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## CURRICULUM VITAE

### **EDUCATION**

1989-1991	B.S. Chemistry, University of Pittsburgh, Pittsburgh, PA.
1991-1997	Ph. D., Chemistry, The Ohio State University, Columbus, OH.

### **MILITARY SERVICE**

•U.S. Army Reserves 1988-1992

### **POST-DOCTORAL APPOINTMENTS**

Oct. 1997- Oct .1998	Post-Doctoral Fellow, Vanderbilt University
Jan. 1999- June 2002	NIH Post-Doctoral Fellow, University of Wisconsin (1 F32 GM20180-01)

### **CURRENT APPOINTMENT**

Aug 1 2002 to June 30, 2008	Asst. Professor of Biochemistry, University of Vermont, Burlington, VT.
July 1, 2008 to June 30, 2020	Assoc. Professor of Biochemistry, University of Vermont, Burlington, VT.
July 1, 2010 to June 30, 2020	Assoc. Professor of Chemistry, University of Vermont, Burlington, VT.
July 1, 2020 to present	Professor of Biochemistry, University of Vermont, Burlington, VT

### **HONORS AND AWARDS**

- The Paul D. Boyer Memorial Award for Post-Doctoral Fellows (2001). This was a new award given by a Biochemistry Department faculty committee at the University of Wisconsin in 2001. This award is given on an annual basis to the post-doctoral fellow in the department determined to be the "most outstanding" post-doctoral scientist.
- The 2009 Journal of Peptide Science Best Publication Award
- 2010-2011 nominee for the UVM Graduate Student Senate Excellence in Teaching Award
- 2015 nominee for the Kroepsch-Maurice Excellence in Teaching Award
- 2017 Office of Undergraduate Research Student Mentoring Award
- 2018 nominee for the Kroepsch-Maurice Excellence in Teaching Award

### **PROFESSIONAL ORGANIZATIONS**

- American Chemical Society
- Society for Redox Biology and Medicine

### **OTHER PROFESSIONAL ACTIVITIES:**

- Member, Cell Signaling and Environmental Pathology Training Program (2004 to 2014)
- Member, M.D./Ph.D. training program (2008 to 2010)
- Member, Hemostasis and Thrombosis Training Program (2003 to 2018)
- Member, UVM Graduate College (2004 to present).
- Member, UVM Cellular, Molecular, and Biomedical Graduate Program (2012 to present)

## RESEARCH

### PEER-REVIEWED PUBLICATIONS

- 66) Hondal RJ. (2023) What is the redox potential of ergothioneine? *Antioxid. Redox. Signal.* Published Online:13 Jan 2023 <https://doi.org/10.1089/ars.2022.0192>
- 65) Hondal RJ. (2022) Flux versus poise: Measuring the dynamic cellular activity of the thioredoxin system with a redox probe. *Redox Biol.* 54, 102376. doi: 10.1016
- 64) Ste.Marie EJ, Hondal RJ. (2022) Application of alpha-methyl selenocysteine as a tool for the study of selenoproteins. *Methods Enzymol.* 662, 297-329. doi: 10.1016/bs.mie.2021.10.016
- 63) Jenny KA, Mose G, Haupt DJ, & Hondal RJ. (2022) Oxidized forms of ergothioneine are substrates for mammalian thioredoxin reductase. *Antioxidants* 11, 185. **PMCID:** PMC8868364
- 62) Colon R, Wheeler M, Joyce EJ, Ste Marie EJ, Hondal RJ, & Rein KS. (2021) The marine neurotoxin brevetoxin (PbTx-2) inhibits *Karenia brevis* and mammalian thioredoxin reductases by targeting different residues. *J Nat Prod.* 84, 2961-2970.
- 61) Jenny KA, Ruggles EL, Liptak MD, Masterson DS & Hondal RJ. (2021) Ergothioneine in a peptide: Substitution of histidine with 2-thiohistidine in bioactive peptides. *J. Pept. Sci.* e3339. **PMCID:** PMC8443123
- 60) Remington J, Liao C, Sharafi M, Ste.Marie E, Ferrell J, Hondal RJ, Wargo M, Schneebeli S & Li, J. (2020) On the aggregation state of synergistic antimicrobial peptides. *J. Phys. Chem. Lett.* 11, 9501-9506.
- 59) Ste.Marie E, Wehrle RJ, Haupt DJ, Wood NB, van der Vliet A, Previs MJ, Masterson DS & Hondal RJ. (2020) Can selenoenzymes resist electrophilic modification? Evidence from thioredoxin reductase and a mutant containing alpha-methylselenocysteine. *Biochemistry* 59, 3300-3315. **PMCID:** PMC7509987
- 58) Ste.Marie E, & Hondal RJ. (2020) 2,2'-Dipyridyl diselenide: A chemoselective tool for cysteine deprotection and disulfide bond formation. *J. Pept. Sci.* 26, e3236. **PMCID:** PMC7509986
- 57) Day BJ, Bratcher PE, Chandler, J, Kilgore M, Min E, LiPuma JJ, Hondal RJ, & Nichols DP. (2020) The thiocyanate analog selenocyanate is a more potent antimicrobial pro-drug that also is selectively detoxified by the host. *Free Radic. Biol. Med.* 146, 324-332. **PMCID:** PMC6951815.
- 56) Jenny KA, Ste.Marie EJ, Mose G, Ruggles EL, & Hondal RJ. (2019) Facile removal of 4-methoxybenzyl protecting group from selenocysteine. *J. Pept. Sci.* 25, e3209. **PMCID:** PMC6851407
- 55) Wehrle RJ, Ste.Marie E, Hondal RJ, & Masterson DS. (2019) Synthesis of alpha-methyl selenocysteine and its utilization as a glutathione peroxidase mimic. *J. Pept. Sci.* 25, e3173. **PMCID:** PMC6785838.
- 54) Alim I, Caulfield JT, Chen Y, Swarup V, Geschwind DH, Ivanova E, Seravalli J, Ai Y, Sansing LH, Hondal RJ, Ste. Marie E, Cave JW, Sagdullaev BT, Karuppagounder SS, & Ratan RR. (2019) Selenium induces an adaptive transcriptional response to inhibit ferroptosis and improve recovery after brain hemorrhage. *Cell* 177, 1262-1279.
- 53) Barber DR, & Hondal RJ (2019) Gain of function conferred by selenocysteine: Catalytic enhancement of one-electron transfer reactions by thioredoxin reductase. *Protein Sci.* 28, 79-89. **PMCID:** PMC6295889.
- 52) Payne NC, Barber DR, Ruggles EL, & Hondal RJ (2019) Can dimedone be used to study selenoproteins? An investigation into the reactivity of dimedone towards oxidized forms of selenocysteine. *Protein Sci.* 28, 41-55. **PMCID:** PMC6295895
- 51) Tuladhar A, Hondal RJ, Colon R, Hernandez EL, & Rein KS. (2019) Effectors of thioredoxin reductase: I Brevetoxins and manumycin A. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology* 217, 76-86. **PMCID:** PMC7485175
- 50) Ste.Marie E, & Hondal RJ. (2018) Reduction of cysteine-S-protecting groups by triisopropylsilane. *J. Pept. Sci.* 24, e3130. **PMCID:** PMC6773273.
- 49) Maroney MJ, and Hondal RJ (2018) Selenium versus sulfur: reversibility of chemical reactions and resistance to permanent oxidation in proteins and nucleic acids. *Free Radic. Biol. Med.* 127, 228-237. **PMCID:** PMC6158117
- 48) O'Keefe JP, Dustin CM, Barber DR, Snider GW, & Hondal RJ (2018) A "seleno-effect" differentiates the roles of redox active cysteine residues in *Plasmodium falciparum* thioredoxin reductase. *Biochemistry* 57, 1767-1778. **PMCID:** PMC5866731

