Donald E. Spratt, Ph.D.

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CURRENT AND PAST APPOINTMENTS

2015 – Present **Assistant Professor**, Gustaf H. Carlson School of Chemistry and Biochemistry
Clark University • Worcester MA USA

2011 – 2015 **Research Associate**, Department of Biochemistry, *Schulich School of Medicine & Dentistry*
University of Western Ontario • London ON Canada

EDUCATION

2008 – 2011 **Postdoctoral Fellow**, Department of Biochemistry, *Schulich School of Medicine & Dentistry*
University of Western Ontario • London ON Canada

- Project: Structure and Mechanism of the E2 Enzyme CDC34 in Ubiquitylation
  - Supervisor: Dr. Gary S. Shaw

2003 – 2008 **Doctorate in Chemistry,** Department of Chemistry, *Guelph-Waterloo Centre for Graduate Work in Chemistry (GWC)²*
University of Waterloo • Waterloo ON Canada

- Thesis: Calmodulin Binding and Activation of Mammalian Nitric Oxide Synthases
  - Supervisor: Dr. J. Guy Guillemette

1999 – 2003 **Bachelor of Science in Biochemistry, Minor in Classical Studies**
Mount Allison University • Sackville NB Canada

SCHOLARSHIPS, FELLOWSHIPS, AND ACADEMIC AWARDS

2015 – 2018	Carl J. and Anna Carlson Endowed Chair, Carlson School of Chemistry and Biochemistry, Clark University
2012	Canadian Institutes of Health Research (CIHR) Postdoctoral Fellowship
2010 – 2011	Natural Sciences & Engineering Research Council of Canada (NSERC) Postdoctoral Fellowship
2008 – 2010	Ontario Ministry of Research and Innovation (OMRI) Postdoctoral Fellowship
2008	W.B. Pearson Medal (Chemistry) – award given to the top University of Waterloo Chemistry PhD thesis
2007 – 2008	Ontario Graduate Scholarship
2007 – 2008	University of Waterloo President's Scholarship
2007 – 2008	University of Waterloo Science Graduate Experience Award
2007	Merck Frosst Biochemistry Award – award given to the top biochemist in the (GWC)²
2007	ASBMB Graduate Travel Award
2007	University of Waterloo Graduate Studies Office Travel Assistantship
2006 – 2007	Ontario Graduate Scholarship in Science and Technology
2004 – 2005	Ontario Graduate Scholarship in Science and Technology
2004	University of Waterloo Graduate Studies Office Travel Assistantship

RESEARCH INTERESTS

The regulation of enzyme catalysis and protein function resulting from specific interactions between two or more proteins plays an integral role in cell division and homeostasis. The development of various human diseases, both genetic and pathogenically linked, can occur when these protein-protein interactions are disrupted or modified. ***My research interests are focused on understanding the molecular basis of human diseases, particularly the biochemical causes of cancer, using state-of-the-art techniques to observe and characterize protein-protein interactions in the cell and at the atomic level.*** Understanding how these protein-protein interactions affect an enzyme's ability to make or break bonds and its underlying mechanism is vital to determining possible pharmacological interventions including drug design.

PUBLICATIONS

Articles Published in Refereed Journals:

1. Kumar, A., Aguirre, J.D., Condos, T.E.C., Martinez-Torres, R.J., Chaugule, V.K., Toth, R., Sundaramoorthy, R., Mercier, P., Knebel, A., **Spratt, D.E.**, Barber, K.R., Shaw, G.S., and Walden, H. (2015) Disruption of the autoinhibited state primes the E3 ligase parkin for activation and catalysis. *EMBO J.* Aug 7. pii: e201592337
    - ❖ This article has been selected for the cover of *EMBO J*.
2. **Spratt, D.E.**, Walden, H., and Shaw, G.S. (2014, invited review) RBR E3 ubiquitin ligases: new structures, new insights, new questions. *Biochem. J.* **458**, 421-437.
    - ❖ This invited review has been downloaded over 3200 times since March 2014 and is the 2nd most downloaded review from the *Biochemical Journal* in the past 3 years.
3. Chong, R.A., Wu, K., **Spratt, D.E.**, Yang, Y., Lee, C., Nayak, J., Xu, M., Elkholi, R., Li, J., Brown, B.D., Chipuk, J.E., Chen, Z., Sanchez, R., Shaw, G.S., Huang, L., and Pan, Z.-Q. (2014) Pivotal role for the ubiquitin Y59-E51 loop in lysine-48 polyubiquitination. *Proc. Natl. Acad. Sci. U.S.A.* **111**, 8434-8439.
4. Kovacev, J., Wu, K., **Spratt, D.E.**, Chong, R.A., Nayak, J., Shaw, G.S., and Pan, Z.-Q. (2014) A snapshot at ubiquitin chain elongation: Lysine 48-tetra-ubiquitin slows down ubiquitination. *J. Biol. Chem.* **289**, 7068-7081.
5. **Spratt, D.E.**, Martinez-Torres, R.J., Noh, Y.J., Mercier, P., Manczyk, N., Barber, K.R., Aguirre, J.D., Burchell, L., Purkiss, A., Walden, H., and Shaw, G.S. (2013) A molecular explanation for the recessive nature of *parkin*-linked Parkinson's disease. *Nat. Commun.* **4**, 1983.
    - ❖ Discussed in two *News & Views* articles in *EMBO J* ((2013) **32**, 2087-2089) and *Current Biology* ((2013) **23**, R691-R693).
    - ❖ Highlighted on the *Michael J. Fox Foundation for Parkinson's Research* Website (August 1, 2013). https://www.michaeljfox.org/foundation/news-detail.php?parkin-big-year-four-newly-released-papers-define-the-structure-of-key-protein-implicated-in
6. **Spratt, D.E.**, Mercier, P., Shaw, G.S. Structure of the HHARI catalytic domain shows glimpses of a HECT E3 ligase. (2013) *PLoS ONE* **8**, e74047.
7. **Spratt, D.E.**, Wu, K., Kovacev, J., Pan, Z.-Q., and Shaw, G.S. (2012) Selective recruitment of an E2~ubiquitin complex by an E3 ubiquitin ligase. *J. Biol. Chem.* **287**, 17374-17385.
8. Piazza, M., Futrega, K., **Spratt, D.E.**, Dieckmann, T., and Guillemette, J.G. (2012) Structure and dynamics of calmodulin (CaM) bound to nitric oxide synthase peptides: effects of a phosphomimetic calmodulin mutation. *Biochemistry* **51**, 3651-3661.
9. **Spratt, D.E.**, and Shaw, G.S. (2011) Association of the disordered C-terminus of CDC34 with a catalytically-bound ubiquitin. *J. Mol. Biol.* **407**, 425-438.
10. Piazza, M., Duangkham, Y., **Spratt, D.E.**, Dieckmann, T., and Guillemette, J.G. (2011) Expression and purification of an isotopically labeled aggregation prone iNOS CaM binding protein for use in NMR studies. *J. Label. Compd. Radiopharm.* **54**, 657-663.
11. **Spratt, D.E.**, Duangkham, Y., Taiakina, V., and Guillemette, J.G. (2011) Mapping the binding and calmodulin-dependent activation of nitric oxide synthase isozymes. *The Open Nitric Oxide Journal* **3**, 16-24.
12. Marlatt, N.M., **Spratt, D.E.**, and Shaw, G.S. (2010) Codon optimization for enhanced *Escherichia coli* expression of human S100A11 and S100A1 proteins. *Protein Expr. Purif.* **73**, 58-64.
13. Feng, C., Dupont, A.L., Nahm, N.J., **Spratt, D.E.**, Weinberg, J.B., Guillemette, J.G., Salerno, J.C., Tollin, G., and Ghosh, D.K. (2009) Intraprotein electron transfer in inducible nitric oxide synthase holoenzyme. *J. Biol. Inorg. Chem.* **14**, 133-142.
14. **Spratt, D.E.**, Taiakina, V., Palmer, M., and Guillemette, J.G. (2008) FRET conformational analysis of calmodulin binding to nitric oxide synthase peptides and enzymes. *Biochemistry* **47**, 12006-12017.
15. **Spratt, D.E.**, Israel, O., Taiakina, V., and Guillemette, J.G. (2008) Regulation of mammalian nitric oxide synthases by electrostatic interactions in the linker region of calmodulin. *Biochim. Biophys. Acta.* **1784**, 2065-2070.
16. **Spratt, D.E.**, Taiakina, V., and Guillemette, J.G. (2007) Calcium-deficient calmodulin binding and activation of neuronal and inducible nitric oxide synthases. *Biochim. Biophys. Acta.* **1774**, 1351-1358.
17. **Spratt, D.E.**, Taiakina, V., Palmer, M., and Guillemette, J.G. (2007) Differential binding of calmodulin domains to constitutive and inducible nitric oxide synthase enzymes. *Biochemistry* **46**, 8288-8300.
18. **Spratt, D.E.**, Newman, E., Mosher, J., Ghosh, D.K., Salerno, J.C., and Guillemette, J.G. (2006) Binding and activation of nitric oxide synthase isozymes by calmodulin EF hand pairs. *FEBS J.* **273**, 1759-1771.
19. Lang, S., **Spratt, D.E.**, Guillemette, J.G., and Palmer, M. (2006) Selective labeling of selenomethionine residues in proteins with a fluorescent derivative of benzyl bromide. *Anal. Biochem.* **359**, 253-258.

