Christopher J. Markworth, Ph.D.

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EDUCATION

Ph.D. Organic Chemistry — **Montana State University**
August 2003 — Bozeman, Montana
Advisor: Professor Paul A. Grieco
Dissertation: I) The Formal Total Synthesis of (-)-Laulimalide
II) Supramolecular Self-Assembly: Transition Metal Encapsulation

A.B. Biochemistry — **Dartmouth College**
June 1993 — Hanover, New Hampshire

ACADEMIC EXPERIENCE

Adjunct Professor of Chemistry — **Western Washington University**
September 2010-Current — Bellingham, Washington

- Courses taught:

General Chemistry I	Chem 121
Elementary Organic Chemistry	Chem 251
Organic Chemistry I	Chem 351
Organic Chemistry II	Chem 352
Organic Chemistry III	Chem 353
Organic Chemistry Lab I	Chem 354
Organic Chemistry Lab II	Chem 356
Medicinal Chemistry	Chem 425c/556

Graduate Research / Teaching Assistant — **Montana State University**
August 1997 – August 2003 — Bozeman, Montana

- Conducted independent research primarily focused on natural product synthesis. Completed a formal total synthesis of the marine antitumor agent (-)-laulimalide. The synthesis featured a lithium perchlorate-mediated carbon Ferrier rearrangement and an organocuprate-mediated epoxide opening with a highly-advanced intermediate.
- **Responsible for mentoring** undergraduate students in the Grieco Laboratory who participated in Montana State University's REU program sponsored by the National Science Foundation. Provided initial training and scientific guidance for undergraduate students over the course of three summers (2001-2003). Students independently completed syntheses of transition metal-mediated supramolecular self-assembly complexes during their summer research experience.
- Taught undergraduate organic chemistry laboratory sections. Duties included pre-laboratory instruction covering the safety and theory relevant to the laboratory experiments.

Associate Instructor — **Indiana University**
August 1996 – August 1997 — Bloomington, Indiana

- Instructor for undergraduate organic chemistry laboratory sections. Provided students with an overview of the experiment and techniques involved in each session.
- Initiated first year graduate research in the laboratory of Professor Paul A. Grieco.

PROFESSIONAL EXPERIENCE

Senior Research Investigator **Icagen, Inc.**
March 2009 – September 2010 Durham, North Carolina
Senior Research Scientist
October 2005 – March 2009

- Member of the medicinal chemistry team that discovered PF-05089771, an Na_V 1.7 selective sodium channel inhibitor for the treatment of neuropathic and inflammatory pain. The compound advanced to Phase II clinical trials.
- Designed and synthesized subtype-selective voltage gated sodium channel inhibitors. Member of an interdisciplinary team that identified several pre-clinical candidates for treating neuropathic and inflammatory pain.
- Co-inventor of a new chemotype of TTXs selective sodium channel (Na_V 1.3) inhibitors. Synthesized the initial hit and expanded the SAR to demonstrate the utility of the series and to establish a suitable IP position. The series served as a major focus in a research collaboration with Pfizer.
- Instrumental in advancing an additional TTXs selective chemotype to lead series designation. Addressed several ADME issues in the process and discovered compounds that demonstrated oral efficacy in animal pain models. The series contributed to the establishment of a research partnership with a major pharmaceutical company.
- Co-led lead optimization efforts on a sodium channel subtype program. Worked with a partner's lead chemist to coordinate research efforts across international sites: target selection, in vivo studies, and IP coverage. Responsibilities included directing project compounds through the testing cascade at Icagen, including primary target screening, selectivity screening, and in vivo testing (pharmacokinetics and efficacy).
- Served as a chemistry liaison for external chemistry resources on the TTXs project. Developed chemistry methodology for use by CROs. Redesigned the synthetic pathway for a chemical series to access a wider array of commercially available materials; use of this chemistry provided a more diverse set of analogues for SAR development and IP protection.
- Managed one associate scientist. Assisted with target selection and career development. Conducted annual reviews.
- Responsible for maintenance of NMR spectrometer.

Research Scientist **Serenex, Inc.**
February 2005 – August 2005 Durham, North Carolina

- Contributed to lead optimization studies of a new family of small molecule heat shock protein 90 (Hsp90) inhibitors unrelated to natural product-based inhibitors. Efforts helped lead to the identification of an orally active clinical candidate (SNX-5422/PF-04929113) that entered Phase I clinical trials for hematologic malignancies.
- Co-developed the synthetic route and purification strategies for the initial scale-up synthesis of the Hsp90 lead compound for pre-clinical investigation.

Senior Scientist **Nuada Pharmaceuticals**
September 2003 – January 2005 Durham, North Carolina

- Designed and synthesized TNF-α and PDE4 inhibitors for the treatment of inflammatory diseases. Efforts were focused on both lead generation and lead optimization.
- Initiated the development of a lead series of compounds that resulted in the discovery of a putative TNF-α inhibitor that has demonstrated efficacy in acute and chronic models of TNBS-induced colitis in rats.

- Led scale-up efforts of lead compounds for use in preliminary animal toxicology and efficacy studies.