- 47) Fredericks GJ, Hoffmann FW, **Hondal RJ**, Rozovsky S, Urschitz J, & Hoffmann PR. (2017) Selenoprotein K increases efficiency of DHHC6 catalyzed palmitoylation by stabilizing the acyl-DHHC6 intermediate. *Antioxidants* 7, E4. **PMCID:** PMC5789314
- 46) Payne NC, Geissler A, Button A, Sasuclark AR, Schroll AL, Ruggles EL, Gladyshev VN & **Hondal RJ**. (2017) Comparison of the redox chemistry of sulfur and selenium-containing analogs of uracil. *Free Radic. Biol. Med.* 104, 249-261. **PMCID:** PMC5328918
- 45) Gladyshev VN, Arnér ES, Berry MJ, Brigelius-Flohé R, Bruford EA, Burk RF, Carlson, BA Castellano S, Chavatte L, Conrad M, Copeland PR, Diamond AM, Driscoll DM, Ferreira A, Flohé L, Green FR, Guigó R, Handy DE, Hatfield DL, Hesketh J, Hoffmann PR, Holmgren A, **Hondal RJ**, Howard MT, Huang K, Kim H-Y, Ick Young Köhrle KJ, Krol A, Kryukov GV, Lee BJ, Lee BC, Lei XG, Liu Q, Lescure A, Lobanov AL, Loscalzo J, Maiorino M, Mariotti M, K. Prabhu KS, Rayman MP, Rozovsky S, Salinas G, Schomburg L, Schweizer U, Simonovic M, Sunde RA, Tsuji PA, Tweedie S, Ursini F, & Zhang Y. (2016) Selenoprotein gene nomenclature. *J. Biol. Chem.* 291, 24036-24040. **PMCID:** PMC5104929
- 44) Ste.Marie E, Ruggles EL & **Hondal RJ**. (2016) Removal of the 5-nitro-2-pyridine-sulfonyl protecting group from selenocysteine and cysteine by ascorbolysis. *J. Pept. Sci.* 22, 571-576. **PMCID:** PMC5098394
- 43) Reich HJ & **Hondal RJ**. (2016) Why Nature chose selenium. *ACS Chem. Biol.* 11, 821-841.
- 42) Ruggles EL, Dekker PB, & **Hondal RJ**. (2014) Conformational analysis of oxidized peptide fragments of the C-terminal redox center in thioredoxin reductases by NMR spectroscopy. *J. Pept. Sci.* 20, 349-360. **PMCID:** PMC4000577
- 41) Lothrop AP, Snider GW, Ruggles EL, Patel AS, Lees WJ, & **Hondal RJ**. (2014) Selenium as an electron acceptor during the catalytic mechanism of thioredoxin reductase, *Biochemistry* 53, 654-663. <https://doi.org/10.1021/bi400658g> **PMCID:** PMC3957198
- 40) Snider GW, Dustin CM, Ruggles EL, & **Hondal RJ**. (2014) A mechanistic investigation of the C-terminal redox motif of thioredoxin reductase from *Plasmodium falciparum*. *Biochemistry* 53, 601-609. **PMCID:** PMC3957191
- 39) Lothrop AP, Snider GW, Ruggles EL, & **Hondal RJ**. (2014) Why is mammalian thioredoxin reductase-1 so dependent upon the use of selenium? *Biochemistry* 53, 554-564. **PMCID:** PMC3957196
- 38) Cunliff B, Snider GW, Fredette N, Stumpff J, **Hondal RJ** & Heintz N. (2014) Resolution of oxidative stress by thioredoxin reductase: cysteine versus selenocysteine. *Redox Biology* 2, 475-484. **PMCID:** PMC3949094
- 37) Lothrop AP, Snider GW, Flemer S. Jr., Ruggles EL, Davidson RS, Lamb A, & **Hondal RJ**. (2014) Compensating for the absence of selenocysteine in high *M<sub>r</sub>* thioredoxin reductases: The electrophilic activation hypothesis, *Biochemistry* 53, 664-674. **PMCID:** PMC3931472
- 36) Cunliff B, Snider GW, Fredette N, **Hondal RJ** & Heintz N. (2013) A direct and continuous assay for the determination of thioredoxin reductase activity in cell lysates. *Anal Biochem* 443, 34-40. **PMCID:** PMC3839276
- 35) Snider GW, Ruggles EL, Khan N, & **Hondal RJ**. (2013) Selenocysteine confers resistance to inactivation by oxidation in thioredoxin reductase: Comparison of selenium and sulfur enzymes. *Biochemistry* 52, 5472-5481. **PMCID:** PMC3760785
- 34) Chandler JD, Nichols DP, Nick JA, **Hondal RJ**, & Day, BJ. (2013) Selective metabolism of hypothiocyanous acid by mammalian thioredoxin reductase promotes lung innate immunity and antioxidant defense. *J. Biol. Chem.* 288, 18421-18428. **PMCID:** PMC3689984
- 33) Randall MJ, Spiess PC, Hristova M, **Hondal RJ**, & van der Vliet, A. (2013) Acrolein-induced activation of mitogen-activated protein kinase signaling is mediated by alkylation of thioredoxin reductase and thioredoxin 1. *Redox Biology* 1, 265-275. **PMCID:** PMC3757691
- 32) **Hondal RJ**, Marino SM, & Gladyshev, VN. (2013) Selenocysteine in thiol-disulfide-like exchange reactions. *Antioxid Redox Signal* 18, 1675-1689. **PMCID:** PMC3613276
- 31) Schroll AL, **Hondal RJ**, & Flemer S. Jr (2012) The use of 2,2' dithiobis(5-nitropyridine) (DTNP) for deprotection and diselenide formation in protected selenocysteine-containing peptides. *J. Pept. Sci.* 18, 155-162. **PMCID:** PMC3437994
- 30) Schroll AL, **Hondal RJ**, & Flemer S. Jr (2012) 2,2' Dithiobis(5-nitropyridine) (DTNP) as an effective and gentle deprotectant for common cysteine protecting groups. *J. Pept. Sci.* 18, 1-9. **PMCID:** PMC3289972
- 29) Spiess PC, Deng B, Matthews DE, **Hondal RJ**, van der Vliet A (2011) Proteomic profiling of acrolein adducts in human lung epithelial cells. *J. Proteomics* 74, 2380-2394. **PMCID:** PMC3196826

