATCC 13382. *ChemBioChem* **2020**, 21, 2659-2666.
53. Tsyplik, O., Makitrynsky, R., Frensch, B., Zechel, D. L., Paululat, T., Teufel, R., and Bechthold, A. Oxidative Carbon Backbone Rearrangement in Rishirilide Biosynthesis. *J. Am. Chem. Soc.* **2020**, 142, 5913–5917
52. Makitrynsky, R., Tsyplik, O., Nuzzo, D., Paululat, T., Zechel, D. L., and Bechthold, A. Secondary nucleotide messenger c-di-GMP exerts a global control on natural product biosynthesis in streptomycetes. *Nucleic Acids Res.* **2020**, 48, 1583–1598.
51. Zhu, J., Zhang, S., Zechel, D. L., Paululat, T., and Bechthold, A.* Rational Design of Hybrid Natural Products by Utilizing the Promiscuity of an Amide Synthetase. *ACS Chem. Biol.* **2019** 14, 1793–1801.
50. Gama SR, Lo BSY, Séguin J, Pallitsch K, Hammerschmidt F, Zechel DL*. 2019. C-H Bond Cleavage Is Rate-Limiting for Oxidative C-P Bond Cleavage by the Mixed Valence Diiron-Dependent Oxygenase PhnZ. *Biochemistry* **2019**, 58, 5271-5280. *Invited submission for special issue on Mechanistic Enzymology (John Gerlt, ed.)*
49. Gama SR, Vogt M, Kalina T, Hupp K, Hammerschmidt F, Pallitsch K*, Zechel DL*. An Oxidative Pathway for Microbial Utilization of Methylphosphonic Acid as a Phosphate Source. *ACS Chem Biol* **2019**, 14, 735–741. *Prior to discovery of this pathway, only C-P lyase was known to degrade the simplest of organophosphonates.*

