Fourteenth Annual

Biotechnology Training Retreat

Saturday,
May 7, 2005

Christian Brothers Retreat & Conference Center
Napa, CA

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Co-sponsored by:

NIH Training Program in Biomolecular Technology
(NIH-1-T32-GM08799)

UC Davis Designated Emphasis in Biotechnology
Graduate Program (DEB)

UC Davis Biotechnology Program

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The Fourteenth Annual Biotechnology Training Retreat

On behalf of the Biotechnology Program, the executive committees of the Designated Emphasis in Biotechnology (DEB) and the NIH Training Grant in Biomolecular Technology, we thank you for joining us, as we honor our **2004-05 fellows and their preceptors**, as well as **our industry affiliates**. We hope that you will enjoy the oral presentations and posters as well as the heavenly scenery and fine cuisine.

Please welcome our biotechnology fellows. Our **5 NIH Fellows** include: **Craig Blanchette** in Biophysics (preceptor is Marjorie Longo); **Gian Oddone** from Chemical Engineering (preceptor is David Block); **Daniel Scott** in Chemistry (preceptor is Michael Toney); **Alan Szmodis** in Biophysics (preceptor is Atul Parikh) and **Robert Ward** from Food Science (preceptor is J. Bruce German). Our **Biotechnology Fellows** (industry and campus fellowships) include: **Tim Cao** from Biomedical Engineering (preceptor is Abdul Barakat), **Robin GrayMerod** from Civil and Environmental Engineering (preceptor is Stefan Wuertz) and **Scott Wong** from Biochemistry and Molecular Biology (preceptors are Kit S. Lam/Earl Sawai). We will be selecting our 2005-06 fellows in early June. Fellowship nominations are due on **May 16, 2005**. Forms can be downloaded from the DEB website.

We would also like to recognize our **First Year Biotechnology Fellows: Douglas Huseby** (Biochemistry and Molecular Biology); **Kiem Vu** (Cell and Developmental Biology); **Vannarith Leang** (Chemical Engineering) and **Robin Lin** (Electrical and Computer Engineering). Please congratulate all of these outstanding predoctoral candidates. Due to the limited time for oral presentations, we will showcase research performed by other students in the DEB program in the poster session.

We are completing our third year of the NIH Biotech Training Grant and have completed a seven-year review of the DEB graduate program in 2004. The consensus is that we are doing a fine job in growing the program. As a reminder, the DEB graduate program is the formal training program for the NIH training grant and the number of **DEB students is close to 70**. Each of our students is showcased on the newly revised DEB website (www.deb.ucdavis.edu).

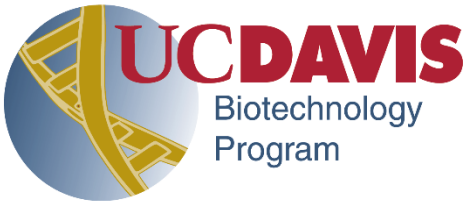
We are having a banner year in placing interns: **Craig Blanchette** completed a rotation at LLNL and **Alan Szmodis** will go to LLNL this summer; **Jennifer Weidhaas** (Civil & Environmental Engineering) spent 3 months doing microbiology in Prof. Kate Scow's lab; **Bob Ward** (Food Science) is interning in Prof. Carlito Cabrilla's chemistry lab; **Tian Bao** (Chemical Engineering) did a rotation at Genentech last summer; **Vidya Kunathigan** (Microbiology) worked on microarray analysis in Prof. Vladimir Filkov's computer science lab; **Scott Wong** spent the summer at Scios; **Sheetal Singh** (BMB) and **Amanda Fischer** (Plant Biology) rotated through Novozymes; **Ze He** (Chemistry) is currently interning at Agilent Technologies; **Tamara Peoples Holst** (BMB) will start at Monsanto-Calgene campus shortly; **Jie-Ren (Jerry) Ku** (Chemical Engineering) is going to Alza this summer; **Tim Cao** (Biomedical Engineering) and **Daniel Scott** (Chemistry) are planning to intern this summer (location still pending). The three Genentech interns still need to be announced

A number of students graduated in 2004 with their PhDs with a DEB: **Chad Green** is currently doing a post-doc in Scot Simon's lab; **Edwin Hagnazari** (BMB) is now a post-doc at Scios [after interning at Scios]; **Albero Iandolino** (Plant Biology) was hired at Monsanto-Calgene campus in March (he also interned at this location); **Viyada Kunithigan** (Microbiology) moved back to Bangkok, Thailand in December to teach (she survived the tsunami); **Manny Torres** (Genetics) joined his wife in Atlanta (she is an MD at the CDC) and was planning to work at Emory University and **Marisa Wong** (Genetics) is a post-doc at CHORI (Children's Hospital Oakland Research Institute) with Ronald Krauss. A number of students will graduate this spring or summer: **Ze He** (Chemistry); **Tamara Peoples Holst** (BMB); **Larry Joh** (Biosystems Engineering); **Jie-Ren (Jerry) Ku** (Chemical Engineering); **Ryann Muir** (Plant Biology) will study patent law at Boston University in the Fall;; **Amanda Ellsmore-Fischer** (Plant Biology) and **Bob Ward** (Food Science). **Sinyoung Park** is now at CuraGen in Connecticut.

This annual event is a great time to officially thank our company affiliates for their support in the form of fellowships, internships and participation on advisory boards. We would like to specifically thank Genentech for their MOU to officially commit to a fellowship and 3 internship slots for the next 3 years.

Last but not least, we want to thank Prof. John Yoder for again offering stimulating bioethics questions for our consideration. As for handling the logistics of the retreat, our gratitude goes out to new staffers, Sharla Harrington and Bjoern Hoffmann. **Please Come Again on April 8, 2006.**

Judy Kjelstrom, Director, UC Davis Biotechnology Program



NIH Training Grant in Biomolecular Technology

(NIH-1-T32-GM08799)

Bruce D. Hammock, Director
Karen McDonald, Co-Director
Martina Newell-McGloughlin, Co-Director

Executive Committee

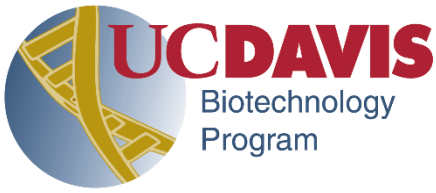
Faculty:

George Bruening (Plant Pathology)
Dan Gusfield (Computer Science)
Ian Kennedy (Mechanical & Aeronautical Engineering)
J. Clark Lagarias (Biochemistry & Molecular Biology)
Kit Lam (MED: Internal Medicine (Hemotology/Oncology)
John Yoder (Plant Sciences)

Industry:

Kenneth Gruys, Monsanto, Calgene campus
Joel Cherry, Novozymes Biotech
Linda Higgins, Scios

Judith A. Kjelstrom, Program Coordinator
(Ex-Officio Member)



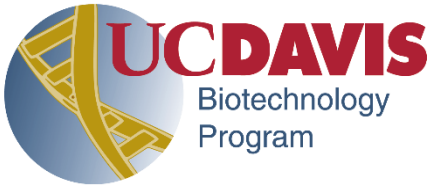
Designated Emphasis in Biotechnology (DEB)

www.deb.ucdavis.edu

Executive Committee

Abhaya Dandekar, Chair
David Rocke (2005-Interim Chair)
Karen McDonald
Robert Rice
Susanne Berglund, Student Member

Judith A. Kjelstrom
Program Coordinator
(Ex-Officio Member)



UC Davis Biotechnology Program

www.biotech.ucdavis.edu

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UC Davis Fourteenth Annual Biotechnology Training Retreat
May 7, 2005
Christian Brothers Retreat & Conference Center

6:45 am – Bus departs Davis, Parking Lot #41

8:00 – 8:30 am	**Registration** **Continental Breakfast**		
8:30 – 8:45 am	**Welcome** Bruce Hammock Director, NIH Training Grant in Biomolecular Technology		
	Morning Session Chair Karen McDonald Co-Director, NIH Training Grant in Biomolecular Technology, DEB Executive Committee		
8:45 – 10:20 am	**Presentations**		
	8:45 am	Bob Ward	*Mentor: Bruce German* SCIOS, Inc.
	9:10 am	Aaron Nguyen	*Mentor: Marjorie Longo*
	9:35 am	Craig Blanchette	*Mentor: David Block*
	10:00 am	Gian Oddone	
10:20 – 10:50 am	**Break / Poster Viewing**		
10:50 am – 12:20 pm	**Presentations**		
	10:50 am	Daniel Scott	*Mentor: Michael Toney*
	11:15 am	Kristen Bennett	Monsanto, Calgene Campus
	11:35 am	Alan Szmodis	*Mentor: Atul Parikh*
	12:00 pm	John Yoder	Bioethics Question (Handout)
12:20 – 2:15 pm	**Lunch / Poster Viewing**		
	Afternoon Session Chair Martina Newell McGloughlin Co-Director, NIH Training Grant in Biomolecular Technology		
2:15 – 3:50 pm	**Presentations**		
	2:15 pm	John Yoder	Bioethics Question (Discussion)
	2:40 pm	Gerd Kleeman	Amgen, Inc.
	3:05 pm	Robin GrayMerod	*Mentor: Stefan Wuertz*
	3:30 pm	Sandra T. Merino	Novozyme Biotech, Inc.
3:50 – 4:00 pm	**Short Break**		
4:00 – 5:15 pm	**Presentations**		
	4:00 pm	Tim Cao (absent)	*Mentor: Abdul Barakat*
	4:25 pm	Scott Wong	*Mentors: Kit Lam & Earl Sawai*
	4:50 pm	Maggie Bynum	Agilent Technologies
	5:15 pm	Eddie Moler	Chiron Corporation
	5:35 pm	Maris Apse	Arcadia Biosciences
5:45 pm	**Closing Remarks** Bruce Hammock / Martina Newell McGloughlin		

6:30 pm – Bus departs Napa

2005 Poster Titles

A. **"*EGFR* and *K-RAS* mutations in bronchioalveolar carcinoma (BAC) from patients treated with the EGFR inhibitor gefitinib on the Southwest Oncology Group (SWOG) S0126 trial"**
Honglin Chen*, Will S. Holland, Wilbur A. Franklin, Jason McCoy, Kari Chansky, John J. Crowley, David R. Gandara, and Paul H. Gumerlock. UCD, U of Colorado, and Southwest Oncology Group Statistical Center.

B. **"A Multi-scale Investigation of Alcohol and Biomembrane Interactions"**
Allison Dickey* and Roland Faller
Chemical Engineering and Material Science, University of California, Davis, CA 95616

C. **"Chemotaxis of Pseudomonas SP. ADP to the Herbicide Atrazine"**
Xianxian Liu*, and Rebecca Parales
Section of Microbiology, University of California, Davis

D. **Identification of Active Site Residues Responsible for Regiospecificity in Nitrobenzene 1,2-Dioxygenase**
Kou-San Ju* and Rebecca E. Parales
Section of Microbiology, University of California, Davis, CA, 95616

E. **Zinc Deficiency Induced Disruption of Iron Metabolism: Changes in Cellular Iron, IRE/IRP Binding, and Proteins Involved in Iron Uptake and Storage**
Brad J. Niles[1*], Michael S. Clegg[1], Susan S. Chou[1], Tony Y. Momma[1], and Carl L. Keen[1, 2];
[1]Departments of Nutrition, and [2]Internal Medicine, at the University of California.

F. **"Regulated Plant Viral Amplicon System for Expression of Recombinant Proteins in Plant Cell Cultures"**
Michael A. Plesha[a,*], Ting-Kuo Huang[a], Mysore Sudarshana[b], Sandra L. Uratsu[c], Bryce W. Falk[b], Abhaya M. Dandekar[c] and Karen A. McDonald[a]
a. Department of Chemical Engineering, b. Department of Plant Pathology, c. Department of Pomology, University of California, Davis, CA, 95616

G. **Trophoblast-Endothelial Interactions *In vitro*: Redistribution of Intercellular Adhesion Molecule-1 (IC AM-1) in Uterine Microvascular Endothelial Cells (UtMVEC) Under Flow**
Tim C. Cao[*], Arlen Soghomonians, Twanda L. Thirkill, Gordon C. Douglas, and Abdul I. Barakat,
Department of Biomedical Engineering, University of California, Davis

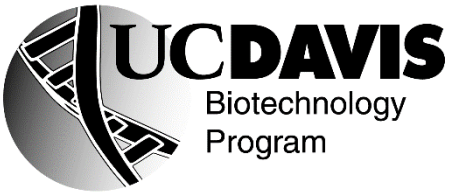
H. **Metabolic Engineering of Omega-3 Fatty Acids in Seed Oil**
Byron Froman, Jennifer Gonzales, AJ Nava, Janet Nelsen, Jeff Haas, Virginia Ursin
Monsanto Company, Calgene Campus

I. **Photochemical implications of tyrosine-176 substitutions in cyanobacterial and plant phytochromes**
Amanda Fischer*, Yi-shin Su, Abigail Yap, Nathan C. Rockwell and J. Clark Lagarias.
Section of Molecular and Cellular Biology, University of California, Davis, CA 95616

J. **Localized Hormone Accumulation and Haustorium Development**
Alexey A. Tomilov, Natalia B. Tomilova, Ibrahim Abdallah, Denneal Jamison McClung, Russell L. Reagan, and John I. Yoder
Department of Plant Sciences, Section of Agricultural Plant Biology, University of California, Davis, CA, USA, 95616

K. **Using Transposon Mutagenesis to Generate Fusion Protein Libraries**
Amanda J. Fischer*, Aubrey Jones[Ω], and Joel R. Cherry[Ω]
UC Davis Biotechnology Training Program*, and Novozymes, Inc. [Ω]

*Member of DEB graduate group **See pages 30 - 38 for abstracts.**



Oral Presentation Abstracts

OVERVIEW OF LAB RESEARCH: J. Bruce German/Robert Ward

German Laboratory

J. Bruce German
Professor of Food Science & Technology
University of California, Davis

Research in the German Lab includes investigation of the role of dietary fat in the structure and function of biological lipids, the role of milk components in food structures and nutrition, and the use of metabolic assessment to personalize health.

