

Nathan Siemers, Ph.D.

Functional Profile

I am an experienced leader of genomics, bioinformatics, and translational research groups in the pharmaceutical/biotech industry. The breadth of my groups' efforts have spanned the full range of pharmaceutical R&D including: new target identification and validation; biomarker driven patient stratification and companion diagnostic development; phase IV research to defend safety and efficacy profiles of approved agents. I am an experienced contributor to target and development asset portfolio management, and have played this role across multiple disease areas. Throughout my career I have created and executed on strategies for the use of new technologies, capabilities, and alliances, across the areas of genomics, bioinformatics, computing, knowledge management, proteomics, next-generation sequencing technologies, and systems biology, to achieve high impact across pharmaceutical R&D.

Experience

Diverse, hands-on training and experience in organic chemistry, molecular biology, molecular immunology, biologics design and production, bioanalytical chemistry/diagnostics, genomics, bioinformatics, and systems biology.

Therapeutic area focus in immunology, immuno-oncology, and oncology with knowledge and experience supporting neuroscience, virology, cardiovascular, metabolic disease, and fibrosis disease areas with omics and systems biology tools.

Line management experience of diverse groups including bioinformatics, sequencing, and proteomics functions.

Roles

2012 - Present **Bristol-Myers Squibb** Hopewell, New Jersey

Director R&D, Applied Genomics

- Translational Research: I lead a team of senior scientists with training in bioinformatics, biostatistics, and systems biology to support translational research efforts across the R&D portfolio.

2004 - 2012 **Bristol-Myers Squibb** Hopewell, New Jersey

Director R&D, Applied Genomics

- Line management of Bioinformatics and Proteomics groups within the Applied Genomics division.

2000 - 2004 **Bristol-Myers Squibb** Hopewell, New Jersey

Associate Director, Applied Genomics

- Led the bioinformatics group with R&D project-facing and computational platform teams.

1998-2000 **Bristol-Myers Squibb** Hopewell, New Jersey

Group Leader, Applied Genomics

- Led the bioinformatics platform group that developed the high-performance computing infrastructure and key genomic software platforms for the company.

1997-1998 **Whitehead Institute** Cambridge, Mass.

Scientist, Functional Genomics (Eric Lander/Todd Golub)

- Validation and analysis of Affymetrix transcriptional profiling device and software technology. Performed the first Affy profiling experiments conducted at BMS.

1996-1997 **Bristol-Myers Squibb** Princeton, New Jersey

Research Investigator, Bioinformatics

- Gene discovery: ion channels, G-protein coupled receptors, TNF receptor family members.
- Methods development for mining of genomic data.
- System administration for Linux, SGI desktop, and SGI Origin supercomputers.
- Staffing and management of BMS Core Sequencing Facility

1993-1996 **Bristol-Myers Squibb** Seattle, Washington

Postdoctoral Fellow, Oncology Drug Discovery

- Phage library construction and biochemical optimization of E. cloacae beta-lactamase activity toward chemotherapeutic prodrugs for use in Antibody-Directed Enzyme-Prodrug Therapy (ADEPT).
- Design, construction, and expression (including process development) of what became Seattle Genetics asset SGN-17 (L49-sfv-bL), an antitumor antibody-beta-lactamase fusion for use in chemotherapy.

1988-1993 **Cornell University** Ithaca, New York

Research Assistant, Department of Chemistry

- Organic Synthesis: Completed total syntheses of sesquiterpene pheromones Periplanones C and D. Advisor: John McMurry
- Computational Chemistry: Molecular Mechanics analyses of macrocycles and ring closure stereochemistry in the low-valent titanium induced coupling of carbonyls.

1985-1988 **Crystal Diagnostics** Woburn, Mass.

Research Scientist

- Explored crystal nucleation as a detection method for chemical and enzymatic diagnostic assays, including applications in Therapeutic Drug Monitoring, Cholesterol testing, and Occupational Exposure.

1982-1983 **Massachusetts Institute of Technology** Cambridge, MA

Undergraduate Research

- Elucidation of selective inhibitory activity of the bioflavonoid quercetin toward isoenzymes of cytochromes P-450 (Michael Marletta, advisor)

Education

Cornell University, Ithaca, New York: PhD in Chemistry, 1993

Massachusetts Institute of Technology, Cambridge, Massachusetts:
B.S. in Chemistry 1985

Whitman College, Walla Walla, Washington.