48. Zhang, S.; Klementz, D.; Zhu, J.; Makitrynsky, R.; Pasternak, A. R. O.; Günther, S.; Zechel, D. L.*; Bechthold, A*. Genome Mining Reveals the Origin of a Bald Phenotype and a Cryptic Nucleocidin Gene Cluster in *Streptomyces asterosporus* DSM 41452. *J. Biotechnol.* **2019**, 292, 23–31. *A genome mining approach was used to find a new producer of nucleocidin, the first in nearly 70 years.*
47. Sarwar, A; Latif, Z; Zhang, S; Zhu, J; Zechel, D; *Bechthold, A. Biological control of potato common scab with rare Isatropolone C compound produced by plant growth promoting *Streptomyces* A1RT. *Front. Microbiol.* **2018**, 9, 1126.
46. Zhang, S.; Zhu, J.; Zechel, D. L.; Jessen-Trefzer, C.; Eastman, R. T.; Paululat, T.; Bechthold, A. New WS9326A Derivatives and One New Annimycin Derivative with Antimalarial Activity Are Produced by *Streptomyces asterosporus* DSM 41452 and Its Mutant. *ChemBioChem* **2018**, 19, 272-279.
45. Horsman G* and Zechel DL*. Phosphonate Biochemistry. *Chem. Rev.* **2017**, 118, 5704-5783. *Invited review that was part of a thematic issue on "Unusual Enzymology in Natural Products Biosynthesis", edited by Wilfred van der Donk (U. Illinois).*
44. Zechel DL*, PhnK: Another piece of the carbon-phosphorus lyase puzzle. *Structure* **2016**, 24, 3-4. *Invited commentary on the cryo-EM structure of the PhnGHJK complex by the Zhang and Raushel labs.*
43. Johnston CW, Skinnider MA, Wyatt MA, Li X, Ranieri MRM, Yang L, Zechel DL, Bin Ma, and Magarvey NA*. An automated Genomes-to-Natural Products platform (GNP) for the discovery of modular natural products. *Nat. Commun.* **2015**, 6, 1–11.
42. Zhu XM, Hackl S, Thaker MN, Kalan L, Weber C, Urgast DS, Krupp EM, Brewer A, Vanner S, Szawiola A, Yim G, Feldmann J, Bechthold A, Wright GD, Zechel DL*: Biosynthesis of the fluorinated natural product nucleocidin in *Streptomyces calvus* is dependent on the *bldA* specified Leu-tRNA(UUA) molecule. *ChemBioChem* **2015**, 16, 2498-2506. *First discovered in 1956, nucleocidin was 're-discovered' in Streptomyces calvus after correcting a mutation in the gene bldA. We also identify the biosynthetic gene cluster.*
41. Gessner A, Heitzler T, Zhang S, Klaus C, Murillo R, Zhao H, Vanner S, Zechel DL*, and Bechthold A*. Changing biosynthetic profiles by expressing *bldA* in *Streptomyces* strains. *ChemBioChem* **2015**, 16, 2244-2252. *Constitutively expressing bldA in Streptomyces can frequently turn on sleeping biosynthetic genes, even when the strains contain native copies of bldA that are normal.*
40. van Staalduinen LM, McSorley FR, Schiessl K, Séguin J, Wyatt PB, Hammerschmidt F, Zechel DL*, Jia Z*: Crystal structure of PhnZ in complex with substrate reveals a di-iron oxygenase mechanism for catabolism of organophosphonates. *Proc. Natl Acad Sci USA* **2014**, 111, 5171-6. *Along with myo-inositol oxygenase, which oxidatively cleaves C-C bonds, PhnZ is a founding member of a family of oxygenases that use a unique mixed-valent diiron co-factor for catalysis.*
39. Hove-Jensen B*, Zechel DL, Jochimsen B: Utilization of glyphosate as a phosphorus source: Biochemistry and genetics of bacterial carbon-phosphorus lyase. *Microbiol. Mol. Biol. Rev.* **2014**, 78, 176-97.
38. Kalan L, Gessner A, Thaker MN, Waglechner N, Zhu X, Szawiola A, Bechthold A, Wright GD, Zechel DL*: A cryptic polyene biosynthetic gene cluster in *Streptomyces calvus* is expressed upon complementation with a functional *bldA* gene. *Chem. Biol.* **2013**, 20, 1214-1224. *Featured in a commentary by the eminent streptomyces geneticist, Keith Chater (<https://doi.org/10.1016/j.chembiol.2013.10.001>). The nucleocidin producer *Streptomyces calvus* is shown to have a bald, non-sporulating phenotype due to a mutation in the gene *bldA*, which is well known to be important for sporulation and secondary metabolite production.*
37. Hove-Jensen B*, McSorley FR, Zechel DL*: Catabolism and detoxification of 1-aminoalkylphosphonic acids: N-acetylation by the *phnO* gene product. *PLoS One* **2012**, 7, e46416. *PhnO is shown to be necessary to allow CP-lyase to cleave the bonds of 1-aminoalkylphosphonates, and additionally provides a protection against toxic compounds.*
36. McSorley FR, Wyatt PB, Martinez A, Delong EF, Hove-Jensen B, Zechel DL*: PhnY and PhnZ comprise a new oxidative pathway for enzymatic cleavage of a carbon-phosphorus bond. *J. Am. Chem. Soc.* **2012**, 134, 8364-7. *Highlighted as a 'Spotlight' article in JACS. In addition to the hydrolase and CP-lyase mechanisms, the PhnY-PhnZ pathway represents a third mechanism that is used by bacteria to extract inorganic phosphate from organophosphonates.*
35. He S-M, Wathier M, Podzelinska K, Wong M, McSorley F, Asfaw, A, Hove-Jensen B, Jia Z, Zechel DL*: Structure and mechanism of PhnP, a phosphodiesterase of the carbon-phosphorus lyase pathway. *Biochemistry*, **2011**, 50, 8603-15. *An extensive kinetic, mutagenic, and crystallographic analysis of the phosphodiesterase that recycles a 'dead-end' intermediate in the CP-lyase pathway.*