- 28) Hondal RJ, & Ruggles EL** (2011) Differing views of the role of selenium in thioredoxin reductase. *Amino Acids* 41, 73-89. **PMCID:** PMC2935959
- 27) Snider G, Grout L, Ruggles EL, & Hondal RJ** (2010) Methaneseleninic acid is a substrate for truncated thioredoxin reductase: Implications for the catalytic mechanism and redox signaling. *Biochemistry* 49, 10329-10338. **PMCID:** PMC3018153
- 26) Lothrop, AP, Ruggles, EL, & Hondal RJ.** (2009) No selenium required: Reactions catalyzed by mammalian thioredoxin reductase that are independent of a selenocysteine residue. *Biochemistry*.48, 6213–6223. **PMCID:** PMC2754045
- 25) Hondal, RJ** (2009) Using chemical approaches to study selenoproteins – focus on thioredoxin reductases. *Biochim. Biophys. Acta* 1790, 1501-1512. **PMCID:** PMC2818346
- 24) Ruggles EL, Dekker PB, & Hondal RJ.** (2009) Synthesis, redox properties, and conformational analysis of vicinal disulfide ring mimics. *Tetrahedron* 65, 1257-1267. **PMCID:** PMC3653589
- 23) Lacey BM, Flemer SJ, Eckenroth BE, & Hondal RJ** (2008) Selenium in thioredoxin reductase: A mechanistic perspective. *Biochemistry* 47, 12810-12821. **PMCID:** PMC3682215
- 22) Ruggles EL, Flemer SJ, & Hondal RJ** (2008) A viable synthesis of *N*-methyl cysteine. *Biopolymers* 90, 61-68. **PMCID:** PMC3691851
- 21) Flemer SJ, Lacey BM & Hondal RJ** (2008) Synthesis of peptide substrates for mammalian thioredoxin reductase. *J. Pept. Sci.* 14, 637-47. **PMCID:** PMC3690199
- 20) Eckenroth BE, Lacey BM, Lothrop AP, Harris KM, & Hondal RJ** (2007) Investigation of the C-terminal redox center of high *M<sub>r</sub>* thioredoxin reductases by protein engineering and semisynthesis. *Biochemistry* 46, 9472-9483. **PMCID:** PMC3682222
- 19) Eckenroth BE, Rould MA, Hondal RJ, & Everse SJ** (2007) Structural and biochemical studies reveal differences in the catalytic mechanisms of mammalian and *Drosophila melanogaster* thioredoxin reductases. *Biochemistry* 46, 4694-4705. **PMCID:** PMC3687216
- 18) Harris KM, Flemer S & Hondal RJ.** (2007) Studies on deprotection of cysteine and selenocysteine side chain protecting groups. *J. Pept. Sci* 13, 81-93. **PMCID:** PMC3689433
- 17) Eckenroth BE, Harris K, Turanov AA, Gladyshev VN, Raines RT, & Hondal, RJ.** (2006) Semisynthesis and characterization of mammalian thioredoxin reductase. *Biochemistry* 45, 5158-5170. **PMCID:** PMC2570056
- 16) Ruggles EL, & Hondal RJ.** (2006) Synthesis and properties of disulfide-bond containing eight-membered rings. *Tet. Lett.* 47, 4281-4284. **PMCID:** PMC3698869
- 15) Lacey BM, & Hondal RJ.** (2006) Characterization of mitochondrial thioredoxin reductase from *C. elegans*. *Biochem. Biophys. Res. Commun.* 346, 629-636. **PMCID:** PMC3687220
- 14) Hondal RJ.** (2005) Incorporation of selenocysteine into proteins using peptide ligation. *Protein and Peptide Letters* 12, 757-764. **PMCID:** PMC3683319
- 13) Nilsson BL, Hondal RJ, Soellner MB, & Raines RT.** (2003) Protein assembly by orthogonal chemical ligation methods. *J. Am Chem. Soc.* 125, 5268-5269.
- 12) Hondal RJ, & Raines RT.** (2002) Semisynthesis of proteins containing selenocysteine. *Methods Enzymol.* 347, 70-83.
- 11) Kubiak RJ, Yue X, Hondal RJ, Mihai C, Tsai M.-D., & Bruzik K.S.**(2001) Involvement of the Arg-Asp-His Catalytic Triad in Enzymatic Cleavage of the Phosphodiester Bond. *Biochemistry* 40, 5422-5432.
- 10) Hondal RJ, Nilsson BL, & Raines RT,** (2001) Selenocysteine in native chemical ligation and expressed protein ligation. *J. Am Chem. Soc.* 123, 5140-5141.
- 9) Hondal RJ, Ma, S Caprioli RM, Hill KE, & Burk RF.** (2001) Heparin-binding histidine and lysine residues of rat selenoprotein P. *J. Biol. Chem.* 276, 15823-15831.
- 8) Hondal RJ, Motley AK, Hill KE, & Burk RF.** (1999) Failure of selenomethionine residues in albumin and immunoglobulin G to protect against peroxynitrite. *Arch. Biochem. Biophys.* 371, 29-34.
- 7) Kubiak RJ, Hondal RJ, Yue X, Tsai M.-D., & Bruzik KS.** (1999) Identification of a novel catalytic triad with dual functions in enzymatic cleavage of the P-O Bond. *J. Am. Chem. Soc.* 121, 488-489.