The goal of the research is to improve scientific knowledge of the mechanisms underlying food consumption and its effect on individual human health. The group works on the biological and functional properties of milk lipids and proteins in addition to lipids and dietary biomolecules from other sources. A major theme of the research has been to attempt, wherever possible, to link the food composition to the nutritional functionality. An understanding of both the value drivers of foods and the value drivers of nutrition will provide the knowledge to make food both delicious and nutritious.

One aspect of the research program is to explore the ways in which evolutionary pressure selected for nutritional functionality in milk. This substance is the only bio-material that has evolved for the sole purpose of nourishing growing mammals. Therefore, a thorough genetic and compositional deconstruction of milk, across a range of species, should yield novel food activities. Parturition is a tenuous period in the mammalian life cycle, for both mother and newborn, and thus successful lactation must provide optimal nutrition at a tolerable metabolic cost to the mother. It is hard to imagine there is much in milk which does not serve a nutritional function, and this makes it an attractive substance for food and nutrition research.

A second focus of the lab is in defining and characterizing health through metabolic profiling. Major developments in genomics and in analytical tools are changing the way diseases are diagnosed, treated and prevented. However, these same technologies will change the way health is assessed. Metabolic profiling looks at the interrelationships of metabolic pathways, and insures that a beneficial change in one measured biomarker is not at the expense of another. The ultimate goal it to provide high-throughput tools which will allow for the rapid measurement of minute changes in body metabolites, allowing personalized medical treatment and nutrition.

NIH FELLOW: Robert Ward

Functional Annotation of Human Milk Oligosaccharides

Presenter:	Robert Ward*
Authors:	**Robert E. Ward*[1], Milady Ninonuevo[2], Carlito Lebrilla[2], J. Bruce German[1]**
Affiliations:	Departments of Food Science and Technology[1] and Chemistry,[2] University of California, Davis, CA 95616

The consumption of human milk during breast feeding provides phenotypic advantages which cannot be explained by our current understanding of its essential nutrient profile. Clearly there are benefits and active ingredients beyond the essential nutrients. Translating such benefits to other foods and health opportunities will be possible if their structures and mechanisms of action are understood. Therefore, deconstruction of the genetic, compositional and structural information content of milk will yield valuable nutritional insight and benefits beyond infancy.

This project addresses a particularly under-appreciated constituent of human milk, the free oligosaccharides. In comparison to other mammals, human milk is particularly rich in soluble oligosaccharides (HMO). After lactose and fat, they are the third most concentrated component in human milk, yet the reason for this is unclear. To date over 130 different HMO have been identified from a pooled sample using mass spectrometry, yet no aspect of our understanding of their functions explains this high concentration and diversity. Furthermore, HMO vary amongst human maternal genotypes, with oligosaccharide species present in each mother's milk varying with Lewis and secretor genes. Reseach is only beginning to address the consequences of this heterogeneity.

HMO are believed to act as prebiotics, or indigestible carbohydrate molecules which selectively stimulate the growth and proliferation of beneficial gut microbes such as *Bifidobacteria* and *Lactobacilli*. However, very little data are available to support this hypothesis much less understand the precise structures and functions of purported prebiotic molecules. The initial goal of this investigation was to use *in vitro* fermentations to determine if HMO can be used as the sole energy source by representatives of the gut microflora of breast-fed infants. In order to create a growth medium to assay the fermentability of the oligosaccharides, a method was first developed to purify gram quantities of these molecules from human milk. Subsequently, pure isolates of *Bifidobacteria* were inoculated, and growth was measured as a function of time. Fructooligosaccharides, a well-characterized prebiotic, and lactose were used as controls. All strains of *Bifidobacteria* tested were able to metabolize the HMO to some extent, yet *B. infantis* was the most active. A total carbohydrate analysis indicated that a maximum of 60% of the HMO was fermentable, and TLC analysis showed these were primarily the smaller species. *B.infantis* was the only species able to cleave terminal sialic acid from the acidic HMO, an activity which may have implications for infant brain development. A mass spectrometry method was used to identify some of the TLC bands which were differentially consumed by the bacterial species.

* Member of the DEB graduate group

COMPANY AFFILIATE: SCIOS, Inc.

SCIO-469, a Potent and Selective Inhibitor of the p38α MAPK, Normalizes the Bone Marow Microenvironment to Inhibit Multiple Myeloma Cell Proliferation and OsteoClast Formation

Presenter:	Aaron N. Nguyen
Authors:	Aaron N. Nguyen,[1*] Elizabeth G. Stebbins,[1] Margaret Henson,[1] Gilbert O' Young,[1] Sun J. Choi,[2] Mamatha Reddy,[1] Jing Y. Ma,[1] Edwin Haghnazari,[1] Ann M. Kapoun,[1] Satyanaryana Medicherla,[1] Andy Protter,[1] George F. Schreiner,[1] G. David Roodman,[2] Tony A. Navas,[1] and Linda S. Higgins[1]
Affiliations:	[1]Scios Inc., Fremont, CA and [2]Division of Hematology-Oncology, University of Pittsburgh

Multiple myeloma (MM) remains incurable despite recent advances in treatment. Accumulating evidence suggests that the MM bone marrow (BM) microenvironment plays a critical role in supporting tumor growth, survival, and drug resistance, as well as in promoting formation of osteolytic bone lesions. A key aspect of this disease-promoting environment is elevated levels of cytokines and other soluble factors. Most prominent among these for tumor support are IL-6 and VEGF. Predominant factors promoting osteolytic lesions are MIP-1α and RANKL. The p38 MAPK is activated by environmental stress and pro-inflammatory cytokines such as TNFα and IL-1β. Furthermore, p38 activation has been shown to be important for the synthesis and secretion of IL-6, VEGF, and TNFα. Consequently, inhibition of p38 is hypothesized to reduce the production of these factors implicated in MM pathology and to have therapeutic benefit by suppressing the tumor-supportive state of the BM microenvironment. Here, we demonstrate that the p38α MAPK inhibitor, SCIO-469, inhibits p38 activity in both BM stromal cells (BMSCs) and myeloma cell lines. Moreover, SCIO-469 reduces IL-6 and VEGF secretion; suppression of such supportive factors leads to inhibition of myeloma cell proliferation in long-term cultures. We also show that SCIO-469 inhibits secretion and expression of osteoclast-activating factors.

OVERVIEW OF LAB RESEARCH: Marjorie Longo/Craig Blanchette

Longo Laboratory

Marjorie Longo
Professor of Chemical Engineering and Materials Science
University of California, Davis

In the Longo laboratory, we study the mechanical, barrier, transport, and adsorptive properties of artificial and real cell membranes that lead to macroscopic behaviors of biological membranes. Examples of these behaviors include viral infection, fertilization, action of anesthetics, membrane transport, and drug delivery. The softness of biological interfaces present special experimental problems associated with the fact that the core membrane component, the lipid bilayer, is fluid under physiological conditions. Therefore, we use mild micromanipulation techniques in which the pressure on the membrane can be varied by as little as one millionth of an atmosphere for measuring membrane mechanical properties and adsorption of water soluble species. We softly image the surface of the lipid bilayer using atomic force microscopy and fluorescence microscopy to examine phenomena at a range of length scales from nanometers to micrometers. Finally, for properties that can't be observed experimentally, we develop computer simulations. Currently, there are four major thrusts: (1) Insertion of amphiphilic peptides into lipid bilayers, with an emphasis on understanding the mechanisms of viral and antimicrobial peptides; (2) Influence of alcohols on the mechanical and energetic properties of lipid bilayers, with an emphasis on understanding the underlying thermodynamics of the process; (3) Utilizing nanometer scale domains in supported lipid bilayers to understand diffusional behavior and multivalent binding behavior in biological membranes. (4) Micron-scale bubbles in medical applications with an emphasis on designing amphiphilic shells for various applications such as drug delivery or contrast agents.

The training project (trainee Craig Blanchette) involves the development of nano-structured supported lipid bilayers for studying the relationship between arrangement and mobility of membrane-associated molecules (e.g. glycosylated lipids) and their binding with proteins. From a biotechnology standpoint, this is an extremely important problem since although high-throughput screening is possible for DNA and some soluble proteins, screening using membrane associated molecule (glycosylated lipids, ion channels, integral membrane proteins) is, relatively, in the dark ages. Since 2/3 of all proteins are membrane associates and many if not, most, drug targets are membrane associated (e.g. ion channels), the ability to display such molecules in the biologically relevant configuration (i.e. the lipid bilayer which is known to be complex, mobile, and structured at the nanometer level) and interpret binding of drugs and proteins to such molecules (where binding can be extremely non-linear) is possibly the greatest challenge of the decade.

NIH FELLOW: Craig Blanchette

The Effects of Cholesterol on Galactosylceramide Domain Microstructure and Binding Properties: A Model Membrane Study

Presenter:	Craig Blanchette*
Authors	Craig Blanchette (cdblanchette@ucdavis.edu), Wan-Chen Lin (wanlin@ucdavis.edu), Timothy V Ratto (ratto7@llnl.gov), Marjorie L. Longo (mllongo@ucdavis.edu)
Affiliations:	Chemical Engineering and Materials Science, UC Davis, Davis, CA

We have studied the effects of cholesterol on Galactosylceramide (GalCer) domain microstructure and binding properties between GalCer and two lectins: gp120, an HIV envelope glycoprotein and *Trichosanthes kirilowi* (TKA). GalCer has been shown to exist on the extracellular leaflet of the cell membrane in nanometer size domains or rafts enriched in cholesterol. The local clustering of GalCer within rafts is thought to facilitate multivalent interaction between receptor proteins and GalCer in the initial attachment of viruses, including HIV-1 (gp120) and bacteria to the host cell membrane. We have chosen to use supported lipid bilayers as a biological interface to mimic the membrane nano-structure observed in cellular membranes. This system allows for characterization of both, GalCer domain microstructure on the nanometer scale (atomic force microscopy) and membrane binding properties (fluorescence microscopy) enabling a structure-function relationship to be established. This model membrane system was used to study the effects of cholesterol on GalCer domain morphology under equilibrium (slow thermal cooling) and non-equilibrium (quenched vesicle fusion) conditions. The addition of cholesterol to bilayers formed through quenched vesicle fusion at high domain area fraction resulted in a networked GalCer domain morphology as opposed to nanometer size circular discs, which occur in the absence of cholesterol. Upon tip-sample contact these domains changed morphology over time, indicating a reduction in transmembrane ordering observed for GalCer domains not containing cholesterol. Using slow cooling techniques we can largely overcome the non-equilibrium effects of the substrate and GalCer domains can be made to exceed 30 μm in radius. To determine if slow cooling methods resulted in equilibrium domain sizes and shapes we utilized an unsupported equilibrium model membrane system, giant unilamellar vesicles (GUVs). The strong correlation between domain size and shape for GUVs and slowly cooled supported lipid bilayers allowed us to conclude slow cooling result in equilibrium domain microstructures. Under slow cooling conditions there was a cholesterol dependent reduction in equilibrium domain radius. This indicates cholesterol alters equilibrium GalCer domain size, an effect which is believed to occur in cellular rafts, but has yet to be observed in model membranes. Based on these results it appears that cholesterol is reducing the line tension at domain edges allowing for domains to rapidly reach equilibrium structures. Using fluorescence microscopy we found that gp120 only binds to slow thermally cooled GalCer domains above a cholesterol mole fraction of 0.075, whereas TKA binds under all domain conditions. This indicates that the micro-structure and display of GalCer within domains can affect the binding properties of the membrane and these effects are protein dependent.

* Member of the DEB graduate group

OVERVIEW OF LAB RESEARCH: David E. Block / Gian Oddone

Block Lab

Dr. David E. Block
Associate Professor
Department of Viticulture and Enology and the Department of Chemical Engineering and Materials Science

The Block Laboratory is focused in three main areas: biopharmaceutical fermentation optimization based on historical data; technology for the prediction and prevention of stuck and sluggish wine fermentations; and the development of methods for modeling the effects of viticultural practices on final wine sensory and chemical characteristics.

In biopharmaceutical fermentation optimization, we are currently developing methods for optimization of recombinant protein production in *E. coli* and lactic acid bacteria (LAB) using existing and developing knowledge bases, along with datamining and artificial intelligence tools. In the latter project, the LAB are being developed as a potential oral delivery device for recombinant vaccines. To date, we have been able to increase cell mass and protein production by an order of magnitude using traditional statistical optimization methods. In order to increase the protein produced per cell, we have begun to utilize a metabolic flux analysis approach to aid in redirecting carbon and nitrogen fluxes toward product formation.

Stuck and sluggish wine fermentations are a chronic industry problem in which yeast sugar utilization stops prior to the exhaustion of sugar leaving an unstable wine. We have taken a variety of mechanistic modeling and data-driven approaches to be able to predict the occurrence of these events prior to inoculation when they can still be readily rectified. While studying these problem fermentations, we initiated a collaborative project examining the effects of ethanol on purified lipid bilayers. These studies have led to the interesting implication of physical changes in yeast cell membrane thickness and lipid spacing in the ability of yeast to transport sugar and sense their environment late in the alcoholic fermentation.