34. Jochimsen B, Lolle S, McSorely FR, Nabi M, Stougaard J, Zechel DL, Hove-Jensen B*: Five phn gene products as components of a multi-subunit complex of the carbon-phosphorus lyase pathway for organophosphonate catabolism. *Proc Natl Acad Sci USA*, **2011**, 108, 11393-8. *First evidence that CP-lyase is comprised, in part, of a multi-protein complex. This complex has since been the target of several structural studies (cryo EM, X-ray), and was an important factor in reconstituting the activity of C-P lyase in vitro by the Raushel lab (Nature 2011, 2013)*
33. Härle J, Günther S, Lauinger B, Weber M, Kammerer B, Zechel DL, Luzhetskyy A, Bechthold A*: Rational design of an aryl-C-glycoside catalyst from a natural product O-glycosyltransferase. *Chem Biol* **2011**, 18, 520-30.
32. Hove-Jensen B*, McSorley F, Zechel DL*: Physiological role of phnP-specified phosphoribosyl cyclic phosphodiesterase in catabolism of organophosphonic acids by the carbon-phosphorus lyase pathway. *J. Am. Chem. Soc.* **2011**, 133, 3617-24. *Identification of the dead-end intermediate that is formed as a product of the CP-bond cleaving step catalyzed by CP-lyase. PhnP is shown to convert this intermediate into a metabolically useful compound.*
31. Groom K, Bhattacharya A, Zechel DL*: Rebeccamycin and staurosporine biosynthesis: Insight into the mechanisms of the flavin-dependent monooxygenases RebC and StaC. *ChemBioChem* **2011**, 12, 396-400.
30. Podzelinska K, Latimer R, Bhattacharya A, Vining LC, Zechel DL*, Jia Z*: The structure of CmlS, a flavin-dependent halogenase involved in the biosynthesis of chloramphenicol. *J. Mol. Biol.* **2010**, 397, 316-331. *In this paper we characterize the 'halogenase' that installs the two chlorine atoms in the iconic antibiotic, chloramphenicol.*
29. Hove-Jensen B*, Rosenkrantz TJ, Zechel DL, Willemoes M: Accumulation of intermediates of the carbon-phosphorus lyase pathway for phosphonate degradation in *phn* mutants of *Escherichia coli*. *J. Bacteriol.* **2010**, 192, 370-374.
28. Nelson GW, Perry M, He SM, Zechel DL, Horton JH*: Characterization of covalently bonded proteins on poly(methyl methacrylate) by X-ray photoelectron spectroscopy. *Colloids. Surf. B Biointerfaces* **2010**, 78, 61-68.

Book Chapters

4. Kamat, S. S.*, Singh, S., Rajendran, A., Gama, S. R., and Zechel, D. L*. (2020) Enzymatic Strategies for the Catabolism of Organophosphonates. In *Comprehensive Natural Products III*, 3rd Ed. (Begley, T. P., and Liu, H.-W. eds), DOI: 9780081026908. *Invited review.*
3. Ulrich, EC; Kamat, SS*; Hove-Jensen, B*; Zechel DL*. Methylphosphonic Acid Biosynthesis and Catabolism in Pelagic Archaea and Bacteria. *Meth. Enzymol.* **2018**, 605, 351-426. *Invited review.*
2. Séguin J and Zechel DL*, "The Di-Iron Oxygenase PhnZ" in the *Encyclopedia of Inorganic and Bioinorganic Chemistry*, Messerschmidt, A., Ed., John Wiley & Sons, Ltd. **2016**. *Invited review.*

Seminars (2010-present)

61. *Guilt by association: chasing down new enzymes through novel natural products*. Seminar, Department of Biochemistry and Biomedical Sciences, McMaster University, June 25th, 2024.
60. *Guilt by association: chasing down new enzymes through novel natural products*. Seminar, Department of Chemistry and Biomolecular Sciences, University of Ottawa, January 17th, 2024.
59. Co-organizer (with Graeme Howe), Canadian Chemistry Conference and Exhibition, symposium on Natural Product Biosynthesis, Enzymology, and Protein Engineering, June 2nd to 6th, 2024.
58. Co-organizer (with Laurence Yang, James McLellan, George diCenzo, and Graeme Howe), annual Open Plastic Symposium, Kingston, April 22nd to 24th.
57. Recent progress in understanding sulfamate and fluorine incorporation during Nucleocidin biosynthesis, 105th, Canadian Chemistry Conference and Exhibition, Vancouver, June 2023
56. Mechanisms of unusual transformations involving organophosphonate natural products mediated by non-heme iron dependent oxygenases, 104th, Canadian Chemistry Conference and Exhibition, Calgary, June 2022.
55. Mechanisms of unusual transformations involving organophosphonate natural products mediated by non-heme iron dependent oxygenases. Dept. of Chemistry, University of British Columbia, October, 2021. **Distinguished Organic Lecture**