**6) Hondal RJ**, Zhao Z, Kravchuk AV, Liao H, Riddle SR, Bruzik KS, & Tsai M.-D. (1998) Mechanism of phosphatidylinositol-specific phospholipase C: A unified view of the mechanism of catalysis" *Biochemistry* 37, 4568-4580.

**5) Hondal RJ**, Riddle SR, Kravchuk AV, Zhao Z, Liao H, Bruzik KS, & Tsai M.-D. (1997) Phosphatidylinositol phospholipase C: Kinetic and stereochemical evidence for an interaction between arginine-69 and the phosphate group of phosphatidylinositol. *Biochemistry* 36, 6633-6642.

**4) Hondal RJ**, Bruzik KS, Zhao Z, & Tsai M.-D. (1997) Mechanism of Phosphatidylinositol-Phospholipase C. 2. Reversal of a Thio Effect by Site-Directed Mutagenesis. *J. Am. Chem. Soc.* 119, 5477-5478.

**3) Hondal RJ**, Zhao Z, Riddle SR, Kravchuk AV, Liao H, Bruzik KS, & Tsai M.-D. (1997) Phosphatidylinositol-specific Phospholipase C. 3. Elucidation of the catalytic mechanism and comparison with ribonuclease A. *J. Am. Chem. Soc.* 119, 9933-9934.

**2) Werneburg BG**, Ahn J, Zhong X, **Hondal RJ**, Kraynov VS, & Tsai M.-D. (1996) DNA Polymerase  $\beta$ : Pre-Steady-State Kinetic Analysis and Roles of Arginine-283 in Catalysis and Fidelity. *Biochemistry* 35, 7041-50.

**1) Hondal RJ & Ulsh RC.** (1992) Studies on the Coprophageal Behavior of the Domestic Rabbit Using Adiabatic Calorimetry. *J. Penn. Acad. Sci.* 66, 107-110.

### Conference Proceedings:

**1) Harris KM & Hondal RJ.** Deprotection of the *p*-methoxybenzyl group of selenocysteine by neighboring group participation. *Understanding Biology Using Peptides: Proceedings of the 19th American Peptide Symposium* (Sylvie E. Blondelle, Ed.). American Peptide Society, 2006. Produced by Springer, New York, pgs 91-92.

**2) Flemer S & Hondal RJ.** An efficient on-resin protocol for on-resin, vicinal disulfide formation: Applications to thioredoxin reductase (2009) *Adv. Exp. Med. Biol.* 611, 93-94.

**3) Schroll A & Hondal RJ.** Further development of new deprotection chemistry for cysteine and selenocysteine side chain protecting groups (2009) *Adv. Exp. Med. Biol.* 611, 135-136.