Finally, we have been studying the effects of viticultural practices on the aroma, flavor, and phenolic profile of finished wines. We have been able to use datamining tools to identify key vineyard inputs that have significant effects on wine quality. With these key inputs identified, model development, again using artificial intelligence tools, will allow the direction of precision viticulture to reduce vineyard heterogeneity and improve overall quality of finished wines.

NIH FELLOW: Gian Oddone

Response Surface Optimization of Recombinant Protein Expression in Fed-batch *L. lactis* Fermentations

Presenter:	Gian Oddone
Authors	Gian Oddone*, David Block, David Mills
Affiliations:	Viticulture and Enology, UC Davis, Davis, CA

An important goal for development of lactic acid bacteria (LAB) vaccines is overcoming the relatively low levels of recombinant protein expression in LAB. To this end, recombinant eGFP expression in *L. lactis* fermentations has been optimized using a central composite response surface experimental design. Three environmental parameters: pH, temperature and Heme concentration, were varied along with two parameters affecting induction of recombinant protein expression. The latter are the concentration of inducer (Nisin) per optical density (OD) unit and the OD at time of induction. All fermentors were batched with identical growth medium consisting of 3x non-buffered M17 and received 50% glucose fed in proportion to agitation speed throughout the run. Cell densities of eGFP-expressing L. lactis have exceeded 12g/L in this medium that lacks the pH buffer glycerophosphate, a component that inhibits growth under conditions of external pH control. The optimal set of conditions found by the response surface for 4L fed-batch fermentations yields protein expression that compares favorably to conventional growth in flasks. The amount of protein per cell, a critical value for determining the potency of an orally delivered LAB vaccine, has been estimated using Western Blot, Bradford, and fluorometer-based assays.

* Member of the DEB graduate group

OVERVIEW OF LAB RESEARCH: Michael Toney / Daniel Scott

Toney Lab

Michael Toney
Associate Professor
Department of Chemistry

The Toney laboratory is interested in both fundamental and applied aspects of enzymes and their catalytic mechanism. Enzymes can catalyze reactions by enormous factors. For example, one of the enzymes our laboratory studies, an amino acid decarboxylase, is the best known biological catalyst. It catalyzes the decarboxylation of simple amino acids ~10^{19}-fold over the nonenzymatic reaction. The sources of the great catalytic powers of enzymes are generally understood in qualitative terms. These include close approximation of reacting groups in the enzyme-substrate complex, general acid/base catalysis, and so on. A quantitative understanding of these catalytic tools is not available and is one of the goals of our research program. On the applied side, enzymes are frequently the targets of pharmaceuticals. We are examining the mechanisms of enzymes that are promising drug targets with the ultimate goal of developing lead compounds for pharmaceutical development.

The experimental techniques employed in our research program include: gene cloning, heterologous expression, and purification of enzymes; enzyme engineering using site-directed mutagenesis and directed evolution; stopped-flow and quenched-flow rapid reaction kinetics of enzyme catalyzed reactions; classical steady-state enzyme kinetics; synthesis of isotopically labeled substrates and measurement of kinetic isotope effects; synthesis of inhibitors and alternate substrates, and X-ray crystallography of enzymes.

One project in the laboratory focuses on the mechanisms of several PLP (vitamin B6) dependent enzymes. PLP dependent enzymes constitute an enormous class of enzymes ubiquitous to biological systems, which are employed extensively in nitrogen metabolism and catalyze a wide variety of reaction types. The unifying feature of these enzymes is the formation of a highly resonance stabilized substrate-based carbanion. Our goals are to understand the fundamental mechanisms by which these enzymes catalyze their cognate reactions, and the mechanisms by which they suppress the many possible side reactions.

A second project involves the mechanistic analysis of enzyme involved in chorismic acid metabolism. The chorismic acid pathways are responsible for the production of carbocyclic aromatic compounds in biological systems and are present only in plants, bacteria, fungi, and some parasites. They are therefore attractive drug targets for antimicrobials.
A third project in the laboratory aims to connect electrically redox enzymes that employ nicotinamide cofactors (e.g. NADH) to macroscopic electrodes such as gold or graphite. This would allow the use of NAD^+-dependent dehydrogenases as enzymes for biofuel cell anodes, for extremely sensitive biosensors, and a variety of other applications. Our approach has been to couple nanotechnology with enzymes, which will be presented here at the Biotechnology Training Grant Retreat.

NIH FELLOW: Daniel Scott

Enzyme Catalyzed Metalic Nanoparticle Synthesis

Presenter:	Daniel Scott*
Authors	Michael Toney
Affiliations:	Department of Chemistry, University of California, Davis, CA

Nanotechnology and biotechnology are two fields of increasing importance that are merging. The former is focused on the synthesis, properties and applications of nanometer-scale structures, while the latter exploits the extraordinary properties of biomolecules to solve significant medical, chemical, and engineering problems. Applications in which these fields currently intersect include quantum dots in optical imaging, biosensors, and gold nanoparticles in immunochemistry[1], as well as facilitation of electron transfer between enzymes and electrodes[2]. Here we describe a novel intersection by showing that the FAD-dependent enzyme glutathione reductase catalyzes the NADPH-dependent synthesis of gold, platinum, and mixed-metal nanoparticles, which are strongly bound to the active site via the redox active cysteines. Juxtaposition of the nanoparticle with the FAD cofactor via the active site cysteines enables the maintenance of the nanoparticle at a low potential in the presence of excess NADPH. This allows layered deposition of metals irrespective of redox potential, and the stabilization of low potential metals toward oxidation in aqueous solution. Thus, biotechnology has been applied to the furtherance of nanotechnology with far-reaching implications, taking us closer to popular conceptions of bionanoassemblers.

* Member of the DEB graduate group

COMPANY AFFILIATE: Monsanto, Calgene Campus

Modification of Seed Oil Content in Soybean (*Glycine max)* by Expression of a *Mortierella ramanniana* Diacylclycerol Aclytransferase

Presenter: Bennett, Kristen A., kristen.a.bennett@monsanto.com

Authors: Bennett, Kristen A. [A] Lardizabal, Kathryn D [A] Keithly, Greg E. [B] Mai, Jennifer T. [A] Hill, Elizabeth K. [B] Ream, Joel E. [B] Wagner, Nicholas N. [A] Colletti, Ronald F. [B] Crow, Laura J [C]

Affiliations:
(A): Monsanto Company, Calgene Campus
(B): Monsanto Company, St. Louis, MO
(C): Monsanto Company, Agracetus Campus

Increased seed oil content of oilseed crops such as canola, sunflower and soybean, has been a target trait of plant breeders for many years. Although modifications of seed fatty acid and amino acid composition have been accomplished through transgenic approaches, there are only a few reports of successful transgenic modification of seed oil content in any crop, and none in the world's leading oilseed crop, soybean. Here we report the first successful transgenic modification to increase soybean seed oil content. This was achieved by modification of a single enzymatic step in the triacylglycerol biosynthetic pathway, the acylation of the sn-3 position of diacylglycerol to form triacylglycerol, by the seed-specific expression of a *Mortierella ramanniana* diacylglycerol acyltransferase (DGAT). This single gene addition significantly increases oil content without impacting protein, is heritable and stable in multiple environments and germplasms.

OVERVIEW OF LAB RESEARCH: Atul Parikh / Alan Szmodis

Parikh Lab

Atul Parikh
Associate Professor
Department of Applied Science, Biophysics Graduate Group

Drawing lessons from nature, we design synthetic material systems with unusual properties and study the relations between their structure, dynamics, and function. These biologically inspired materials often surpass biological specificity and complexity and are expected to find applications in a range of technologies in life sciences (biomedical sensors, early detection of diseases, and drug discovery), as well as in new materials for micro electronics (e.g., resists and molecular electronics), and surface coatings (e.g., adhesives and biofilms). Currently, we explore and exploit the self-assembly strategies employed by biological systems in the design of cell membranes. A focus in our group is to develop phospholipid based strategies to design novel lipid and protein microarrays for applications in functional proteiomics and fundamental biophysics.

NIH FELLOW: Alan Szmodis

Studies Utilizing Patterned 2D Model Biomembranes

Presenter: Alan Szmodis*
Authors Alan Szmodis, Sanhita Dixit, Chanel Yee, & Atul Parikh
Affiliations: Department of Applied Science, Biophysics Graduate Group, University of California, Davis, CA,

The ability to create biomimetic model constructs, in which an investigator has domain over the constituents present, allows for studies to be conducted in simplified and well-characterized systems compared to native analogs. We have recently demonstrated the controlled patterning of supported lipid membranes through a deep-UV lithographic approach. This process affords one the ability to control the size, shape, and placement of biological molecules in a lipid matrix on a solid support. It is then possible to increase biological complexity, from the bottom up, allowing us to scrutinize the effects of new component addition as systems progress. We have produced arrays of proteins in a matrix of lipid bilayers using this patterning process, with future goals of creating arrays with multiple functionalities. These arrays have possible uses as sensing devices as well as high throughput laboratory testing constructs.

* Member of the DEB graduate group

COMPANY AFFILIATE: Amgen, Inc.

From Discovery to Market: The role of Formulation in the Production of Protein Therapeutics

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Our mission in the Pharmaceutics Department at Amgen is to develop formulations and delivery systems for Amgen's clinical and marketed products and to support discovery research as needed with preclinical characterization and formulations.

Formulation development is one of the critical steps in developing a protein as a therapeutic product. Because proteins are complex molecules composed of numerous reactive chemical groups and delicate three-dimensional structures, identifying a set of conditions to keep all components stable is a tremendous challenge and virtually impossible. Therefore, the main objective becomes one of maintaining the appropriate efficacy and safety of the protein product. In order to achieve this objective, it is imperative to develop an in-depth understanding of protein properties and the broad spectrum of degradation pathways affecting protein stability.

To this end our formulation development focuses on determining the potential degradation pathways assessing the significance of each and optimizing variables to minimize the degradation products that are clinically significant.

OVERVIEW OF LAB RESEARCH: Stefan Wuertz / Robin GrayMerod

Wuertz Laboratory

Stefan Wuertz
Professor of Civil and Environmental Engineering
University of California, Davis

Dr. Wuertz's environmental engineering and microbiology laboratory is in the Dept. of Civil and Environmental Engineering. The lab conducts research on biological wastewater treatment, biofilms, and public health aspects of storm water runoff. The Wuertz laboratory investigates the use of horizontal gene transfer in biofilms to facilitate the removal of xenobiotic and recalcitrant compounds. Sequencing batch reactors (SBR) and membrane bioreactors are studied for their potential to treat endocrine disrupting compounds in addition to traditional biological removal of nitrogen and phosphorus. The Wuertz laboratory utilizes epifluorescent microscopy, confocal laser scanning microscopy and microelectrodes coupled with techniques like fluorescent *in situ* hybridization (FISH) and quantitative image analysis to study the spatial distribution of single cells and communal groups of cells within complex microbial communities. Studies are conducted for their application in environmental engineering to determine the relationship between structure and function of microbial populations and wastewater treatment performance. Additionally, the Wuertz group detects pathogens in storm water runoff using hollow-fiber ultrafiltration technology and quantitative real time PCR. In addition, *Bacteroides* and *E. coli* are explored as cultivation-independent and –dependent marker organisms for microbial source tracking to distinguish between human and non-human fecal contamination.

NIH FELLOW: Robin GrayMerod

Plasmid DNA Uptake in Biofilms: Facilitating the Bioenhancement of Wastewater Treatment

Presenter:	Robin GrayMerod*
Authors:	Robin GrayMerod and Stefan Wuertz
Affiliations:	Department of Civil and Environmental Engineering, University of California, Davis

Natural transformation, a means of horizontal gene transfer, has been shown to be a potential technique for bioaugmentation in biofilm bioreactors for wastewater treatment. Such a method targets indigenous microbes competent for natural genetic transformation with naturally occurring plasmids containing biodegradative genes to facilitate the degradation of xenobiotic and recalcitrant compounds. *Acinetobacter* sp. BD413, a well-characterized bacterial strain capable of forming relatively homogenous biofilms and displaying a high frequency of transformation is used as the model organism in lab-scale experimentation. Clay is being investigated for its potential as a carrier material for plasmid DNA destined for genetic transformation. Clay particles have been shown to not only protect free DNA from degradation by environmental factors but also positively affect biofilm architecture, activity, and resistance to stress while increasing wastewater treatment performance. Since very little is known about the relation between biofilm architecture and transformation efficiency we are examining biofilm structure and its potential to play a role in influencing the efficiency of genetic transformation. Additionally, while a monoculture BD413 biofilm has been shown as a potential technique for the method of plasmid-mediated bioenhancement, the potential of BD413 has not been investigated in a mixed culture biofilm. Thus we will investigate the feasibility of plasmid-mediated bioenhancement of BD413 with the plasmid pWDL7 in a mixed culture biofilm and subsequent removal of 3-chloroaniline. Current results concerning biofilm monitoring and reproducibility will also be presented.

* Member of the DEB graduate group

COMPANY AFFILIATE: Novozyme Biotech, Inc.

Novozymes: Unlocking The Magic Of Nature

Sandra T. Merino
Senior Scientist
Novozymes, Inc.
1445 Drew Avenue
Davis, CA

Novozymes is the biotech-based world leader in enzymes and microorganisms, having developed over 600 products that are used every day around the world. In January of 2001, Novozymes began work on a DOE-sponsored contract to reduce, by a factor of ten, the cost of enzymes used in the conversion of lignocellulosic waste to ethanol. Over the past four years we have utilized all the biotechnological tools at our disposal to discover new, more efficient cellulase enzymes and to improve enzyme production to meet this challenge. This talk will describe some aspects of this work and our role in making cellulosic ethanol a significant fuel in the years to come.