54. Mechanisms of unusual transformations involving organophosphonate natural products mediated by non-heme iron dependent oxygenases, Dept. of Chemistry, Simon Fraser University, October, 2021.
53. "Unusual Transformations in the Biosynthesis of the Halogenated Organophosphonate Fosfonochlorin", 51st IUPAC / 104th CCCE, Biosynthesis Symposium (Virtual meeting due to covid-19), August, 2021.
52. "Genomics driven discovery of new enzyme reactions and molecules", Dept. of Chemistry, Acadia University, Wolfville, NS, November 2019.
51. "Genomics driven discovery of new enzyme reactions and molecules", Dept. of Chemistry, Mt. Allison University, Sackville, NB, November 2019.
50. "Genomics driven discovery of new enzyme reactions and molecules", Dept. of Chemistry, St. Francis Xavier University, Antigonish, NS, November 2019.
49. "Genomics driven discovery of new enzyme reactions and molecules", Dept. of Chemistry, Dalhousie University, Halifax, NS, November 2019.
48. "Genomics driven discovery of new microbial enzymes and natural products", Dept. of Chemistry, University of Manitoba, May 2019.
47. "Follow the chemistry: Making and breaking odd bonds with enzymes." Dept. of Chemistry, Université Laval, Quebec, December 2018. **Invited seminar.**
46. "A Short History of Methylphosphonate". RTG1976 Co-factor Retreat, Felberg-Falkau, Germany, April **2018. Keynote speaker.**
45. "Activation of Molecular Oxygen for Microbial Biosynthesis and Catabolism", RTG1976 Enzyme Co-factor Working Group, Albert-Ludwigs-Universität Freiburg, Freiburg, Germany, February, **2018. Invited seminar.**
44. "New enzyme mechanisms from microbial catabolism of organophosphonates", DPhG seminar series, Institute for Pharmaceutical Sciences, Albert-Ludwigs-Universität Freiburg, November **2017**, Freiburg, Germany. **Invited seminar.**
43. "New chemistry from the sea: Enzymatic cleavage of phosphonate CP bonds via CH bond activation", 100th Canadian Chemistry Conference and Exhibition, Symposium on Reactivity in Organic and Biological Chemistry, Toronto, June **2017. Invited seminar.**
42. "Biosynthesis of fluorometabolites and the perplexing case of a missing molecule" 100th, Canadian Chemistry Conference and Exhibition, Symposium on Fluorinated Molecules: Syntheses, Analysis, and Applications, Toronto, June **2017. Invited seminar.**
41. "Follow the chemistry: making and breaking odd-bonds with enzymes". Molecular and Cellular Biology group, Department of Biology, Queen's University, March 28th, 2017. Invited seminar.
40. "Follow the chemistry: making and breaking odd-bonds with enzymes". Department of Chemistry, University of Toronto, March 10th, 2017. **Invited seminar.**
39. "*Raising the dead: A cure for baldness and cryptic biosynthesis in Streptomyces calvus*", International VAAM-Workshop 2016, Biology of Bacteria Producing Natural Products, Freiburg, Germany, September 2016. **Plenary speaker.**
38. "*A cure for baldness and cryptic biosynthesis in Streptomyces calvus*", Maritimes Natural Products Conference, Dalhousie University, Halifax, August 2016. **Plenary speaker.**
37. "*Follow the chemistry: Making and breaking odd bonds with enzymes.*" Trent University, March 2nd, 2016.
36. "*Follow the chemistry: Making and breaking odd bonds with enzymes.*" Wilfrid Laurier University Jan. 29th, 2016.
35. "*A cure for baldness and cryptic biosynthesis in Streptomyces calvus.*" Pacificchem 2015 - Biosynthesis of Natural Products symposium, Waikiki, USA, December 2015. **Invited seminar.**
34. "*A new oxidative pathway for enzymatic cleavage of phosphonate CP bonds.*" 250th American Chemical Society National Meeting, Symposium celebrating Gordon Hammes Award recipient Frank Raushel, Boston, August, 2015. **Invited seminar.**
33. "*A cure for baldness and cryptic biosynthesis in Streptomyces calvus*". American Society of Pharmacognosy Annual Meeting, Copper Mountain, Colorado, USA, July 2015. **Invited seminar.**
32. "*Eliminating bottlenecks in natural product discovery: the role of TTA codons in the expression of biosynthetic pathways in Streptomyces.*" Canadian Society for Chemistry national meeting, Natural

