ARRTI

Alberta RNA Research and Training Institute

ANNUAL REPORT

2018 – 2019

University of Lethbridge

FIAT LUX

MAY 1, 2018 TO
APRIL 30, 2019

WWW.ULETH.CA/RESEARCH/ARRTI
TWITTER: @ARRTI_RNA

Mandate

ARRTI is dedicated to foster and facilitate RNA research and training excellence at the University of Lethbridge and to contribute to the multidisciplinary research and teaching community at the University of Lethbridge and its surrounding communities.

Members

Director – Hans-Joachim Wieden (Department of Chemistry and Biochemistry)
Associate Director – Tony Russell (Department of Biological Sciences)
Research Members –

- Borries Demeler (Department of Chemistry and Biochemistry)
- Ute Kothe (Department of Chemistry and Biochemistry)
- Marc Roussel (Department of Chemistry and Biochemistry)
- Nehal Thakor (Department of Chemistry and Biochemistry)
- Stacey Wetmore (Department of Chemistry and Biochemistry)
- Trushar Patel (Department of Chemistry and Biochemistry)
- Athanasios Zovoilis (Department of Chemistry and Biochemistry)

Recruitment

1. Canada 150 Research Chair in Biophysics
    - Dr. Borries Demeler (Started August 1, 2018, joined ARRTI in December 2018)
2. Postdoctoral Fellows
    - Dr. Maulik Badmalia (Patel lab)
    - Dr. Jumai Abioye (Wieden lab)
    - Dr. Preethi Balasundaram (Wieden lab)
    - Dr. Harmen Steele (Demeler lab, U of Montana)
3. Research Associates
    - Dr. Laura Keffer-Wilkes (RNA Innovation Manager - NSERC CREATE)

Trainees

Total trainees between May 1, 2018 and April 30, 2019: 98

Postdoctoral Fellows – 11

- Two Postdoctoral Fellows completed their programs at ARRTI
    - Dr. Govardhan Reddy Veerareddygari is now the Central Stores Manager in the new Science and Academic Building at the University of Lethbridge
    - Dr. Soumya Deo was recruited to a start-up company (Polyamyna Nanotech Inc.) through a MITAC fellowship

Research Associates – 11

PhD Students – 20

- Two students successfully defended their dissertation during this reporting period
  - Dr. Stefan Lenz is now a Postdoctoral Fellow at the University of Calgary
  - Dr. Katie Wilson is now a Postdoctoral Fellow at the Australian National University in Canberra, Australia

MSc Students – 20

- Three students successfully defended their thesis during this reporting period
  - Rhys Hakstol is now a lab technician at Lethbridge College
  - Erin Kelly is attending medical school at the University of Calgary
  - Dominic Czekay is now a lab technician at the University of Lethbridge

Undergraduate Students – 33

High School Students – 3

Note: Trainees who completed a BSc or MSc and moved on to an MSc or PhD, respectively, are only listed under their current category, to avoid counting any trainee twice.

ARRTI Lab Representatives (2018-19)

- Demeler – Catrione Lee
- Kothe – Dominic Czekay
- Patel – Tyler Mrozowich
- Roussel – Hossein Hosseini
- Russell – David McWatters
- Thakor – Jean Claude Nshozabahizi
- Wetmore – Ryan Kung
- Wieden – Taylor Sheahan
- Zovoilis – Chris Isaac

RNA Bioengineering and Innovation Network

RNA Innovation is a unique partnership between the University of Lethbridge, Université de Sherbrooke, and industry collaborators, providing trainees with an exceptional learning experience during their graduate studies program. This NSERC Collaborative Research and Training Experience (CREATE) program aims to produce highly qualified personnel with skills in advanced RNA research, scientific leadership, and industry experience.

Industry Experience

The major advantage of RNA Innovation will be access to industry collaborations. Each trainee cohort will work together with an industry partner to solve an R & D problem as part of the deepYellow Challenge. Together the trainees will learn to apply their research training, work as a team, and develop a final product. Trainees will also receive funding for on-site industry training and project development through the Twinning Program. All participants will be matched with a specific internship, receive mentorship and a personalized networking experience.

Professional Skills

In addition to academic and research skills, trainees will develop skills in management, leadership, communication, teaching, integrity and ethics through complementary workshops and courses. Participation in the deepYellow challenge will encourage development of project management and entrepreneurial skills. Additional workshops providing some theoretical foundation in management will supplement the trainee's learning experience. All trainees will be required to participate in a new graduate level Scientific Leadership course. Modules will include professional communication, integrity & ethics, and leadership with respect to gender and minority representation.

Highly Qualified Personnel

Graduates of the RNA Innovation program will be uniquely trained, "job-ready" with knowledge of applied and basic research, and possess a diverse set of leadership skills. This multidisciplinary background will make them ideally suited to careers in a multitude of biotechnology fields. RNA Innovation is the ideal program for students that desire real-world, hands-on experience during their research program. Funding is available for graduate students (MSc and PhD), as well as undergraduate students and post-doctoral fellows.

Check out www.rnainnovation.ca for more information!

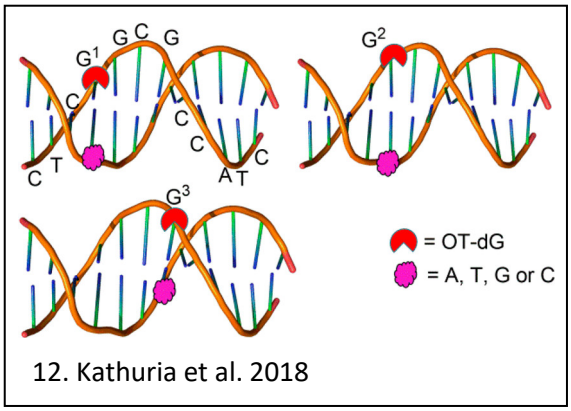
Research Dissemination

Journal articles published – 41

1. van Marle, G., and **Patel, T.R.** (2018) Proceedings of the Alberta Virology Conference, University of Alberta, 1–2 June 2017; edited by Guido van Marle and Trushar R. Patel. *Biotechnol. Genet. Eng. Rev*. 34(1): 1-2. DOI: 10.1080/02648725.2018.1478662 (IF: 1.7) (***editorial***)
2. Meier-Stephenson, V., Mrozowich, T., Pham, M., and **Patel, T.R.** (2018) DEAD-box helicases: the Yin and Yang roles in viral infections. *Biotechnol. Genet. Eng. Rev*. 34(1): 3-32. DOI: 10.1080/02648725.2018.1467146 (IF: 1.7)
3. Dzananovic, E., McKenna, S.A., and **Patel, T.R.** (2018) Viral proteins targeting host protein kinase R to evade an innate immune response: a mini review. *Biotechnol. Genet. Eng. Rev*. 34(1): 33-59. DOI: 10.1080/02648725.2018.1467151 (IF: 1.7)