Research Assistant **GlaxoWellcome**
March 1994 – July 1996 Research Triangle Park, North Carolina

- Synthesized chemical libraries on a variety of solid-phase formats utilizing both combinatorial and parallel synthesis techniques.
- Contributed to the discovery and development of isotope-based encoding strategies for library synthesis.
- Designed and synthesized a peptoid-based library to demonstrate the utility of the encoding strategy.

PATENTS AND PATENT APPLICATIONS

Markworth, C.J.; Marron, B.E.; Rawson, D.J.; Storer, R.I.; Swain, N.A.; West, C.W.; Zhou, S. Sulfonamide Compounds. U.S. Patent 9,145,407, September 29, 2015.

Beaudoin, S.; Laufersweiler, M.C.; **Markworth, C.J.**; Marron, B.E.; Millan, D.S.; Rawson, D.J.; Reister, S.M.; Sasaki, K.; Storer, R.I.; Stupple, P.A.; Swain, N.A.; West, C.W.; Zhou, S. Sulfonamide Derivatives. U.S. Patent 8,907,101, December 9, 2014.

Marron, B.E.; Fritch, P.C.; **Markworth, C.J.**; Maynard, A.T.; Swain, N.A. Inhibitors of Ion Channels. U.S. Patent 8,741,934, June 3, 2014.

Beaudoin, S.; Laufersweiler, M.C.; **Markworth, C.J.**; Marron, B.E.; Millan, D.S.; Rawson, D.J.; Reister, S.M.; Sasaki, K.; Storer, R.I.; Stupple, P.A.; Swain, N.A.; West, C.W.; Zhou, S. Sulfonamide Derivatives. U.S. Patent 8,541,588, September 24, 2013.

Marron, B.E.; Fritch, P.C.; **Markworth, C.J.**; Maynard, A.T.; Swain, N.A. Heterocyclic Sulfonamides as Inhibitors of Ion Channels. U.S. Patent 8,357,711 January 22, 2013.

Beaudoin, S.; Laufersweiler, M.C.; **Markworth, C.J.**; Marron, B.E.; Millan, D.S.; Rawson, D.J.; Reister, S.M.; Sasaki, K.; Storer, R.I.; Stupple, P.A.; Swain, N.A.; West, C.W.; Zhou, S. Sulfonamide Derivatives. U.S. Patent 8,153,814, April 10, 2012.

Fulp, A.B.; Johnson, M.S.; **Markworth, C.J.**; Marron, B.E.; Seconi, D.C.; West, C.W.; Wang, X.; Zhou, S. Sodium Channel Inhibitors. U.S. Patent 8,124,610, February 28, 2012.

Markworth, C.J.; Marron, B.E.; Swain, N.A. Benzamide Derivatives as Modulators of SCN3A and SCN5A Sodium Channel Subunits and Their Preparation, Pharmaceutical Compositions, and Use in the Treatment of Pain. PCT Int. Appl. WO10/035166, **2010**.

Didsbury, J. R.; Dyakonov, T.; Haydar, S.N.; Jones, M.L.; Li, F.F.; **Markworth, C.J.**; Matthew, J.; Schoenen, F.J.; Scicinski, J.J.; Middlemiss, D.; Burns, J.F.; Cabana, L.A.; Collupy, G.C.; Vanvliet, D.N. Antiinflammatory Indole, Benzimidazole, and Benzolactam Boronic Acid Compounds. U.S. Pat. Appl. Publ. US 20090264384, **2009**.

Didsbury, J.R.; Dyakonov, T.; Haydar, S.N.; Jones, M.L.; Li, F.F.; **Markworth, C.J.**; Scicinski, J.J.; Cabana, L.A.; Mathew, J.; Middlemiss, D.N.; Collupy, G.C.; Schoenen, F.J.; Burns, J.F.; VanVliet, D.N. Preparation of Heterocyclylalkylboronic Acids and Related Compounds Which Inhibit Inflammatory Cytokines. PCT Int. Appl. WO07/134169, **2007**.

PUBLICATIONS

Swain, N.A.; Batchelor, D.; Beaudoin, S.; Bechle, B.M.; Bradley, P.A.; Brown, A.D.; Brown, B.; Butcher, K.J.; Butt, R.P.; Chapman, M.L.; Denton, S.; Ellis, D.; Galan, S.; Gaulier, S.M.; Greener, B.S.; de Groot, M.J.; Glossop, M.S.; Gurrell, I.K.; Hannam, J.; Johnson, M.S.; Lin, Z.; **Markworth, C.J.**; Marron, B.E.; Millan, D.S.; Nakagawa, S.; Pike, A.; Printzenhoff, D.; Rawson, D.J.; Ransley, S.J.; Reister, S.M. Kosuke, S.; Storer, R.I.; Stupple, P.A.; West, C.W. Discovery of Clinical Candidate 4-[2-(5-Amino-1*H*pyrazol-4-yl)-4-chlorophenoxy]-5-chloro-2-fluoro-*N*-1,3-thiazol-4-ylbenzenesulfonamide (PF-05089771): Design and Optimization of Diaryl Ether Aryl Sulfonamides as Selective Inhibitors of $Na_V1.7$. *J. Med. Chem.*, **2017**, *60*, 7029-7042.

