

Curriculum Vitae

Stephen Cochrane MSci PhD MRSC

Senior Lecturer in Organic Chemistry
School of Chemistry, Queen's University Belfast
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EDUCATION AND EMPLOYMENT HISTORY

Senior Lecturer in Organic Chemistry, Queen's University Belfast (Aug 2019 – present)

Lecturer in Organic Chemistry, Queen's University Belfast (April 2017 – July 2019)

Sir Henry Wellcome Postdoctoral Fellow, University of Oxford (Jan 2016 – March 2017)

PhD in Organic Chemistry, University of Alberta (Sept 2010 – Dec 2015)

MSci in Chemistry, Queens University Belfast (Sept 2006 – June 2010)

RESEARCH EXPERIENCE

Sir Henry Wellcome Postdoctoral Fellow (Feb 2016 – Mar 2017)

Department of Chemistry, University of Oxford, Oxford, UK

Research Sponsors: Prof. Benjamin G. Davis and Prof. James H. Naismith (St. Andrews)

Project: Uncovering the mode of action of lipid II flippase: A new antibiotic target

PhD Student (Sept 2010 – Dec 2015)

Department of Chemistry, University of Alberta, Edmonton AB, Canada

Supervisor: Prof. John C. Vederas

Project: Structural and mechanistic studies on antimicrobial lipopeptides

Undergraduate Research Project (Sept 2009 – May 2010)

School of Chemistry, Queens University Belfast, Belfast, Northern Ireland, UK

Supervisor: Dr. William P. D. Goldring

Project: Synthesis of cationic lipids for gene therapy

Summer Research Project (June 2009 – Sept 2009)

Department of Chemistry, University of Alberta, Edmonton AB, Canada

Supervisor: Prof. John C. Vederas

Project: Solid supported syntheses of both components of the lantibiotic lactacin 3147

Summer Research Project (Aug 2008 – Sept 2008)

Queens University Ionic Liquids Laboratory, Belfast, Northern Ireland, UK

Supervisor: Dr. Martin J. Earle

Project: Novel reactions of selenium in ionic liquids

Summer Research Project (June 2008 – July 2008)

Department of Pharmacy, University of Oslo, Oslo, Norway

Supervisor: Dr. Trond V. Hansen

Project: Synthesis of a SIRT1 inhibitor for the treatment of type II diabetes

INDEPENDENT RESEARCH GRANTS*

*PI = Principal Investigator, Col = Co-investigator, % = percent ownership of funds

12. **£26,704** (PI, 100%) – EPSRC Impact Acceleration Award, Jan – June 2024
Chemical Optimization of in-silico-Generated Drug Leads
11. **£1,270,245** (PI, 100%) – European Research Council Starting Grant covered by UKRI Frontier Research Guarantee, Oct 2023 – Sept 2028
NEW HOPE: New Approaches to Overcome the Problem of Antimicrobial Resistance
10. **£965,055** (Col, 5%) – EPSRC (EP/W021390/1), Feb 2022 – Jan 2024
A solid-state NMR instrument for Northern Ireland
9. **£243,690** (PI, 100%) – EPSRC (EP/V032860/1), Dec 2021 – Nov 2023
Interrogating the Nisin:lipid II Interaction: A Chemical Biology Approach
8. **£14,831** (PI, 100%) – EPSRC Impact Acceleration Award, Sept – Dec 2020
Immobilization of Antibiotic Targets
7. **£54,450** (PI, 100%) – EPSRC Equipment Grant, Sept 2020
Purchase of spectrofluorimeter
6. **£391,380** (PI, 100%) – EPSRC (EP/T01783X/1), Sept 2020 – Aug 2023
Synthesis of novel brevicidine and laterocidine analogues active against multi-drug-resistant Gram-negative bacteria
5. **£26,491** (PI, 100%) – QUB Interdisciplinary Fund, Jul 2019 – Jun 2020.
Solid-Supported Enzymatic Synthesis of Glycolipids (SEGS): New tools for antibiotic discovery
4. **£112,500** (Col, 10%) – Invest NI, Dec 2018 – Nov 2019
Pharmaceutical development of novel antimicrobial peptides
3. **£215,788** (PI, 100%) – EPSRC (EP/S015892/1), Jan 2019 – Dec 2020
One size fits all – The semi-synthesis of new undecaprenol analogues for the study of multiple undecaprenyl-processing enzymes
2. **£20,000** (PI, 100%) – Royal Society (RSG\R1\180063), April 2018 – March 2019
Clickaprenol, a new semi-synthetic probe to study the mechanism of several different bacterial flippases
1. **£30,136** (PI, 100%) – Wellcome Trust (110270/A/15/Z), April 2017 – Jan 2020
Uncovering the Mode of Action of Lipid II Flippase: A New Antibiotic Target

