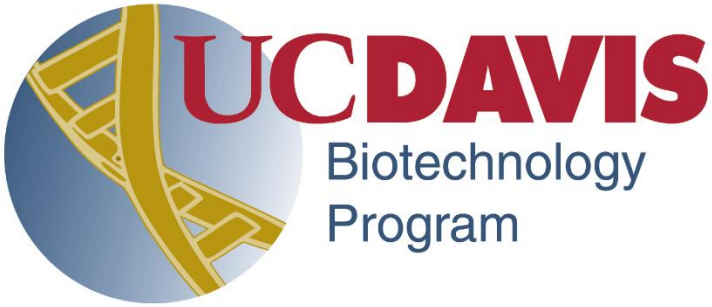


Thirteenth Annual

Biotechnology Training Retreat

Christian Brothers Retreat Center
Napa Valley

Saturday, March 27, 2004

**Co-Sponsored by the NIH Training Grant
in Biomolecular Technology
(NIH-1-T32-GM08799-01A1) and the
UC Davis Biotechnology Program**

The Thirteenth 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 2003-04 fellows and their preceptors, as well as our company affiliates. It is also a time to share good science, network with new people and old friends, and most of all …… enjoy good food & wine along with beautiful scenery.

Our biotechnology fellowships are highly competitive, so we want the biotechnology community to meet these scholars and share in their exciting research projects. Our **NIH Fellows** include: Craig Blanchette (preceptor is Marjorie Longo); Chad Green (preceptor is Scott Simon); Larry Joh (preceptor is Jean VanderGheynst); and Scott Wong (preceptors are Kit S. Lam/Earl Sawai). Amanda Ellsmore (preceptor is J. Clark Lagarias) and Bob Ward (preceptor is J. Bruce German) are our **Biotechnology Fellows** (industry and campus fellowships). We will be selecting our 2004-05 fellows in May. Fellowship nominations are due on April 19, 2004 and forms can be downloaded from the DEB website (www.deb.ucdavis.edu).

We would also like to recognize our **first year Biotechnology Fellows:** Michael Cabbage (Plant Biology); Katherine Chang (Biological & Agricultural Engineering); Allison Dickey (Chemical Engineering); and Alan Szmodis (Biophysics). Due to the limited time for oral presentations, we will showcase research performed by other students in the DEB program in the poster session. Please congratulate all of these outstanding predoctoral candidates.

We have a few program updates. We are completing our second year of the NIH Biotech Training Grant and a seven-year review of the DEB graduate program. As a reminder, the DEB graduate program is the formal training program for the NIH training grant. In the spring of 2003, Prof. Rosemary Smith moved to Maine, so Prof. Karen McDonald was named as her replacement as a co-director on the Training Grant. As for the DEB program, Prof. Abhaya Dandekar and the rest of the executive committee have been working for months on the self-review of the program and we still have a 2-day site visit to complete on April 20 and 22. We really need help… please sign up.

The DEB program now boasts 23 graduate programs with close to 100 faculty trainers. The number of DEB students has more than doubled in the last two years to over 60 active members. We placed students in a wide variety of internship sites over the last year: Berlex Biosciences (Marisa Wong); CAH&FS (Angelica Giuffre); Gladstone Institute at UCSF (Moraima Guadelupe) ICOS (Chad Green); Monsanto (Alberto Iandolino); Novozymes Biotech (Vidhya Ramakrishnan); and Scios (Edwin Hagnazari).

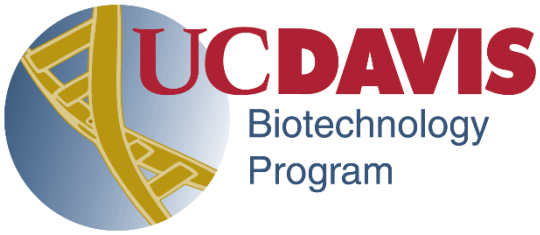
A number of students graduated in 2003 with their PhD, along with a DEB: Angelica Giuffre (Microbiology) is doing a post-doc at Plum Island working with exotic viral pathogens; Denneal Jamison McClung (Genetics) is a finalist for a faculty position in Molecular Genetics at CSUS; Sinyoung Park (Chemical Engineering) is at Bayer; and Vidhya Ramakrishnan (Microbiology) is continuing as a post-doc in the Bisson Lab.

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 thank our affiliates: Chiron, Monsanto, and Novozymes Biotech for coming today. We also welcome Agilent Technologies and Amgen. We hope that they can become more deeply involved in our DEB program.

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 Jennifer Lee and Erica Seitz Chédin.

Bon Appetit!