OVERVIEW OF LAB RESEARCH: Abdul I. Barakat & Tim Cao

Barakat Laboratory

Abdul I. Barakat
Associate Professor, Mechanical and Aeronautical Engineering
University of California, Davis

Research in Dr. Barakat's Biofluids and Cellular Mechanics Laboratory focuses primarily on the following four areas:

(1) Elucidating the role of arterial fluid mechanics in the development and progression of atherosclerosis: The pathological complications of atherosclerosis, namely heart attacks and strokes, are a leading cause of mortality. Early atherosclerotic lesions develop preferentially in regions of arterial branching and curvature where blood flow is multi-directional and highly disturbed. The goal of our studies is to elucidate the basis of atherosclerotic lesion development in regions of disturbed flow. To this end, we perform both macroscopic (whole vessel) and microscopic (cellular) studies. The macroscopic studies involve experimental and computational studies of arterial flow fields and of the transport of macromolecules within the arterial wall. The microscopic studies use a combination of experimental and computational methods to probe the impact of fluid mechanical forces on the structure and function of vascular endothelial cells, the cells lining the inner surfaces of blood vessels. A related project involves investigations of targeted endovascular drug delivery and the enhancement of drug delivery capabilities via acoustic modalities.

(2) Understanding the role of flow in regulating trophoblast cell migration during pregnancy: During pregnancy, fetal trophoblast cells invade and migrate within maternal spiral arteries. This process is essential for the proper development of the fetal unit. A particularly interesting aspect of trophoblast cell migration within spiral arteries is that it occurs with the trophoblast cells moving on arterial endothelium in a direction opposite to that of blood flow. The goal of our research is to establish the mechanisms governing trophoblast counter-flow migration. Within this context, we are interested in the effect of flow on trophoblast cells and spiral artery endothelial cells as well as in the mechanisms governing communication between these two cell types.

(3) Optimizing the performance of endovascular stents: The placement of a stent within an arterial segment injures underlying vascular endothelium. It is essential for the endothelial injury to heal sufficiently rapidly in order for the stenting procedure to be successful. We have recently shown that the body of the stent significantly disturbs the flow field in the vicinity of the stent. Moreover, the detailed nature of the flow disturbance depends on the design of the stent. Therefore, one goal of our research is to optimize stent design in order to minimize the extent of flow disturbance. An additional objective is to understand the impact of flow disturbance on endothelial cell wound healing.

(4) Impact of metal-based nanoparticles on endothelial cells: Epidemiological studies demonstrate that exposure to fine particulate matter is associated with enhanced cardiovascular mortality. We are investigating the impact of metal-based nanoparticles on inflammation in vascular endothelial cells. Of particular interest is the dependence of the inflammatory response on nanoparticle composition and the mechanisms governing nanoparticle-induced inflammation.

NIH FELLOW: Tim Cao

Trophoblast-Endothelial Interactions *In vitro*: Redistribution of Intercellular Adhesion Molecule-1 (IC AM-1) in Uterine Microvascular Endothelial Cells (UtMVEC) Under Flow

Presenter: Abdul I. Barakat

Authors: Tim C. Cao*, Arlen Soghomonians, Twanda L. Thirkill, Gordon C. Douglas, and Abdul I. Barakat,

Affiliations: Department of Biomedical Engineering, University of California, Davis

A poorly understood but crucial event during human fetal development is trophoblast cell invasion and remodeling of the uterine vasculature. Abnormalities in trophoblast remodeling of the uterine endothelium are associated with pregnancy complications such as pre-eclampsia and intrauterine growth restriction. In this study we used an *in vitro* coculture system, consisting of macaque trophoblasts cultured on top of uterine microvascular endothelial cells, to investigate trophoblast-mediated endothelial remodeling under shear stress conditions. Using immunocytochemistry and image analysis, we observed that endothelial ICAM-1 was redistributed towards the downstream edge when the cells were cocultured with trophoblasts under a steady shear stress of 15 dyn/cm^2 for 24 h. This ICAM-1 asymmetry was less pronounced at 7.5 dyn/cm^2 for 24 h, and not observed when cocultures were maintained under static conditions or when endothelial cells were cultured alone under steady shear stress conditions. Redistribution of ICAM-1 to the downstream edge was also observed when endothelial cells were incubated with trophoblast-conditioned culture medium and subjected to flow, although the extent of the redistribution was not as great as that seen under coculture conditions. These data suggest that endothelial ICAM-1 expression is regulated by direct contact with trophoblasts and as yet unknown secreted factors. Analysis of cocultures by confocal microscopy showed that some trophoblasts had penetrated and migrated under the endothelial monolayer. The incidence of sub-endothelial trophoblasts was greater under flow than under static conditions. ICAM-1 asymmetry has been associated with endothelial cell migration, and ICAM-1 plays a major role in leukocytic and metastatic transmigration across endothelium. We therefore speculate that trophoblasts and fluid shear induce uterine endothelial mobility, which reduces the extent or strength of endothelial cell-cell adhesion and facilitates penetration of the monolayer by trophoblasts during placentation.

* Member of the DEB graduate group

OVERVIEW OF LAB RESEARCH: Earl Sawai & Kit S. Lam/Scott Wong

Sawai Laboratory

Earl Sawai
Med: Pathology
University of California, Davis

Our lab is focused on characterizing the biologic and biochemical function(s) of the regulatory protein Nef from HIV-1 and SIV. Using a molecular genetic approach we determine whether specific Nef functions are important for viral replication. To investigate whether these functions are critical for development of disease, we utilize the SIV/rhesus macaque model for simian AIDS.

We have discovered that a cellular serine-threonine kinase, p21-activated kinase (PAK), associates and with and activates both HIV-1 and SIV Nef. Our studies using SIV Nef mutants indicate that there is a strong correlation between the ability of SIV Nef to associate with PAK and the induction of high viral loads and disease in SIV-infected rhesus macaques. We are mapping the domains of both HIV-1 and SIV Nef that are important for PAK association and activation. By using SIV/HIV Nef chimeras, where specific domains of Nef can be swapped. We are characterizing the functional differences between HIV and SIV Nef domains. Recently we have identified another domain on the N-terminus of Nef that is important for binding a different cellular serine kinase. Studies are underway to map this region.

We are also studying the structure-function relationship between the cytoplasmic tail of HIV-1 and SIV envelope protein and Nef. We have discovered that the cytoplasmic tail of HIV-1 and SIV envelope is capable of downregulating the Nef-associated kinase activity in a dose dependent manner. Current work focuses on mapping the domains of the cytoplasmic tail that are important for this inhibitory activity.

Our goal is to develop novel therapeutic approaches to inhibit HIV replication and disease progression. Because Nef is an important determinant of pathogenesis, it serves as an attractive target for antiviral approaches. In collaboration with Kit Lam, we are screening one bead-one compound combinatorial small molecule libraries for compounds that bind to HIV-1 and SIV Nef. Small molecules identified in these binding assays will be tested for their ability to inhibit Nef functions such as Nef-PAK interactions. These compounds will also be tested for their ability to inhibit viral replication in T cell lines and peripheral blood mononuclear cells (PBMCs).

NIH Fellow: Scott Wong

Identification of Small Molecule Inhibitors of the Simian Immunodeficiency Virus Nef and the Cellular p21-Activated Kinase

Presenter: Scott Wong
Authors: Scott Wong*[1], Ruiwu Liu[2], Alan Lehman[2], Erwin Antonio[1], Michael Ye[1], Kit Lam[2], Earl Sawai[1].
Affiliation: Department of Pathology and Laboratory Medicine[1], Department of Hematology /Oncology[2], University of California, Davis, CA, 95616

Nef, a viral protein encoded by the Simian Immunodeficiency Virus (SIV) and the Human Immunodeficiency Virus (HIV), is capable of enhancing virion infectivity, down-regulating CD4 and MHC-I proteins from the cell surface and participating in cellular activation. We have shown that Nef binds and activates a member of the p21-activated kinase (PAK) family, a group of cellular serine-threonine kinase. Earlier *in vivo* studies with SIVΔnef mutations result in pathogenic revertants that restore PAK binding by generation of truncated forms of Nef. The selection for this Nef mutant demonstrates the importance of this interaction for the virus.

To further study the Nef-PAK interaction, we have identified small molecule compounds that inhibit PAK activation by Nef. We have expressed and purified wild-type SIV Nef in *E.coli* as a poly-hisitidine tagged fusion protein. Recombinant SIV protein was used to screen one-bead one-compound combinatorial small molecule libraries to identify ligands that bind Nef.

After screening 400,000 compounds from 3 different libraries, we have identified small molecules that bind to SIV*mac239* Nef. Compounds were tested for their ability to inhibit Nef mediated PAK activation using an *in vitro* kinase assay on COS7 cells transfected with SIV and HIV Nef. One compound was found to inhibit a kinase bound to the N-terminus of SIV Nef. Another family of ligands was found to inhibit SIV and HIV Nef activity by reducing Nef associated PAK auto-phosphorylation. These compounds can also inhibit the Nef-PAK interaction with *in vitro* kinase assay performed on SIV infected cultures. We will next determine if inhibiting the Nef-PAK interaction in SIV infected cells will affect viral replication, infectivity and CD4/MHC-I down-regulation assays. If these compounds are effective in cultures, testing will continue *in vivo* with the rhesus macaque model for SIV pathogenesis. It is hoped that compounds identified in these studies will represent a new class of HIV inhibitors.

* Member of the DEB graduate group

COMPANY AFFILIATE: Agilent Technologies

Protein Microarrays for Cardiovascular Research

Maggie Bynum
Scientist
Agilent Technologies
Palo Alto, CA 94306

After a brief overview of Agilent Technologies, I will describe a collaborative project between Agilent Labs and Stanford University.

The identification and quantification of proteins are essential for understanding molecular events leading to disease. We have fabricated an antibody microarray to detect serum proteins related to cardiovascular disease. Using proprietary thermal inkjet technology, we print eight identical arrays on surface-modified microscope slides. The array selectively captures 37 proteins from serum with bound monoclonal antibodies. Captured proteins are detected with labeled secondary antibodies. Results will be shown demonstrating the multiplexed protein measurement is potentially a valuable tool for the study of cardiovascular disease.

COMPANY AFFILIATE: Chiron Corporation

Novel Antibody and Small-Molecule Oncology Therapeutics

E. J. Moler
Chiron Research
Chiron Corporation
4560 Horton Street
Emeryville CA 94608

Chiron is applying an advanced understanding of cancer and infectious disease to create high-value products that address major medical needs. The company has maintained and broadened its focus on infectious-disease research since its groundbreaking work with hepatitis B antigens in the early 1980s. Since introducing the cancer therapy Proleukin® (aldesleukin) interleukin-2 to the market in 1992, Chiron has been committed to expanding its research and development of products for cancer patients.

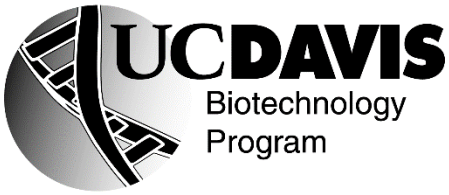
Chiron has initiated Phase I and II trials for antibody and small-molecule based cancer therapies. An overview of these novel therapeutic agents will be presented.

COMPANY AFFILIATE: Arcadia Biosciences

Arcadia Biosciences – Current Projects

Maris Apse
Principal Scientist, Project Lead – Salt Tolerant Plants
Arcadia Biosciences
Davis, CA 95616

Arcadia Biosciences is an ag-biotech startup company in Davis. Arcadia seeks to develop technologies whose application benefits the environment or enhances human health. Current projects at Arcadia include salt-tolerant plants, nitrogen use efficient plants, and omega-6 fatty acid enriched plant oils. Overviews of each of these projects will be discussed, with an additional emphasis on the development and advances of the salinity tolerance technology in crop plants.



Bioethics

September 2, 2003

Going to Great Lengths

By VIRGINIA POSTREL

Getty Images

The Food and Drug Administration recently approved a new use for biosynthesized human growth hormone: treating unusually short children who don't have any other known disorder. In clinical studies, the drug, which is called Humatrope and made by Eli Lilly & Company, added several inches to kids' eventual height without producing any significant health risks. Humatrope, in other words, met the regulatory tests for safety and efficacy. But bioethicists greeted the decision with protests.

"We will start to treat the normal as a disease," Arthur Caplan of the University of Pennsylvania told The Washington Post, adding that "whenever you take people on the low end of a distribution curve and say they have a disorder, you're starting down a slippery slope."

It does seem ridiculous to treat otherwise healthy short people as disabled. A man who is 5-foot-3 or a woman who is 4-foot-11 is hardly in the same position as someone who can't walk or see.

Still, being short does, on average, hurt a person's prospects. Short men, in particular, are paid less than tall men. The tall guy gets the girl. The taller presidential candidate almost always wins. And many parents desperately want Humatrope for their short children -- not to treat a "disease" but to make their kids' futures more pleasant. These parents care more about the real stigma of being short than about the theoretical stigma of calling shortness a disorder. If adding a few inches means accepting a medical diagnosis of excessively small stature, they'll do it. Why quibble about definitions?

One reason, of course, is insurance, which covers "diseases" but not discretionary treatments. If every new cure defines a new disease, the argument goes, the insurance system will eventually crash.

But insurance doesn't cover everything. Contracts can exclude care that, while life-enhancing, isn't essential. Most insurance doesn't cover Lasik eye surgery, for instance, even though it cures myopia.