**4) Flemer S, Schroll A, & Hondal RJ** DTNP as a gentle and effective method of deprotection for side-chain protectants on commercially available Cys and Sec SPPS derivatives. *Building Bridges: The Proceedings of the 22<sup>nd</sup> American Peptide Symposium* (Michal Lebl, Ed.). American Peptide Society, 2011. Produced by Prompt Scientific Publishing, San Diego, CA, pgs 24-25.

### Book Chapters:

**1) Ruggles EL, Snider GW, & Hondal RJ** (2012) Chemical basis for the use of selenocysteine. In *Selenium: Its Molecular Biology and Role in Human Health*. 3<sup>rd</sup> ed, D.L. Hatfield, M.J. Berry, V.N. Gladyshev, Eds. Pgs 73-83. Springer, New York.

**2) Hondal RJ**, Zhao Z, Kravchuk AV, Liao H, Riddle SR, Bruzik KS, & Tsai M.-D. (1998) The Mechanism of Phosphatidylinositol-Specific Phospholipase C Revealed by Protein Engineering and Thio-PI Analogs. In *Phosphoinositides: Chemistry, Biochemistry and Biomedical Applications*, K. S. Bruzik, Ed. ACS Symp. Ser. 718, 109-120.

### Newsletters:

**1) Hondal RJ**, and Schaeffer C. (1995) Preparation of competent cells using transformation and storage solution, *Epicentre Forum* 2, 5.

### Patents:

**1) Direct assay of thioredoxin reductase activity** (2014) US 20150050682 A1, **Robert J. Hondal**, Nicholas H. Heintz, Brian Cuniff, Nicholas Fredette, Gregg W. Snider.

**2) Selenocystine Derivatives, Alpha-Methylselenocysteine, Alpha-Methylselenocysteine Derivatives, and Methods of Making and Using Same** (2015) Provisional Patent# 62/110,943, **Robert J. Hondal**, Erik L Ruggles.

**3) Substitution of histidine with 2-thiohistidine in bioactive peptides.** WO WO2022226360A1 **Robert J. Hondal**,

## **INVITED LECTURES**

- Hondal, R.J.** *Cheating on Selenium. Gordon Research Conference: Thiol-Based Redox Regulation & Signaling.* July 9-15, 2022, Barcelona, Spain.
- Hondal, R.J.** *The Chemical Advantage of Selenium in Enzymes and RNA.* University of New Hampshire, Durham, NH. November 5<sup>th</sup>, 2019.
- Hondal, R.J.** *Everything I learned about thiol/disulfide exchange, I learned from selenium (and Ron)* Massachusetts Institute of Technology, Cambridge, MA. RTR-60 Symposium. July 27<sup>th</sup>, 2019.
- Hondal, R.J.** *Selenium in enzymes and tRNA: Is there a common chemical connection?* Yale University, New Haven, CT. November 16<sup>th</sup>, 2017.
- Hondal, R.J.** *Why Nature uses Selenium in Enzymes and tRNA.* Florida International University, Miami, Florida. October 20<sup>th</sup>, 2017.
- Hondal, R.J.** *Selenium in enzymes and RNA: Is there a common chemical connection?* SUNY Albany, Albany, NY. September 12<sup>th</sup>, 2017.
- Hondal, R.J.** *Selenium confers resistance to oxidative inactivation: Enzymes, model compounds, and molecular mechanisms.* 10<sup>th</sup> International Peroxidase Meeting, August 29<sup>th</sup> – 31<sup>st</sup>, 2017. Breckenridge, Colorado.
- Hondal, R.J.** *Selenium versus sulfur: reversibility of chemical reactions and resistance to permanent oxidation in proteins and nucleic acid.* Se2017, The 11th International Symposium on Selenium in Biology and Medicine. Stockholm, Sweden. August 13-17, 2017.
- Hondal, R.J.** *Selenium in proteins and RNA: A chemical and biological rationale.* Northeast Regional Meeting of the American Chemical Society, Binghamton, NY, October 5-8, 2016.
- Hondal, R.J.** *Why Nature Chose Selenium.* University of Southern Mississippi, Hattiesburg, MS. March 11<sup>th</sup>, 2016.
- Hondal, R.J.** *Why Nature Chose Selenium.* St. Michael's College, Colchester, VT. April 15<sup>th</sup>, 2016.
- Hondal, R.J.** *The Essential Poison: Connecting the Chemistry of Selenium with Biology.* 2014 American Association for the Advancement of Science Annual Meeting, Nexus of Cell Signaling and Drug Discovery: Oxygen, Phosphorus, Sulfur, and Nitrogen, February 15<sup>th</sup>, 2014.
- Hondal, R.J.** *The Selenium Paradox: The Chemical Basis for the Use of Selenocysteine in Enzymes.* Stonehill College, Easton, MA, November 22<sup>nd</sup>, 2013.
- Hondal, R.J.** *The Selenium Paradox: The Chemical Basis for the Use of Selenocysteine in Enzymes.* SUNY-Potsdam, March 5<sup>th</sup>, 2013.
- Hondal, R.J.** *The Selenium Paradox: The Chemical Basis for the Use of Selenocysteine in Enzymes.* Florida International University, October 5<sup>th</sup>, 2012.
- Hondal, R.J.** *The Selenium Paradox: The Chemical Basis for the Use of Selenocysteine in Enzymes.* Gordon Research Conference – Enzymes, Coenzymes, and Metabolic Pathways. Waterville Valley Resort, July 15-20, 2012.
- Hondal, R.J.** *Selenium: It's Chemistry and Biology Among the Elements of Life.* Hobart and William Smith Colleges, Department of Chemistry, March 7<sup>th</sup>, 2012.
- Hondal, R.J.** *The Chemical and Biological Function of Selenium in Thioredoxin Reductase.* Brown University, Department of Molecular Pharmacology, Physiology & Biotechnology September 16<sup>th</sup>, 2011.
- Hondal, R.J.** *The Chemical and Biological Function of Selenium in Enzymes.* University of Kansas, Department of Molecular Biosciences. January 24<sup>th</sup>, 2011.
- Hondal, R.J.** *A Chemico-Biological Rationale for the Use of Selenocysteine.* The 9th International Symposium on Selenium in Biology and Medicine. Kyoto, Japan, May 31 - June 4, 2010.
- Hondal, R.J.** *Differing Views of the Role of Selenium in Thioredoxin Reductase.* Cell Signaling/Environmental Seminar Series, University of Vermont. February 22<sup>nd</sup>, (2010).
- Flemer S, Jr. Schroll A, **Hondal R.J.** *New Orthogonal Se-Protection Protocol for Selenocysteine in Fmoc SPPS: Progress Toward Stepwise Diselenide Formation.* 36th Northeast Regional Meeting of the American Chemical Society, Hartford, CT, United States, October 7-10 (2009) AN: 2009:1216291
- Hondal, R.J.** *Differing Views of the Role of Selenium in Thioredoxin Reductase.* Department of Chemistry, College of The Holy Cross, Worcester, MA October 16<sup>th</sup>, 2009.