Judy Kjelstrom, acting director, UC Davis Biotechnology Program



NIH Training Grant in Biomolecular Technology

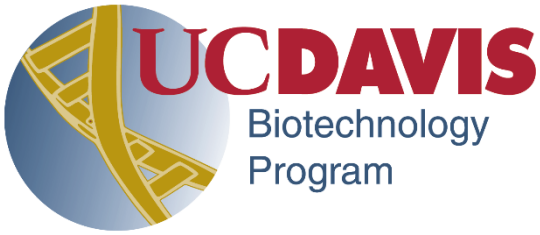
Bruce D. Hammock, Director
Martina Newell-McGloughlin, Co-Director
Karen McDonald, Co-Director

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 (Hem/Onc)
John Yoder (Vegetable crops)

Company Representatives:
Monsanto, Calgene campus: Nordine Cheikh
Novozymes Biotech: Joel Cherry
Scios: designee TBA

Judith A. Kjelstrom, Program Coordinator
Erica Seitz Chédin, Assistant Director
Cathy Miller, Grant Administrator
Jennifer Lee & Gail Stroup, Administrative Assistants



Designated Emphasis in Biotechnology (DEB) Executive Committee

Abhaya Dandekar, Chair
Karen McDonald
Robert Rice
David Rocke

UC Davis Biotechnology Program

Acting Director
Judith A. Kjelstrom
(DEB Program Coordinator & Ex-Officio Member
of the DEB Executive Committee)

Erica Seitz Chédin, Assistant Director
Jennifer Lee, Administrative Assistant

UC Davis Thirteenth Annual Biotechnology Training Retreat
March 27, 2004
Christian Brothers Retreat & Conference Center

PROGRAM OVERVIEW

6:45am	Bus Departs UC Davis, Parking Lot #41
8:15 am	Registration & Continental Breakfast
8:30 am	Welcome by Martina Newell-McGloughlin NIH Training Grant in Biomolecular Technology- Co-director
	Morning Session Chair- Abhaya Dandekar DEB Executive Committee- Chair
8:45 – 9:10	Marjorie Longo/Craig Blanchette
9:15 – 9:40	Stephen Brown (Novozymes Biotech)
9:45 – 10:10	Kit Lam & Earl Sawai/Scott Wong
10:15 – 10:40	Scott Simon/Chad Green
10:45 – 11:05	Break/poster viewing
11:10 – 11:35	John Purcell (Monsanto Company)
11:40 – 12:05pm	Clark Lagarias/Amanda Ellsmore-Fisher
12:10	John Yoder- Bioethics Question (Handout)
12:15 – 2:15pm	Lunch/poster viewing
	Afternoon Session Chair- George Bruening Biotechnology Program Advisory Committee- Chair
2:15 – 2:30	John Yoder- Bioethics Question (Discussion)
2:30 – 2:55	Jean VanderGheyst/Larry Joh
3:00 – 3:25	Bruce German/Bob Ward
3:30 – 3:40	Break/poster viewing (optional)
3:40 – 4:05	Eddie Moler (Chiron Corporation)
4:10 – 4:25	Tim Osslund (Amgen Inc.)
4:30 – 4:45	David Hirshberg (Agilent Technologies)
4:45	Close
5:00pm	Bus Departs Napa

POSTER TITLES

A. "Novel Probes for Multimodality Molecular Imaging"
B. Jarrett, J. Ross, S. Wang, S. Youens, and A. Louie

B. "*In Silico* Analysis of the Grape (*Vitis Vinifera* L.) Transcriptome and Functional Genomic Approaches to Unveil Organ-specific Developmental responses to Abiotic Stresses and Host Interactions with Pierce's Disease"
Alberto B. Iandolino*, Francisco Goes da Silva, Hyunju Lim, Hongkyu Choi, Jong Min Baek, Anna Leslie, Jane Xu, Larry E. Williams and Douglas R. Cook

C. Transgenic Livestock for Human Health: Changing the Composition of Milk
James D. Murray, Wade Reh*, Gary B. Anderson and Elizabeth A. Maga

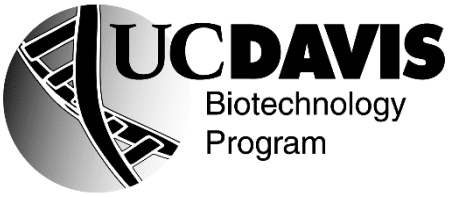
D. Conservation of Mechanism in Three Chorismate Utilizing Enzymes and the Design for Mechanism-based Antimicrobials for 4-amino-4-deoxychorismate Synthase
Ze He*, Michael Toney

E. Crystal Structures of γ-Aminobutyrate Aminotransferase and its Complex with Aminooxyacetate
Wenshe Liu*, Pete Peterson, Rich Carter, Xianzhi Zhou, Jimmy Langston, Andrew Fisher, and Michael Toney

F. α-Tubulin Detyrosination: A Redox-Sensitive Regulatory Switch for Vascular Smooth Muscle Cell Growth
Anh Phung*, Lukas Kubal, Andrés Kamaid, Rebecca Arnold, J. David Lambeth, J. Chlöe Bulinski, and Jason Eiserich

See pages 26 to 31 for abstracts.

