

Keith T. Gagnon, Ph.D.

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EDUCATION

2000-2003 B.S. Biochemistry
 North Carolina State University
 Summa Cum Laude, weighted GPA 4.0

2003-2007 Ph.D. Biochemistry
 North Carolina State University
 Ph.D. Advisor: Dr. E. Stuart Maxwell
 "Assembly, Structure and Function of Archaeal Box C/D sRNPs"
 Awarded: December 12, 2007

POST-DOCTORAL TRAINING

2008 - 2014 Postdoctoral Fellow
 UT Southwestern Medical Center
 Departments of Pharmacology and Biochemistry
 Dr. David R. Corey laboratory

HONORS AND AWARDS

Outstanding Young Alumni Award, College of Agriculture & Life Sciences, NC State Univ. (2016)
UT Southwestern Postdoctoral Association Travel Award (2013)
UT Southwestern Biological Chemistry Travel Award (2010)
NIH (F32) Postdoctoral Fellowship, NICHD (2009-2012)
A.R. Main-Becton Dickinson Award for Outstanding Graduate Research (2007)
A. Tab Williams Endowment (2002-2003)
Col. Henry E. Kendall Scholarship (2000-2003)

TEACHING

Southern Illinois University, CHEM 350, Biochemistry (2015-present)
Southern Illinois University, CHEM 595B, Biochemistry Seminar (2015-present)
Problem-Based Learning, SIU Medical School, Neurological, Muscular and Behavioral Unit (NMB) (2015-present)
UT Southwestern Postdoctoral Training Certificate in Education (Fall 2012)

PROFESSIONAL ACTIVITIES

Member, RNA Society (2006-present)
Scientific Advisory Committee, Oligonucleotide Therapeutics Society (2014-present)
Member, Oligonucleotide Therapeutics Society (2010-present)
Member, American Chemical Society (2014-present)
NSF Reviewer (2015, 2016)
NIH Reviewer, *Therapeutic Approaches to Genetic Diseases (TAG)* study section (2017)
Journal Reviewer - *Nucleic Acids Research, Journal of Biological Methods, Gene, Molecular Therapy, ACS Synthetic Biology, Human Molecular Genetics*