Publications 1-5

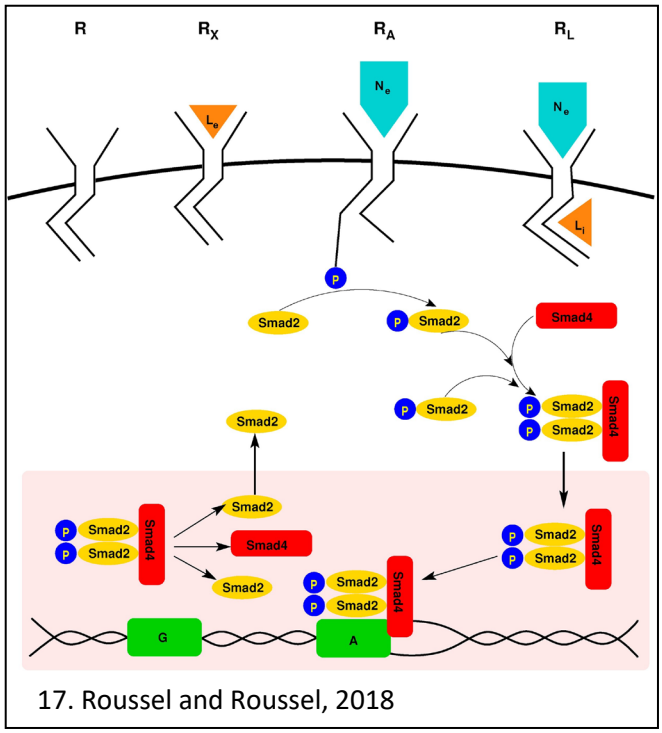
4. Roberts, L. and **Wieden, H.-J.*** (2018) Viruses, IRESs, and A Universal Translation Initiation Mechanism. *Biotechnol. Genet. Eng. Rev*. 34(1): 60-75. DOI: 10.1080/02648725.2018.1471567 (IF: 1.7)
5. Isaac, C., **Patel, T.R.** and **Zovoilis, A.** (2018) Non-coding RNAs in Virology: an RNA Genomics Approach. *Biotechnol. Genet. Eng. Rev.* 34(1): 90-106. DOI: 10.1080/02648725.2018.1471642 (IF: 1.7)
6. Meier, M.*, Moya, A., Krahn, N., McDougal, M., McRae, E.K.S., Booy, E.P., **Patel, T.R.**, McKenna, S.A. and Stetefeld, J.* (2018). Structure and hydrodynamics of a DNA G-quadruplex with a cytosine bulge. *Nucleic Acids Res*. 46(10): 5319-5331. DOI: 10.1093/nar/gky307 (IF: 11.561)
7. Ross, J.A. and **Thakor, N.*** (2018) Toeprinting Analysis of Translation Initiation Complex Formation on Mammalian mRNAs. *J. Vis. Exp.* 135: e57519. DOI: 10.3791/57519 (IF: 1.232)
8. Van Riesen, A.J., Fadock, K.L., Deore, P.S., Desoky, A., Manderville, R.A.*, Sowlati-Hashjin, S. and **Wetmore, S.D.*** (2018) Manipulation of a DNA aptamer-protein binding site through arylation of internal guanine residues. *Org. Biomol. Chem.* 16(20): 3831-3840. DOI: 10.1039/c8ob00704g (IF: 3.564)
9. Dahlman, H.A., Berger, F.D., Kung, R.W., Wyss, L.A., Gubler, I., McKeague, M., **Wetmore, S.D.**, and Sturla, S.J. (2018) Fluorescent elongated hydrophobic nucleobase analogues stabilize DNA duplexes containing O^6-alkylguanine adducts. *Helv. Chim. Acta.* 101: e1800066. DOI: 10.1002/hlca.201800066 (IF: 1.071)
10. Cai, A., Wilson, K.A., Patnaik, S., **Wetmore, S.D.** and Cho, B.P.* (2018) DNA Base Sequence Effects on Bulky Lesion-Induced Conformational Heterogeneity during Simulated Translesion Synthesis. *Nucleic Acids Res*. 46(12):6356-6370. DOI: 10.1093/nar/gky409 (IF: 11.561)
11. Kung, R.W., Sharma, P., and **Wetmore, S.D.*** (2018) Effect of the size and shape of nitrogen-containing aromatics on the conformational preferences of DNA containing damaged guanine: Insights from quantum chemical calculations and molecular dynamics simulations. *J. Chem. Info. Model*. 58(7): 1415-1425. DOI: 10.1021/acs.jcim.8b00238 (IF: 3.804)
12. Kathuria, P., Sharma, P., Manderville, R.A., and **Wetmore, S.D.*** (2018) Molecular dynamics simulations of mismatched DNA duplexes associated with the major C8-linked 2'-deoxyguanosine adduct of the food mutagen ochratoxin A: Influence of opposing base, adduct ionization state and sequence on the structure of damaged DNA. *Chem. Res. Toxicol.* 31(8): 712-720. DOI: 10.1021/acs.chemrestox.8b00064 (IF: 3.432)



12. Kathuria et al. 2018

13. **Roussel, M.R.*** (2018) The Mackey-Glass models, 40 years later. *Biomath Commun.* 5: 140-158. DOI: 10.11145/bmc.2018.10.277. (IF: N/A) (***Invited perspective article***)
14. Kotb, A., Hyndman, E. and **Patel, T.R.*** (2018) The role of zyxin in regulation of malignancies. *Heliyon* 4(7): e00695. DOI: 10.1016/j.heliyon.2018.e00695 (IF: N/A)

15. Byron, O., Nischang, I., and **Patel, T.R.** (2018) Analytical ultracentrifugation (AUC): a seminal tool offering multiple solutions. *Eur. Biophys. J.* 47(7): 693-696. DOI: 10.1007/s00249-018-1333-z. (IF: 1.935)
16. Moore, A.N., McWatters, D.C., Hudson, A.J., and **Russell, A.G.** (2018) RNA-Seq employing a novel rRNA depletion strategy reveals a rich repertoire of snoRNAs in *Euglena gracilis* including box C/D and Ψ-guide RNAs targeting the modification of rRNA extremities. *RNA Biol.* 15(10): 1309-1318. DOI: 10.1080/15476286.2018.1526561 (IF: 5.216)