*Member of DEB graduate group



Oral Presentation Abstracts

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

"Multivalent Interactions Between Gp120, an HIV Envelope Glycoprotein, and Galactosylceramide (GalCer): A Force Spectroscopy Study"

Craig Blanchette*, Marjorie Longo
Department of Chemical Engineering and Materials Science
University of California, Davis

We are interested in studying the multivalent interaction between gp120, an HIV envelope glycoprotein, and one of its receptors Galactosylceramide (GalCer). HIV-1 has two different fusion pathways, which depend largely on cell type. Infection of hepatocytes, vagina, colon and neural epithelial cells and sperm cells occur through an initial interaction between gp120 and GalCer, a glycosphingolipid containing a galactose sugar head group. GalCer has been shown to exist on the extracellular leaflet of the cell membrane in nanometer size domains or rafts. The local clustering of GalCer within rafts is thought to facilitate the multivalent interaction between gp120 and GalCer in the initial attachment of HIV-1 to the host cell. It is believed that the display of GalCer ligands within these rafts can affect the strength of the polyvalent interaction between GalCer and gp120. We propose to use model membranes to study the effects of GalCer density, mobility and molecular arrangement on the binding force between GalCer and gp120 at the single molecule level. We have developed a series of techniques in which we are able to form supported bilayers containing GalCer micro-domains of varying density, fluidity, and size. GalCer domain size can be varied by controlling the rate of cooling or quenching past its phase transition temperature during the formation of supported bilayers. By regulating this parameter we have been able to form GalCer domains as small as 25 nm and as large as 5 um. We have also been able to vary the degree of mobility and density of GalCer, within these domains, through the addition of cholesterol. Our goal is to measure the binding force between gp120 and GalCer micro-domains, under the varying conditions, using an atomic force microscope and quantify the effects of GalCer mobility, density and domain size on the strength of the multivalent interaction between GalCer and gp120.

*** Member of the DEB graduate group**

COMPANY AFFILIATE: Novozymes Biotech

"Hyaluronic Acid Production by Recombinant *Bacillus subtilis* Strains"

Stephen Brown, Bill Widner, Regine Behr, Alan Sloma, Tiah Hue, Steve Von Dollen, and David Sternberg
Novozymes Biotech
Davis, CA 95616

Hyaluronic acid (HA) is a biopolymer with a wide range of technical and biomedical applications, and a worldwide annual market valued at over $1 billion. HA is currently obtained commercially from rooster combs, and certain strains of *Streptococcus* that synthesize this compound naturally to form an outer capsule. However, these are less than ideal sources. Recovery of HA from rooster combs necessitates extensive purification to remove antigenic avian proteins, while Streptococci are fastidious organisms that can be expensive to grow, and have the potential to produce exotoxins. Thus, it would be advantageous to develop an alternative host for producing HA that avoids these complications.

Recombinant *Bacillus* species have been used for several decades to produce industrial enzymes and small molecules such as riboflavin. These organisms are capable of secreting copious amounts of product and are very economical to grow in industrial fermentors. In addition, many products made by *Bacillus* have achieved GRAS (Generally Recognized As Safe) status. Thus, these organisms offer several advantages as possible hosts for producing HA. Here we report the metabolic engineering of a *B. subtilis* strain that is capable of secreting large amounts of high molecular weight HA. The *has*A gene from *Streptococcus equisimilis,* which encodes the enzyme hyaluronan synthase, has been introduced into *Bacillus subtilis* and expressed, resulting in the production of authentic HA in the 1-2 MDa range. Artificial operons were assembled and tested, all of which contain the *has*A gene along with one or more genes encoding enzymes involved in the synthesis of the UDP-precursor sugars that are required for HA synthesis. *B. subtilis*-derived HA was shown to be secreted and of high quality, comparable to other commercially available sources. Thus, recombinant *B. subtilis* strains offer a new, competitive production system for the large-scale manufacture of HA.

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 Simian Immunodeficiency Virus Nef and the Cellular p21-Activated Kinase"

Scott Wong*[1], Ruiwu Liu[2], Alan Lehman[2], Erwin Antonio[1], Michael Ye[1], Kit Lam[2] and Earl Sawai[1]
Department of Medical Pathology[1]/ Hematology[2], University of California, Davis 95616

Nef is a viral protein encoded by the Simian Immunodeficiency Virus (SIV) and Human Immunodeficiency Virus (HIV). Nef is capable of enhancing virion infectivity, down-regulating cellular surface proteins from the plasma membrane and participating in cellular activation. One way Nef increases cellular activation is by binding and activating a cellular p21-activated kinase (PAK). In our earlier *in vivo* studies with SIV∆nef, pathogenic revertants were found to restore PAK binding through the generation of truncated forms of Nef.

To further study this interaction, we will be identifying small molecules that inhibit the Nef-PAK interaction. Wild-type SIV Nef was expressed in *E.coli* with a poly-Histidine tag and purified using nickel affinity chromatography. The recombinant protein was used to screen one-bead one-compound encoded small molecule libraries to identify compounds that bind Nef. These libraries have functional small molecules on the outer bead surface while a coding tag attached to the bead interior that can be used to identify the small molecule by microsequencing. Beads that have Nef bound to small molecules are identified using a colormetric method.

Preliminary studies have resulted in the identification of several compounds that bind SIVmac239 Nef. These candidate molecules are being characterized for their ability to affect PAK binding and activation. Furthermore, these small molecules will be used to determine if they are capable of inhibiting virus replication in cell culture. If effective *in vitro*, lead compounds we be tested *in vivo* with SIV infected rhesus macaques. It is hoped that compounds identified in these studies will represent a new class of HIV inhibitors.