PUBLICATIONS

Peer-Reviewed Articles

- Kartje, Z.K., Barkau, C.L., Rohilla, K.J., and Gagnon, K.T. (2017) DNA Substitutions Tune CRISPR-Cas9 Activity, *in review*.
- Ageely, E.A., Kartje, Z.J., Rohilla, K., Barkau, C.L., and Gagnon, K.T. (2016) Quadruplex-flanking stem structures modulate the stability and metal ion preferences of RNA mimics of GFP. *ACS Chem. Biol.*, 11:2398-2406.
- Kalantari, R., Hicks, J.A., Li, L., Gagnon, K.T., Sridhara, V., Lemoff, A., Mirzaei, H., and Corey, D.R. (2016) Stable Association of RNAi Machinery is Conserved Between the Cytoplasm and Nucleus of Human Cells. *RNA*, 22:1-14.
- Dodd, D.W., Tomchick, D.R., Corey, D.R., and Gagnon, K.T. (2016) Pathogenic C9ORF72 Antisense Repeat RNA Forms a Double Helix with Tandem C:C Mismatches. *Biochemistry*, 55:1283-1286.
- Hu, J., Liu, J., Gagnon, K.T., and Corey, D.R. (2015) Engineering Duplex RNAs for Challenging Targets: Recognition of GGGGCC/CCCCGG repeats at the ALS/FTD C9ORF72 locus. *Chem. Biol.*, 22:1505-1511.
- Gagnon, K.T., Li, L., Janowski, B.A., and Corey, D.R. (2014) Analysis of Nuclear RNA Interference in Human Cells by Subcellular Fractionation and Argonaute Loading. *Nat. Protoc.*, 9:2045-2060.
- Gagnon, K.T., Li, L., Chu, Y., Janowski, B.A., and Corey, D.R. (2014) RNAi Factors Are Present and Active in Human Cell Nuclei. *Cell Reports*, 6:211-221.
- Matsui, M., Zhang, H., Chu, J., Gagnon, K.T., Shaikh, S., Kuchimanchi, S., Manoharan, M., Corey, D.R., and Janowski, B.A. (2013) Promoter RNA Links Transcriptional Regulation of Inflammatory Pathway Genes. *Nucl. Acids Res.*, 41:10086-10109.
- Dodd, D.W., Gagnon, K.T., and Corey, D.R. (2013) Digital Quantitation of Potential Therapeutic Target RNAs. *Nucl. Acid Therap.*, 23:188-194.
- Gagnon, K.T., Biswas, S., Zhang, X., Brown, B.A. II, Wollenzien, P., Mattos, C., and Maxwell, E.S. (2012) Structurally Conserved Nop56/58 N-Terminal Domain Facilitates Efficient Box C/D Ribonucleoprotein-guided Methyltransferase Activity. *J. Biol. Chem.*, 287:19418-19428.
- Gagnon, K.T., Watts, J.K., Pendergraff, H.M., Potier, P., Thai, D., Montallier, C., and Corey, D.R. (2011) Antisense and antigene inhibition of gene expression by cell-permeable oligonucleotide-oligospermine conjugates. *J. Am. Chem. Soc.*, 133:8404-8407.
- Biswas, S., Buhrman, G., Gagnon, K.T., Mattos, C., Brown II, B.A., and Maxwell, E.S. (2011) Comparative Analysis of the 15.5kD Box C/D snoRNP Core Protein in the Primitive Eukaryote *Giardia lamblia* Reveals Unique Structural and Functional Features. *Biochemistry*, 50:2907-2918.
- Hu, J., Gagnon, K.T., Lui, J., Watts, J.K., Syeda-Newaz, J., Bennett, C.F., Swayze, E.E., Randolph, J., Chattopadhyaya, J. and Corey, D.R. (2011) Allele-selective inhibition of ataxin-3 (ATX3) expression by antisense oligomers and duplex RNAs. *Biol. Chem.*, 392:315-325.
- Gagnon, K.T., Pendergraff, H.M., Deleavey, G.F., Swayze, E.E., Potier, P., Randolph, J., Roesch, E.B., Chattopadhyaya, J., Damha, M.J., Bennett, C.F., Montallier, C., Lemaitre, M., and Corey, D.R. (2010) Allele-Selective Inhibition of Mutant Huntingtin Expression with Antisense Oligonucleotides Targeting the Expanded CAG Repeat. *Biochemistry*, 49:10166-10178.
- Yue, X., Schwartz, J. C., Chu, Y., Younger, S. T., Gagnon, K.T., Elbashir, S., Janowski, B. A., and Corey, D. R. (2010) Transcriptional regulation by small RNAs at sequences downstream from 3' gene termini. *Nat. Chem. Biol.*, 6:621-629.

- Gagnon, K.T., Zhang, X., Qu, G., Biswas, S., Suryadi, J., Brown II, B.A., and Maxwell, E.S. (2010) Signature Amino Acids Enable the Archaeal L7Ae Box C/D RNP Core Protein to Recognize and Bind the K-loop RNA Motif. *RNA*, 16:79-90.
- Bleichert, F., Gagnon, K.T., Brown II, B.A., Maxwell, E.S., Leschziner, A.E., Unger, V.M., and Baserga, S.J. (2009) A Dimeric Structure for Archaeal Box C/D Small Ribonucleoproteins. *Science*, 325(5946):1384-1387.
- Gagnon, K.T., Ju, S.Y., Goshe, M.B., Maxwell, E.S., and Franzen, S. (2009) A Role for Hydrophobicity in a Diels-Alder Reaction Catalyzed by Pyridyl-Modified RNA. *Nucl. Acids Res.*, 37(9):3074-3082.
- Hu, J., Matsui, M., Gagnon, K.T., Schwartz, J.C., Gabillet, S., Arar, K., Wu, J., Bezprozvanny, I., and Corey, D.R. (2009) Allele-Specific Silencing of Mutant Huntingtin and Ataxin-3 Genes by Targeting Expanded CAG Repeats in mRNAs. *Nat. Biotechnol.*, 27(5):478-484.
- Gagnon, K.T., Zhang, X., Agris, P.F., and Maxwell, E.S. (2006) Assembly of the Archaeal Box C/D sRNP Can Occur Via Alternative Pathways and Requires Temperature-Facilitated sRNA Remodeling. *J. Mol. Biol.*, 362(5):1025-1042.

