KARL E. GRISWOLD
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RESEARCH INTERESTS

My primary research interests relate to molecular engineering of biological catalysts for use as therapeutic agents. We use natural protein scaffolds as a starting point, and employ iterative combinatorial algorithms that search the adjacent protein sequence space for functionally improved variants. This methodology, termed directed evolution, combines cutting edge genetic diversification technologies with carefully designed high throughput screens to create enzyme variants with enhanced properties. The strategy is being applied to develop: variants of current therapeutic agents with improved activity and biological properties, novel enzymes that catalyze reactions relevant to treatment of clinical disorders and conditions, and therapeutic proteins that exhibit decreased immunogenicity in human patients.

Related interests include engineering enzymes for practical application in the synthesis of small molecule pharmaceutical drugs, for use in bioremediation, and as catalysts in the conversion of biomass.

PROFESSIONAL EXPERIENCE

- 2007-Present **Assistant Professor,** Thayer School of Engineering, Dartmouth College, Hanover, NH
  A broad interest in biotechnology underlies a research program focused on engineering proteins with enhanced performance characteristics in practical industrial and clinical settings. A particular emphasis is being placed on developing biotherapeutic agents that exhibit low immunogenicity.
- 2005-2007 **Postdoctoral Fellow,** University of Texas at Austin, Austin, TX
  Advisor: George Georgiou
  Research projects included molecular engineering of glutathione transferases, esterases, and therapeutic enzymes for treatment of human disease. Novel screens for enzyme activity were developed based on detection of pH changes, *in vitro* compartmentalization, and genetic selection *via* growth on customized synthetic substrates. All of these assays continue to be employed for screening combinatorial libraries of enzyme variants with potential applications in synthetic chemistry and cancer therapy.
- 1999-2005 **Graduate Research Assistant,** University of Texas at Austin, Austin, TX
  Advisors: Brent L. Iverson and George Georgiou
  Dissertation research involved development of new strategies for directed evolution of enzyme activities. Results included the first experimental demonstration that random homology-independent recombination can yield highly active chimeric enzymes. These studies also lead to the design of novel high throughput flow cytometric screens for enzymatic activity.
- 1997-1999 **Applications Chemist**, Huntsman Corporation, Austin, TX
  Group Supervisor: Robert Zimmerman
  Division Manager: Dave McCoy
- 1995-1997 **Final Test Technician**, Finnigan Corporation (Now Thermo Electron), Austin, TX
  Manager: Ed McCauley

EDUCATION

- 1999-2005 Ph.D., Chemistry, University of Texas at Austin, Austin, TX.
  Focus on Protein Engineering – GPA 4.0
  Advisors: George Georgiou and Brent L. Iverson

  Dissertation: *Engineering Highly Active Enzymes with Altered Substrate Selectivity*

- 1991-1995 B.S. Southwest Texas State University, San Marcos, TX.
  Major-chemistry, Minor-mathematics, Graduated Summa Cum Laude
  Focus on Organic Synthesis – GPA 3.9
  Research Advisor: Michael T. Blanda

AWARDS AND HONORS

- Early Career Translational Research Award in Biomedical Engineering, Wallace H. Coulter Foundation (2008)
- Professional Development Award, University of Texas (2005)
- NIH Biotechnology Training Grant (2000-2003)
- Royston M. Roberts - Regents Fellowship, University of Texas (1999)
- DOW Chemical Foundation Scholar, Southwest Texas State University (1991-1995)
- Presidential Upper Division Scholar, Southwest Texas State University (1994-1995)
- ACS Polymer Education Committee Award for Organic Chemistry (1993)

PUBLICATIONS

10) Parker, A.S., Zhang, W., Griswold, K.E., Bailey-Kellogg, C. Optimization algorithms for functional deimmunization of therapeutic proteins. Submitted to the *17th Annual International Conference on Itelligent Systems for Molecular Biology* (2009), to be published in *Bioinformatics*.

9) Zhang, W., Griswold, K.E., Bailey-Kellogg, C. Protein fragment swapping: A method for asymmetric, selective site-directed recombination. Accepted for publication in the *Proceedings of the 13th Annual International Conference on Research in Computational Molecular Biology* (2009), Tuscon, AZ, United States

8) Griswold, K.E., Aiyappan, N.S., Iverson, B.L., Georgiou, G. The Evolution of Catalytic Efficiency and Substrate Promiscuity in Human Theta Class 1-1 Glutathione Transferase. *Journal of Molecular Biology* (2006), **364**(3), 400-10.