Pryde, D.C.; Swain, N.A.; Stupple, P.A.; West, C.W.; Marron, B.; **Markworth, C.J.**; Printzenhoff, D.; Lin, Z.; Cox, P.J.; Suzuki, R.; McMurray, S.; Waldron, G.J.; Payne, C.E.; Warmus, J.S.; Chapman, M.L. The discovery of a potent $Na_V1.3$ inhibitor with good oral pharmacokinetics. *Med. Chem. Commun.*, **2017**, *8*, 1255-1267.

Huang, K.H.; Barta, T.E.; Rice, J.W.; Smith, E.D.; Ommen, A.J.; Ma, W.; Veal, J.M.; Fadden, R.P.; Barabasz, A.F.; Foley, B.E.; Hughes, P.F.; Hanson, G.J.; **Markworth, C.J.**; Silinski, M.; Partridge, J.M.; Steed, J.M.; Hall, S.E. Discovery of novel aminoquinazolin-7-yl-6,7-dihydro-indol-4-ones as potent, selective inhibitors of heat shock protein 90. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 2550-2554.

Huang, K.H.; Veal, J.M.; Fadden, P.; Rice, J.W.; Eaves, J.; Strachan, J.-P.; Barabasz, A.F.; Foley, B.E.; Barta, T.E.; Ma, W.; Silinski, M.A.; Hu, M.; Partridge, J.M.; Scott, A.; DuBois, L.G.; Freed, T.; Steed, P.M.; Ommen, A.J.; Smith, E.D.; Hughes, P.F.; Woodward, A.R.; Hanson, G.J.; McCall, W.S.; **Markworth, C.J.**; Hinkley, L.; Jenks, M.; Geng, L.; Lewis, M.; Otto, J.; Pronk, B.; Verleysen, K.; Hall, S.E. Discovery of Novel 2-Aminobenzamide Inhibitors of Heat Shock Protein 90 as Potent, Selective and Orally Active Antitumor Agents. *J. Med. Chem.* **2009**, *52*, 4288-4305.

Mio, M.J.; Kopel, L.C.; Braun, J.B.; Gadzwika, T.L.; Hull, K.L.; Brisbois, R.G.; **Markworth, C.J.**; Grieco, P.A. One-Pot Synthesis of Symmetrical and Unsymmetrical Bisarylethynes by a Modification of the Sonogashira Coupling Reaction. *Org. Lett.* **2002**, *4*, 3199-3202.

Strobel, G.A.; Dirkse, E.; Sears, J.; **Markworth, C.J.** Volatile antimicrobials from *Muscodor albus*, a novel endophytic fungus. *Microbiology* **2001**, *147*, 2943-2950.

Malkin, B.D.; Thickman, K.R.; **Markworth, C.J.**; Wilcox, D.E.; Kull, F.J. Inhibition of Potato Polyphenol Oxidase by Anions and Activity in Various Carboxylate Buffers (pH 4.8) at Constant Ionic Strength. *J. Enzym. Inhib.* **2001**, *16*, 135-145.

Grieco, P.A.; **Markworth, C.J.** Selective Deprotection of Alkyl t-Butyldimethylsilyl Ethers in the Presence of Aryl t-Butyldimethylsilyl Ethers. *Tetrahedron Lett.* **1999**, *40*, 665-666.

Wagner, D.S.; **Markworth, C.J.**; Wagner, C.D.; Schoenen, F.J.; Rewerts, C.E.; Kay, B.K.; Geysen, H.M. Ratio Encoding Combinatorial Libraries with Stable Isotopes and Their Utility in Pharmaceutical Research. *Comb. Chem. High T. Scr.* **1998**, *1*, 143-153.

Geysen, H.M.; Wagner, C.D.; Bodnar, W.M.; **Markworth, C.J.**; Parke, G.J.; Schoenen, F.J.; Wagner, D.S.; Kinder, D.S. Isotope or Mass Encoding of Combinatorial Libraries. *Chem. Biol.* **1996**, *3*, 679-688.

CONTRIBUTED PRESENTATIONS (presenter in bold)

Mensinger, Z.L.; Brisbois, R.G.; Erickson, H.L.; Rodwogin, M.D.; Gadzikwa, T.L.; Alfonzo, C.G.; Markworth, C.J.; Diep, N.K.; Grieco, P. A. Investigation of Transition Metal-mediated Supramolecular Self-Assemblies Featuring Endohedral Ethylenediamine Palladium(II) Moieties. *Abstracts of Papers*, 227th ACS National Meeting, Anaheim, CA, March 28-April 1, 2004, ORGN-384.

Markworth, C.J.; Grieco, P.A. Progress Toward the Total Synthesis of (-)-Laulimalide. 58th Northwest Regional Meeting of the American Chemical Society, Bozeman, MT, June 12-14, 2003, 54.