Public Schools of Texas, Illinois, and Oregon

Awards

Campbell Scholar, Whitman College, 1982
Mattin Research Fellow, Cornell University, 1990, 1992
United States Department of Education Fellow, 1991
John James Blackmore Prize, Cornell University, 1992
President's Award, Pravastatin Research, Bristol-Myers Squibb, 1998
Applied Biotechnology Collaboration Award, Bristol-Myers Squibb, 2003
Triumph Award, Target Validation and Due Diligence via Bioinformatics, Bristol-Myers Squibb, 2003
Triumph Award, Metabonomics in Toxicology, 2005

Associations

Member of the New York Academy of Sciences
Member of the American Association of Cancer Research
Member of the American Society for Mass Spectrometry
Manuscript review for the journals *Bioconjugate Chemistry* and *Bioinformatics*.
Grant reviewer for the Canadian Network Centres of Excellence Program.
Panel Member, National Science Foundation.
Grant reviewer, National Genome Research Network (NGFN), Germany

Interests

Music Performance (currently cellist in Westminster Conservatory Orchestra as well as various chamber ensembles in Princeton, NJ), Photography.

Publications

Luz D. Orozco, Brian J. Bennett, Charles R. Farber, Anatole Ghazalpour, Calvin Pan, Nam Che, Pingzi Wen, Hong Xiu Qi, Adonisa Mutukulu, **Nathan Siemers**, Isaac Neuhaus, Roumyana Yordanova, Peter Gargalovic, Matteo Pellegrini, Todd Kirchgessner, Aldons J. Lusis *Unraveling inflammatory responses using systems genetics and gene-environment interactions in macrophages* **Cell** 2012, 151, 658-670.

Ross-Macdonald P, de Silva H, Patel V, Truong A, He A, Neuhaus I, Tilford C, Ji R, **Siemers N**, Greer A, Carboni J, Gottardis M, Menard K, Lee F, Dodier M, Frennesson D, Sampognaro A, Saulnier M, Trainor G, Vyas D, Zimmermann K, Wittman M. *Biochemical and transcriptional profiling to triage additional activities in a series of IGF-1R/IR inhibitors.* **Bioorganic & Medicinal Chemistry** 2012, 20(6), 1961-72.

Rui-Ru Ji, Scott D. Chasalow, Lisu Wang, Omid Hamid, Henrik Schmidt, John Cogswell, Suresh Alaparthi, David Berman, Maria Jure-Kunkel, **Nathan O. Siemers**, Jeffrey R. Jackson, and Vafa Shahabi: *An immune-active tumor microenvironment*

favors clinical response to Ipilimumab **Cancer Immunology, Immunotherapy** 2012, 61(7), 1019-1031. DOI: 10.1007/s00262-011-1172-6

Rui-Ru Ji, **Nathan O. Siemers**, Ming Lei, Liang Schweizer, Robert E. Brucoleri: *SDRS – an algorithm for analyzing large scale dose response data.* **Bioinformatics** 2011, 27 (20), 2921-2923. DOI: 10.1093/bioinformatics/btr489

Han Chang, Donald G. Jackson, Paul S. Kayne, Petra B. Ross-Macdonald, Rolf-Peter Ryseck, and **Nathan O. Siemers**: *Exome Sequencing Reveals Comprehensive Genomic Alterations across Eight Cancer Cell Lines.* **PLoS One** 2011, 6(6), e21097.

Bennett Brian J, Farber Charles R, Orozco Luz, Kang Hyun Min, Ghazalpour Anatole, **Siemers Nathan**, Neubauer Michael, Neuhaus Isaac, Yordanova Roumyana, Guan Bo, Truong Amy, Yang Wen-pin, He Aiqing, Kayne Paul, Gargalovic Peter, Kirchgessner Todd, Pan Calvin, Castellani Lawrence W, Kostem Emrah, Furlotte Nicholas, Drake Thomas A, Eskin Eleazar, Lusic Aldons J. *A high-resolution association mapping panel for the dissection of complex traits in mice..* **Genome Research**. 2010, 20(2), 281-90.

Charles Tilford, **Nathan Siemers**: *Gene Set Enrichment Analysis.* **Methods Mol Biol**. 2009, 563, 99-121

Friedrichs F, Zugck C, Rauch GJ, Ivandic B, Weichenhan D, Müller-Bardorff M, Meder B, El Mokhtari NE, Regitz-Zagrosek V, Hetzer R, Schäfer A, Schreiber S, Chen J, Neuhaus I, Ji R, **Siemers NO**, Frey N, Rottbauer W, Katus HA, Stoll M.: *HBEGF, SRA1, and IK: Three cosegregating genes as determinants of cardiomyopathy.* **Genome Res**. 2009, 19(3), 395-403.