MAJOR SCHOLARSHIPS AND AWARDS

Independent Awards and Fellowships

- 2019 : N/A – Thieme Chemistry Journals Award for Early-Career Researchers
2016 : £250,000 – Sir Henry Wellcome Postdoctoral Fellowship

Graduate Awards and Scholarships

- 2015 : \$5,000 – Andrew Stewart Memorial Prize
2014 : \$60,000 – Alberta Innovates Health Solutions Graduate Scholarship
2013 : N/A – CHEM 502 Graduate Seminar Award
2011 : \$150,000 – Vanier Canada Graduate Scholarship
2011 : \$18,000 – Presidents Doctoral Prize of Distinction
2010 : \$9,000 – Provost Doctoral Entrance Award

Undergraduate Awards and Scholarships

- 2010 – Cecil Wilson Top Graduate Award
2009 – Level 3 Foundation Award
2008 – IAESTE NI Trainee of the Year
2006 – Queens University Belfast Entrance Scholarship

PEER-REVIEWED PUBLICATIONS

28. Buijs, N. P.; Matheson, E. J.; **Cochrane, S. A.***; Martin, N. I.*; Targeting membrane-bound bacterial cell wall precursors; A tried and true antibiotic strategy in nature and the clinic. *Chem. Comm.* **59**, 7685 (2023).
27. Ballantine, R. D.; Ayed, K. A.; Bann, S. J.; Hoekstra, M.; Martin, N. I.* and **Cochrane, S. A.***; Linearization of the Brevicidine and Laterocidine Lipopeptides Yields Analogues that Retain Full Antibacterial Activity. *J. Med. Chem.* **66**, 6002 (2023).
26. Ballantine, R. D.; Ayed, K. A.; Bann, S. J.; Hoekstra, M.; Martin, N. I.* and **Cochrane, S. A.***; Synthesis and Structure-Activity Relationship Studies of N-Terminal Analogues of the Lipopeptide Antibiotics Brevicidine and Laterocidine. *RSC Med. Chem.* **13**, 1640 (2022).
25. Ayed, K. A.; Ballantine, R. D.; Hoekstra, M.; Bann, S. J.; Wesseling, C. M. J.; Bakker, A. T., Zhong, Z.; Li, Y-X., van der Stelt, M.; **Cochrane, S. A.***; Martin, N. I.* Synthetic Studies with the Brevicidine and Laterocidine Lipopeptide Antibiotics Including Analogues with Enhanced Properties and in vivo Efficacy. *Chem. Sci.* **13**, 3563 (2022).
24. Kotsogianni, I.; Wood, T. M.; Alexander, F. M.; **Cochrane, S. A.** and Martin N. I. Binding Studies Reveal Phospholipid Specificity and Its Role in the Calcium-Dependent Mechanism of Action of Daptomycin. *ACS Infectious Diseases* **7**, 2612 (2021).
23. Bann, S. J.; Ballantine, R. D and **Cochrane, S. A.** The Tridecaptins: Non-Ribosomal Peptides That Selectively Target Gram-Negative Bacteria. *RSC Med Chem* **12**, 538 (2021).