- Hondal, RJ.** *Selenium in Thioredoxin Reductase: A Mechanistic Perspective.* Department of Chemistry, University of Rochester, Rochester, NY. October 31<sup>st</sup>, 2008.
- Hondal, RJ.** *Selenium vs. Sulfur in Enzymes: The Case of Thioredoxin Reductase.* College of Pharmacy, University of Wisconsin-Madison, Madison, WI. October 12<sup>th</sup>, 2007.
- Hondal, RJ.** *LEGO Proteins: The Use of Protein Building Blocks to Study Protein Function.* State University of New York-Plattsburgh, Plattsburgh, NY. September 7<sup>th</sup>, 2007.
- Eckenroth BE & **Hondal RJ.** *Selenium vs. Sulfur Thioredoxin Reductases: A Conformation Switching Mechanism Explains Differences in the Catalytic Mechanisms.* Gordon Research Conference – Enzymes, Coenzymes, and Metabolic Pathways. University of New England, July 8-13, (2007).
- Hondal, RJ.** *Selenium in Proteins: The Case of Thioredoxin Reductase.* Department of Chemistry, The Ohio State University, Columbus, OH. March 29<sup>th</sup>, 2007.
- Hondal, RJ.** *Selenium vs. Sulfur Thioredoxin Reductases: Structure studies by X-ray crystallography and functional analysis using semisynthesis.* Department of Chemistry & Biochemistry, The Florida State University, Tallahassee, FL. January 30<sup>th</sup>, 2007.
- Flemer, SF, Harris, KM, & **Hondal RJ.** *A New Method for Deprotecting p-Methoxybenzyl and Acetamidomethyl Groups from Cysteine and Selenocysteine.* Northeast Regional Meeting of the American Chemical Society, Binghamton, NY, October 5-7, (2006)
- Eckenroth BE, & **Hondal RJ.** *Structure-Function Relationships of the Conserved GCUG Tetrapeptide Motif of Thioredoxin Reductase Investigated by Protein Semisynthesis.* The 8th International Symposium on Selenium in Biology and Medicine, Madison, WI. July 25-30, (2006).
- Hondal, RJ.** *I. New orthogonal deprotection strategies for cysteine and selenocysteine. II. Semisynthetic selenoproteins.* Department of Biochemistry, University of Nebraska, Lincoln, NE. October 11, 2005.
- Hondal, RJ.** *Inserting Selenocysteine into Proteins – Problems and Advances.* New England Biolabs, Beverly, MA. November 4<sup>th</sup>, 2005.
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#### **ABSTRACTS PRESENTED AS POSTERS**