Reviews, Book Chapters, Protocols, and Commentaries

- Rohilla, K.J., and Gagnon, K.T. (2017) RNA Biology of Disease-Associated Microsatellite Repeat Expansions. *Acta Neuropath. Comm.*, accepted.
- Gagnon, K.T. (2016) "Loading of Argonaute Protein with Small Duplex RNA in Cellular Extracts" in *Meth. Mol. Biol.*, Ren-Jang Lin editor, Humana Press, 1421:53-67.
- Gagnon, K.T., and Corey, D.R. (2015) Stepping Toward Therapeutic CRISPR. *Proc. Natl. Acad. Sci., USA*, 112:15535-15537.
- Gagnon, K.T., and Maxwell, E.S. (2015) Assessing Intermolecular RNA:RNA Interactions Within a Ribonucleoprotein Complex Using Heavy Metal Cleavage Mapping. *Meth. Mol. Biol.*, 1240:125-134.
- Gagnon, K.T., and Watts, J.K. (2014) 10th Annual Meeting of the Oligonucleotide Therapeutics Society. *Nucl. Acid Therap.*, 24:428-434.
- Gagnon, K.T., and Corey, D.R. (2012) Argonaute and the Nuclear RNAs: New Pathways for Controlling Gene Expression. *Nucl. Acid Therap.*, 1:3-16.
- Gagnon, K.T., and Maxwell, E.S. (2011) "Electrophoretic Mobility Shift Assay for Characterizing RNA-Protein Interaction." in *Meth. Mol. Biol.*, Henrik Nielsen editor, Humana Press, 703:275-291.
- Gagnon, K.T. (2010) HD Therapeutics – CHDI 5th Annual Conference. *IDrugs*, 13(4):219-223.
- Franzen, S., and Gagnon, K.T. (2010) Advertising Science for High Impact Publication. *The Open Ethics J.*, 4:1-9.
- Gagnon, K.T., Qu, G., and Maxwell, E.S. (2009) "Multicomponent 2'-O Ribose Methylation Machines: Evolving Box C/D RNP Structure and Function." in *DNA and RNA Modification Enzymes: Structure, Function, Mechanism and Evolution*, H. Grosjean editor, LANDES BioScience, p.436-449.
- Gagnon, K.T., Zhang, X., and Maxwell, E.S. (2008) "The Box C/D RNPs: Evolutionarily Ancient Nucleotide Modification Complexes." in *RNA and DNA Editing: Molecular Mechanisms and their Integration into Biological Systems*, H. Smith editor, John Wiley and Sons, Inc., p.313-339.
- Gagnon, K.T., Zhang, X., and Maxwell E.S. (2007) *In Vitro* Reconstitution and Affinity Purification of Catalytically Active Archaeal Box C/D sRNP Complexes. *Meth. Enzym.*, 425:263-282.

Patents

Corey, D.R., Gagnon, K.T., Bennett, C.F., Swayze, E.E. "Methods and Compositions Useful in Treatment of Diseases or Conditions Related to Repeat Expansion." Patent application 61/405,157. Filed 10/20/2010. Licensed to Isis Pharmaceuticals 07/2011.

Gagnon, K.T., Damha, M.J. "Tuning CRISPR/Cas9 Activity with Chemically Modified Nucleotide Substitutions." Provisional. Filed on 9/23/2016.

ORAL CONFERENCE PRESENTATIONS and INVITED SEMINARS

Invited Seminar, Department of Chemistry, St. Louis University, St. Louis, Missouri, February, 2017. "Broccoli and CRISPR and What's Cooking in the RNA Kitchen."