Rui-Ru Ji, Heshani de Silva, Yisheng Jin, Robert E. Brucoleri, Jian Cao, Aiqing He, Wenjun Huang, Paul S. Kayne, Isaac M. Neuhaus, Karl-Heinz Ott, Becky Penhallow, Mark I. Cockett, Michael G. Neubauer, **Nathan O. Siemers** & Petra Ross-Macdonald: *Transcriptional profiling of the dose response: a novel approach for characterizing drug activities.* **Bioinformatics** (2007) 23 (20): 2716-2724.

Chang, H, Obenauer-Kutner, L, He, A, Xing, G, Truong, A, Kayne, P, Flesher, A, **Siemers, N**, Jure-Kunkel, M, Grace, M: *Expression profiling demonstrates co-stimulatory activity of BMS-663513, and anti-CD137 antibody.* **20th EORTC-NCI-AACR Symposium.**

Duygu Ucar, Isaac Neuhaus, Petra Ross-MacDonald, Charles Tilford, Srinivasan Parthasarathy, **Nathan Siemers**, Rui-Ru Ji: *Construction of a reference gene association network from multiple profiling data: application to data analysis.* **Bioinformatics** 23(20): 2716-2724 (2007)

Huttenhower, C., Flamholz, A., Landis, J., Sahi, S., Myers, C., Hibbs, M., **Siemers, N.**, Troyanskaya, O. and Collier, H.A. (2007) *Nearest Neighbor Networks: Clustering expression data based on gene neighborhoods.* **BMC Bioinformatics**. 2007 Jul 12; 8:250.

Constantine KL, Krystek SR, Healy MD, Doyle ML, **Siemers NO**, Thanassi J, Yan N, Xie D, Goldfarb V, Yanchunas J, Tao L, Dougherty BA, Farmer BT 2nd. (2005) *Structural and functional characterization of CFE88: evidence that a conserved and essential bacterial protein is a methyltransferase.* **Protein science: a publication of**

the Protein Society 14 (6), 1472-84.

Vivekananda M. Vrudhula, David E. Kerr, **Nathan O. Siemers**, Gene M. Dubowchik and Peter D. Senter (2003) *Cephalosporin prodrugs of paclitaxel for immunologically specific activation by L-49-sFv-beta-Lactamase fusion protein*. **Bioorg Med Chem Lett**, 13, 539.

David E. Kerr, Vivekananda M. Vrudhula, Hakan P. Svennson, **Nathan O. Siemers**, and Peter D. Senter (1999) *Comparison of recombinant and synthetically formed monoclonal antibody-beta-lactamase conjugates for anticancer prodrug activation*. **Bioconjugate Chemistry** 10, 1084.

Trachette L. Jackson, Sharon R. Lubkin, **Nathan O. Siemers**, David E. Kerr, Peter D. Senter, and James D. Murray (1999) *Mathematical and Experimental Analysis of the Localization Characteristics of Anti-Tumor Antibody-Enzyme Conjugates*. **British Journal of Medicine**. 80, 1747.

David E. Kerr, **Nathan O. Siemers**, Peter D. Senter, and Vivekananda M. Vrudhula (1998) *Development and Activities of a New Melphalan Prodrug Designed for Tumor-Selective Activation*. **Bioconjugate Chemistry** 9, 255.

Nathan O. Siemers and Peter D. Senter (1998) The Activation of Anticancer Prodrugs by Monoclonal Antibody-Enzyme Conjugates. **Antibodies in Diagnosis and Therapy: Technologies, Mechanisms and Clinical Data**. S. Matzku and R.A. Stahel, Ed. Taylor & Francis.

Nathan O. Siemers, Susan Yarnold, Mark Stebbins, David E. Kerr, Vivekananda M. Vrudhula, Ingegerd Hellström, Karl Erik Hellström, and Peter D. Senter (1997) *Construction, Expression, and Activities of L49-sFv-β-Lactamase, a Single-Chain Antibody Fusion Protein for Anticancer Prodrug Activation*. **Bioconjugate Chemistry** 8, 510.

Nathan O. Siemers, Dale E. Yelton, Jürgen Bajorath, and Peter D. Senter (1996) *Modifying the Specificity and Activity of the Enterobacter cloacae P99 β-Lactamase by Mutagenesis Within an M13 Phage Vector*. **Biochemistry** 35, 2104.

John E. McMurry and **Nathan O. Siemers** (1994) *Periplanone Total Synthesis via Intramolecular Pinacol Coupling*. **Tetrahedron Letters** 35, 4505.

Nathan O. Siemers (1993) *The Development of a Molecular Mechanics Based Model to Predict Diol Stereochemistry in Low Valent Titanium Mediated Pinacol Coupling Reactions. Successful Application of this Model Toward the Synthesis of Periplanones C, D, and A*. Dissertation, Cornell University.

John E. McMurry and **Nathan O. Siemers** (1993) *The Stereochemistry of the Titanium Induced Intramolecular Pinacol Coupling Reaction*. **Tetrahedron Letters** 34, 7891.