*** Member of the DEB graduate group**

OVERVIEW OF LAB RESEARCH: Scott Simon/Chad Green

Molecular and Biophysical Mechanisms Regulating Leukocyte Recruitment in Inflammation and the Development of Rational Therapeutics to Block Their Inappropriate Adhesion During Diseases Including Myocardial Infarction and Sepsis

Scott Simon
Professor of Biomedical Engineering
University of California, Davis

In the Simon Lab, we are interested in blood-cell function, specifically the behavior of one type of white blood cell called the neutrophil. Neutrophils are in concentrations of about a billion per liter and circulate in the vasculature for only a few hours before being cleared in organs. Their goal over this interval is to surveil the circulation and peripheral tissues for bacteria and other foreign invaders and to home to sites of inflammation. To perform this bacteriocidal function, they are endowed with active motile machinery, can detect the "molecular scent" of invaders through receptor-ligand interaction, and contain enzymes both to kill invaders and to help initiate wound repair. Research focuses on the mechanics of adhesion and the movement of neutrophils. Neutrophils interact with endothelial cells that line the walls of blood vessels. The flow of blood sets up repellent stresses and the cells roll until they are activated by sensory receptors. Once activated, they adhere to sites of inflammation and also aggregate with each other. In addition to stimulatory receptors, neutrophils express several classes of adhesion receptors that make them very "sticky." These molecules enable them to adhere to sites of inflammation and at sites of injured tissue, such as the myocardium during a heart attack. These studies have a number of important applications. For example, some kinds of cell aggregation may be very sensitive indicators of inflammation, and understanding the basic mechanisms that control the adhesion and migration of neutrophils may lead to new therapeutics in fighting heart disease and cancer. In the laboratory, technologies are developed to "sense" molecular scale forces associated with neutrophil adhesion, such as a phase contrast microscopy linked to piezo-controlled force transducers. Direct imaging of the dynamics of cellular adhesion as they interact with vascular endothelial monolayers in parallel plate flow chambers is accomplished by real-time video microscopy, coupled with automated image analysis. Flow cytometry coupled with shear flow chambers provides "electronic imaging" of the molecular events supporting cellular adhesion and functional activation.

NIH FELLOW: Chad Green

"β_2-Integrin Dynamics on Neutrophils Imaged in Real-Time during Arrest"

Chad E. Green*, Aaron F. Lum and Scott I. Simon
Department of Biomedical Engineering
University of California, Davis

Two adhesive events critical to efficient capture and transmigration of neutrophils (PMN) at vascular sites of inflammation are upregulation of selectins on endothelium (EC) that bind to sLe^x decorated glycoproteins on PMN, and activation of β_2-integrins (CD18) to bind ICAM-1 on EC. A classical pathway activating leukocyte arrest is via ligation of endothelial expressed chemotactic factors such as IL-8, which triggers G-protein signaling that in turn activates β_2-integrins. Recently we identified a second mechanism for PMN activation that involves E-selectin recognition of sLe^x expressed on L-selectin and PSGL-1. Within seconds of PMN rolling on activated HUVEC or a cell monolayer expressing E-selectin and ICAM-1 (L-E/I), L-selectin and PSGL-1 colocalize in clusters at the trailing cell membrane. On HUVEC or L-E/I, PMN rolling transitioned to β_2-integrin mediated cell arrest within two cell diameters. Current efforts have focused on visualizing how β_2-integrins are activated and participate in arrest and transmigration. Real time immunofluorescence coupled with phase contrast microscopy of PMN flowing over activated HUVEC indicate highly mobile clusters of β_2-integrin forming at dynamic sites of contact. At a shear stress of 2 dynes/cm^2, LFA-1 and mAb 327C, an antibody that recognizes the ligand binding conformation of CD18, both redistribute to the neutrophil uropod and to small punctate clusters at pseudopod projections. In contrast, neutrophils adherent to the L-E/I substrate lacking surface chemotactic agents do not exhibit significant shape change or uropod formation. However, punctate clusters of β_2-integrin persist at the cell contact with the substrate. Taken together, the data shows that binding of E-selectin and surface chemokine to neutrophils provide distinct signals driving the assembly of the *inflammatory synapse*, a macromolecular signaling complex formed as PMN roll on inflamed endothelium.

*** Member of the DEB graduate group**

COMPANY AFFILIATE: Monsanto Company

"Current and Future Impact of Agricultural Biotechnology"

John P. Purcell, Ph.D.
Global Lead
Scientific Affairs
Monsanto Company
St. Louis, MO 63167

The use of agricultural biotechnology has grown rapidly since its introduction in the mid-1990s. Over 700 million acres of crops improved through biotechnology have been grown from 1996-2003. Farmers around the globe have adopted the products at a record pace with double-digit percent increases in acres each year. This commercial success has not been without controversy. A great number of studies have now been published that document the impact biotechnology is having and address many of the concerns raised about the technology. In this presentation, I will present findings from a number of key studies that address the economic, environmental and social impact of the current agricultural biotechnology products. I will also discuss the future trends in the industry and the potential impact of products in development.