The deeper dispute is cultural. We think some biological phenomena deserve treatment and sympathy and others don't. If you have chronic migraines, we'll help. If you're ugly, too bad. If we say that being short is treatable and offer medicine to change that biological fate, then we're saying there's something wrong with being short.

We need a new, less pejorative category: "biological conditions we don't like." Not diseases or disabilities, simply dislikes - conditions that keep us from being whom we want to be. We can treat dislikes without shame. Or we can leave them untreated without entitlement. Otherwise, we will label everything we don't like a disease, no matter how absurd the consequences. The law is already headed in that direction.

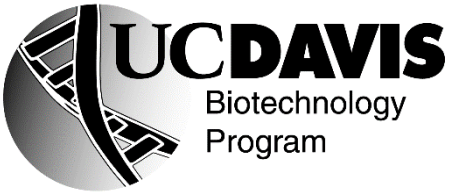
Consider a complaint filed by the Equal Employment Opportunity Commission in March charging an Alabama McDonald's franchise with violating the Americans With Disabilities Act. The restaurant had refused to let Samantha Robichaud, whose face is almost entirely covered with a port-wine-stain birthmark, work the front counter. Robichaud had held other jobs in the restaurant, but promotion to management requires experience in several positions, including the front counter. The E.E.O.C. claims that she was told she would never be promoted because of her appearance.

"The opportunity to make a living and succeed in the workplace is not restricted to models and movie stars but is the promise held out to every person with talent, skills and ambition," said Charles E. Guerrier of the E.E.O.C's Birmingham office.

The litigation is still pending, but Robichaud's lawsuit is a classic example of "hard cases make bad law." The E.E.O.C. is using a sympathetic client to outlaw a perfectly natural, if unkind, phenomenon: preferring good-looking employees to unattractive ones. The agency is effectively trying to define ugliness as a disease. Looks are, after all, a biological condition. But so, to some extent, are intelligence and personality. So, to some extent, is every trait that distinguishes one person from another. At the end of this slippery slope is a rule that says that the only fair way to choose employees is by random draw. Nobody wants to go down that road.

Better, then, to rethink the way we've conflated medicine and moral judgment. Biological fate doesn't just give us disabilities and disorders. To a large degree, it gives us who we are. Our bodies are us. Yet our inner selves do not always match our physical forms. Our bodies impose definitions and limitations that falsify our identities and frustrate our purposes.

Writing about her own and other people's experiences with plastic surgery, the author Joan Kron refers to "those of us who feel misrepresented by our faces." Those false faces are not diseased, disordered or disabled. But that doesn't mean we don't want the power to change them.



Poster Abstracts

A. "*EGFR* and *K-RAS* mutations in bronchioalveolar carcinoma (BAC) from patients treated with the EGFR inhibitor gefitinib on the Southwest Oncology Group (SWOG) S0126 trial."

Honglin Chen*, Will S. Holland, Wilbur A. Franklin, Jason McCoy, Kari Chansky, John J. Crowley, David R. Gandara, and Paul H. Gumerlock.
UCD, University of Colorado, and Southwest Oncology Group Statistical Center.

Background: S0126 was a phase II trial testing *EGFR* inhibitor gefitinib in BAC, an uncommon non-small cell lung cancer subtype with distinctive epidemiological, clinical, pathologic, and radiographic characteristics. Molecular markers in the EGFR: HER2-Ras-Raf-MeK-MAPK pathway have been examined for prognostic and predictive value under the influence of gefitinib therapy in BAC patients. Gandara et al (Clin Cancer Res, 2004) reported that high level of p-MAPK is correlated with poorer survival following the treatment of ZD1839 in S0126. We hypothesized that oncogenic mutations in *EGFR* or *K-RAS*, exclusively, may be the potential cause for activation of the MAPK pathway, high levels of p-MAPK, and failure to benefit from gefitinib in S0126. **Methods:** DNA was extracted from 64 pre-treatment, paraffin-embedded tumor tissues. Mutations in the exons 18, 19 and 21 in EGFR, and codon 12^{th} and 13^{th} in Kras were examined based on methods described by Lynch et al., and Davis et al., respectively. Mutations were confirmed by direct sequencing using an automated DNA sequencing approach. Results were correlated with patient clinical data. **Results:** EGFR mutations were found in 8 (8/62=13%) patients, with 6 containing point mutations at either codon 858 or 861 or both in exon 21, 1 at codon 719 in exon 18, and 1 deletion mutation in exon 19. Three EGFR mutation patients showed partial or complete response to the treatment of gefitinib. Out of 64 patients, 19 mutations (30%) in Kras codon 12^{th} were identified, but none in codon 13^{th}. The mutations were found marginally correlated with smoking history (p=0.08) with an equal frequency of G to T transversion and G to A transition. 18 patients containing Kras codon 12^{th} mutation did not respond to the gefitinib therapy. The overall survival curve after 26 months of administration of gefitinib showed a split of patients with Kras mutation and those with wt Kras, but not statistic significant (P=0.53). The correlations of *EGFR* and *Kras* mutations with the high level of nMAKP and poor survival are ongoing. **Conclusions:** 1) This study demonstrates that mutations in *EGFR* and *Kras* occur relatively frequently in BAC patients. 2) The value of Braf mutations in prognostic and prediction of the outcome of gefitinib treatment is ongoing 3) Correlation of these molecular findings with patient histology, response and overall survival is ongoing (The Hope Foundation, CA32102, CA38926, U10 CA46441)

* Member of the DEB graduate group

B. "A Multi-Scale Investigation of alcohol and biomembrane interactions"

Allison Dickey* and Roland Faller
Chemical Engineering and Material Science, University of California, Davis, CA 95616

The first line of defense for a cell against intrusive extracellular molecules is the lipid membrane. This protective barrier must be resilient to prevent unwanted small molecules from passing through the membrane because a change in the delicate intracellular ion balance could be detrimental to the cell. Experimentally, it has been shown that as the chain length and concentration of alcohols near the membrane increase, the area per lipid expands, increasing the likelihood of membrane permeation.[1] We use molecular dynamics to study the interactions between short-chain alcohols and a pure DPPC lipid bilayer using both atomistic and coarse-grained models. Using an atomistic model, we characterize the effect of alcohol chain-length and concentration on the mechanical properties of the lipid bilayer through parameters such as area per head group, order parameter, and density profile. These interactions are also of interest to wine producers because of a problem known as a stuck fermentation. It is suggested that this occurs when yeast transmembrane proteins are denatured as a result of an increase in lateral pressure from alcohols interacting with the lipid bilayer.[2] We also examine the effects of lipid\alcohol interactions on membrane curvature and use a coarse-grained model[3] to reach relevant scales.

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* Member of the DEB graduate group

C. Chemotaxis of *Pseudomonas* SP.ADP to the Herbidcide Atrazine

Xianxian Liu*, and Rebecca Parales
Section of Microbiology, University of California, Davis

Atrazine is a widely used man-made herbicide. Several recent studies have reported its negative impacts on amphibians and mammals, and concerns about residual atrazine in the environment are increasing. The atrazine-degrading bacterial strain *Pseudomonas* sp. ADP utilizes atrazine as its sole nitrogen source, mineralizing it in the process. Chemotaxis is a behavioral response that allows bacteria to sense and locate specific chemicals in the environment. The goal of this research project is to characterize the chemotactic responses of atrazine-degrading bacteria and determine whether chemotaxis plays a role in the biodegradation of atrazine. Using quantitative capillary assays and temporal assays, we have shown that atrazine and the atrazine metabolites cyanuric acid and N-isopropylammelide are chemoattractants for *Pseudomonas* sp. ADP. ADP cells grown either in the presence or absence of atrazine were attracted to all three chemicals, indicating that the chemotactic response is constitutively expressed in *Pseudomonas* sp. ADP. Genes encoding atrazine degradation enzymes are located on a large catabolic plasmid in strain ADP. We have demonstrated that a cured strain, ADP-M1, which does not contain the atrazine catabolic plasmid, also responds to atrazine, cyanuric acid and N-isopropylammelide as chemoattractants. These results indicate that specific genes required for atrazine chemotaxis are not carried on the atrazine catabolic plasmid. In addition, the results demonstrate that atrazine metabolism is not required for the chemotactic response, because ADP-M1 is unable to degrade atrazine. Therefore, atrazine must be detected directly. We are currently developing strategies to identify the specific protein that functions as the atrazine chemoreceptor.

* Member of the DEB graduate group

D. Identification of Active Site Residues Responsible for Regiospecificity in Nitrobenzene 1,2-Dioxygenase

Kou-San Ju* and Rebecca E. Parales
Section of Microbiology, University of California, Davis, CA, 95616

Contamination of soil and groundwater with nitroaromatic compounds poses a significant risk to human health due to their acute toxicity and suspected carcinogenicity. In addition, nitroaromatic compounds are recalcitrant to biodegradation because the electron-withdrawing nature of the nitro-groups renders them resistant to electrophilic attack. *Comamonas* sp. strain JS765 is unique in its ability to use nitrobenzene for carbon and energy by an oxidative pathway. Nitrobenzene 1,2-dioxygenase (NBDO) is the key enzyme that specifically attacks nitrobenzene at the nitro-substituted carbon, forming catechol. In an effort to identify the determinants of NBDO specificity, we generated variants of NBDO with amino acid substitutions at the active site. Oxidation of nitrotoluenes and nitrochlorobenzenes was tested using recombinant strains expressing the wild-type and mutant dioxygenase genes. These substrates provide several possible oxidation sites (methyl group; unsubstituted aromatic ring carbons; nitro-substituted carbon; chloro-substituted carbon). Analysis of the reaction products by GC-MS showed that wild-type NBDO preferentially targeted the nitro-substituted carbons of most of the tested substrates, forming methylcatechols or chlorocatechols. Amino acid substitutions at positions 258 and 350 of the oxygenase large subunit increased oxidation at the chloro-substituted positions of nitrochlorobenzenes (to form nitrocatechols) and at the methyl groups of nitrotoluenes. The results suggest that Asn-258 and Ile-350 are critical for controlling enzyme regiospecificity. Differences in substrate regiospecificities between wild-type and mutant enzymes reflect changes in the chemical environment of the active site that can be correlated with crystal structures of NBDO containing bound nitrobenzene or 3-nitrotoluene.

* Member of the DEB graduate group

E. Zinc Deficiency Induced Disruption of Iron Metabolism: Changes in Cellular Iron, IRE/IRP Binding, and Proteins Involved in Iron Uptake and Storage

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Zinc deficiency is associated with a number of pathologies, including inappropriate apoptosis that results from multiple biochemical lesions at the cellular level. A consistent observation of Zn deficiency is the accumulation of iron in multiple tissues, including testis, liver, kidney, and spleen. The oxidative stress associated with Zn deficiency may be a result of an increased iron load. However, the mechanisms behind this rise in Fe are unknown. In this study, we examined the mechanisms underlying Fe accumulation during Zn deficiency. 3T3 cells were cultured in Zn depleted (-Zn; 0.5 μM Zn), Zn Supplemented (+Zn; 50 μM Zn) or untreated (Con) media. After 24h of culture, -Zn cells were characterized by a 50% decrease in intracellular Zn, and 35% increase in intracellular Fe relative to cells in the +Zn and Con groups. The increase in cellular Fe was associated with a significant increase in levels of transferrin receptor (TfR) and ferritin L proteins. This is most likely the source of iron accrual, as it was found that DMT1 mRNA levels were decreased. Examination of -Zn cells indicated increased IRP-2, and decreased IRP-1 binding, respectively, to a consensus IRE. Accumulation of IRP-2 has been previously noted with increases in Nitric Oxide (NO) levels. Increased NO measured by DAF fluorescence was measured in the –Zn cells. Thus, we suggest that the Fe accumulation that is characteristic of Zn deficiency is due in part to increased TfR levels resulting from differential IRE/IRP regulation possibly due to NO-induced changes in IRP-2 levels

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F. Regulated Plant Viral Amplicon System for Expression of Recombinant Proteins in Plant Cell Cultures

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The human protein alpha-1-antitrypsin (AAT) is genetically engineered into tobacco plant cells to investigate the feasibility of human protein production using recombinant plant cell cultures. AAT is produced using three different production systems; a constitutive, an inducible, and a viral amplicon system. In the constitutive system the CaMV 35S promoter drives the production of AAT. In the inducible system, the XVE promoter[1] which is activated in the presence of estradiol is used to directly drive the production of AAT. In the plant viral amplicon expression system, the complete *Cucumber mosaic virus* (CMV) genome is inserted into the plant genome with the AAT gene substituted for the native viral coat protein gene. Transcription of CMV RNA1 which codes for the 1a protein (a component of the viral replicase) is under the control of the XVE inducible promoter, while CMV RNA2 and RNA3 are constitutively expressed. Using this method, complete replication-competent virus will only be produced following induction. Using transient agroinfiltration of *Nicotiana benthamiana* tobacco leaves we have demonstrated that active rAAT is produced using the viral amplicon expression system following estradiol treatment at levels between 2-4% total soluble protein.

1. Zuo, J., Niu, Q.-W., and Chua, N.-H., An estrogen receptor-based transactivator XVE mediates highly inducible gene expression in transgenic plants. *The Plant Journal*, **2000**, 24: 265-273.