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- Hondal, RJ** The Selenium Paradox: The Chemical Basis for the Use of Selenocysteine in Enzymes. *Gordon Research Conference – Enzymes, Coenzymes, and Metabolic Pathways*. Waterville Valley Resort, NH. July 15-20, 2012.
- Flemer S, & **Hondal RJ**. DTNP as a gentle and effective method of deprotection for side-chain protectants on commercially available Cys and Sec SPPS derivatives. *22<sup>nd</sup> American Peptide Symposium – Building Bridges*. June 25<sup>th</sup> – June 30<sup>th</sup>, 2011. San Diego, CA.
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- Flemer, S, **Hondal, RJ**. Native Chemical Ligation as An Important Tool in Protein Engineering. *37th Northeast Regional Meeting of the American Chemical Society*, Burlington, VT, United States, June 29-July 2 (2008), AN 2008:788522
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- Ruggles EL, & **Hondal RJ**. Viable construction of *N*-methyl cysteine and its use in peptide synthesis. *234<sup>th</sup> Meeting of the American Chemical Society*. Boston, MA. Aug 19<sup>th</sup> – 23<sup>rd</sup>. (2007) AN2007: 884125
- Lacey BM, Flemer, S. & **Hondal RJ**. Contribution of ring strain to catalysis: Comparison of cyclic and acyclic forms of octapeptides as substrates for high *M<sub>r</sub>* thioredoxin reductases. *234<sup>th</sup> Meeting of the American Chemical Society*. Boston, MA. Aug 19<sup>th</sup> – 23<sup>rd</sup>. (2007) AN2007: 878899
- Stevenson Flemer Jr. & **Hondal RJ**. An Efficient Protocol for On-Resin, Vicinal Disulfide Formation: Applications to Thioredoxin Reductase. *20<sup>th</sup> American Peptide Society Symposium: Peptides for Youth*. Montreal, Canada. June 26-30, (2007).
- Alayne L Schroll & **Hondal RJ**. Further Development of New Deprotection Chemistry for Cysteine and Selenocysteine Side Chain Protecting Groups. *20<sup>th</sup> American Peptide Society Symposium: Peptides for Youth*. Montreal, Canada. June 26-30, (2007).
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- Eckenroth, BE, Everse, SJ, Adams, TE, & **Hondal, RJ**. Crystallization of mammalian thioredoxin reductase for structural studies using synthetic active site peptides. *FASEB Meeting*. April 2-6 (2005), San Diego, CA. Abstract #2600. *FASEB Abstracts*.
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- Harris, KM & **Hondal RJ**. Deprotection of the *p*-methoxybenzyl group of selenocysteine by neighboring group participation. *19<sup>th</sup> American Peptide Symposium*. San Diego, CA. (2005).
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- Hondal, RJ**, Kravchuk, AV, & Tsai, M.-D. Using Protein Engineering and Thio-PI Analogs to Probe the Mechanism of PI-PLC. *ACS National Meeting*, Las Vegas, Nevada. (1997), AN1997:485974.
- Liao, H., **Hondal, RJ**, & Tsai, M.-D. Site-directed mutagenesis studies of phosphatidylinositol-specific phospholipase C: the substrate binding residues. *17th International Congress of Biochemistry and Molecular Biology. Annual Meeting of the American Society for Biochemistry and Molecular Biology*. San Francisco, CA. Aug. 24-29, (1997). Abstract #2628, pg A1307, *FASEB Abstracts*.

## **Ongoing Research Support**

### **LCOM Internal Grant Program**

Cunniff B and Hondal RJ, co-PIs	01/01/2023 – 12/31/2025	no salary
<i>Improved version of Elamipretide with greatly enhanced antioxidant function</i>		\$75,000

The goals of this project are to: (i) Synthesize antioxidant peptides that target the mitochondria. (ii) Test whether these peptides can be reduced by in vivo antioxidant systems. (iii) Test the hypothesis that these peptides protect the mitochondria from oxidative injury.

<b>NIH-NHLBI</b> (Day, BJ and Hondal RJ, co-PIs)	01/01/19 – 11/30/22	1.2 months
1 R01 HL141146-01A1	\$1,604,808.00	

#### *Selenocyanate as a novel treatment of cystic fibrosis lung disease*

The proposal has three specific aims: (i) Specific aim 1 will determine the chemical mechanism by which Sec-containing TrxR resists inactivation by HOSCN/HOSeCN oxidation and Cys-containing TrxR are inactivated by HOSCN/HOSeCN. (ii) Specific aim 2 will examine CFTR's and Sec-TrxR's role in the importance of <sup>-</sup>SCN/HOSCN - mediated lung host defense against bacterial infection. (iii) Specific aim 3 is designed to examine <sup>-</sup>SeCN as a potential therapy for treatment of lung inflammation and infection using wild type and CFTR KO and  $\beta$ -ENaC Tg mouse models.

### **American Heart Association: 2020 Collaborative Sciences Award**

Bouchard BA, Hondal RJ (co-PIs)	07/01/20 – 06/30/23	no salary
20CSA35320087	\$250,000	

Development of appropriate, targeted therapies to prevent thrombosis by modulation of platelet FV/Va levels

The major goal of this project is to develop appropriate, targeted therapies to prevent thrombosis by modulation of platelet factor V/Va levels.

**TEACHING EXPERIENCE**

BIOC 205 (1 hour)	Proteomics	Fall 2002
BIOC 351 (1.5 hours)	Protein semisynthesis	Fall 2002
BIOC 381 (14 hours)	Graduate Seminar (protein engineering)	Spring 2003
BIOC 207 (entire course)	Biochemistry Laboratory	Fall 2003
BIOC 207 (entire course)	Biochemistry Laboratory	Spring 2004
BIOC 207 (entire course)	Biochemistry Laboratory	Fall 2004
BIOC 351 (1.5 hours)	Peptide synthesis & sequencing	Fall 2004
BIOC 207 (entire course)	Biochemistry Laboratory	Spring 2005
BIOC 371 (4.5 hours)	NMR theory & applications	Spring 2005
BIOC 381 (14 hours)	Graduate Seminar (oxidative stress & cell signaling)	Spring 2005
BIOC 207 (entire course)	Biochemistry Laboratory	Fall 2005
BIOC 353 (15 hours)	Enzyme mechanism	Fall 2005
BIOC 207 (entire course)	Biochemistry Laboratory	Spring 2006
BIOC 381 (14 hours)	Graduate Seminar (translational control mechanisms)	Spring 2006
MMG 198 (3 credits)	Undergraduate Research	Spring 2006
BIOC 207 (entire course)	Biochemistry Laboratory	Fall 2006
BIOC 351 (12 hours)	Protein structure & function	Fall 2006
BIOC 191 (3 credits)	Undergraduate Research	Spring 2007
CHEM 291 (2 credits)	Undergraduate Research	Spring 2007
BIOC 371 (6 hours)	NMR theory & applications	Fall 2007
BIOC 353 (16.5 hours)	Enzyme mechanism	Spring 2008
BIOC 381 (14 hours)	Graduate Seminar (highly cited papers-JBC/Biochem)	Spring 2008
BIOC 192 (2 credits)	Undergraduate Research	Spring 2008
BIOC 381 (14 hours)	Graduate Seminar (protein S-nitrosylation)	Fall 2008
BIOC 191 (2 credits)	Undergraduate Research	Fall 2008
BIOC 351 (12 hours)	Protein structure & function	Spring 2009
BIOC 191 (2 credits)	Undergraduate Research	Spring 2009
BIOC 371 (10.5 hours)	NMR theory & applications	Fall 2009
	Circular dichroism, mass spectrometry	
BIOC 191 (2 credits)	Undergraduate Research	Fall 2009
BIOC 353 (18 hours)	Enzyme mechanism	Spring 2010
BIOC 192 (1 credits)	Undergraduate Research	Spring 2010
CHEM 40	Introduction to Research	Spring 2010
BIOC 205 (entire course)	Biochemistry for majors	Fall 2010
MMG 199 (1 credit)	Undergraduate research	Fall 2010
BIOC 351 (21 hours)	Protein structure & function	Spring 2011
BIOC 192 (1 credit)	Undergraduate research	Spring 2011
BIOC 205 (entire course)	Biochemistry for majors	Fall 2011
BIOC 191 (3 credit)	Undergraduate research	Fall 2011
BIOC 353 (21 hours)	Enzyme mechanism	Spring 2012
BIOC 207 (3 comp labs)	Biochemistry Laboratory	Spring 2012