17. Roussel and Roussel, 2018

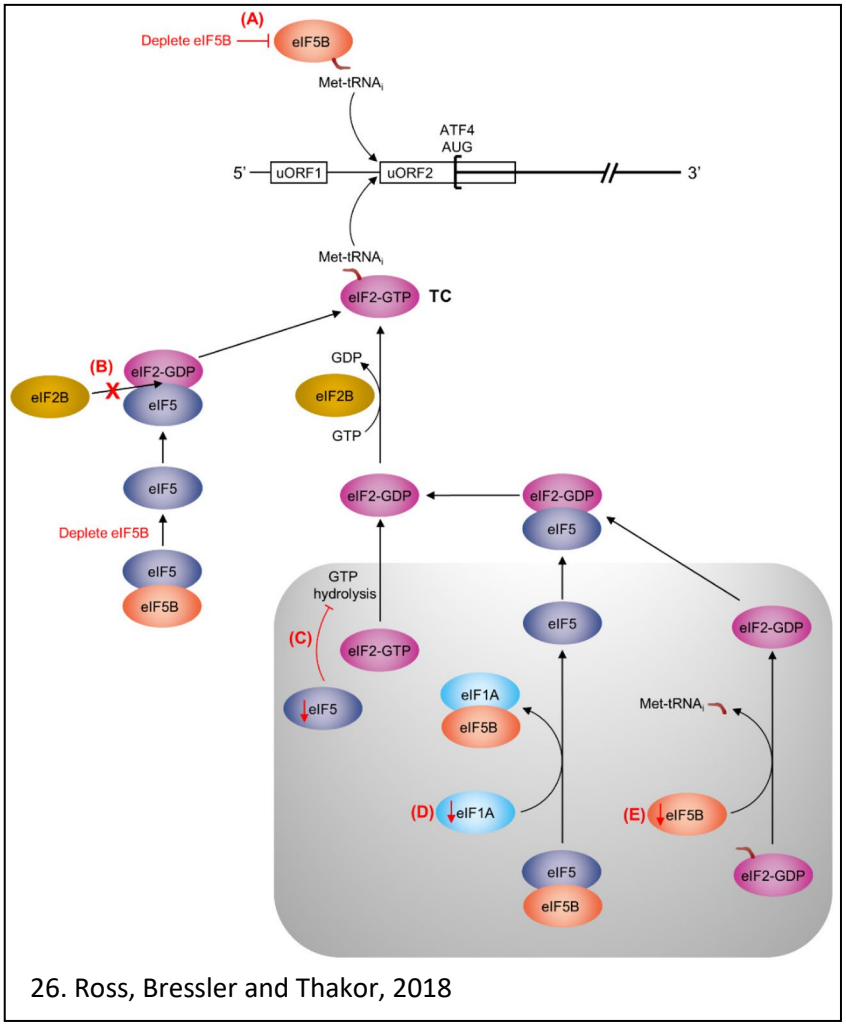
17. Roussel, C.J., and **Roussel, M.R.** (2018) A mathematical model of the biochemical network underlying left-right asymmetry establishment in mammals. *Biosystems* 173: 281-297. DOI: 10.1016/j.biosystems.2018.10.003 (IF: 1.619)
18. Meier-Stephenson, V., Bremner, W.T.R., Dalton, C.S., van Marle, G., Coffin, C.S., and **Patel, T.R.** (2018) Comprehensive Analysis of Hepatitis B Virus Promoter Region Mutations. *Viruses* 10(11): E603. DOI: (IF: 3.761)
19. Salveson, P.J., Haerianardakani, S., Thuy-Boun, A., Yoo, S., Kreutzer, A.G., **Demeler, B.**, and Nowick, J.S. (2018) Repurposing Triphenylmethane Dyes to Bind to Trimers Derived from Aβ. *J. Am. Chem. Soc.* 140(37): 11745-11754. DOI: 10.1021/jacs.8b06568 (IF: 14.357)
20. Turnbull, D., Kostiuk, N., **Wetmore, S.D.**, and Gerken, M. (2018) Syntheses, characterisation, and computational studies of tungsten hexafluoride adducts with pyridine and its derivatives. *J. Fluor. Chem.* 215: 1-9. DOI: 10.1016/j.jfluchem.2018.08.007 (IF: 2.055)
21. Wilson, K.A., Garden, J.L., Wetmore, N.T., and **Wetmore, S.D.** (2018) Computational insights into the mutagenicity of two tobacco-derived carcinogenic DNA lesions. *Nucleic Acids Res.* 46(22): 11858-11868. DOI: 10.1093/nar/gky1071 (IF: 11.561)
22. Wilton, E.E., Opyr, M.P., Kailasam, S., Kothe, R.F., and **Wieden, H.-J.** (2018) sdAb-DB: The Single Domain Antibody Database. *ACS Synth. Biol.* (11): 2480-2484. DOI: 10.1021/acssynbio.8b00407 (IF: 5.316)
23. Mrozowich, T., McLennan, S., Overduin, M. and **Patel, T.R.** (2018) Structural Studies of Macromolecular Interactions in Solution using Small Angle X-Ray Scattering. *J. Vis. Exp*. 141: e58538. DOI:10.3791/58538 (IF: 1.184)
24. Lenz, S.A.P. and **Wetmore, S.D.** (2018) Structural explanation for the tunable substrate specificity of an E. coli nucleoside hydrolase: insights from molecular dynamics simulations. *J. Comput. Aided Mol. Des.* 32(12): 1375-1388. DOI: 10.1007/s10822-018-0178-y (IF: 2.356)

25. Lloyd, D., Murray, D.B., Aon, M.A., Cortassa, S., **Roussel, M.R.**, Beckmann, M., and Poole, R.K. (2018) Temporal metabolic partitioning of the yeast and protist cellular networks: the cell is a global scale-invariant (fractal or self-similar) multioscillator. *J. Biomed. Opt*. 24(5): 1-17. DOI: 10.1117/1.JBO.24.5.051404. (IF: 2.367)

26. Ross, J.A., Bressler, K.R., and **Thakor, N.** (2018) Eukaryotic Initiation Factor 5B (eIF5B) Cooperates with eIF1A and eIF5 to Facilitate uORF2-Mediated Repression of ATF4 Translation. *Int. J. Mol. Sci.* 19(12): E4032. DOI: (IF: 3.687)

27. Wilson, K.A., Holland, C.D., and **Wetmore, S.D.** (2018) Uncovering a unique approach for damaged DNA replication: A computational investigation of a mutagenic tobacco-derived thymine lesion. *Nucleic Acids Res*. 47(4): 1871-1879. DOI: 10.1093/nar/gky1265 (IF: 11.561)