* Member of the DEB graduate group

G. Trophoblast-Endothelial Interactions *In vitro*: Redistribution of Intercellular Adhesion Molecule-1 (IC AM-1) in Uterine Microvascular Endothelial Cells (UtMVEC) Under Flow

Tim C. Cao*, Arlen Soghomonians, Twanda L. Thirkill, Gordon C. Douglas, and Abdul I. Barakat,
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A poorly understood but crucial event during human fetal development is trophoblast cell invasion and remodeling of the uterine vasculature. Abnormalities in trophoblast remodeling of the uterine endothelium are associated with pregnancy complications such as pre-eclampsia and intrauterine growth restriction. In this study we used an *in vitro* coculture system, consisting of macaque trophoblasts cultured on top of uterine microvascular endothelial cells, to investigate trophoblast-mediated endothelial remodeling under shear stress conditions. Using immunocytochemistry and image analysis, we observed that endothelial ICAM-1 was redistributed towards the downstream edge when the cells were cocultured with trophoblasts under a steady shear stress of 15 dyn/cm^2 for 24 h. This ICAM-1 asymmetry was less pronounced at 7.5 dyn/cm^2 for 24 h, and not observed when cocultures were maintained under static conditions or when endothelial cells were cultured alone under steady shear stress conditions. Redistribution of ICAM-1 to the downstream edge was also observed when endothelial cells were incubated with trophoblast-conditioned culture medium and subjected to flow, although the extent of the redistribution was not as great as that seen under coculture conditions. These data suggest that endothelial ICAM-1 expression is regulated by direct contact with trophoblasts and as yet unknown secreted factors. Analysis of cocultures by confocal microscopy showed that some trophoblasts had penetrated and migrated under the endothelial monolayer. The incidence of sub-endothelial trophoblasts was greater under flow than under static conditions. ICAM-1 asymmetry has been associated with endothelial cell migration, and ICAM-1 plays a major role in leukocytic and metastatic transmigration across endothelium. We therefore speculate that trophoblasts and fluid shear induce uterine endothelial mobility, which reduces the extent or strength of endothelial cell-cell adhesion and facilitates penetration of the monolayer by trophoblasts during placentation.

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H. Metabolic Engineering of Omega-3 Fatty Acids in Seed Oil

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Monsanto Company, Calgene Campus

Polyunsaturated fatty acids (PUFA) are nutritionally important fatty acids that have long been recognized for their biological activity. Current dietary guidelines suggest a balance of ω-6 and ω-3 PUFA of approximately 4:1. Dietary preferences and the availability of a low cost PUFA source have lead to an imbalance in the ω-6:ω-3 ratio in the typical American diet. Dietary balance could be addressed by the development of ω-3 containing functional foods. Current ω-3 sources are either costly to stabilize (algal, fish), come from a non-sustainable source (fish), or have low bioactivity (vegetable). Recent clinical studies showed that stearidonic acid (SDA), a plant-based ω-3, has ~4-fold improved bioavailability over current vegetable oil ω-3. Furthermore, SDA has higher chemical stability than algal and fish ω-3 oils, allowing for expanded applications in functional foods. An oilseed crop capable of producing SDA-rich vegetable oil could increase supply, lower cost, and provide the benefits of ω-3 to a growing world population. The fatty acid composition of crop plants is primarily controlled by the expression of fatty acid desaturases with different regiospecificities. These enzymes are ubiquitous in nature, however, crop species do not contain a Δ6 desaturase that is necessary for production of SDA. Accumulation of >20% SDA in canola oil was achieved by expression of a Δ6 and Δ15 desaturase under seed specific regulation.

I. Photochemical implications of tyrosine-176 substitutions in cyanobacterial and plant phytochromes

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Directed evolution of a cyanobacterial phytochrome (Cph1) was undertaken to elucidate the structural basis of its light sensory activity by remodeling the chemical environment of its linear tetrapyrrole prosthetic group. Our studies revealed a single tyrosine-to-histidine (YH) mutation that transformed phytochrome into an intensely red fluorescent biliprotein. Tyrosine-176 is conserved in the GAF domain of all members of the phytochrome superfamily, implicating its direct participation in phytochrome's primary photochemistry. To better understand how tyrosine-176 of Cph1 functions as a photochemical gate, it was subjected to saturation mutagenesis. Seventeen amino acid substitutions that yielded soluble proteins exhibited greatly altered spectroscopic properties, indicating that tyrosine-176 is essential for WT photochemistry. The YH mutation was introduced into representative plant phytochromes (Phy's), bacterial and fungal phytochromes (BphP's) and Cph2 class of phytochromes. Plant phytochrome YH mutants displayed reduced photochemistry and enhanced fluorescence, similar to those of the Cph1 mutant. By contrast, YH mutants of Bphs and Cph2s were not similarly altered indicating that bilin-protein interactions are different from Phy and Cph1 phytochromes. Transgenic Arabidopsis plant lines were constructed in which constitutively expressed YH alleles of plant phytochromes were introduced. The biological activity and subcellular localization of the YH transgenes will be presented.

This work was supported in part by the National Institutes of Health (GM068552-02), National Science Foundation Center for Biophotonics Science and Technology (PHY-0120999), and the University of California, Davis, Biotechnology Program.

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J. Localized Hormone Accumulation and Haustorium Development

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Most obvious phenotype associated with chemical signaling between plants is manifested by parasitic species of Orobanchaceae. The development of haustoria – an invasive root structure that allow hemiparasitic plants to transition from autotrophic to heterotrophic growth, is rapid, highly synchronous and readily observed *in vitro*. Haustorium development is initiated in aseptic roots of the facultative parasite *Triphysaria versicolor* when exposed to chemicals associated with host root exudates and rhizosphere bioactivity. Morphological features of early haustorium ontogeny include rapid cessation of root elongation, expansion and differentiation of epidermal cells into haustorial hairs, and cortical cell expansion followed by host root invasion and xylem differentiation.

We used a variety of approaches to assay localized changes in auxin and ethylene during early haustorium development. We show that auxin accumulation at the site of haustorium initiation results from a block in acropetal transport is critical early events in haustorium development. Auxin action induces ethylene biosynthesis and the two hormones in cooperation initiate epidermal hair proliferation and cortical cells expansion. Our experiments show that *T. versicolor* uses existing plant regulatory mechanism for realizing early haustorium development. Auxin and ethylene regulatory pathways have repeatedly been recruited in the association between plant roots and other organisms; this has now been extended to at least one association between roots of different plants.

The genetic determinants that distinguish parasitic from non parasitic plants have yet to be identified but presumably function at a stage prior to hormone action. In order to understand the genetic mechanism of haustoria formation we have created a subtractive libraries enriched with genes upregulated and downregulated by different haustoria inducing factors or by contact of host roots with roots of parasite. 10000 ESTs from the libraries have being sequenced and investigated in detail. The microarray experiments and analysis of others are under way.

This work was funded by NSF award # 0236545

K. Using Transposon Mutagenesis to Generate Fusion Protein Libraries

Amanda J. Fischer*, Aubrey Jones[Ω], and Joel R. Cherry[Ω]
UC Davis Biotechnology Training Program*, and Novozymes, Inc. [Ω]

A transposon-mediated insertional mutagenesis method has been established that combines the highly efficient Gateway™ sub-cloning system (Invitrogen) and the Transposon Mutation Generation System™ (MGS-Finnzymes). This method makes it possible to select for gene-targeted mutants, eliminating selection of clones containing transposon insertions outside of the gene of interest. In addition to complementing commonly employed mutagenesis techniques (e.g. error-prone PCR) used to generate libraries for directed enzyme evolution screens, this method was subsequently adapted to generate random-length fusion proteins for pathway engineering purposes. The mutagenesis libraries generated using this technology have randomly distributed, 15 bp in-frame insertions and a very low frequency of wild-type (un-mutated genes), thereby increasing the efficiency of screening. The β-glucosidase (BG) gene from *Aspergillus oryzae* was mutagenized and heterologously expressed in *Saccharomyces cerevisiae* for colorimetric screening. BG transposon mutants displayed a range of glucosidase activity, suggesting that this system was successful in altering BG's enzymatic activity. Libraries of BG and *H. insolens* Cel45A endoglucanase (EG) fusion proteins were generated and again heterologously expressed in *Saccharomyces cerevisiae* for colorimetric screening. In order to generate fusion protein libraries, transposon mutagenesis libraries were generated for both the BG and EG genes, and these libraries were subsequently ligated together at the transposon insertion site, leaving a unique NotI restriction recognition site. EG:BG fusion protein libraries were screened for both BG and EG activity and multiple active fusion proteins were identified. This form of transposon-mediated insertional mutagenesis will serve as a starting point for engineering systems that create other more useful (less deleterious) types of mutations including single aa insertions or deletions, single or multiple amino acid replacements, and serial truncations

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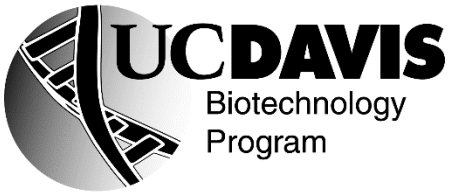

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**These Biotechnology companies have donated at least $20,000 per year for a Biotechnology fellowship, have offered an internship site for our Biotechnology graduate students and have presented at the annual Biotechnology Training Retreat. Company representatives also serve as advisors for training grants and other educational programs.

The success of our program depends on the continued support of our affiliates and the Biotechnology Program would like to thank them for their continued support.

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Our seven key product categories include microarrays; microfluidics; gas chromatography; liquid chromatography; mass spectrometry; software and informatics products; and related consumables, reagents and services.

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Amgen is a leading human therapeutics company in the biotechnology industry. For 25 years, the company has tapped the power of scientific discovery and innovation to dramatically improve people's lives. Amgen pioneered the development of novel products based on advances in recombinant DNA and molecular biology and launched the biotechnology industry's first blockbuster medicines. Today, as a Fortune 500 company serving millions of patients, Amgen continues to be an entrepreneurial, science-driven enterprise dedicated to helping people fight serious illness.

Over the past quarter century, Amgen has pioneered the methods by which human proteins that play a role in disease processes are identified, isolated, produced in quantity and used as therapeutics. Today, Amgen has research programs in inflammation, metabolic disorders and osteoporosis, neurology, oncology and hematology. The company has R&D facilities in Thousand Oaks, CA; San Francisco, CA; Cambridge, MA; Cambridge, UK; Regensburg, Germany; and Seattle, WA. With expertise in proteins, small molecules, antibodies, peptibodies, and nucleic acids, Amgen's scientists can pursue the study of disease, choose the best target for a disease and then use the modality most likely to have an effect on that target. This approach positions Amgen as one of the only companies with capabilities across a range of modalities. Mastering the tools of therapeutic development, as they emerge, is crucial to Amgen's ongoing success. Accordingly, the company has invested at least 20 percent of product sales in research and development each year since 1994—a total of approximately $2.0 billion in 2004.

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Berlex's singular approach to developing and making specialized medicines already has yielded innovations in treating multiple sclerosis, dermatological disorders, female health concerns, cancer and in the creation of new diagnostic imaging techniques. For the future, the pipeline of new products and the potential for developing better treatments will help make medicine work for those who need it most in the years ahead.

Whether you are a patient or caregiver, a physician, an investor, a job-seeker, or a neighbor, we hope this section will give you the information you need about the medicines we make today, and about the responsibility we have to the communities where we operate and to the families whose lives we touch.

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Mission
Chiron strives to be a leading biotechnology company by creating products that transform human health worldwide. We aim to prevent and treat diseases and improve people's lives.

Leadership Strategy
We will accomplish our mission through technological leadership, product-oriented research, superior manufacturing, and commercial strategies that create and expand markets.

Ethical Standards
We adhere to the highest legal and ethical principles in the conduct of all aspects of our business. We are committed to adhering to proven standards of financial and operational performance.

Values
Our purpose is to find solutions to human suffering caused by disease. Because disease does not wait for solutions, we are driven by a sense of urgency. As a result, our environment is intense, challenging, and focused on creating value for those who use our products and delivering sustained profitable growth for those who invest in our company.

Quality
Our goal at Chiron is to deliver quality products and services on time to all customers, internal and external. We provide employees with training and resources to meet or exceed customer requirements. We monitor processes and products to identify opportunities for continuous improvement.

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Genentech is a leading biotechnology company that discovers, develops, manufactures, and commercializes biotherapeutics for significant unmet medical needs. A considerable number of the currently approved biotechnology products originated from, or are based on, Genentech science. Genentech manufactures and commercializes multiple biotechnology products directly in the United States and licenses several additional products to other companies. The company has headquarters in South San Francisco, Calif., and is traded on the New York Stock Exchange under the symbol DNA.

Corporate Overview
Genentech, the founder of the biotechnology industry, is a company with a quarter-century track record of delivering on the promise of biotechnology. Today, Genentech is among the world's leading biotech companies, with multiple protein-based products on the market for serious or life-threatening medical conditions and over 30 projects in the pipeline. With its strength in all areas of the drug development process — from research and development to manufacturing and commercialization — Genentech continues to transform the possibilities of biotechnology into improved realities for patients.

Marketed Products:
Delivering innovative medicines to patients with serious or life-threatening medical conditions is what Genentech is all about. Since its beginning in 1976, the company has focused its drug discovery efforts on therapies that would fill unmet needs. Today, Genentech manufactures and commercializes multiple protein-based biotherapeutics for serious or life-threatening medical conditions — giving Genentech one of the leading product portfolios in the biotech industry.

Development Pipeline:
As a biotechnology leader, Genentech has a long-standing tradition of reinvesting a significant percentage of revenues back into research and development — a practice that has proved successful in transforming promising candidates into important new products. With the projects below under way, Genentech's development pipeline has never been more robust and promising. More than half of Genentech's pipeline is composed of potential antibody therapies.