22. Baker, R. B.; Ives, C. M.; Bray, A.; Caffrey, M. and **Cochrane, S. A.** Undecaprenol Kinase: Function, Mechanism and Substrate Specificity of a Potential Antibiotic Target. *Eur. J. Med. Chem.* **210**, 113062 (2021).
21. Cochrane, R. V. K.; Alexander, F. M.; Boland, C.; Fetis, S.; Caffrey, M. and **Cochrane, S. A.** From Plant to Probe: Semi-Synthesis of Labelled Undecaprenol Analogues Allows Rapid Access to Probes for Antibiotic Targets. *Chem. Commun.* **56**, 8603 (2020).
20. **Cochrane, S. A.** and Lohans, C. T. Breaking Down the Cell Wall: Strategies for Antibiotic Discovery Targeting Bacterial Transpeptidases. *Eur. J. Med. Chem.* **194**, 112262 (2020).
19. Calabrese, C.; Uriarte, I.; Insausti, A.; Vallejo-López, M.; Basterretxea, F. J.; **Cochrane, S. A.**; Davis, B. G.; Corzana, F. and Cocinero, E. J. Observation of the Unbiased Conformers of Putative DNA-Scaffold 2 Ribosugars. *ACS Cent. Sci.* **6**, 293-303 (2020).
18. Chiorean, S.; Antwi, I.; Carney, D. W.; Kotsogianni, I.; Giltrap, A. M.; Alexander, F. M.; **Cochrane, S. A.**; Payne, R. J.; Martin, N. I.; Henninot, A. and Vederas, J. C. Dissecting the Binding Interactions of Teixobactin with the Bacterial Cell-Wall Precursor Lipid II. *ChemBioChem* **21**, 781-792 (2020).
17. Bann, S. J.; Ballantine, R. D.; McCallion, C. E.; Qian, P-Y.; Li, Y-X. and **Cochrane, S. A.** A Chemical-Intervention Strategy to Circumvent Peptide Hydrolysis by D-Stereoselective Peptidases. *J. Med. Chem.* **62**, 10466-10472 (2019).
16. Ballantine, R. D.; McCallion, C. E.; Nassour, E.; Tokajian, S. and **Cochrane, S. A.** Tridecaptin-Inspired Antimicrobial Peptides with Activity Against Multidrug-Resistant Gram-Negative Bacteria. *Med. Chem. Commun.* **10**, 484-487 (2019).
15. Ballantine, R. D.; Li, Y-X.; Qian, P-Y. and **Cochrane, S. A.** Rational Design of New Cyclic Analogues of the Antimicrobial Lipopeptide Tridecaptin A₁. *Chem. Commun.* **54**, 10634-10637 (2018).
14. Dong, Y. Y.; Wang, H.; Pike, A. C. W.; **Cochrane, S. A.**; Hamedzadeh, S.; Wyszynski, F. J.; Bushell, S. R.; Royer, S. F.; Widdick, D. A.; Sajid, A.; Boshoff, H. I.; Park, Y.; Lucas, R.; Liu, W-M.; Lee, S. S.; Machida, T.; Minnal, L.; Mehmood, S.; Belaya, K.; Liu, W-W.; Chu, A.; Shrestha, L.; Mukhopadhyay, S. M. M.; Strain-Damerell, R.; Chalk, N. A.; Burgess-Brown, N. A.; Bibb, M. J.; Barry 3rd, C. E.; Robinson, C. V.; Beeson, D.; Davis, B. G. and Carpenter, E. P. Structures of DPAGT1 Explain Glycosylation Disease Mechanisms and Advance TB Antibiotic Design. *Cell* **175**, 1045-1058 (2018).