OVERVIEW OF LAB RESEARCH: J. Clark Lagarias/Amanda Ellsmore

The Lagarias Laboratory

J. Clark Lagarias
Professor of Molecular and Cellular Biology
University of California, Davis

In the natural environment, plants are exposed to extremes in light intensity and spectral quality and therefore must continuously optimize light capture for photosynthesis. This is accomplished by the action of numerous light receptors that serve to mediate adaptive changes in plant growth and development. Our studies focus on the phytochromes, light sensing biliproteins found in plants and cyanobacteria, which mediate responses mainly to red and far-red light in the environment. The long term goal of these investigations is to rationally alter the natural responses of plants to their light environment through modification of the biosynthesis, structure and function of phytochromes. Three major avenues of research in our laboratory are outlined below.

Molecular Mechanism of Phytochrome Signaling (NIH Supported)**.** The recent discovery of phytochromes in nonphotosynthetic bacteria and fungi document that phytochrome ancestors and their ancient signaling partners have evolved into components of signaling systems found in higher eukaryotes. Our studies seek to define how tetrapyrrole and light signals are perceived by the phytochrome molecule and transduced to downstream target molecules, addressing the hypothesis that prokaryotic and eukaryotic phytochromes transduce both signals by protein phosphorylation via distinct biochemical mechanisms. Through purification and molecular characterization of the photoreceptor from evolutionarily-diverged organisms, structural features that may confer common and novel functions can be deduced and experimentally tested. Our recent research investigations are based upon a body of evidence gathered over the past twenty years which have led to unifying hypotheses for a mechanism of phytochrome signaling. For the development of these hypotheses, we have exploited publically available genomic databases, along with research using recombinant systems for expression/reconsitution of photoactive holophytochromes and *in vitro* biochemical assays for phytochrome function - methodologies developed in this laboratory over many years.

Phytochrome Chromophore Biosynthesis (USDA CGRI Supported)**.** Phytobilins are linear tetrapyrrole pigments whose optical and photochemical properties are tuned by the proteins with which they are associated. When bound to phycobiliproteins, phytobilins harvest light throughout the visible spectrum and efficiently transfer this energy to photosynthetic reaction centers, enabling cyanobacteria, red algae and cryptophytes to colonize light-limiting environments unsuitable for other photosynthetic organisms. Phytobilins also play a key role as sensors of light quality, intensity, duration and direction when associated with the protein moiety of plant and cyanobacterial phytochromes. Our investigations focus on the HY2 family of ferredoxin-dependent bilin reductases, enzymes responsible for the biosynthesis of the phytobilin precursors of phytochrome and phycobiliprotein chromophores. Utilizing recombinant enzymes, biochemical and biophysical approaches have been used to determine cofactor composition, substrate/inhibitor specificity and kinetic parameters for individual members of this family. Chemical modification studies, in combination with site-directed

mutagenesis, domain swapping and collaborative x-ray crystallographic analyses, seek to elucidate the structural basis for the catalytic specificity of each family member. By introduction of different combinations of bilin reductase genes into plants and cyanobacteria, we seek to tailor the wavelength sensitivity of phytochromes and phycobiliproteins. Compounds affecting bilin reductase activity also could be used to prevent germination of undesirable plant species, growth of toxin-producing cyanobacteria and the length of time needed for plants to flower.

Directed Evolution of Phytochromes (NIH Biotech & CBST Supported)**.** Our laboratory has developed tools for biochemical synthesis, modification and *de novo* design of phytochrome-based biliproteins with a range of photophysical properties that span the visible and near infrared region of the light spectrum. The same technology also enables the synthesis of novel phycobiliproteins in cells. By exploiting and/or genetically altering the double bond regiospecificity of the ferredoxin-dependent bilin reductases (see above), in combination with (semi)synthesis of novel linear tetrapyrrole precursors and directed evolution of apophytochrome genes, our studies seek to develop new biliprotein reagents with novel chemical proteins and biochemical functions. Among the target applications of our studies are 1) NIR-emitting fluorescent proteins that can be produced within living cells, 2) phytochrome- and phycobiliprotein-based fluorescent labels, 3) phytochrome-based chemical- and pH-sensing fluorescent/photochemical detection reagents ,and 4) light-regulated gene expression delivery systems. By error-prone mutagenesis and a combination of digital imaging and fluorimaging methods, we seek to engineer novel functions for biliproteins that nature never intended. This work is funded by a combination of public and private funds.

BIOTECHNOLOGY FELLOW: Amanda Fischer

"Directed Evolution of Phytochrome"

Amanda J. Ellsmore* and J. Clark Lagarias
Plant Biology Graduate Group, Section of Molecular and Cellular Biology
University of California, Davis

Phytochromes are biliprotein photoreceptors that exist in two photointerconvertible forms - the red light absorbing Pr form and the far-red light absorbing Pfr form. We previously showed that unnatural bilin precursors yield strongly fluorescent adducts with apophytochromes in living cells [1]. These fluorescent phytochrome adducts, known as phytofluors, hold great promise for numerous cell biological applications, however, unlike the green fluorescent protein (GFP), exogenous unnatural bilin-precursors are needed for phytofluor formation in cells.