7) Griswold, K.E., Kawarasaki, Y., Ghoneim, N., Benkovic, S.J., Iverson, B.L., Georgiou, G. Evolution of highly active enzymes by homology-independent recombination. *Proceedings of the National Academy of Sciences, USA* (2005), **102**(29), 10082-7

6) Levy, M., Griswold, K.E., Ellington, A.D. Direct selection of trans-acting ligase ribozymes by *in-vitro* compartmentalization. *RNA* (2005), **11**(10):1555-62

5) Georgiou, G., Harvey, B.R., Griswold, K.E., Iverson, B.L. (2005). Applications of Flow Cytometry in Protein Engineering. (Chapter 12) In Larry A. Sklar (Ed), Flow Cytometry in Biotechnology. Oxford University Press

4) Kawarasaki, Y., Griswold, K.E., Stevenson, J.D., Selzer, T., Benkovic, S.J., Iverson, B.L., Georgiou, G. Enhanced crossover SCRATCHY: construction and high-throughput screening of a combinatorial library containing multiple non-homologous crossovers. *Nucleic Acids Research* (2003), **31**(21), e126/1-e126/8

3) Griswold, K.E., Mahmood, N.A., Iverson, B.L., Georgiou, G. Effects of codon usage versus putative 5'-mRNA structure on the expression of *Fusarium solani* cutinase in the *Escherichia coli* cytoplasm. *Protein Expression and Purification* (2003), **27**(1), 134-42

2) Griswold, K.E. pH sensing agar plate assays for esterolytic enzyme activity. *Methods in Molecular Biology* (Totowa, NJ, United States) (2003), **230**, 203-11

1) Blanda, M.T., Griswold, K.E. Synthesis of a Symmetric Octathio Bis(calix[4]arene) Cage Molecule. *Journal of Organic Chemistry* (1994), **59**(15), 4313-15, Erratum (1994), **59**(26), 8315

PATENTS

- Griswold, Karl E. and Scanlon, Thomas C. **Therapeutic Charge Engineered Variants of Lysozyme and Methods for using the Same to Treat Infections.** Provisional US Patent Application (2009), 29 pp. Attorney Docket Number KEGTCS11609
- Griswold, Karl E. **Primary alkanolamides, their preparation and their uses.** PCT Int. Appl. (2000), 23 pp. CODEN: PIXXD2 WO 2000066543 A1 20001109 CAN 133:335966 AN 2000:790464 CAPLUS

PRESENTATIONS

- **Karl E. Griswold** and Thomas C. Scanlon. **New Designs for Catalytic Antimicrobial Agents.** Presented at: 2nd International Conference on Biomolecular Engineering, Santa Barbara, CA, January 18-23, 2009

- **Karl E. Griswold** (invited speaker), Bum Yeol Hwang, Brent Iverson, George Georgiou. **High Throughput Screens for Evolutionary Engineering by Designed Selection.** Presented at: Society for Industrial Microbiology Annual Meeting, San Diego, CA, August 10-14, 2008

- **Karl E. Griswold** (presenter), Thomas C. Scanlon, Laurie A. Whittaker. **Genetically Engineered Lysozyme for Treatment of Pulmonary Infections**. Poster Presented at: WHCF Annual Early Career Award Meeting, Ft. Lauderdale, FL, August 4-7, 2008

- **Karl E. Griswold** (invited speaker). **Protein Engineering: Retooling Nature's Molecular Machines.** Presented at: Jones Seminar Series, Thayer School of Engineering, Dartmouth College, April 7, 2006

- **Karl E. Griswold** (speaker), Yasuaki Kawarasaki, Nada Ghoneim, Stephen J. Benkovic, George Georgiou. **Enzyme humanization and the creation of novel enzymes by combinatorial non-homologous recombination.** Presented at: *Biotechnology Secretariat*, 229th ACS National Meeting, San Diego, CA, March 13-18, 2005

- Levy, Matthew (presenter), **Griswold, Karl E.**, Ellington, Andrew. **Trans-acting ribozyme selection via *in-vitro* compartmentalization.** Poster Presented at: Gordon Research Conference - Origin of Life, Ventura, CA, January 16-21, 2005

- **Griswold, Karl E.** (speaker); Kawarasaki, Yasuaki; Benkovic, Stephen; Iverson, Brent L.; Georgiou, George. **Engineering Enzyme Substrate Selectivity in Recombinant *E. coli***. Presented at: [549] – *Advances in Biocatalysis and Protein Engineering II*, Annual AIChE Meeting, San Francisco Hilton; San Francisco, CA, November 16-21, 2003

- **Griswold, Karl E.** (speaker); Kawarasaki, Yasuaki; Selzer, Tzvia; Stevenson, James D.; Benkovic, Stephen; Iverson, Brent L.; Georgiou, George. **Flow cytometric screening of**

chimeric glutathione transferase libraries expressed in *Escherichia coli*. Presented at: 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003

•**Griswold, Karl E.** (presenter); Blanda, Michael T. Poster Presented at: 208th ACS National Meeting, Washington, DC August 21-25, 1994

PROFESSIONAL SOCIETIES

•Member AIChE •Member ACS •Member ASEE •Member SIM

REFERENCES

1. Dr. Joseph Helble
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   University of Texas at Austin
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4. Dr. Brent Iverson
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