Product Biosynthesis symposium, Ottawa, June 2015

31. "*Raising the dead: cryptic biosynthesis in Streptomyces calvus*". Cellular and Molecular Biology group meeting, Dept. of Biology, Queen's University, Kingston, Ontario, January 2015.
30. "*New chemistry from the sea: Enzymatic cleavage of phosphonate CP bonds via CH bond activation*." 20th International Conference on Phosphorus Chemistry (ICPC), Dublin, Ireland, June 2014. **Invited seminar.**
29. "*Mechanistic and structural analysis of a new di-iron dependent oxygenase that cleaves carbon-phosphorus bonds*." Canadian Society for Chemistry national meeting, Enzymology Session, Vancouver, June 2014
28. "*New enzyme mechanisms for the cleavage of carbon-phosphorus bonds*." Canadian Society for Chemistry national meeting, Quebec, May, 2013.
27. "*Expression and analysis of cryptic biosynthetic genes in Streptomyces*.", Canadian Society for Chemistry national meeting, Quebec, May, 2013.
26. "*Advances in the structure and mechanisms of microbial enzymes that transform organophosphonates to phosphate*" Dept. of Chemistry, York University, October, 2012.
25. "*Necessity is the mother of invention: enzymatic cleavage of carbon-phosphorus bonds*." BioMOLAR Network, Dept. of Chemistry, University of Ottawa, April 2012.
24. "*Waking the dead: Cryptic biosynthesis in Streptomyces calvus*." Depts. of Biochemistry and Molecular Biology, Dalhousie University, September 2011.
23. "*Necessity is the mother of invention: enzymatic cleavage of carbon-phosphorus bonds*." Dept. of Chemistry, McMaster University, September 2011.
22. "*Flavin-dependent enzymes in natural product biosynthesis*." Helmholtz Institute for Pharmaceutical Sciences (HIPS), Saarbrücken University, Germany, May, 2011.
21. "*New frontiers in enzymatic organophosphonate degradation*." Biochemisches Institut, Universität Zürich, Switzerland, March, 2011.
20. "*Breaking up is hard to do: Analysis of bacterial enzymes involved in the metabolism of organophosphonates*." Albert-Ludwigs-Universität, Dept. of Pharmaceutical Sciences, Freiburg, Germany, November, 2010.
19. "*Halogenases: better living through 'natural' chemistry*." Canadian Society for Chemistry national meeting, Toronto, June, 2010.
18. "*Oxidative Enzymes in Natural Product Biosynthesis*." Dept. of Biochemistry, University of Victoria, April, 2010.

RESEARCH TEAM (current team in blue)

PhD

1. Samantha Hollands (2019 – present, NSERC PGS-D). Biosynthesis of cyanobactins.
2. Sahar Shokrgozar (2022 – present). Biodegradation of plastics.
3. Alessia Rizzello (2022 – present). Biosynthesis of nucleocidin.
4. Liwah Keller (2022 – present). Biodegradation of plastics.
5. Shaoyan Wang (2024 – present). Biodegradation of plastics.
6. Julia Tasch (2022 – present, co-supervised with Bechthold, U. Freiburg). Cyanobactin biosynthesis.
7. Tamara Dinhof (2022 – present, co supervised with Pallistch, U. Vienna). CP-lyase inhibitors.
8. Ola Pasternak (2016 – 2022). Biosynthesis of the fluorometabolite nucleocidin by *Streptomyces calvus*.
9. Mirjam Bernhardt (2017-2020, co-supervised with Bechthold), U. Freiburg). Biosynthesis of a non-ribosomal peptide.
10. David Simon (PhD student, 2013 – 2019, co-supervised with Oleschuk, Queen's Chem). Influence of the *bldA* gene on the proteomes and secondary metabolite profiles in *Streptomyces*.

11. Usman Aftab (April – Oct., 2013, visiting Ph.D. student, University of the Punjab). Discovery of anticancer compounds in *Streptomyces* isolated in Pakistan
12. Fern McSorley (Ph.D., 2008 – 2013). Enzymatic cleavage of carbon-phosphorus bonds.
13. Katie Groom (Ph.D., 2005 – 2013, co-supervised with Snieckus, Queen's Chem.). Studies into the Biosynthesis and Chemical Synthesis of Indolocarbazoles and Related Heterocyclic Compounds. Metalation of Indole-6- Carboxamide.
14. Arne Gessner (PhD 2015-2018, co-supervised with Bechtold, U. Freiburg). The effect of the *bldA* gene on *Streptomyces* secondary metabolite production.