A directed evolution approach was undertaken with the goal of creating fluorescent phytochrome mutants that utilize endogenous bilin precursors found in plants and cyanobacteria. Our strategy employed error-prone PCR for generating point mutations at random positions within the phototsensory regionof the cyanobacterial phytochrome 1 (Cph1) [2]. In addition, *in vitro* DNA shuffling was used to generate diversity within these point mutation libraries [3]. The photosensory region was targeted for mutagenesis because its structure is critical for the spectroscopic properties of phytochrome [4,5]. We hypothesize that alterations in this region will result in spectrally shifted holophytochrome mutants that are 'locked' in either the Pr or Pfr form, thereby enhancing their red and far-red fluorescence. As a collateral approach, three classes of divergent phytochromes were cloned and will be subjected to directed evolution as well.

Mutated phytochrome proteins were expressed in different bilin producing strains of *E.coli* and screened for spectral abnormalities using digital imaging spectroscopy [6]. These libraries were also screened for fluorescence using flow cytometry. Multiple classes of mutant with altered spectral properties were identified and their lesions determined.

References

1. Murphy J. T. and Lagarias J.C. The Phytofluors: A new class of fluorescent protein probes. *Current Biology*, 1997. 7(11): 870-876.
2. Henke E. and Bornscheuer U. T. directed evolution of an esterase from *Psuedomonas fluorescens. Biological Chemistry*, 1999. 380 (7): 1029-1033.
3. Stemmer W.P.C. Rapid evolution of a protein in vitro by DNA shuffling. *Nature*, 1994. 370: 389-391.
4. Cherry J.R., Hondred D., Walker J.M., Keller J.M., Hershey H.P., and Vierstra R.D. Carboxy-terminal deletion analysis of oat phytochrome a reveals the presence of separate domains required for structure and biological activity. *Plant Cell*, 1993. 5:565-575.
5. Wu S. H. and Lagarias J. C. Defining the bilin lyase domain: Lessons from the extended phytochrome superfamily. *Biochemistry*, 2002. 39 (44): 13487-13495.
6. Gambetta G. and Lagarias J.C. Genetic engineering of phytochrome biosynthesis in bacteria, *Proc. Natl. Acad. Sci.* USA, 2001. 98 (19): 10566-10571.

*** Member of the DEB graduate group**

OVERVIEW OF LAB RESEARCH: Jean VanderGheynst/Larry Joh

VanderGheynst Laboratory

Jean VanderGheynst
Associate Professor of Biological & Agricultural Engineering
University of California, Davis

Our laboratory research area is Bioprocess Engineering with an emphasis on agricultural and environmental biotechnology. She is particularly interested in the application of biological engineering to the production and delivery of microbial agents for the control of plant pathogens and insects, and in value-added processing of plant biomass for production of high-value proteins and commodity chemicals.

NIH FELLOW: Larry Joh

"Value-Added Processing of Tomato for Production of Monoclonal Antibodies"

Larry Joh*, and Jean S. VanderGheynst
Department of Biological and Agricultural Engineering
University of California, Davis

The demand for existing biopharmaceuticals and new therapeutic proteins discovered through genomics research is expected to rise considerably in the future. Large-scale production of antibodies and other proteins in transgenic plants has been proposed as a cost-effective option for meeting this demand. Antibodies are relatively large and complex molecules that are not made well in many conventional systems such as *E. coli* and yeast but are typically made well in plants. The plant system of interest for our research is the UC82b processing tomato. Tomato provides several advantages over other plant expression systems, including amenability to large-scale greenhouse production and potentially simpler purification due to lower native protein content. Although a number of different biopharmaceutical proteins have been expressed in transgenic plants, surprisingly few reports have been published on protein extraction and purification, collectively termed downstream processing. Purification is likely to represent most of the cost of biopharmaceutical production in plants. We are using statistically designed experiments to develop and optimize the extraction and purification processes, and will use the computer software package SuperPro Designer (Intelligen, Inc., Piscataway, NJ) to estimate economics and scale-up the optimized bench-scale process to a 10 kg/yr base-case commercial antibody production unit. Our initial experiments have focused on extraction of soluble proteins from tomatoes, separation and concentration of protein extract from tomato pulp, and purification of immunoglobulin G (IgG) from native tomato proteins. We have observed that protein extraction yield from tomato is quite sensitive to extraction conditions and to unit procedures involved with blending and solid separation. To prevent fouling of filtration membranes and clogging of chromatography columns, a two-step process of centrifugation and microfiltration was needed. The microfiltered extract was then concentrated by ultrafiltration to reduce the size of chromatography columns. We have found that Protein A chromatography is very effective in separating IgG from a concentrated solution of IgG and native tomato proteins.

*** Member of the DEB graduate group**

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.