20. Lang, S., **Spratt, D.E.**, Guillemette, J.G., and Palmer, M. (2005) Dual-targeted labeling of proteins using cysteine and selenomethionine residues. *Anal. Biochem.* **342**, 271-279.
21. Newman, E., **Spratt, D.E.**, Mosher, J., Cheyne, B., Montgomery, H.J., Wilson, D.L., Weinburg, J.B., Smith, S.M.E., Salerno, J.C., Ghosh, D.K., and Guillemette, J.G. (2004) Differential activation of nitric-oxide synthase isozymes by calmodulin-troponin C chimeras. *J. Biol. Chem.* **279**, 33547-33557.

Invited Presentations: (9 of 10)

1. London Health Research Day, Academic Careers Panelist – University of Western Ontario, London ON, April 1st, 2015
2. Department of Physiology and Pharmacology – University of Western Ontario, London ON, February 23rd, 2015
3. Department of Chemistry and Biochemistry – Texas State University, San Marcos TX, USA, December 5th, 2014
4. Gustaf H. Carlson School of Chemistry – Clark University, Worcester MA, USA, November 24th, 2014
5. Departments of Chemistry and Biology – Syracuse University, Syracuse NY, USA, January 9th, 2014
6. Department of Chemistry – Wilfrid Laurier University, Waterloo ON, June 10th, 2013
7. Institute of Biochemistry and Molecular Biology Seminar – University of Waterloo, Waterloo ON, March 20th, 2012
8. Biochemistry Forum, Department of Biochemistry – University of Western Ontario, London ON, February 17th, 2012.
9. Canadian Cancer Society Kitchener-Waterloo *Relay for Life* Event, Kitchener ON, June 18th 2010.

Conference Presentations: (13 of 24)