MSc

1. [Mosorire Tajudeen \(2023 – present\). Biodegradation of polyurethane.](#)
2. [Danica Levesque \(2024 – present\). Carbon-phosphorus lyase.](#)
3. Maame Yaa Yamoah (2021 – present). Microbial degradation of plastic.
4. Kendall Hupp (4th year thesis, 2018 – 2019; MSc, 2019 – 2021). Novel pathways for organophosphonate degradation and biosynthesis.
5. Suhayla Sequeira (MSc student, 2017 – 2019). Biosynthesis of the fluorometabolite nucleocidin by *Streptomyces calvus*.
6. Isobel Barber (MSc student 2018-2019, on exchange from Durham University, UK). Biosynthesis of a cyanobactin.
7. Jorge Antonio Tzec Interián (MSc student, summer of 2018, on exchange from the Instituto de Ecología A.C., Xalapa, México). Application of a promoter assay to improve nucleocidin production in *S. calvus*.
8. Becky Lo (2017 – 2018). Mechanistic analysis of the phosphonate degrading enzymes PhnY* and PhnZ.
9. Kaitlyn Pinkett (MSc student, 2015 – 2017). Biosynthesis of the fluorinated natural product nucleocidin by *S. calvus*.
10. Jacqueline Séguin (M.Sc., 2013 – 2015). Mechanistic analysis of the organophosphonate degrading enzymes PhnY and PhnZ.
11. Alyssa Brewer (M.Sc., 2013 – 2015). Analysis of cryptic biosynthetic pathways in *Streptomyces calvus*.
12. XiMing Zhu (M.Sc., 2012 – 2014). Exploration of cryptic biosynthetic pathways activated with a functional *bldA* gene in *Streptomyces calvus*.
13. Ryan Latimer (M.Sc., 2008 – 2010). Studies on the chloramphenicol halogenase CmlS.
14. Di Hu (M.Sc., 2007 – 2010, co-supervised with Derek Pratt). Computational Studies of Lipid Autoxidation and Solvent-Mediated Antioxidant Activity and a Kinetic Study of a Halogenase in the Pyrrolnitrin Biosynthetic Pathway.
15. Meagan Perry (M.Sc., 2006 – 2009). Improving protein solubility via directed evolution.
16. Shu-Mei He (M.Sc., 2005-2008). Towards the structure and function of CP-lyase enzymes.

Postdoctoral Fellows

1. [Dr. Maria Cleveland \(2022 – present\). Plastic biodegradation](#)
2. [Dr. Jaeick Lee \(2024 – present\). Plastic biodegradation](#)
3. Dr. Sheng Li (2023 – present). Synthesis of substrate probes for polyurethane degrading enzymes.
4. Dr. Luana Cunha (2022 – present). Nucleocidin biosynthesis.
5. Dr. Tripti Dadheech (2022). Plastic biodegradation.
6. Dr. Simanga Gama (2018 – 2021). Characterization of glyphosate degradation enzymes.
7. Dr. Manisha Patel (2018 – 2020). Biosynthesis of cyanobactins.
8. Dr. Daria Trofimova (2008 – 2010). Production of reactive oxygen species by antibodies (joint with Derek Pratt).

9. Dr. Anupam Bhattacharya (2005 – 2007). Indolocarbazole biosynthesis and halogenases.

10. Dr. Yan Luo (2004 – 2006). Analysis of bacterial CP-lyase enzymes.

Visiting Professors

Prof. Bjarne Hove-Jensen, Dept. of Biology, University of Copenhagen (2010 – 2012). Analysis of the pathway for organophosphonate degradation by carbon-phosphorus lyase.

Undergraduate

Supervised 54 undergraduates since 2004. This includes 4th year honours thesis projects, NSERC USRAs, co-op placements, volunteers, and visiting students.

COLLABORATIONS

National

Zongchao Jia, DBMS, Queen's University (2005 – present)

Jia is a Canada Research Chair in Structural Biology. I have long collaborated with his lab to determine the X-ray crystal structures of our enzymes. We have published several papers together on CP-bond cleaving enzymes and halogenases (*PNAS* **2014**, *Biochemistry* **2011**, *J Mol Biol* **2010**, *J Biol Chem* **2009**, *J Bacteriol* **2008**).