Published

Lee, Liana, M. ; Feder, John, N.; Siemers, Nathan, O.; Wu, Shujian; Chen, Jian (2004) Novel human cell surface protein with immunoglobulin folds, BGS-19 (US20040025195, WO2003083078).

Patents

Lee, Liana, M. ; Feder, John, N.; Siemers, Nathan, O.; Wu, Shujian (2003) Polynucleotides encoding novel two splice variants of a human cell surface protein with immunoglobulin folds, BGS5G and BGS5I (WO2003083076).

Feder, John, N. ; Lee, Liana, M.; Chen, Jian; Jackson, Donald; Ramanathan, Chandra, S.; Siemers, Nathan, O.; Chang, Han (2003) Polynucleotide encoding a novel human potassium channel beta- subunit, K⁺ Mbeta1 (US20030181711, WO200248369).

Feder, John N. ; Lee, Liana; Chen, Jian; Jackson, Donald; Ramanathan, Chandra S.; Siemers, Nathan O.; Chang, Han; Ryseck, Rolf-Peter; Watson, Andrew J.; Carroll, Pamela (2003) Polynucleotide encoding a novel human potassium channel beta-subunit, K⁺ betaM3 (US20030114371, WO2002068587).

Feder, John N. ; Lee, Liana; Chen, Jian; Jackson, Donald; Ramanathan, Chandra S.; Siemers, Nathan O.; Chang, Han; Duclos, Franck; Krystek, Stanley R. (2003) Polynucleotide encoding a novel potassium channel with homology to the ether-a-go-go family, HEAG2 (US20030114354).

Feder, John N. ; Lee, Liana M.; Chen, Jian; Jackson, Donald; Ramanathan, Chandra; Siemers, Nathan; Chang, Han (2003) Polynucleotide encoding a novel human potassium channel alpha-subunit, K⁺ alphaM1, and variants thereof (US20030059923, WO2002064732).

Feder, John N. ; Lee, Liana; Chen, Jian; Jackson, Donald; Ramanathan, Chandra S.; Siemers, Nathan O.; Chang, Han; Carroll, Pamela (2003) Polynucleotide encoding two novel human potassium channel beta-subunits, K⁺betaM4 and K⁺betaM5 (US20030054989, WO2002068604).

Feder, John N. ; Lee, Liana; Chen, Jian; Jackson, Donald; Ramanathan, Chandra S.; Siemers, Nathan O.; Chang, Han (2003) Polynucleotide encoding a novel human potassium channel beta-subunit, K⁺ betaM6, expressed highly in the small intestine (US20030036115, WO2002070727).

Chang, Han ; Chen, Jian; Feder, John; Jackson, Donald; Lee, Liana; Ramanathan, Chandra S.; Siemers, Nathan O.; Carroll, Pamela (2003) Polynucleotide encoding a novel human potassium channel beta-subunit, K⁺ betaM2 (US20030032786, WO2002066601).

Feder, John N. ; Lee, Liana; Chen, Jian; Jackson, Donald; Ramanathan, Chandra S.; Siemers, Nathan O.; Chang, Han (2003) Polynucleotides encoding a novel glycine receptor alpha subunit expressed in the gastrointestinal tract, HGRA4, and splice variant thereof (US20030032608, WO2002066606).

Jackson, Donald, G. ; Feder, John; Nelson, Thomas; Mintier, Gabe; Ramanathan, Chandra; Lee, Liana; Siemers, Nathan; Bol, David; Schieven, Gary; Finger, Joshua; Todderud, C, Gordon.; Bassolino, Donna; Krystek, Stanley; Mcatee, Patrick; Suchard, Susan; Bana (2002) POLYNUCLEOTIDES ENCODING NOVEL HUMAN PHOSPHATASES (WO2002057460).

Siemers, Nathan O.; Yarnold, Susan; Senter, Peter D. (2000) Recombinant antibody-enzyme fusion proteins (US6132722, EP0986576).

Bowen, Michael, A. ; Siemers, Nathan (2000) TUMOR NECROSIS FACTOR RECEPTOR HOMOLOGUE-1 ("TRH1") (WO0034294).

Koocher, Martin ; Siemers, Nathan O. (1989) Method and Apparatus for Detecting an Analyte of Interest Capable of Being converted Into a Carbonyl Containing Composition (US4816414).

Invited

Biopharmaceutical Statistics Workshop, Muncie, Indiana (2000). "Escape from Noise: Pre-Processing Transcriptional Profiling Data".

Presentations

1st Ontario Microarray Network Technology Symposium (2000). Invited Speaker: "Know Thy Neighbor – An Exploration of KNN Techniques".