13. Bakhtiary, A.; **Cochrane, S. A.**; Mercier, P.; McKay, R. T.; Miskolzie, M.; Sit, C. S. and Vederas, J. C. Insights into the Mechanism of Action of the Two-Peptide Lantibiotic Lacticin 3147. *J. Am. Chem. Soc.* **139**, 17803-17810 (2017).
12. **Cochrane, S. A.**; Findlay, B.; Bakhtiary, A.; Acedo, J. Z.; Rodriguez-Lopez, E. M.; Mercier, P.; and Vederas, J. C. The Antimicrobial Lipopeptide Tridecaptin A₁ Selectively Binds to Gram-Negative Lipid II. *Proc. Natl. Acad. Sci. USA* **113**, 11561-11566 (2016).
11. **Cochrane, S. A.**; and Vederas, J. C. Lipopeptides from *Bacillus* and *Paenibacillus* spp.: A Gold Mine of Antibiotic Candidates. *Med. Res. Rev.* **36**, 4-31 (2016).
10. **Cochrane, S. A.**; Li, X.; He, S.; Yu, M.; Wu, M.; and Vederas, J. C. Synthesis of Tridecaptin-Antibiotic Conjugates with in Vivo Activity Against Gram-Negative Bacteria. *J. Med. Chem.* **58**, 9779-9785 (2015).
9. **Cochrane, S. A.**; Surgenor, R. R.; Khey, K. M. W.; and Vederas, J. C. Total Synthesis and Stereochemical Assignment of the Antimicrobial Lipopeptide Cerexin A₁. *Org. Lett.* **17**, 5428-5431 (2015).
8. **Cochrane, S. A.**; Lohans, C. T.; van Belkum, M. J.; Bels, M.; and Vederas, J. C. Studies on Tridecaptin B₁, a New Tridecaptin Analogue with Activity Against Multidrug Resistant Gram-Negative Bacteria. *Org. Biomol. Chem.* **13**, 6073-6081 (2015).
7. Kwon, M.; **Cochrane, S. A.**; Vederas, J. C.; and Ro, D-K. Molecular Cloning and Characterization of Drimenol Synthase from Valerian (*Valeriana officinalis*). *FEBS Lett.* **588**, 4597-4603 (2014).
6. **Cochrane, S. A.**; and Vederas, J. C. Unacylated Tridecaptin A₁ Acts as an Effective Sensitizer of Gram-Negative Bacteria to Other Antibiotics. *Int. J. Antimicrob. Agents* **44**, 493-499 (2014).
5. **Cochrane, S. A.**; Findlay, B.; Vederas, J. C.; and Ratemi, E. S. Key Residues in Octyl-tridecaptin A₁ Analogs Linked to Stable Secondary Structure in the Membrane. *ChemBioChem* **15**, 1295-1299 (2014).
4. **Cochrane, S. A.**; Lohans, C. T.; Brandelli, J. R.; Mulvey, G.; Armstrong, G. D.; and Vederas, J. C. Synthesis and Structure-Activity Relationship Studies of N-Terminal Analogues of the Antimicrobial Peptide Tridecaptin A₁. *J. Med. Chem.* **57**, 1127-1131 (2014).
3. Lohans, C. T.; van Belkum, M. J.; **Cochrane, S. A.**; Huang, Z.; Sit, C. S.; McMullen, L. M.; and Vederas, J. C. Biochemical, Structural and Genetic Characterization of Tridecaptin A₁, an Antagonist of *Campylobacter jejuni*. *ChemBioChem* **15**, 243-249 (2014).
2. **Cochrane, S. A.**; Huang, Z.; and Vederas, J. C. Investigation of the Ring-Closing Metathesis of Peptides in Water. *Org. Biomol. Chem.* **11**, 630-639 (2013).
1. Liu, W.; Chan, A. S. H.; Liu, H.; **Cochrane, S. A.**; and Vederas J. C. Solid Supported Chemical Synthesis of Both Components of the Lantibiotic Lacticin 3147. *J. Am. Chem. Soc.* **133**, 14216-14219 (2011).

PATENTS

1. United Kingdom Priority Patent Application No. 2101165.5; Title: Antibiotic Natural Product Analogues Inventors: Ballantine, R. D.; **Cochrane, S. A.**; Al Ayed, K. and Martin, N.I. Priority date: January 28, 2021.

CONFERENCE PRESENTATIONS AND VISITING SPEAKER INVITATIONS

22. **Cochrane, S. A.** (June 9th, 2023) Plenary Speaker at Pathogen Biology Ireland Symposium, Galway, Ireland.
21. **Cochrane, S. A.** (May 21st, 2023) Speaker at 56th ESBOC Chemical Biology in Europe Symposium, Gregynog Hall, Wales, UK.
20. Organized 2023 RSC Chemical Biology and Bioorganic Group Forum, Belfast, UK.
19. **Cochrane, S. A.** (Aug 28th – Sept 2nd, 2022) Speaker at European Peptide Symposium, Barcelona, Spain.
18. **Cochrane, S. A.** (Aug 8th – 9th, 2022) Invited Speaker for Chemical Biology Ireland, Dublin.