Nathan Magarvey, McMaster University (2014-2015)

We worked with the Magarvey lab to use his pioneering "Genes to Natural Products" methodology (GNP), a combination of bioinformatics, chemoinformatics, and MS/MS. GNP allows one to predict the structure of a natural product based on a microbial biosynthetic gene cluster. We share co-authorship on a paper describing the versatility of GNP (*Nat. Commun.* **2015**).

Gerry Wright, McMaster University (2010-2015)

We collaborated with the Wright lab to sequence the genome of *Streptomyces calvus*. It was through this collaboration that we discovered the role of *bldA* in the expression of cryptic biosynthetic pathways, including that of the rare fluorinated natural product, nucleocidin. We share co-authorship on our *Chem Biol* **2013** and *ChemBioChem* **2015** papers.

International

Katharina Pallitsch and Friedrich Hammerschmidt, University of Vienna, Austria (2013 – present)

Analysis of the mechanisms of carbon-phosphorus bond cleavage by PhnY and PhnZ using substrate analogues synthesized by the Pallitsch and Hammerschmidt labs. We have co-authored several papers together, including *PNAS* **2014**, *ACS Chem Biol* **2019**, *Biochemistry* **2019**, *ChemBioChem* **2022**, and *Biochem. Soc. Trans.* **2023**.

Ditlev Brodersen, Aarhus University, University of Copenhagen (2022 – present)

Structural analysis of CP-lyase with mechanism-based inhibitors. The Ditlev lab has published milestone papers describing the C-P-lyase complex using X-ray crystallography (*Nature* **2015**) and cryo-EM spectroscopy (*Nature Comm.* **2023**). Along with Katharina Pallitsch (U. Vienna) we are using mechanism-based inhibitors to identify and structurally characterize the active sites of the complex.

Amie K. Boal and J. Martin Bollinger, Jr, Penn State University (2022 – present)

Structural and mechanistic analysis of iron dependent oxygenases related to phosphonate biochemistry. This new collaboration seeks to understand how iron dependent oxygenases generate and control reactive oxygen species in demanding reactions such as C-H bond cleavage. Examples include the fosfonochlorin biosynthetic enzyme FfnD recently characterized by our lab (*ChemBioChem* **2022**).

Andreas Bechthold, Albert-Ludwigs-Universität-Freiburg, Germany (2010 – present)

Analysis of cryptic biosynthetic pathways in *Streptomyces*. This highly successful collaboration began during my sabbatical in the Bechthold lab in 2010-2011. This collaboration initiated our studies into the biosynthesis of the annimycin and nucleocidin in *Streptomyces calvus*. We have co-authored several papers, including *Chem Biol* (**2013**), *ChemBioChem* (**2015**, **2018**, **2020**, **2022**), *J. Biotechnol* (**2019**), *JACS* (**2020**), *NAR* (**2020**), and *ACS Chem Biol* (**2019**). We continue to collaborate on the effect of the *bldA* gene on expression of cryptic biosynthetic genes in *Streptomyces*. This has involved the exchange of students between our labs.

Jorg Feldmann, University of Aberdeen, United Kingdom (2014-2015)

Feldmann has developed a novel spectroscopic method called continuum source molecular absorption spectroscopy (CS-MAS) which can be coupled to HPLC for the detection of molecules that contain fluorine. We collaborate with his lab to analyze culture extracts from *Streptomyces calvus* for the presence of organofluorine secondary metabolites, including nucleocidin. He is a co-author on our *ChemBioChem* 2015 paper on nucleocidin.

Edward F. DeLong, MIT, USA (2011 – 2012)

Use of genetic screens to discover new organophosphonate catabolic pathways in microbes. The DeLong lab shared metagenomic data that contributed to our *JACS* (2012) paper on the novel oxidative PhnY / PhnZ pathway.

Bjarne Hove-Jensen, Aarhus University, University of Copenhagen (2007 – 2018)

Analysis of the *E. coli* carbon-phosphorus (CP) lyase pathway for organophosphonate degradation. This was a very fruitful collaboration, producing 12 co-authored papers and reviews concerning the CP-lyase pathway, including publications in *JACS* (2011, 2012) and *PNAS* (2011). Hove-Jensen visiting my lab on two occasions (Feb 2010 - Sept 2010, Apr 2011 - Sept 2011) for a total of 14 months which provided a unique opportunity for my students to work alongside an expert in *E. coli* genetics.