28. Chung, A.J., Deore, P.S., Al-Abdul-Wahid, S., Aboelnga, M.M., **Wetmore, S.D.**, and Manderville, R.A. (2018) Acceptor Influence on Thiolate Sensing by Hemicyanine Dyes. *J. Org. Chem*. 84(4): 2261-2268. DOI: 10.1021/acs.joc.9b00066 (IF: 4.805)

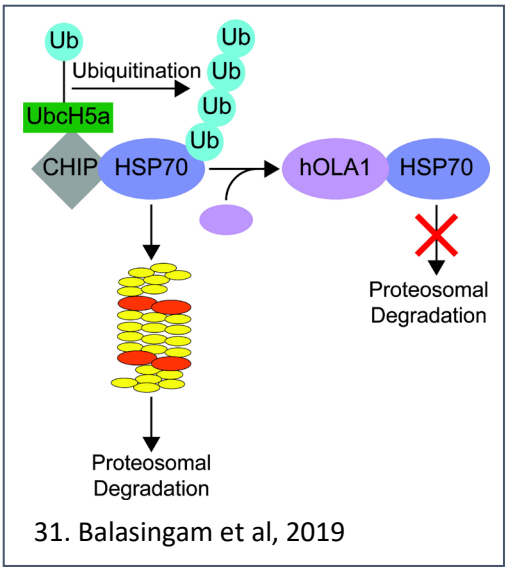


26. Ross, Bressler and Thakor, 2018

29. Ross, J.A., Dungen, K.V., Bressler, K.R., Fredriksen, M., Khandige Sharma, D., Balasingam, N., **Thakor, N.** (2019) Eukaryotic initiation factor 5B (eIF5B) provides a critical cell survival switch to glioblastoma cells via regulation of apoptosis. *Cell Death Dis.* 10(2): 57. DOI: 10.1038/s41419-018-1283-5 (IF: 6.187)

30. Wilson, K.A., Fernandes, P.A., Ramos, M.J., and **Wetmore, S.D.*** (2019) Exploring the Identity of the General Base for a DNA Polymerase Catalyzed Reaction Using QM/MM: The Case Study of Human Translesion Synthesis Polymerase η. *ACS Catal.* 9(3): 2543-2551. DOI: 10.1021/acscatal.8b04889 (IF: 12.221)

31. Balasingam, N., Brandon, H.E., Ross, J.A., **Wieden, H.-J.**, and **Thakor, N.** (2019) Cellular roles of the human Obg-like ATPase 1 (hOLA1) and its YchF homologs. *Biochem. Cell Biol.* 2019 Feb 11:1-11. DOI: 10.1139/bcb-2018-0353 (IF: 2.250)



31. Balasingam et al, 2019

32. Ranaivoson, F.M., Turk, L.S., Ozgul, S., Kakehi, S., von Daake, S., Lopez, N., Trobiani, L., De Jaco, A., Denissova, N., **Demeler, B.**, Özkan, E., Montelione, G.T., and Comoletti, D. (2019) A Proteomic Screen of Neuronal Cell-Surface Molecules Reveals IgLONs as Structurally Conserved Interaction Modules at the Synapse. *Structure* 27(6):893-906. DOI: 10.1016/j.str.2019.03.004 (IF: 4.907)
33. Ferens F.G., **Patel, T.R.**, Oriss, G., Court, D.A., and Stetefeld, J. (2019) A Cholesterol Analog Induces an Oligomeric Reorganization of VDAC. *Biophys. J.* 116(5): 847-859. DOI: 10.1016/j.bpj.2019.01.031 (IF: 3.495)
34. Bansal, A., Karanth, N.M., **Demeler, B.**, Schindelin, H., and Sarma, S.P. (2019) Crystallographic Structures of IlvN·Val/Ile Complexes: Conformational Selectivity for Feedback Inhibition of Aceto Hydroxy Acid Synthases. *Biochemistry* 58(15):1992-2008. DOI: 10.1021/acs.biochem.9b00050 (IF: 2.997)
35. Stuart, D., **Wetmore, S.D.**, and Gerken, M. (2019) Syntheses, characterization, and computational study of AsF5 adducts with ketones. *J. Fluor. Chem.* 221: 9-16. DOI: 10.1016/j.jfluchem.2019.02.011 (IF: 2.055)
36. Nshozabahizi, J.C., Aubrey, K.L., Ross, J.A., and **Thakor, N.** (2019) Applications and limitations of regulatory RNA elements in synthetic biology and biotechnology. *J. Appl. Microbiol. In press.* DOI: 10.1111/jam.14270. (IF: 2.16)
37. Gemmill, D., D'souza, S., Meier-Stephenson, V., and **Patel, T.R.** (2019) Current approaches for RNA labelling to identify RNA-binding proteins. *Biochem. Cell Biol. In press*. DOI: 10.1139/bcb-2019-0041 (IF: 2.250)
38. Kagra, D., Preethi, S.P., and Sharma, P. (2019) Interaction of aspartic acid and asparagine with RNA nucleobases: a quantum chemical view. *J. Biomol. Struct. Dyn. In press.* DOI: 10.1080/07391102.2019.1592025 (IF: 3.107)
39. Koul, A., Deo, S., Booy, E.P., Orriss, G., Genung, M., and McKenna, S.A. (2019) Impact of double-stranded RNA characteristics on the activation of human 2'-5'-oligoadenylate synthetase 2 (OAS2) *Biochem. Cell Biol*. *In press*. DOI: 10.1139/bcb-2019-0060. (IF: 2.250)
40. Kaur, S., Sharma, P., and **Wetmore, S.D.** (2019) Can Cyanuric Acid and 2,4,6-Triaminopyrimidine Containing Ribonucleosides be Components of Prebiotic RNA? Insights from QM Calculations and MD Simulations. *Chemphyschem. In press*. DOI: 10.1002/cphc.201900237 (IF: 2.947) (***Invited journal cover***)

41. Turnbull, D., **Wetmore, S.D.**, and Gerken, M. (2019) Synthesis, Characterization, and Lewis Acid Behavior of $[W(NC_6F_5)F_4]_x$ and Computational Study of $W(NR)F_4$ (R = H, F, CH_3, CF_3, C_6H_5, C_6F_5), $W(NC_6F_5)F_4(NCCH_3)$, and $W(NC_6F_5)F_4(NC_5H_5)_n$ (*n*= 1, 2). *Inorg. Chem.* 58(9): 6363-6375. DOI: 10.1021/acs.inorgchem.9b00574 (IF: 4.85)

Magazine articles – 2

1. Mrozowich, T., Meier-Stephenson, V., and **Patel, T.R.** (2019) Microscale thermophoresis: warming up to a new biomolecular interaction technique. *The Biochemist* 41(2): 8-13.
2. **Demeler, B.** (2019) Measuring molecular interactions in solution using multi-wavelength analytical ultracentrifugation: combining spectral analysis with hydrodynamics. *The Biochemist* 41(2): 14-19.