17. **Cochrane, S. A.** (Jan 28th, 2022) Visiting Speaker at Wayne State University (virtual).
16. **Cochrane, S. A.** (Nov 16th, 2020) 3rd SCI/RSC Symposium on Antimicrobial Drug Discovery in London, UK. *Cancelled due to Covid-19.*
15. **Cochrane, S. A.** (Aug 17th – 18th, 2020) Irish Chemical Biology Symposium in Dublin, Ireland. *Cancelled due to Covid-19.*
14. **Cochrane, S. A.** (Jun 7-12th, 2020) Virtual FASEB Microbial Glycobiology Conference.
13. **Cochrane, S. A.** (Jan 30th, 2020) Visiting Speaker at Trinity College Dublin, Ireland.
12. **Cochrane, S. A.** (Nov 29th, 2019) Visiting Speaker at Maynooth University, Ireland.
11. **Cochrane, S. A.** (Sept 6th, 2019) Speaker at the Chemical Biology and Bio-organic Chemistry Group Meeting in Fribush, UK.
10. **Cochrane, S. A.** (Aug 28th, 2019) Speaker at the International Meeting on Antimicrobial Peptides in Utrecht, Netherlands.
9. **Cochrane, S. A.** (Mar 25th, 2019) Speaker at the 10th RSC Chemical Biology and Bio-organic Chemistry Group Forum in Manchester, UK.
8. **Cochrane, S. A.** (2018) Speaker at Chemistry as Innovating Science (CHAINS) 2018 in Leiden, Netherlands.
7. **Cochrane, S. A.** (2018) Speaker at the 101st Canadian Chemistry Conference and Exhibition in Edmonton, Alberta, Canada.
6. **Cochrane, S. A.**; and Davis, B. G. (2017) Poster presentation at the 25th American Peptide Symposium in Whistler, BC, Canada.
5. **Cochrane, S. A.**; Findlay, B.; Bakhtiary, A.; Acedo, J. Z.; Rodriguez-Lopez, E. M.; and Vederas, J. C. (2016) Poster presentation at the 34th European Peptide Symposium in Leipzig, Germany.
4. **Cochrane, S. A.**; and Vederas, J. C. (2015) Poster presentation at the 24th American Peptide Symposium in Orlando, FL, USA.
3. **Cochrane, S. A.**; and Vederas, J. C. (2014) Speaker at the 33rd European Peptide Symposium in Sofia, Bulgaria.
2. **Cochrane, S. A.**; and Vederas, J. C. (2013) Speaker at the 2013 Volcano Conference in Chemical Biology in Pack Forest, WA, USA.
1. **Cochrane, S. A.**; Huang, Z.; and Vederas, J. C. (2012) Poster presented at the 95th Canadian Chemistry Conference and Exhibition in Calgary, Alberta, Canada.

TEACHING EXPERIENCE

Queen's University Belfast (April 2017 – present)

Lectures: CHM4007 – Frontiers in Drug Discovery (course coordinator); CHM3016 – Drug Development; CHM3002 – Organic Chemistry III; CHM1004 – Structure, Reactivity and Mechanism in Organic and Bioorganic Chemistry

Tutorials: CHM1101 – Organic Chemistry I; CHM2003 – Organic Chemistry II

Lab classes: CHM3015 – Advanced Practical Work in Medicinal Chemistry (course coordinator)

University of Oxford (Feb 2016 – March 2017)

Tutorials: Organic Chemistry Tutor for Year 2 and 3 students at Pembroke College

Laboratory Manager: Laboratory manager of one of the Davis group labs (8 people)

University of Alberta (Sept 2010 – Dec 2015)

Teaching Assistant: Organic Chemistry lab instructor and help-session instructor