1. Aguirre, J.D., Kumar, A., Condos, T.E.C., Mercier, P., Martinez-Torres, J., Barber, K.R., **Spratt, D.E.**, Walden, H, and Shaw, G.S. Disruption of an autoinhibited state primes the E3 ligase parkin for activation and catalysis. 2015 EMBO Ubiquitin Meeting, Cavtat, Croatia, Poster Presentation, September 18-22, 2015. (PDF work)
2. **Spratt, D.E.**, Marlatt, N.M., Macklin, J.A., and Shaw, G.S. *In vitro* analysis of human S100 protein heterodimer complex formation. 19th Internation Symposium on Calcium Binding Proteins and Calcium Function in Health and Disease, Nashville TN, USA, Poster Presentation, May 30–June 3, 2015. (PDF work)
3. Aguirre, J.D., George, S., **Spratt, D.E.**, O'Donoghue, P., and Shaw, G.S. Recoding the *E. coli* genome for production of recombinant phosphoproteins. London Health Research Day, London ON, Poster presentation, April 1, 2015. (PDF work)
4. **Spratt, D.E.**, and Shaw, G.S. Deciphering the Mechanism of E2 and E3 enzymes in Ubiquitylation. MOOT XXVI NMR Conference, Kingston ON, Oral presentation. October 26-27, 2013. (PDF work)
5. **Spratt, D.E.**, Martinez-Torres, R.J., Noh, Y.J., Mercier, P., Manczyk, N., Barber, K.R., Aguirre, J.D., Burchell, L., Purkiss, A., Walden, H., and Shaw, G.S. A molecular explanation for the recessive nature of *parkin*-linked Parkinson's disease. 2013 CSHL Meeting on "The Ubiquitin Family", Cold Spring Harbor NY, USA, Poster presentation. May 14-18, 2013. (PDF work)
6. **Spratt, D.E.**, Mercier, P., Manczyk, N., and Shaw, G.S. The unique structure of a RING domain from parkin provides insight into the development of autosomal recessive Parkinson disease. 25th International Conference on Magnetic Resonance in Biological Systems, Lyon Rhône, France, Poster Presentation. August 19-24, 2012. (PDF work)
7. **Spratt, D.E.**, and Shaw, G.S. Probing the autoinhibition of a cullin-RING E3 ubiquitin ligase by NMR spectroscopy. 25th International Conference on Magnetic Resonance in Biological Systems, Lyon Rhône, France, Poster Presentation. August 19-24, 2012. (PDF work)
8. **Spratt, D.E.**, Cook, B.W., Barber, K.R. and Shaw, G.S. Protein interactions of ubiquitin within E2 and E3 enzyme complexes. 94th Canadian Chemistry Conference and Exhibition, Montreal PQ, Oral Presentation. June 5-9, 2011. (PDF work)
9. **Spratt, D.E.** and Shaw G.S. Rbx1 preferentially binds to the CDC34~ubiquitin complex during SCF-dependent polyubiquitin chain assembly. 2011 CSHL Meeting on "The Ubiquitin Family", Cold Spring Harbor NY, USA, Poster presentation. May 17-21, 2011. (PDF work)
10. **Spratt, D.E.** and Shaw G.S. The structure of Rbx1/ROC1 and its site of interaction with CDC34 provide insights into SCF-dependent polyubiquitin chain assembly. 24th International Conference on Magnetic Resonance in Biological Systems, Cairns QLD, Australia, Poster presentation. August 22-27, 2010. (PDF work)
11. **Spratt, D.E.**, Rintala-Dempsey, A.C., Barber, K.R., and Shaw, G.S. Interactions within the E2 enzyme CDC34-ubiquitin complex are transient. Biophysical Society 54th Annual Meeting, San Francisco CA, USA, Poster presentation. February 20-24, 2010. (PDF work)
12. Guillemette, J.G., **Spratt, D.E.**, Montgomery, H.J., Newman, E., Perdicakis, B., and Jervis E.J. Control of nitric oxide synthase activity by calmodulin and a caged inhibitor. 90th Canadian Chemistry Conference and Exhibition, Winnipeg MB, CANADA, Oral presentation. May 26-30, 2007. (Ph.D work)
13. **Spratt, D.E.**, Taiakina, V., and Guillemette, J.G. FRET analysis of calmodulin binding to nitric oxide synthase peptides and enzymes. Experimental Biology – ASBMB Annual Meeting, Washington DC, USA, Poster presentation. April 28-May 2, 2007. (Ph.D work)

Published Abstracts/Number of Notes:

1. **Spratt, D.E.**, Taiakina, V., and Guillemette, J.G. (2008) Dynamic conformation changes of calmodulin when bound to nitric oxide synthase using FRET. *FASEB J.* **22**, 1009.1.
2. Israel, O.K., **Spratt, D.E.**, Taiakina, V., and Guillemette, J.G. (2008) The binding and activation of nitric oxide synthase by modified central linker and "phosphomimetic" calmodulin proteins. *FASEB J.* **22**, 612.1.
3. **Spratt, D.E.**, Taiakina, V., and Guillemette, J.G. (2007) FRET analysis of calmodulin binding to nitric oxide synthase peptides and enzymes. *FASEB J.* **21 (5)**, A645.
4. Newman, E., **Spratt, D.E.**, Mosher, J., Cheyne, B., Montgomery, H.J., Wilson, D.L., Weinberg, J.B., Smith, S.M.E., Salerno, J.C., Ghosh, D.K., and Guillemette, J.G. (2004) Differential activation of the three nitric oxide synthase isozymes by calmodulin-troponin C chimeras. *FASEB J.* **18 (8)**, C20.
5. Salerno, J.C., Newman, E., **Spratt, D.E.**, Mosher, J., Cheyne, B., Montgomery, H.J., Wilson, D.L., Weinberg, J.B., Smith, S.M.E., Ghosh, D.K., and Guillemette, J.G. (2004) Differential activation of the three nitric oxide synthase isozymes by calmodulin-troponin C chimeras. *Nitric Oxide-Biology and Chemistry* **11 (1)**, 69-70.

ELECTRONIC MEDIA PUBLICATIONS

Three-dimensional Structure Coordinates:

1. Mercier, P., **Spratt, D.E.**, and Shaw, G.S. Solution structure of the catalytic domain of HHARI (2013) *RCSB Protein Data Bank* (www.rcsb.org) Accession Code 2M9Y
2. Mercier, P., **Spratt, D.E.**, Noh, Y.J., Mancyzk, N., and Shaw, G.S. NMR structures of the RING2 and IBR-RING2 domains from parkin (2013) *RCSB Protein Data Bank* (www.rcsb.org) Accession Codes 2LWR and 2M48
3. **Spratt, D.E.**, and Shaw, G.S. NMR structure of human cullin-free Rbx1 (2012) *RCSB Protein Data Bank* (www.rcsb.org) Accession Code 2LGV
4. Piazza, M., Futrega, K., **Spratt, D.E.**, Guillemette, J.G., and Dieckmann, T. Solution NMR structure of CaM bound to the iNOS CaM binding domain peptide (2012) *RCSB Protein Data Bank* (www.rcsb.org) Accession Code 2LL6
5. Piazza, M., Futrega, K., **Spratt, D.E.**, Guillemette, J.G., and Dieckmann, T. Solution NMR structure of CaM bound to the eNOS CaM binding domain peptide (2012) *RCSB Protein Data Bank* (www.rcsb.org) Accession Code 2LL7

Protein Assignments by NMR Spectroscopy:

6. Mercier, P., **Spratt, D.E.**, and Shaw, G.S. Backbone and side-chain ^{1}H, ^{13}C, and ^{15}N resonance assignments of the HHARI catalytic domain (2013) *Biological Magnetic Resonance Data Bank* (www.bmrb.wisc.edu) Accession Code BMRB 19315
7. Mercier, P., **Spratt, D.E**, Noh, Y.J., Mancyzk, N., and Shaw, G.S. Backbone and side-chain ^{1}H, ^{13}C, and ^{15}N resonance assignments of RING2 and IBR-RING2 domains from parkin (2013) *Biological Magnetic Resonance Data Bank* (www.bmrb.wisc.edu) Accession Codes BMRB 18642 and 18990
8. **Spratt, D.E.**, and Shaw, G.S. Backbone and side-chain ^{1}H, ^{13}C, and ^{15}N resonance assignments of human cullin-free Rbx1 (2012) *Biological Magnetic Resonance Data Bank* (www.bmrb.wisc.edu) Accession Code BMRB 17824
9. Piazza, M., Futrega, K., **Spratt, D.E.**, Guillemette, J.G., and Dieckmann, T. Backbone and side-chain ^{1}H, ^{13}C, and ^{15}N resonance assignments of calmodulin bound to the iNOS CaM binding domain peptide (2012) *Biological Magnetic Resonance Data Bank* (www.bmrb.wisc.edu) Accession Codes BMRB 18027
10. Piazza, M., Futrega, K., **Spratt, D.E.**, Guillemette, J.G., and Dieckmann, T. Backbone and side-chain ^{1}H, ^{13}C, and ^{15}N resonance assignments of calmodulin bound to the eNOS CaM binding domain peptide (2012) *Biological Magnetic Resonance Data Bank* (www.bmrb.wisc.edu) Accession Codes BMRB 18028