Conference publications – 2

1. Mrozowich, T., Meier-Stephenson, V., Vigar, J.A., Bujnicki, J.M., **Wieden, H.-J.**, and **Patel, T.R.*** (2019) Towards Obtaining a Nanoscale Structure of Terminal Regions of Japanese Encephalitis Virus Genome. 63rd Annual Meeting, Biophysical Society, Baltimore, USA, Mar 2-6, 2019. *Biophys. J.* 14: 404a. DOI: 10.1016/j.bpj.2018.11.1924 (IF: 3.495)
2. Meier-Stephenson, V., Schultz, S., Coffin, C.S., and **Patel, T.R.*** (2018) Identification of a G4-quadruplex structure motif in hepatitis B virus genome: a potential novel drug target. Canadian Liver Meeting 2018, Toronto, Canada, Feb 9-11, 2018. *Journal of the Canadian Association of Gastroenterology* 1: 491-492. DOI: 10.1093/jcag/gwy009.340 (IF: N/A)

Mathematical reviews – 5

1. MR3850003: Asymptotic analysis of a TMDD model: when a reaction contributes to the destruction of its product. By L.I. Michalaki, D.A. Goussis. (Review by **Roussel, M.R.**)
2. MR3811780: The structure of MESSI biological systems. By P. Millán, A. Dickenstein (Review by **Roussel, M.R.**)
3. MR3776244: Global behaviors analysis for tryptophan operon system with bounded noise. By X. Zhu, M. Li, C. Liu, J. Yuan, C. Li. (Review by **Roussel, M.R.**)
4. MR3754603: Nonmonotone invariant manifolds in the Nagylaki-Crow model. By B. Seymenoglu, S. Baigent. (Review by **Roussel, M.R.**)
5. MR3735285: Conservation laws in biochemical reaction networks. By A. Mahdi, A. Ferragut, C. Valls, and W. Carsten. (Review by **Roussel, M.R.**)

Theses – 4

1. Erin Kelly, M.Sc. (2018) Distinguishing features of guide and substrate RNA recognition by H/ACA snoRNPs. Supervisor: **Dr. Ute Kothe**
2. Dominic Czekay, M.Sc. (2018) Structure-based H/ACA guide RNA design and testing explains the structure-function relationship of H/ACA guide RNA. Supervisor: **Dr. Ute Kothe**
3. Katie Wilson, Ph.D. (2018) Computational insights into the molecular basis for the replication of flexible tobacco-derived DNA lesions. Supervisor: **Dr. Stacey Wetmore**
4. Stefan Lenz, Ph.D. (2018) Computational insight into the broad substrate specificity of enzymes that process nucleic acids. Supervisor: **Dr. Stacey Wetmore**

Other research dissemination – 127

- 27 presentations by PIs
  - 16 of these presentations invited or keynote lectures
- Over 100 presentations by trainees (poster and oral presentations)

Funding

ARRTI Principal Investigators received approximately $1.9 million in operating grants in 2018-19. This includes:

- $326,000 from the Natural Sciences and Engineering Research Council
- $439,890 from the Canadian Foundation for Innovation
- >$1,200,000 from Research Chairs
  - Dr. Borries Demeler – Canada 150 Research Chair in Biophysics
  - Dr. Ute Kothe – Alberta Innovates Strategic Chair in Transcriptomics of RNA Modification
  - Dr. Trushar Patel – Canada Research Chair in RNA & Protein Biophysics
  - Dr. Nehal Thakor – Campus Alberta Innovation Program (CAIP) Chair of Synthetic Biology and RNA-based Systems
  - Dr. Stacey Wetmore – Canada Research Chair in Computational Chemistry
  - Dr. HJ Wieden – Alberta Innovates Strategic Chair in RNA Bioengineering
  - Dr. Athanasios Zovoilis – Canada Research Chair in RNA Bioinformatics and Genomics

Also, > $1 million in funding was received from the following sources:

- $205,289 resource allocation from Compute Canada
- US $22,067 resource allocation from NSF XSEDE
- $379,058 in beamtime from Diamond Light Source Limited
- $247,500 from Alberta Innovates (Strategic Project Grant)
- $150,000 from NSERC Collaborative Research and Training Experience (CREATE) Program

In addition, $166,000 in funding was received by ARRTI students and postdoctoral fellows from NSERC, Alberta Innovates, and the Alberta Government.

This makes a total of **> $3 million** in funding in the 2018-19 reporting year.

Note: The above list of funding may not be comprehensive and indicates a minimum amount of funding for the reporting period.

Events

12th Annual Chinook Symposium for Chemistry and Biochemistry (Annual Activity)

- Annual student conference hosted by the Department of Chemistry and Biochemistry at the University of Lethbridge to showcase student research.
- Organized by Susan Hill, Susan Findlay and **Dr. Trushar Patel**.
- Of the 15 awards given, 8 were received by ARRTI trainees.

14th Annual RiboWest Conference (Standalone Activity)

Organizers: **Dr. Trushar Patel**, **Dr. Nehal Thakor, Dr. Athan Zovoilis, and Dr. Ute Kothe**

Event Manager: Ms. Emily Wilton

June 10-13, 2018

Gairdner Lecture: Dr. Nahum Sonenberg

- McGill University
- Title: *Diverse Functions of the Cap-binding Protein 4EHP-Complex in Control of mRNA Translation*

Alberta Epigenetics Network (AEN) sponsored Opening Keynote Lecture: Dr. Steven Jones

- Canada's Michael Smith Genome Sciences Centre, BC Cancer Agency
- Title: *Using genomics and transcriptomics to develop a platform for precision medicine in oncology*

AEN Sponsored "Breakthrough in Epigenetics" Lecture: Dr. Martin Hirst

- University of British Columbia
- Title: *Exploiting cis-regulatory enhancers as therapeutic targets in cancer*

Invited RiboClub Lecture: Dr. Michelle Scott

- Université de Sherbrooke
- Title: *A pan-transcriptome view of mid-size RNAs*

Closing Keynote Lecture: Dr. Jennifer Kugel

- University of Colorado Boulder
- Title: *Regulation of RNA polymerase II by SINE encoded ncRNAs*

RiboWest 2018 - over 100 attendees! (Photo credit to Elaine Van Rootselaar)

RNA and Epigenetics Symposium with Gairdner Keynote (Standalone Activity)

Organizers: **Dr. Ute Kothe** and **Dr. Trushar Patel** together with Emily Wilton