12th Annual Meeting of the Oligonucleotide Therapeutics Society, September 25-28, 2016, Montreal, Quebec, Canada. Selected abstract: "Nucleotide Substitutions Tune CRISPR/Cas9 Cleavage Activity."

47th American Chemical Society (ACS) Central Regional Meeting (CERM), May 18-21, 2016, Covington, KY. Invited Talk: "Tuning Cas9 Activity with CRISPR RNA Modification."

CRISPR & Genome Engineering Conference, May 26-27, 2016, Boston, MA. Invited Talk: "Tuning Cas9 Activity with CRISPR RNA Modification."

Invited Seminar, Physiology Department, Southern Illinois University, Carbondale, Illinois, October, 2015. "Adventures in Noncoding RNA Biochemistry: A Collection of Short Stories."

Invited Seminar, South Dakota State University, Brookings, South Dakota, March 2014. "Seeing Biochemistry and Disease Through RNA Lenses."

Invited Seminar, Chemistry and Biochemistry Department, Southern Illinois University, Carbondale, Illinois, February 2014. "Seeing Biochemistry and Disease Through RNA Lenses."

Invited Seminar, Anatomy and Cell Biology Department, Rosalind Franklin Medical University, North Chicago, Illinois, January 2014. "Viewing Biology and Disease Through RNA Lenses."

Invited Seminar, Chemistry and Biochemistry Department, Baylor University, Waco, Texas, December 2013. "Viewing Biochemistry and Disease Through RNA Lenses."

16th Annual Meeting of the American Society for Gene and Cell Therapy, May 15-18, 2013, Salt Lake City, Utah. Invited Talk: "Noncoding RNAs Link Transcriptional Regulation of Inflammatory Pathway Genes."

Keystone Symposia on RNA Silencing, March 19-24, 2013, Whistler Conference Centre, Whistler, British Columbia, Canada. Selected Abstract: "Argonaute and RNAi in the Mammalian Cell Nucleus."

Invited Seminar, Department of Biological Sciences, University of South Carolina, Columbia, South Carolina, February 2013. "Noncoding RNA and Repeat Expansion RNA in Human Biology and Disease."

17th Annual Meeting of the RNA Society, May 29-June 3, 2012, University of Michigan, Ann Arbor, Michigan. Selected abstract: "Argonaute and RISC in the Mammalian Cell Nucleus."

6th Annual Meeting of the Oligonucleotide Therapeutics Society, October 20-23, 2010, Dana Point, California. Selected abstract: "Allele-Selective Inhibition of Mutant Huntingtin Expression with Antisense Oligonucleotides Targeting the Expanded CAG Repeat."

RESEARCH SUPPORT

Ongoing

Amyotrophic Lateral Sclerosis Therapeutic Idea Award

Department of Defense Gagnon (PI) 06/01/16 - 05/31/18

“Chemical Library Screening for Potential Therapeutics Using Novel Cell-Based Models of ALS”

Goal: Develop and apply a high throughput chemical screening workflow to cell-based models of ALS for discovery of compounds with therapeutic potential.

Judith and Jean Pape Adams Charitable Foundation

Gagnon (PI) 01/01/17 - 12/31/17

Title: “C9ORF72 transcription and splicing as therapeutic targets for a genetic form of ALS”

Goal: Target C9ORF72 splicing with antisense oligonucleotides for intron skipping or target C9ORF72 promoter with CRISPR to block transcription in cell models of ALS.

Completed (last 3 years)

ALS Association Starter Grant

Amyotrophic Lateral Sclerosis Association Gagnon (PI) 08/01/15 - 07/31/16

“Flexible and Accessible Cell-Based Models of c9FTD/ALS”

Goal: Develop and validate cell-based models of c9FTD/ALS designed to facilitate accessibility to a broad research community and to be amenable to mechanistic investigations.

School of Medicine Team Development Grant

Southern Illinois University Gagnon (PI) 01/01/15 - 12/31/16

“Demystifying Aggregation in c9FTD/ALS to Enable Therapeutic Development”

Goal: Seed grant to develop a multi-disciplinary team to investigate the process of repeat expansion RNA aggregation in c9FTD/ALS using infrared spectroscopy and other novel tools.