TEACHING EXPERIENCE

Sept. 2008 – June 2015 ***Mentoring of Students***, University of Western Ontario • London ON
Trained and mentored 17 graduate students and 9 undergraduate students during their honours theses or summer projects

Sept. 2003 – April 2008 ***Undergraduate Training Co-supervisor***, University of Waterloo • Waterloo ON
Co-supervised, trained and mentored 9 undergraduate students during their honours theses or CO-OP placement

Sept. 2003 – April 2008 ***Teaching Assistant***, University of Waterloo • Waterloo ON
Assisted and supervised undergraduate students, led tutorial sessions, and marked assignments and exams.

Courses – 110 hours/term (# of students per term, student assessment /4.8):

CHEM 430 – Biochemical Pharmacology (~40 students)
- Pharmacodynamics, pharmacokinetics, drug design and metabolism, and the pharmacology of nitric oxide.

CHEM 433 – Advanced Biochemistry (~30 students)
- Nitrogen fixation, assimilation of nitrogen, amino acid metabolism, metabolic regulation, proteolytic enzymes, ubiquitin, blood coagulation, signal transduction and amplification.

CHEM 331 – Fundamentals of Metabolism 1 (~50 students)
- Thermodynamics of metabolism. Metabolism of carbohydrates and lipids.

CHEM 333 – Metabolism 1 (~120 students)
- Metabolic pathways of carbohydrates, lipids and amino acids.

CHEM 335L – Advanced Biochemistry (laboratory • ~20 students, 4.5/4.8)
- NMR, allostery, enzymology, electrophoresis, carbohydrates, lipids, photosynthesis, and respiration.

CHEM 233 – Fundamentals of Biochemistry, (~80 students)
- Chemistry of amino acids, carbohydrates, lipids and nucleic acids, and enzymes.

CHEM 237 and 237L – Introductory Biochemistry (~200 students, 4.4/4.8)
- Introduction to the chemistry of amino acids, carbohydrates, lipids, proteins and nucleic acids.

Jan. 2006 – April 2008 ***Tutor – Centre for Accessible Learning***, Wilfrid Laurier University • Waterloo ON

CONTINUING EDUCATION

2009 – 2015	***Future Professor Workshop Series***, University of Western Ontario • London ON
2010 – 2015	***Continuing Professional Development***, *Schulich School of Medicine & Dentistry,* University of Western Ontario • London ON
August 15-20, 2011	***Biomolecular NMR Training Course***, University of Alberta • Edmonton AB Course Host: NANUC – National High Field Nuclear Magnetic Resonance Centre
August 16-20, 2010	***Advanced Course on Multidimensional NMR***, James Cook University • Cairns, QLD, Australia
October 23, 2009	***OMRI Postdoctoral Workshop***, MaRS Discovery District • Toronto ON
Sept. 2002 – April 2003	***Undergraduate Research Assistant***, Mount Allison University • Sackville NB Supervisor: Dr. A. G. Grant
May-August 2001, 2002	***Undergraduate Research Assistant – Enviropig™ Project***, University of Guelph • Guelph ON Supervisors: Dr. C. W. Forsberg and Dr. M. Z. Fan

ADMINSTRATIVE & LEADERSHIP

February/March 2012, 2014 University of Western Ontario • London ON
National Scholarship Program - Evaluator

May 2009 – present University of Western Ontario • London ON
Biochemistry Outreach Program – Demonstrator, led high school students through a week-long biotechnology module

March 2009, 2010 University of Western Ontario • London ON
Margaret Moffat Research Day - Judge

May 2005 – Aug. 2006 University of Waterloo • Waterloo ON
President of the Chemistry Graduate Student Society

Jan. 2004 – May 2005 University of Waterloo • Waterloo ON
Social Coordinator of the Chemistry Graduate Student Society