Keynote Speaker: Dr. Azim Surani

October 19, 2018

Gairdner Laureate Dr. Azim Surani

- Dr. Azim Surani is a recipient of the 2018 Canada Gairdner International Award for the discovery of mammalian genomic imprinting that causes parent-of-origin specific gene expression and its consequences for development and disease.
- Dr. Surani has been Marshall-Walton Professor of Physiology and Reproduction at the Wellcome Trust Cancer Research UK Gurdon Institute at the University of Cambridge since 1992, and Director of Germline and Epigenomics Research since 2013.
- This prize was awarded to both Dr. Surani and Dr. Davor Solter, as they released parallel studies on genomic imprinting. Faulty imprints can lead to developmental, physiological and behavioural anomalies in mice, and result in diseases in humans. There is growing evidence for the importance of imprinting in disease susceptibility from developmental syndromes like Beckwith-Wiedemann, Angelman and Prader-Willi, to a variety of cancers and neurological disorders and obesity. It also has effects on diverse aspects of mammalian development and physiology, such as stem cells, core body temperature, nutrition and behaviour. Their work is one of the key discoveries that started the field of epigenetics, the study of heritable changes in gene function without changes in the DNA sequence.
- Dr. Surani's talk was titled "*From genomic imprinting to the human germline*."
- Following the keynote address, nine speed talks were presented by students as part of the RNA and Epigenetics Symposium, sponsored by the Alberta Epigenetics Network.
- During his visit, Dr. Surani also gave a presentation at high school, and led a career development discussion at a graduate student luncheon.

ARRTI Speaker Series (Ongoing Activity)

In order to broaden the knowledge base of ARRTI members, a monthly speaker series has been established. The speaker series is intended to bring leading researchers to the University of Lethbridge for lectures on a broad range of topics relating to RNA research.

For the 2018-19 year, this series of events was funded by the RNA Salon initiative by the RNA Society, with additional funding by Lexogen.

RNA SOCIETY

LEXOGEN
Enabling complete transcriptome sequencing

This year's speaker series:

1. Dr. Jane Jackman (June 28, 2018)
    - The Ohio State University
    - "Non-canonical enzymes catalyze critical steps in tRNA processing and modification"
    - Hosted by **Dr. Kothe**
2. Dr. Gareth Williams (August 21, 2018)
    - Biochemistry & Molecular Biology Department, University of Calgary
    - "Biochemical and structural basis for how the human RAD51 paralogs promote homologous recombination repair"
    - Hosted by **Dr. Patel**
3. Dr. Alexey Savelyev (November 15, 2018)
    - Department of Chemistry and Biochemistry, University of Montana
    - "Multi-Scale Computational Modeling of DNA and Applications to Biophysical Problems"
    - Hosted by **Dr. Demeler**
4. Dr. Emre Brookes (November 15, 2018)
    - Department of Chemistry and Biochemistry, University of Montana
    - "Advancements in analysis of small angle scattering experiments, hydrodynamic computations and putting your software on the web"
    - Hosted by **Dr. Demeler**
5. Dr. Nils Walter (November 26, 2018)
    - University of Michigan
    - "Single Molecules Come Into Focus: Understanding RNA-Driven Regulation From First Principles"
    - Hosted by **Dr. Kothe**
6. Dr. Gregg Morin (December 5, 2018)
    - Canada's Michael Smith Genome Sciences Center
    - "Chemo-proteogenomic analyses of CDK12's role in mRNA processing"
    - Hosted by **Dr. Wieden**
7. Dr. Artur Luczak (January 28, 2019)
    - Department of Neuroscience, University of Lethbridge
    - "Decoding brain and behavior using artificial intelligence"
    - Hosted by **Dr. Wieden**
8. Dr. Borries Demeler (February 27, 2019)
    - Department of Chemistry and Biochemistry, University of Lethbridge
    - "Probing molecular interactions in the solution phase by multi-wavelength analytical ultracentrifugation"
9. Dr. Karen Glass (March 15, 2019)
    - Associate Professor, Department of Pharmaceutical Sciences, Albany College of Pharmacy and Health Sciences (Colchester, Vermont campus)
    - "Combinatorial Recognition of Histone Modifications"
    - Hosted by **Dr. Demeler**

10. Dr. Harmen Steele (April 18, 2019)
    - Postdoctoral fellow, University of Montana
    - "The human cytochrome c domain-swapped dimer: tight regulation of intrinsic apoptosis"
    - Hosted by **Dr. Demeler**
11. Ms. Michelle Nemetchek (April 18, 2019)
    - Ph.D. candidate, University of Montana (Dr. Travis Hughes lab)
    - "Mechanisms of biased agonism in the nuclear receptor PPARγ"
    - Hosted by **Dr. Demeler**

Average attendance: 45 attendees total

ARRTI Seminar Series (Ongoing Activity)

To foster a greater awareness of the research being conducted within the institute, members of ARRTI have participated in a monthly seminar series, where a member of each research group presented their research to members of the institute.

Average attendance: 40 attendees total

Journal Club (Ongoing Activity)

Members of ARRTI participate in weekly journal club meetings, where members choose a work of contemporary scientific research to present to colleagues within the institute

Average attendance: 30 total attendees

RiboClub Webconferences (Ongoing Activity)

Members of ARRTI participate in monthly RiboClub videoconferences. RiboClub is a pan-Canadian research association founded in Sherbrooke, Quebec, whose members study the evolution, structure and function of RNA. Each monthly videoconference has four presentations from researchers representing RNA laboratories across Canada.

Presentations by ARRTI members:

- **Kamiko Bressler** (Thakor): *Eukaryotic initiation factor 5B (eIF5B) cooperates with eIF1A and eIF5 to regulate uORF-mediated translation of ATF4*
- **Dominic Czekay** (Kothe): *Specificity and structural requirements of H/ACA guide RNA – substrate RNA interactions*
- **Tyler Mrozowich** (Patel): *Biophysical Characterization of Flaviviral Non-Coding Terminal Regions* (Best presentation award in MSc category)
- **Harland Brandon** (Wieden): *Molecular Mimicry and the Ribosome: The conserved ATPase YchF interacts with tRNA and the ribosome*
- **Chris Isaac** (Zovoilis): *Dissecting the role of SINE non-coding RNAs in amyloid pathology: An integrative RNA genomics approach*

Average attendance: 30 total attendees

International Genetically Engineered Machine (iGEM) Competition (Ongoing Activity)

ARRTI trainees make part of the collegiate iGEM team, as well as acting as mentors and trainers for the Lethbridge high school team. In the 2018 Giant Jamboree, the high school team won a silver medal and the collegiate team won a gold medal. The high school team was also nominated for Best Model.