BIOC 192 (3 credit)	Undergraduate research	Spring 2012
BIOC 205 (entire course)	Biochemistry for majors	Fall 2012
BIOC 191 (7 credits)	Undergraduate research	Fall 2012
CHEM 291 (1 credit)	Undergraduate research	Fall 2012
PATH 305 (1.5 hours)	thioredoxin system lecture	Fall 2012
BIOC 192 (5 credit)	Undergraduate research	Spring 2013
PHRM 303 (3 credit)	Pharmacological Techniques	Spring 2013
BIOC 212 (1 hours)	Small group – Diabetes	Spring 2013
BIOC 284 (2 hours)	Small group – evaluation of student presentations	Spring 2013
BIOC 205 (entire course)	Biochemistry for majors	Fall 2013
BIOC 191 (11 credits)	Undergraduate research	Fall 2013
BIOC 351 (25.5 hours)	Protein structure & function	Spring 2014
BIOC 351 (3 hours)	small group discussion leader	Spring 2014
BIOC 212 (1 hour)	small group discussion leader	Spring 2014
PATH 395 (1 hour)	Readings in Pathology: Redox Biology	Spring 2014
HON 196B (2 credits)	Honors College Research	Spring 2014
BIOC 192 (7 credits)	Undergraduate research	Spring 2014
CHEM 040 (7 week lab rotation)	Introduction to Research	Spring 2014
BIOC 301 (31 hours)	Biochemistry I for grad students	Fall 2014
BIOC 191 (3 credits)	Undergraduate research	Fall 2014
HON 196B (2 credits)	Honors College Research	Fall 2014
BIOC 296B (42 hours)	Nutritional biochemistry	Spring 2015
BIOC 192 (4 credits)	Undergraduate research	Spring 2015
HON 196B (2 credits)	Honors College Research	Spring 2015
CHEM 292 (2 credits)	Undergraduate research	Spring 2015
HLTH 095 (2 hour panel)	Exploring Anat. & Phys.	Summer 2015
BIOC 195 (1.5 hours)	Preparation for Biochemistry	Summer 2015
BIOC 191 (2 credits)	Undergraduate research	Fall 2015
CHEM 292 (3 credits)	Undergraduate research	Fall 2015
BIOC 263 (42 hours)	Nutritional biochemistry	Spring 2016
BIOC 192 (6 credits)	Undergraduate research	Spring 2016
CHEM 291 (4 credits)	Undergraduate research	Fall 2016
HON 196B (4 credits)	honors thesis research	Fall 2016
BIOC 263 (43 hours)	Nutritional biochemistry	Spring 2017
BIOC 302 (43 hours)	Biochemistry II for grad students	Spring 2017
BIOC 191 (6 credits)	Undergraduate research	Fall 2017
BIOC 263 (43 hours)	Nutritional biochemistry	Spring 2018
BIOC 302 (43 hours)	Biochemistry II for grad students	Spring 2018
BIOC 192 (6 credits)	Undergraduate research	Spring 2018
BIOC 191	Undergraduate research	Fall 2018
BIOC 263 (43 hours)	Nutritional biochemistry	Spring 2019
BIOC 192 (6 credits)	Undergraduate research	Spring 2019
BIOC 191	Undergraduate research	Fall 2019
BIOC 263 (43 hours)	Nutritional biochemistry	Spring 2020

BIOC 192 (6 credits)	Undergraduate research	Spring 2020
BIOC 191 (6 credits)	Undergraduate research	Fall 2020
BIOC 263 (43 hours)	Nutritional biochemistry	Spring 2021
BIOC 192 (6 credits)	Undergraduate research	Spring 2021
BIOC 191 (6 credits)	Undergraduate research	Fall 2021
BIOC 263 (43 hours)	Nutritional biochemistry	Spring 2022
BIOC 192 (6 credits)	Undergraduate research	Spring 2022
BIOC 002 (15 hours)	Modern Perspective II	Spring 2022
BIOC 191 (6 credits)	Undergraduate research	Fall 2022
BIOC 263 (43 hours)	Nutritional biochemistry	Spring 2023
BIOC 192 (6 credits)	Undergraduate research	Spring 2023