BIOTECHNOLOGY FELLOW: Robert Ward

"Metabolism of Human Milk Oligosaccharides by Gut Microflora"

Robert E. Ward[1*], Youmie Park[2], Carlito Lebrilla[2] and J. Bruce German[1]
Department of Food Science and Technology[1], Department of Chemistry[2], University of California, Davis, CA 95616

Human milk is a complete food tailored by evolutionary pressure to nourish and improve the success of neonates. Its consumption results in phenotypic advantages to infants which cannot be explained by our understanding of its nutrient profile. Therefore there are components with nutritional activity beyond our understanding, and translating such benefits to other foods will be possible if the structures and mechanisms are understood. Deconstructing the genetic, compositional and structural information content of this bio-fluid will thus yield valuable nutritional insight and result in benefits to all. This project addresses an under-appreciated constituent of human milk, the oligosaccharides. In comparison to other mammals, human milk is rich in soluble oligosaccharides (HMO). After lactose and fat, they are the third most concentrated component. Over 130 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 maternal genotypes, the Lewis and secretor genes being prominent polymorphisms. They are believed to act as prebiotics, or indigestible carbohydrates which stimulate the growth and proliferation of beneficial gut microbes. However, little data are available to support this hypothesis, much less to provide an understanding of the precise structures and functions of the purported prebiotic molecules. The goal of this investigation is to use *in vitro* fermentation system to examine the metabolism of HMO by the gut microflora of infants. Using mass spectrometry and HPLC, we will monitor the time changes in the oligosaccharide profile of a growth media prepared with these molecules as the sole source of fermentable carbohydrate. Fructooligosaccharides, a well-characterized prebiotic, will be used as a positive control. The follow-up study will focus on understanding the basis of the microbial population differences between breast-fed and bottle-fed infants. Further work will establish the effect of maternal genotype, and the effect of varying HMO in modifying the competitive growth of different bacteria within complex microbial populations.

*** Member of the DEB graduate group**

COMPANY AFFILIATE: Chiron Corporation

"In-vitro Drug Combination Studies: The Good, the Bad, and the Ugly"

E. J. Moler*, K. Rendahl, Y. Shao, B. Hibner
Chiron Research
Chiron Corporation
4560 Horton Street
Emeryville CA 94608

Preclinical i*n-vitr*o studies of the effects of drug combinations on cancer cell-line cultures are frequently used to guide clinical trial design. While there is a voluminous literature base of published studies claiming synergistic and/or antagonistic interactions, relatively little attention has been paid to certain crical details of the experiment design and analysis methodology. Thse include the sensitivity of the interaction models to the parameters used to derive the conclusions, the statistical analysis of the data, the effects of systematic errors on the analysis, and the design of appropriate controls.

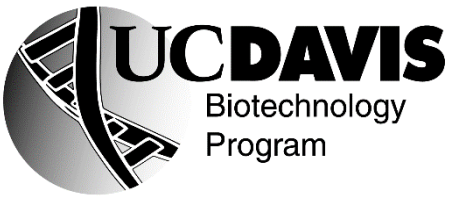
We have developed a robotically performed drug combination assay based on the Response Surface Analysis (RSA) approach analyzed by Loewe's additivity model. We have identified critical elements of the experiment design based on a) sensitivity analysis of the parameters used in the models to interpret the data and b) the practical realities of implementing a cell-based assay.

We will present a discussion of:

- the theory of drug interaction elucidation
- the selection of interaction models
- sensitivity analysis of model parameters and the implications for experiment design
- methods of visualization and statistical analysis
- essential elements of the experiment and controls design

References:

W. R. Greco, et. al., "The Search for Synergy: A Critical Review from a Response Surface Perspective", Pharmacological Reviews, 47(2), pp 331-385.



Poster Abstracts

A. "Novel Probes for Multimodality Molecular Imaging"

Jarrett, J. Ross, S. Wang, S. Youens, A. Louie
Department of Biomedical Engineering, UC Davis

Our laboratory focuses on the development of novel imaging tools for probing molecular events *in vivo* for application in the diagnosis and study of human disease. Current efforts in the lab are directed towards multimodality probes that can be detected by magnetic resonance imaging (MRI), fluorescence microscopy or positron emission tomography (PET). PET has exquisite sensitivity but relatively poor resolution. Fluorescence techniques provide highest resolution but limited depth of interrogation. MRI has a few orders of magnitude better resolution than PET and unlimited depth of interrogation in the human system. By combining these imaging techniques we can draw upon the strengths of each to provide more complete information about a system of interest. Projects in progress in the lab include development of dual-mode PET-MRI agents directed towards atherosclerotic plaques; activatable agents that are triggered by membrane hyperpoloarization/depolarization for study of retinal function; and dual-mode optical/MRI nanoparticles for tumor imaging.

