

Nathan Siemers, Ph.D.

- Functional Profile** Current role: Director of Genomics in a pharmaceutical company with line management of bioinformatics and proteomics groups. I oversee and direct the use of genomic and systems biology tools across preclinical and clinical R&D, with particular focus on oncology, immunology, and immuno-oncology. Responsible for identification, acquisition, and implementation of major knowledge integration platforms across the enterprise as well as the architect of enterprise high performance computing platforms for genomics. Cross-trained in chemistry, biology, genomics, oncology, drug delivery, medical diagnostics, and bioinformatics, my training and experience has made me adept at integrating and synthesizing across domains to practically identify and validate drugs, drug targets, biomarkers, and patient populations.
- Experience** 21 years experience in the Pharmaceutical and Biotechnology/Diagnostics industries.
- Extensive background in the application of Genomic methods and Integrative Biology to all stages of Pharmaceutical R&D, from Exploratory Discovery to Phase IV Development support of product labeling and new product indications.
- Hands on experience in: bioinformatics; genomics; molecular biology; targeted delivery of anticancer drugs; biochemistry; molecular diagnostics; organic synthesis.
- 28 years experience in the use, development, and architecture of Informatics and High Performance Computing platforms.
- Effective at identifying and retaining invaluable Scientific staff.
- Roles** 2004 - Present **Bristol-Myers Squibb** Hopewell, New Jersey
Director R&D, Applied Genomics
- Direct activities of Proteomics and Bioinformatics departments responsible for support of Genomics activities across the corporation.
 - Coordinate all aspects of Genomics support for Oncology, Immunology, and Immuno-Oncology Disease areas.
 - Champion and coordinate the use of Systems Biology methods to identify targets in

preclinical discovery efforts and stratify patient populations in the clinical domain.

- Areas of direct development and support: Next generation sequencing; Profiling Technologies (RNA, Protein, Metabolite) for target, drug, and biomarker validation.; Systems Biology and Chemistry/Biology data integration; Model Systems Biology; Toxicogenomics; Proteomics; High Content Screening; RNA interference technologies and screening; DNA sequencing/analysis, clinical virology; Human Genetics and Pharmacogenetics; Biomarker identification, validation; Sequence databases, analysis and mining; Enterprise-wide Knowledge Management and Knowledge Bases.
- Identify, establish, and manage diverse Alliances in the areas of Target and Compound Validation
- Laboratory workflow support for all areas of Genomics
- Control software and hardware budgets for Corporate-wide Genomics IT infrastructure, vendor selection and negotiation.
- Coordination of Bioinformatics activities with Discovery and Corporate Informatics.
- Communication of strategic needs and initiatives to R&D Leadership.
- Training and education of Research and Development staff in the use of Genomic tools.

2000 - 2004 **Bristol-Myers Squibb** Hopewell, New Jersey
Associate Director, Applied Genomics

1998-2000 **Bristol-Myers Squibb** Hopewell, New Jersey
Group Leader, Applied Genomics

1997-1998 **Whitehead Institute** Cambridge, Mass.
Scientist, Functional Genomics (Eric Lander/Todd Golub)

- Early validation and analysis of Affymetrix transcriptional profiling device and software technology

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 Seattle Genetics SGN-17 (L49-sfv-bL), an antitumor antibody-bL fusion for use in chemotherapy. L49 antibody and sfv Fusion protein licensed to Seattle Genetics,

although development has been halted.

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

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**
DOI: 10.1007/s00262-011-1172-6

Rui-Ru Ji, **Nathan O. Siemers**, Ming Lei, Liang Schweizer, Robert E. Bruccoleri: *SDRS – an algorithm for analyzing large scale dose response data.* **Bioinformatics**
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).

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, Lusk 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.: *HBEFG, SRA1, and IK: Three cosegregating genes as determinants of cardiomyopathy.* **Genome Res**. 2009 Mar;19(3):395-403.

Rui-Ru Ji, Heshani de Silva, Yisheng Jin, Robert E. Bruccoleri, 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 costimulatory 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
Patents**

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).

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).

**Public
Software
Releases
(myself and my
group)**

Oracle Table Browser: advanced relational database browsing and mining tool. <http://otb.sourceforge.net> (John Hinsdale)

Xpress-Analyzer: analytical and statistical tools, including Analysis of Variance, Principal Components Analysis , General Linear Models. <http://sourceforge.net/projects/xpress-analyzer> (Isaac Neuhaus)

Flickr Hive Mind: data mining of the Flickr (<http://flickr.com>) database of photography. An exercise in the use of modern Web APIs and Web Services. Over 11 million individuals have used the tool. <http://flickrhivemind.net> (Nathan Siemers)

**Invited
Presentations**

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

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