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Calgene was founded in 1980 and is perhaps best known for the development of the first commercialized genetically engineered food, the FLAVR SAVR tomato. Monsanto acquired Calgene in 1997 and it is now a research and development site within Monsanto AG. Current research at Calgene focuses primarily on improving quality traits for feed and food, as well as nutritional approaches for the enhancement of health. Calgene has approximately 100 employees and it is the primary site within Monsanto for the canola biotech pipeline. Current projects include increasing the value of field crops by optimizing the micronutrient and oil profile of the grain. Several genomic-based approaches are being utilized for gene discovery. Functionality of candidate genes is then assessed in model systems. Examples of the use of genomic-based approaches to identify interesting gene leads will be presented.

Monsanto provides a wide array of integrated solutions to help meet the needs of growers and commercial customers who need to control unwanted vegetation safely and effectively. Monsanto also provides products to the dairy industry to increase the efficiency of milk production, and seeds for several cropping systems.

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Enzymes are the natural solution to industrial problems. With enzymes we can reduce the consumption of water, energy and harmful chemicals and still make production more efficient. Novozymes is the world leader in enzyme solutions. Based on an advanced biotech platform we produce and sell more than 500 enzyme products in 120 countries. Since 1941 Novozymes has introduced almost every new industrial enzyme on the market, making us the world's largest manufacturer of enzymes today. With our minds set on innovation, we will continue to be so in the future.

Novozymes has introduced, with few exceptions, every new enzyme to the industry, from lipases, which remove grease stains during washing, to amylases, which are used to manufacture sweeteners. In our work we use the following technologies: microbiology, bioinformatics, gene technology, protein chemistry, computer chemistry, directed evolution, fermentation and recovery technology.

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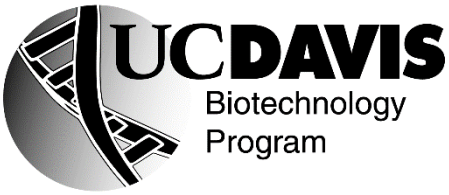
The overall objective of Scios' research program is to discover innovative new treatments for specific cardiorenal and inflammatory diseases and Alzheimer's disease. These disease areas are associated with substantial unmet medical needs. Scios scientists have developed an in-depth understanding of the molecular basis of these diseases and have discovered numerous product candidates, including those currently in the Scios clinical development pipeline.

The application of advanced technologies in the traditional areas of cellular and molecular biology, protein chemistry, medicinal chemistry, and pharmacology supports the ongoing discovery process. Over recent years, the Company has taken steps to develop and apply state-of-the-art platform technologies to facilitate the discovery of naturally occurring proteins and novel small molecules that can serve as potential new therapeutic agents. These technologies include genomics, combinatorial chemistry, high throughput screening and advanced models of diseases of interest. The application of these technologies has factored centrally in our success with numerous projects, like our P38-Kinase inhibitor program. In less than two years, our scientists have applied these advanced methods to identify highly potent and selective inhibitors of this key pro-inflammatory enzyme.



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Scott Wong
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Susanne Berglund
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Corey Dodge
Chemical Engineering & Material Science

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Plant Sciences-Vegetable Crops

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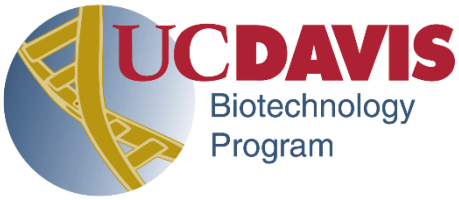

www.biotech.ucdavis.edu

The Mission of the Biotechnology Program:

The Biotechnology Program was created in 1986, to assist in the organization of university activities related to biotechnology and to coordinate such activities with other efforts on the Davis campus. It is a central facility of the Office of Research. The Program's missions include:

- Promoting and coordinating the development of biotechnology and biotechnology-related research on the campus;
- Assisting with development of new and improved facilities for biotechnology research;
- Promoting research interactions between faculty and private industry and public agencies;
- Recommending and implementing curriculum development and training in biotechnology;
- Serving as an information and education resource on biotechnology for the campus and the public.

The Program serves as the **Administrative Home** for pre-doctoral programs:

- Designated Emphasis in Biotechnology (**DEB**) www.deb.ucdavis.edu
- Advanced Degree Program (**ADP**) for corporate employees
  - A PhD program for the working professional
- NIH Training Program in Biomolecular Technology

Biotechnology Program Office:

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NIH Training Grant in Biomolecular Technology
July 1, 2002- June 30, 2007

UC Davis has been awarded a prestigious NIH training grant in biomolecular technology in recognition of the quality of multidisciplinary research and training provided by the campus. The grant is under the directorship of Bruce Hammock, Department of Entomology, and The Cancer Research Center with co-directors Karen McDonald*, Department of Chemical Engineering and Materials Science, and Associate Dean of the College of Engineering; and Martina Newell-McGloughlin, UC Systemwide Biotechnology Program, and Department of Plant Pathology. *Rosemary Smith was the original co-director from engineering, but she left campus in 2003. Karen McDonald is the current co-director from engineering.

The name, Biomolecular Technology, is chosen to reflect the emphasis of the program as an area of scientific endeavor, which is characterized by the following three elements:

1. Emphasis on the analysis of model systems of obvious significance to medicine and biotechnology;
2. The synthesis of information and research approaches from disciplines such as cellular physiology, genetics, physical biochemistry, and chemical engineering; and
3. The translation of biological information into a quantitative framework.

Through this focus the program provides well-coordinated multidisciplinary training of predoctoral graduate students in critical areas of biotechnology research and a structure for interdisciplinary research environments that integrate basic biological science and engineering disciplines as well as academic and industrial experiences. The program is designed to recruit and support trainees who show exceptional promise coupled with the drive to reach out across disciplines and forge new research directions in biotechnology.

The Faculty of the DEB have been successful in obtaining a NIH training grant within the time period of this review. The NIH Training Grant in Biomolecular Technology (1-T32-GM08799) was awarded on July 1, 2002 for 5 years. Having the formal DEB training program along with industrial internships definitely strengthened our grant proposal. Currently, there are 14 NIH biotechnology training grants funded nationwide and only three in California. UC Berkeley and Stanford have the other two grants in the State.

A question of the relationship between the DEB and the Training Program in Biomolecular Technology often arises. The answers are as follows:

- The DEB is a formal training program for the NIH Training Grant.
- The DEB provides training and a structure for interdisciplinary interaction, in addition to our established graduate programs.
- The DEB provides a formal accreditation (on diploma & transcript) to reflect biotechnology training in cross-disciplines.
- Not all the DEB students will be funded by the NIH Biotechnology Training Program. The fellows are a select subset based on a highly competitive nomination & selection process:
  1. Nomination by a Faculty Trainer and completion of an application by the student.
  2. Ranking by the Executive Committee of the NIH Biotechnology Training Program. It is based on: academic merit; quality of the research; interdisciplinary nature of research; and willingness to complete an internship.

Information about the NIH Biotechnology Training Grant is publicized on the DEB (www.ucdavis,edu) website. **2005-06 Fellowship Nominations are due on May 16, 2005 .**

NIH Training Grant Faculty

Directorship of Bruce Hammock
Co-Directors are Karen McDonald and Martina Newell-McGloughlin

Gary Anderson
Animal Science

Matthew Augustine
Chemistry

Enoch Baldwin
Molecular & Cellular Biology

Craig Benham
Biomedical Engineering / Genome Center

David Block
Chemical Engineering

George Bruening
Plant Pathology

Alan Buckpitt
VM: Molecular Biosciences

Kenneth Burtis
Molecular & Cellular Biology / Genome Center

Daniel Chang
Molecular & Cellular Biology

Abhaya Dandekar
Plant Sciences-Pomology

Michael Denison
Environmental Toxicology

Bryce Falk
Plant Pathology

Katherine Ferrara
Biomedical Engineering

Andrew Fisher
Chemistry

J. Bruce German
Food Science & Technology

Jeffrey Gregg
MED: Pathology

Daniel Gusfield
Computer Science

Bruce Hammock
Entomology / UCD Cancer Center

Alan Jackman
Chemical Engineering & Material Sciences

Ian Kennedy
Mechanical & Aeronautical Engineering

Hsing-Jien Kung
MED: Biochemistry / UCD Cancer Center

J. Clark Lagarias
Molecular & Cellular Biology

Kit Lam
MED: Hematology & Oncology/Chemistry

Kent Lloyd
VM:Anatomy, Physiology & Cell Biology

Marjorie Longo
Chemical Engineering & Material Sciences

Karen McDonald
Chemical Engineering & Material Sciences

Claude Meares
Chemistry

Juan Medrano
Animal Science

Richard Michelmore

Plant Sciences - Vegetable Crops

James Murray
Animal Science / Genetic Engineering Large Animals

Atul Parikh
Applied Science

Martin Privalsky
Microbiology

Robert Rice
Environmental Toxicology

David Rocke
Applied Science

Simon Scott
Biomedical Engineering

Kate Scow
Land, Air & Water Resources

Michael Toney
Chemistry

Jean VanderGheynst
Biological & Agricultural Engineering

Craig Warden
Neurobiology, Physiology & Behavior

David Wilson
Molecular & Cellular Biology

Stefan Wuertz
Civil & Environmental Engineering

John Yoder
Plant Sciences – Vegetable Crops

NIH Training Program in Biomolecular Technology

The DEB is a **formal training program** for the NIH Training Grant.

The DEB provides **training and a structure for interdisciplinary interactions**, in addition to our established graduate programs.

The DEB provides a **formal accreditation** (on diploma & transcript) to reflect biotechnology training in cross-disciplines.

Not all the DEB students will be part of the NIH Biotechnology Training Program. The fellows are a **select subset** based on a highly competitive nomination & selection process:

- Nomination by a Faculty Trainer and completion of an application by the student.

- Ranking by the Executive Committee of the Program based on academic merit, quality of the research, interdisciplinary nature of research, and a willingness to complete an internship.

Designated Emphasis in Biotechnology Program (DEB)

Goals and Mission of the DEB

The Designated Emphasis in Biotechnology (DEB) is an inter-graduate group program that allows Ph.D. students to receive and be credited for training in the area of biotechnology. The DEB provides a nurturing interactive environment to promote integration of multiple disciplinary approaches to the conduct of research and to promote learning in biotechnology. The mission is to prepare well-educated students to approach problems with creativity and flexibility. The program will provide tools for the students to be leaders, visionaries, entrepreneurs, researchers and teachers in the broad area of biomolecular technology.

DEB Mission:

To provide well-coordinated, cross-disciplinary training of graduate students in critical areas of biomolecular technology research.

To promote interdisciplinary research environments that integrate basic biological science, engineering and computational disciplines.

To allow cross-disciplinary training and trainee experience in a biotechnology company or cross-college laboratory.

Students come from a wide array of disciplines: Participating graduate programs currently include **23 programs**: Agricultural and Environmental Chemistry; Biochemistry and Molecular Biology; Biological Systems Engineering (formerly Biological & Agricultural Engineering); Biomedical Engineering; Biophysics; Cell & Developmental Biology; Chemical Engineering; Chemistry; Civil and Environmental Engineering; Comparative Pathology; Entomology; Genetics; Immunology; Materials Science and Engineering; Mechanical and Aeronautical Engineering; Food Science; Microbiology ; Molecular, Cellular and Integrative Physiology (formerly Physiology); Nutrition; Pharmacology & Toxicology; Plant Biology; Plant Pathology; and Statistics. The DEB program supplements a student's Ph.D. curriculum and those completing the program will obtain an official designation on their diploma & transcript indicating a qualification in biotechnology. Example: **Doctoral Degree in Microbiology with a Designated Emphasis in Biotechnology**

Brief History:

The DEB was formally established in 1997 as an outgrowth of the first NIH Training Grant in Biotechnology (funded in the early 1990s). The DEB became the formal training program for the current NIH Training Grant in Biomolecular Technology (1-T32-GM08799: July 1, 2002-June 30, 2007). The DEB provides a very effective multidisciplinary biotechnology concentration, which includes exposure to bioethics, business and legal aspects of biotechnology as well as a 3-6 month

internship in a biotechnology company or research laboratory in another college or national laboratory. As of December 2003, the DEB has 23 affiliated graduate groups or departmentally based graduate programs and we are in the process of adding Biostatistics and Electrical & Computer Engineering. The number of students in the Designated Emphasis in Biotechnology has increased dramatically over the last two years and now boasts over 50 members, with many being first year students. We have graduated 14 students with a DEB notation on their diplomas as of December of 2003.

Program Administration:

The administrative home for the DEB and the NIH Training Grant in Biomolecular Technology is the UC Davis Biotechnology Program. Dr. Judith Kjelstrom serves as the DEB and NIH Training Grant program coordinator for the DEB, in addition to directing the Biotechnology Program. She works closely with the DEB chair, Abhaya Dandekar (Department of Pomology) and the rest of the executive committee: Karen McDonald (Chemical Engineering and Materials Science), Robert Rice (Environmental Toxicology) and David Rocke (Applied Science/Biostatistics) to oversee the day-to-day activities of the graduate program.

Course Work:

The DEB has a required core curriculum for students regardless of whether their graduate major is in biological science, engineering, statistics, etc. A key feature of the DEB is its requirement for a research internship at a cooperating biotechnology company or a cross-college site. When the students complete their Ph.D. requirements as well as the DEB requirements, their diploma notes not only their graduate major, but also that they have completed the DEB (e.g., "Ph.D. in Chemical Engineering with a Designated Emphasis in Biotechnology").

We have created a website for the Designated Emphasis in Biotechnology (http://www.deb.ucdavis.edu/) to advertise the program as well as the NIH Training Grant. The announcement of the grant is on the site. Program information, forms, pictures and other pertinent information is listed on the site. We have linked the website to graduate home pages of most of the 23 DEB program affiliates in the Division of Biological Sciences, College of Engineering, College of Letters and Science and the College of Agriculture and Environmental Sciences.