The collegiate project was VInCEnT, a Viral-Inspired Novel Cargo Encapsulation Toolkit, a standardized toolkit for simple design and assembly of custom protein nanocompartments (PNCs) for delivery of small molecules, nucleic acids, or proteins to specific cell targets. PNCs have user-specified surface proteins, encapsulation proteins, and cargo-loading approaches with wide-ranged applicability including targeted antibiotic delivery, rapid vaccine development, gene therapy, materials synthesis, improved cell culture transfection, specific biological control agents, and more. This team was led by **Dr. Trushar Patel**, **Dr. Hans-Joachim Wieden** and Dr. Angeliki Pantazi.

The high school project (Cu-Later) aimed to use a system of biological components to sequester and remove toxic metal ions (such as copper, nickel and lead) from oil and mining tailings ponds. This team was led by Dr. Laura Keffer-Wilkes, **Dr. Hans-Joachim Wieden** and Dr. Angeliki Pantazi.

Let's Talk Science (Ongoing Activity)

Dr. Ute Kothe serves as faculty supervisor for graduate student co-ordinators of Let's Talk Science, a national science outreach program. ARRTI trainee Darren Gemmill (M.Sc. candidate in the **Patel** lab) is an LTS coordinator.

Let's Talk Science organized or participated in the following events:

1. Middle School Day (May 25, 2018) – Target audience: Middle school students (90 students involved)
2. Spooky Science Weekend (November 2 & 3, 2018) – Target audience: Elementary students (300 children attended)
3. Let's DO Science Day (November 15, 2018) – Target audience: High school students (60 students involved)
4. Play Day (February 18, 2019) – Target audience: Families with children
5. Lethbridge Regional Science Fair and Science Olympics (March 23, 2019)

In addition to these events, LTS performed 38 school visits, offering a variety of chemistry, biology, and physics experiments, and provided hands-on science activities for 23 community groups. Through all the activities, the Let's Talk Science Program has engaged more than 3500 students and 500 adults.

Media Coverage

"Breadth of research program highlighted as three U of L researchers are named Canada Research Chairs" - University of Lethbridge UNews, May 3, 2018

- **Dr. Trushar Patel** awarded Tier 2 Canada Research Chair in RNA & Protein Biophysics, funded by the Canadian Institutes of Health Research.
- https://www.uleth.ca/communications/breadth-research-program-highlighted-three-u-l-researchers-are-named-canada-research

"RiboWest Conference 2018 brings together top RNA researchers from Western Canada and beyond" - University of Lethbridge UNews, June 10, 2018

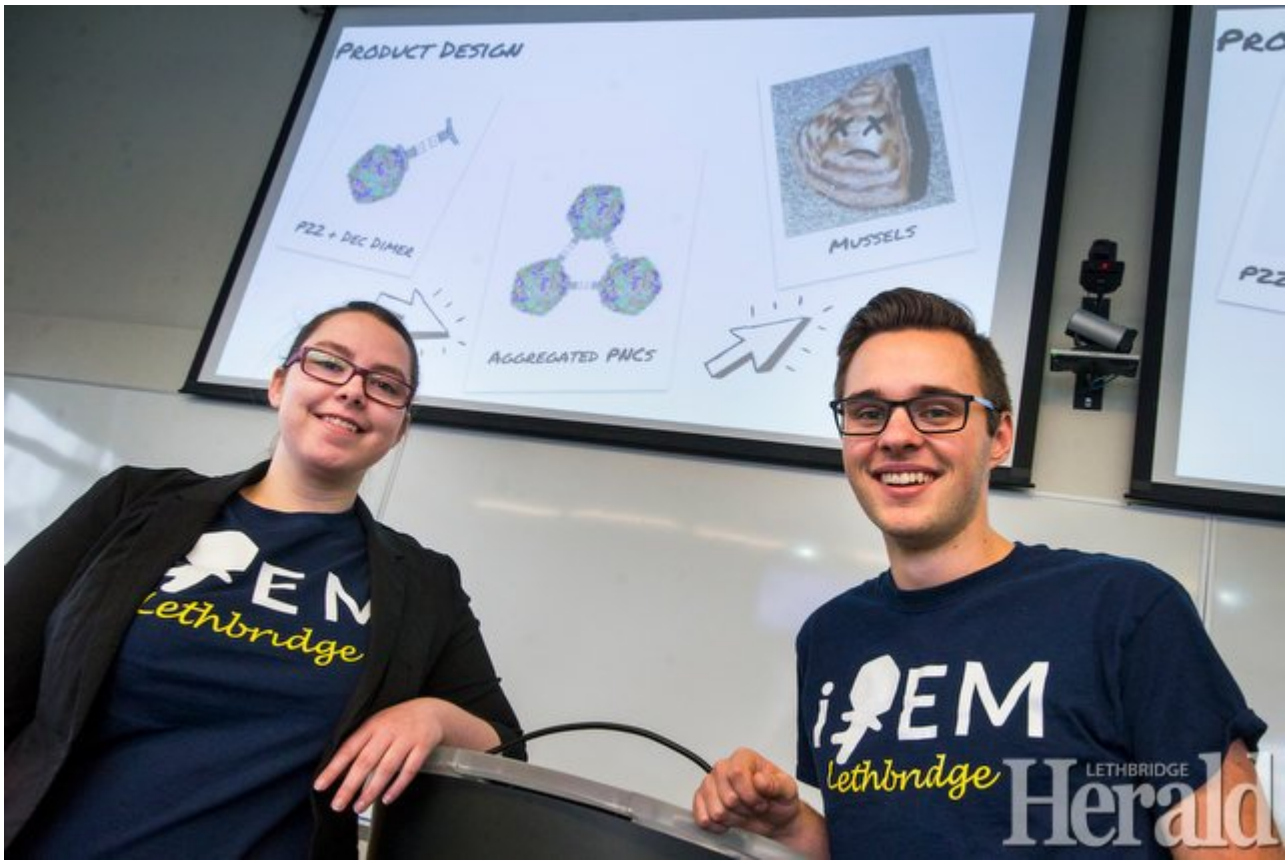
- Announcement of RiboWest 2018 conference at the University of Lethbridge.
- https://www.uleth.ca/unews/article/ribowest-conference-2018-brings-together-top-rna-researchers-western-canada-and-beyond
- Also covered by: "RNA Conference Begins" - Lethbridge Herald, June 12, 2018

"CREATE grant funding to support development of RNA Bioengineering and Innovation Network" - University of Lethbridge UNews, July 16, 2018

- The University of Lethbridge, in partnership with the Université de Sherbrooke, has been awarded $1.65 million over the span of six years to develop the RNA Bioengineering and Innovation Network Collaborative Research and Training Experience (CREATE).
- https://www.uleth.ca/unews/article/create-grant-funding-support-development-rna-bioengineering-and-innovation-network
- Also covered by: "New federal funding for the U of L will support development of RNA Bioengineering and Innovation Network" - Lethbridge News Now, July 17, 2018
- Also covered by: "University recognized for RNA research" - Lethbridge Herald, July 21, 2018

"U of L iGEM teams tackling relevant issues, awarded gold and silver at Giant Jamboree" - University of Lethbridge UNews, November 6, 2018

- From over 300 teams, representing countries from all over the world, the U of L's collegiate team secured a gold medal and the high school entry a silver at the 2018 International Genetically Engineered Machine (iGEM) competition in Boston, MA.
- https://www.uleth.ca/communications/university-lethbridge-igem-teams-tackling-relevant-issues-awarded-gold-and-silver
- Also covered by: "Gold medal winning research project" - CTV News at 5, November 6, 2018
- Also covered by: "Local iGEM teams earn gold, silver at 'Giant Jamboree' in Boston" - Lethbridge Herald, November 7, 2018



Lethbridge Collegiate iGEM members, Syndee Calhoun and Luke Saville

"Shining New Light on Virus Pandemics: Celebrating Research and Creative Excellence at the University of Lethbridge" - University of Lethbridge UNews, January 2019

- **Dr. Trushar Patel** discusses his lab's research into viruses and potential methods to inhibit them.
- https://www.uleth.ca/unews/video/shining-new-light-dr-trushar-patel

"New NSERC program links RNA research and industry partners" - University of Lethbridge UNews, March 8, 2019

- Announcement of competitive funding opportunities for RNA CREATE.
- https://www.uleth.ca/unews/article/new-nserc-program-links-rna-research-and-industry-partners

"Alberta Innovates grant facilitates joint research project on the hepatitis B virus" - University of Lethbridge UNews, April 30, 2019

- **Dr. Trushar Patel** and collaborator Dr. Carla Coffin at the University of Calgary have secured Alberta Innovates funding worth $639,000 to further research aimed at developing innovative strategies to combat hepatitis B virus (HBV) infection.
- http://www.uleth.ca/unews/article/alberta-innovates-grant-facilitates-joint-research-project-hepatitis-b-virus

Facilities

SynBridge Maker-Space

SynBridge usage in the 2018-19 reporting year was very similar to the last two years, with over 3000 hours of usage by nine different research groups on campus.

Details about SynBridge equipment and rates can be found on our website:
http://www.uleth.ca/research/centres-institutes/alberta-rna-research-and-training-institute/synbridge-synthetic-biology-maker-space

Mass Spectrometry Facility

The Mass Spectrometry Facility (Orbitrap Fusion™ Tribrid™ Mass Spectrometer) is operational and serves as a core facility at the University of Lethbridge. Our Mass Spectrometry Facility Manager (**Fan Mo**) processed and analyzed over 500 samples in the reporting year, for several different research groups on campus.

For more information about the facility and its fees, please visit our website:
http://www.uleth.ca/research/centres-institutes/alberta-rna-research-and-training-institute/arrti-mass-spectrometry-facility

Notable Accomplishments

Chemical Institute of Canada (CIC) Fellowship

- Dr. Stacey Wetmore

Canadian Science Policy Centre – Science Meets Parliament delegate

- Dr. Trushar Patel – one of 29 selected, only delegate from Alberta

14th Annual RiboWest Conference Awards (Lethbridge, Alberta)

- Luc Roberts (Wieden) – 2nd Place Oral Presentation (PI judged), 1st Place Oral Presentation (student judged)
- Anileen Pageni (Kothe) – 1st Place Poster Presentation (PI judged)
- Saskia Funk (Kothe) – 2nd Place Poster Presentation (PI judged)
- Dora Capatos (Wieden) – 3rd Place Poster Presentation (PI judged)
- Dylan Girodat (Wieden) – 3rd Place Oral Presentation (student judged)
- Elijah Dueck (Kothe) – 2nd Place Poster Presentation (student judged)
- Govardhan Reddy Veerareddygari (Kothe) – Best Postdoctoral Fellow Poster (student judged)
- Sydnee Calhoun (Wieden) – Poster Recognition (student judged)
- Aroura Gagnon (Russell) – Poster Recognition (student judged)

12th Annual Chinook Symposium for Chemistry and Biochemistry (Lethbridge, Alberta)

- Hope Vienneau (Kothe) – 1st Place Undergraduate Biochemistry
- Sydnee Calhoun (Wieden) – 2nd Place Undergraduate Biochemistry
- Priya Bhutani (Wetmore) – 1st Place MSc Chemistry
- Elijah Dueck (Kothe) – 1st Place MSc Biochemistry, Canadian Journal of Chemistry Award for Best Student Presentation (Graduate Award)
- Ryan Kung (Wetmore) – 1st Place PhD Chemistry
- Taylor Sheahan (Wieden) – 1st Place PhD Biochemistry
- Dustin Smith (Wieden) – 2nd Place PhD Biochemistry

101st Canadian Chemistry Conference and Exhibition (Edmonton, Alberta)

- Priya Bhutani (Wetmore) - Tied for 1st Place for Graduate Student Poster Presentation in the Theoretical and Computational Division

CSV2018: The 2nd Symposium of the Canadian Society for Virology

- Tyler Mrozowich (Patel) – Travel Award
- Vanessa Meier-Stephenson (Patel) – Travel Award

2018 International Hepatitis B Virus Meeting

- Vanessa Meier-Stephenson (Patel) – Travel Award

Spring Convocation 2019 (University of Lethbridge)

- Gold Medal of the Governor General – Katie Wilson (Wetmore)
- School of Graduate Studies Silver Medal of Merit, Doctor of Philosophy – Katie Wilson (Wetmore)

NSERC University Undergraduate Student Research Awards

- Jeffrey McDonald (Kothe)
- Daniel Rocca (Kothe)
- Anileen Pageni (Kothe)
- Tim Vos (Kothe)
- Simmone D'souza (Patel)
- Lindey Felske (Wetmore)
- Janelle Bykowski (Wetmore)
- Cynthia Etondi Fonderson (Wetmore)
- Dylan Nikkel (Wetmore)

University of Lethbridge – Chinook Summer Research Awards

- Hope Vienneau (Kothe)
- Keara Cheredaryk (Kothe)

Alberta Innovates Heritage Youth Researcher Summer (HYRS)

- Abel Belay (Kothe)
- Justin Pitcher (Patel)
- Emma Arnell (Wetmore)