1. **Course Requirements**:

a. **MCB 263** (2 units): Biotechnology Fundamentals and Application (winter quarter, alternate odd numbered years)

An interdisciplinary course which includes: introduction to modern recombinant DNA technology; rate processes of biological systems, optimization of bioreactor performance; practical issues in biotechnology; and some specific case studies of the development of biotechnology products and processes. Grading: Letter grade; two one-hour exams, one research paper (team project) on a selected topic relevant to biotechnology, and regular reading assignments.

b. **MCB 282** (variable): Biotechnology Internship (may be done any quarter)

The internship will expose qualified graduate students to research activities in a biotechnology company, to company culture, to legal and business aspects of industry, and to another career option. A minimum of 3 months internship at a local biotechnology company or cross college or national laboratory (i.e. Lawrence Berkeley Laboratory, Lawrence Livermore National Laboratory, etc.). S/U grading; research performance (student report) will be evaluated by the professor in charge and in consultation with the company trainer.

c. **MCB/ECH 294** (1 unit): Current Progress in Biotechnology (fall, winter and spring quarters). Three quarters of seminar are required for the DEB Program.

This course is an interdisciplinary seminar, featuring speakers from industry as well as academia. The students will have an opportunity to discuss the seminar topic with the lecturers, to learn about biotechnology research activities at companies and to network with speaker. Grading: S/U grading, attendance is required, and a summary report on the seminars is required at the end of the quarter.

d. **MIC 292** (1 unit): From Discovery to Product - An Introduction to Biotechnology at the Industrial Level. (winter quarter; even numbered years). MIC 292 is an approved **seminar elective** for the DEB program (may substitute for one quarter of MCB/ECH 294).

This course is designed to provide a unique opportunity to gain insight into basic and applied biotechnology at the industrial level. Lectures are presented by senior scientists from Novozymes Biotech, Inc. in Davis California (http://www.novozymesbiotech.com/). A tour of the industrial facilities will be arranged. Grading: S/U grading, attendance is required, and a summary report on the seminars is required at the end of the quarter.

e. **GGG 296** (2 units): Scientific Professionalism and Integrity (fall quarter)

The course will allow the student to become familiar with their roles and responsibilities as a professional scientist and/or instructor. While some standards of acceptable scientific behavior will be presented in class, most of the time will be spent discussing various "gray zone" scenarios, in which proper conduct is unclear. Grading: S/U grading; active class participation in class discussions is required. **This course is currently highly recommended, but will be required, pending approval.**

2. **Qualifying Exam Requirements**:

The Ph.D. qualifying exam should demonstrate appropriate knowledge with the area of biotechnology. At least one faculty member of the designated emphasis shall participate in the qualifying examination.

3. **Thesis Requirements**:

The dissertation committee shall include at least one faculty member of the designated emphasis. The major professor must be a participating DEB member.

4. **Additional Requirements**:

Regular attendance at the annual Biotechnology Training retreat and at the informal Pizza Chalk Talk Seminars (talks by students and faculty on current research) is expected.

DEB Program Students 2004-2005

Suzanne Balko
Chemical Engineering

Tian Bao
Chemical Engineering

Jason Bell
Biochemistry & Molecular Biology

Sandra Bennun Serrano
Chemical Engineering

Susanne Berglund (aka Kuhlman)
Microbiology

Craig Blanchette
Biophysics

Jerry Boonyaratanakornkit
Biochemistry & Molecular Biology

Monica Britton
Genetics

Tim Cao
Biomedical Engineering

Honglin Chen
Genetics

Jerome Diaz
Food Science

Allison Dickey
Chemical Engineering

Corey Dodge
Chemical Engineering

Amanda Enstrom
Immunology

James Evans
Biochemistry & Molecular Biology

Wen-Ying Feng
Statistics (Biostatistics Emphasis)

Amanda Fisher
Plant Biology

Robin GrayMerod
Civil & Environmental Engineering
Moraima Guadalupe
Comparative Pathology

Ze He
Chemistry

Laura Higgins
Molecular, Cellular & Integrative Physiology

Kevin Holden
Microbiology

Tamara Holst (aka Peoples)
Biochemistry & Molecular Biology

Jennifer Horner
Biochemistry & Molecular Biology

Yi-Hwa (Patty) Hwang
Biochemistry & Molecular Biology

Aminah Ikner
Biochemistry & Molecular Biology

Kou-San Ju
Microbiology

Michael Kareta
Biochemistry & Molecular Biology

Pinar Kocabas
Chemical Engineering

Jie-Ren (Jerry) Ku
Chemical Engineering

Pavan Kumar
Plant Biology

Nathaniel Leachman
Cell & Developmental Biology

Vannarith Leang
Chemical Engineering

Young Lee
Biochemistry & Molecular Biology

Xianxian (Janice) Liu
Microbiology

Wenshe Liu
Chemistry

Riccardo LoCascio

Microbiology

Ruixiao Lu
Statistics

Thomas Luu
Biochemistry & Molecular Biology

Caroline Meloty-Kapella
Cell & Developmental Biology

Ryann Muir
Plant Biology

Brad Niles
Nutrition

Gian Odonne
Chemical Engineering

Ying Peng
Genetics

Anh Phung
Biochemistry & Molecular Biology

Warren Place
Microbiology

Michael Plesha
Chemical Engineering

Wade Reh
Genetics

Rowena Romano
Biological Systems Engineering

Ahmad Rushdi
Electrical and Computer Engineering

Andres Schwember
Plant Biology

Daniel Scott
Chemistry

David Sela
Food Science

Jillian Silva
Biochemistry & Molecular Biology

Sheetal Singh
Biochemistry & Molecular Biology

Samir Singh
Chemical Engineering

Cheng Song
Cell & Developmental Biology

James Stice
Molecular, Cellular & Integrative Physiology

Alan Szmodis
Biophysics

Esra Talu
Chemical Engineering

Jennifer Taylor
Comparative Pathology

Vu Trinh
Biochemistry & Molecular Biology

Robert Ward
Food Science

Jennifer Weidhaas
Civil and Environmental Engineering

Scott Wong
Biochemistry & Molecular Biology

Andrew Wong
Genetics

Chun-Yi (Jimmy) Wu
Pharmacology & Toxicology

Liang Yang
Biochemistry & Molecular Biology

Melinda Zaragoza
Microbiology

Erin Zumstein
Biochemistry & Molecular Biology

DEB Faculty Participants

Agricultural & Environmental Chemistry
Linda Bisson
Andrew Clifford
Michael Denison
J. Bruce German
Bruce Hammock
You-Lo Hsieh
Fumio Matsumura
Krishnan Nambiar
Kate Scow

Biochemistry & Molecular Biology
Steffen Abel
Everett Bandman
Alan Bennett
Linda Bisson
Sean Burgess
Frederic Che□din
Ronald Chuang
Gino Cortopassi
Michael Denison
Charles Gasser
Bruce Hammock
Thomas Jue
Clarence Kado
Dan Kliebenstein
Stephen Kowalczykowski
Hsing-Jien Kung
J. Clark Lagarias
Kit Lam
Janine LaSalle
Su-Ju Lin
Paul Luciw
Claude Meares
Marty Privalsky
Robert Rice
Pam Ronald
Robert Rucker
Dewey Ryu
Earl Sawai
Kazuhiro Shiozaki
Henning Stallberg
Steven Theg
Valerie Williamson
David Wilson
Reen Wu
John Yoder
Glenn Young

Biological Systems Engineering
(formerly "Biological & Agricultural Engineering")
David Slaughter
Jean VanderGheynst
Ruihong Zhang

Biomedical Engineering
Abdul Barakat
Craig Benham
Roland Faller
Katherine Ferrara
Ian Kennedy
Tonya Kuhl
Kit Lam
Marjorie Longo
Claude Meares
Atul Parikh
Dewey Ryu
Scott Simon
Pieter Stroeve

Biophysics
Abdul Barakat
Craig Benham
John H. Crowe
Thorsten Dieckmann
Roland Faller
Andrew Fisher
Ching Yao Fong
Thomas Jue
Stephen Kowalczykowski
Tonya Kuhl
Janine LaSalle
Marjorie Longo
Atul Parikh
Scott I. Simon
Henning Stallberg
Steven Theg
Michael D. Toney
David Wilson
Yin Yeh

Cell & Developmental Biology
Gary Anderson
Everett Bandman
Ron Baskin
Frederic Che□din
Jason Eiserich
Paul FitzGerald
Su-Ju Lin
Bo Liu
Robert Rice
Reen Wu

Chemical Engineering & Materials Science Engineering
David Block
Stephanie Dungan
Nael El-Farra
Roland Faller
Tonya Kuhl
Marjorie Longo
Karen McDonald
Ron Phillips
Robert Powell
Dewey Ryu
Pieter Stroeve

Chemistry
Matthew Augustine
Alan Balch
Thorsten Dieckman
Andrew Fisher
Bruce Hammock
J. Clark Lagarias
Carlito Lebrilla
Claude Meares
Krishnan Nambiar
Michael Toney

Civil & Environmental Engineering
Daniel Chang
Stefan Wuertz

Comparative Pathology
Peter Barry
Stephen Barthold

Satya Dandekar
Jeff Gregg
Rivkah Isseroff
Kit Lam
Thomas North
Earl Sawai
Jay Solnick
Alice Tarantal
Jose Torres
Reen Wu
Tilahun Yilma

Entomology
Bruce Hammock

Food Science
Diane Barrett
Linda Bisson
David Block
Christine Bruhn
Stephanie Dungan
J. Bruce German
David Mills
Krishnan Nambiar
Robert Powell
David Reid
Dewey Ryu
Glenn Young

Genetics
Steffan Abel
Alan Bennett
Linda Bisson
George Bruening
Sean Burgess
Frederic Che□din
Douglas Cook
Gino Cortopassi
Abhaya Dandekar
Bryce Falk
Charles Gasser
David Gilchrist
Tom Gradziel
Stacy Harmer
Clarence Kado
Dan Kliebenstein
Stephen Kowalczykowski
Janine LaSalle
Su-Ju Lin
Juan Medrano
Richard Michelmore
James Murray
Marty Privalsky
Pam Ronald
Earl Sawai
Alison Van Eenennaam
Valerie Williamson
Reen Wu
John Yoder

Immunology
Satya Dandekar
Kit Lam
Jose Torres
Tilahun Yilma

Material Science & Engineering
Subhash Risbud

Mechanical & Aeronautical Engineering
Abdul Barakat
Ian Kennedy

Microbiology
Stephen Barthold
Blaine Beaman
Linda Bisson
Richard Bostock
George Bruening
Sean Burgess
Ronald Chuang
Satya Dandekar
Bruce Hammock
Paul Luciw
Clarence Kado
Stephen Kowalczykowski
Su-Ju Lin
Karen McDonald
David Mills
David Ogrydziak
Rebecca Parales
Marty Privalsky
Dewey Ryu
Earl Sawai
Kate Scow
Kazuhiro Shiozaki
Jay Solnick
Jose Torres
Tilahun Yilma
Glenn Young

Molecular, Cellular and Integrative Physiology *(formerly "Physiology")*
Gary Anderson
Christopher Calvert
Jason Eiserich
Dewey Ryu
John Rutledge
Judith Stern
Alice Tarantal
Barry Wilson
Reen Wu

Nutrition
Christopher Calvert
Andrew Clifford
J. Bruce German
Judith Stern

Pharmacology & Toxicology
Ronald Chuang
Gino Cortopassi
Michael Denison
Jason Eiserich
Bruce Hammock
Hsing-Jien Kung
Jerold Last
Fumio Matsumura
Robert Rice
Robert Rucker
Barry Wilson
Reen Wu

Plant Biology
Steffen Able
Diane Barrett
Alan Bennett
Richard Bostock
Kent Bradford
Douglas Cook
Abhaya Dandekar
Katayoon "Katy" Dehesh
Don Durzan
Bryce Falk
Charles Gasser
Tom Gradziel
Stacy Harmer

Dan Kliebenstein
J. Clark Lagarias
Bo Liu
Terence Murphy
Michael Reid
Pam Ronald
Valerie Williamson
John Yoder

Plant Pathology
Richard Bostock
George Bruening
Douglas Cook
Bryce Falk
David Gilchrist
Clarence Kado
Richard Michelmore
Pam Ronald
Steven Theg

Statistics
Andrew Clifford
Shu Geng
David Rocke

The Value of Internships

Over the last 13 years (even before the formal DEB program was established), we have placed pre-doctoral students in a variety of biotechnology companies for their industrial research experience. They include:

Agilent Technologies
Alza
Amgen
Bayer
Berlex Biosciences
Celera AgGen
Chiron
DuPont
Exelixis
Genentech
ICOS
Maxygen
Monsanto, Calgene Campus;
Novozymes Biotech
Scios
Syntex
Recovery Sciences
Roche Biosciences
Ventria Biosciences
and others

Industry Partners gain many things from internships:

- Access to highly talented creative researchers
- Opportunity to gain inside tract on future employees
- Through students, further collaboration with scientists on campus
- Participate in the annual retreat to meet UC scientists students, potential interns, other company scientists
- Potential to use UC facilities through the collaboration
- Opportunity to participate in weekly campus seminars

Students gain much from internships:

- Ability to work in a highly creative non-academic environment
- Opportunity to participate in focused team approach to defined research goals
- Ability to use equipment and facilities not available on campus
- Discover the type of environment, which suits future career goals
- Participate in industry seminars
- Enhanced curriculum vitae: reference letters and new skills
- Access to potential employment opportunities

Close to 70 students are currently enrolled, so we need more Academic-Industry Partnerships