B. "*In Silico* Analysis of the Grape (*Vitis Vinifera* L.) Transcriptome and Functional Genomic Approached to Unveil Organ-specific Developmental responses to Abiotic Stresses and Host Interactions with Pierce's Disease"

Alberto B. Iandolino[2*], Francisco Goes da Silva[1], Hyunju Lim[1], Hongkyu Choi[1], JongMin Baek[3], Anna Leslie[3], Jane Xu[1], Larry E. Williams[2] and Douglas R. Cook[1]
[1]Department of Plant Pathology; [2]Department of Viticulture and Enology. [3]CA&ES Genomics Facility, University of California Davis, 1 Shields Avenue, Davis, CA 95616

Grapes (*Vitis vinifera* L.) are the most widely cultivated fruits in the world. Their genome harbors genes encoding for unique sets of phenotypic and molecular traits expressed at different stages of development. We analyzed ~135,000 grape Expressed Sequence Tags (ESTs) derived from 58 cDNA libraries to identify molecular phenotypes correlated with berry development, response to abiotic stresses or resistance and susceptibility to the Pierce's Disease (PD) bacterial pathogen *Xylella fastidiosa*. Contigs were assembled and annotated using CAP3 and homology match against the GeneBank non-redundant database. Information about the current grape unigene set was organized in an on-line relational database (http://cgf.ucdavis.edu). EST frequencies per contig were used to estimate their tissue, developmental stage or treatment specific expression levels. Putative contig differential expression was estimated *in-silico* by frequency analysis against random generated expression datasets. Trends in expression profiles among libraries and contigs were also unveiled by correlation, hierarchical cluster and principal component analysis. This *in-silico* analysis strategy allowed the identification of gene sets with putative specific expresion patterns associated with different organs and networks involved in responses to biotic and abiotic stresses. In particular, several *X. fastidiosa* responsive genes were identified and further confirmed by real-time reverse transcriptase PCR. We are currently characterizing leaves and berries in response to water and nitrogen stress as well as host-*X. fastidiosa* interactions combining transcriptional profiling with the Affymetrix *Vitis* GeneChip® and metabolite analysis HPLC-DAD-MS or GC-MS.

*** Member of the DEB graduate group**

C. "Transgenic Livestock for Human Health: Changing the Composition of Milk"

James D. Murray, Wade Reh*, Gary B. Anderson and Elizabeth A. Maga
Department of Animal Science, University of California, Davis

Since the generation of the first transgenic mice over 20 years ago, the genetic engineering of plant and animal species has held great potential. Progress has been made in the field of transgenic plants as many have entered production. In animals, however, this promise has yet to be realized. We have been working towards applying genetic engineering to dairy animals in order to improve the nutritional and health benefits of milk for consumers. As a model for the dairy cow, transgenic goats were generated by pronuclear microinjection with transgenes designed to express either human lysozyme or desaturase in lactating mammary gland epithelial cells. Preliminary results indicate that the presence of human lysozyme in milk conferred anti-bacterial properties to the milk and acted to decrease the growth of bacterial contaminants in the milk. Such milk would be of value in assisting with micorflora establishment in the gut and maintaining the health of consumers of this milk. It was also demonstrated that expression of the desaturase transgene during lactation resulted in milk with decreased saturated fatty acid levels, increased mono- and polyunsaturated fatty acids and increased levels of conjugated linoleic acid (CLA). The consumption of lower levels of saturated fatty acids could lower the risk for cardiovascular disease. In addition, CLA has been reported to have immuno-modulating and anti-carcinogenic properties that may benefit the consumer if delivered in milk.

*** Member of the DEB graduate group**

D. "Conservation of Mechanism in Three Chorismate Utilizing Enzymes and the Design for Mechanism-based Antimicrobials for 4-amino-4-deoxychorismate Synthase"

Ze He*, Michael Toney
Chemistry Department, University of California-Davis

The shikimate pathway, the endproduct of which is chorismate, is central to the biosynthesis of carbocyclic aromatic compounds in plants, bacteria, fungi, and some parasites. Chorismate is the common branchpoint for the production of several metabolites. Compounds that are derived from chorismate include: aromatic amino acids, vitamins K and E, folate, coenzyme Q, plastoquinones, menaquinones, salicylate, phenoxazinones, and others. The absence of these pathways in mammals makes them very attractive targets for the development of antibiotics and herbicides. Useful inhibitors have long been commercially employed, including glyphosate (broad spectrum herbicide) and the sulfa class of antibiotics.

Our initial interest is in the enzymes that convert chorismate into *p*-aminobenzoic acid (PABA) in folate biosynthesis. Here, we provide evidence that 4-amino-4-deoxychorismate, the intermediate between chorismate and PABA, is formed via a S_N2'' mechanism in which an active site lysine acts as a nucleophile in the formation of a covalent intermediate. This mechanism resolves long-standing questions regarding chorismate-utilizing enzymes and suggests strategies for mechanism-based inhibition. The anti-bacterial properties of (6*S*)-6-fluoroshikimate can be rationalized in this light as well.

*** Member of the DEB graduate group**

E. Crystal Structures of γ-Aminobutyrate Aminotransferase and its Complex with Aminooxyacetate

Wenshe Liu*, Pete Peterson, Rich Carter, Xianzhi Zhou, Jimmy Langston, Andrew Fisher, and Michael Toney
Department of Chemistry, University of California, Davis, CA 95616

γ – Aminobutyrate (GABA), which is the major amino acid neurotransmitter in brain, has been suggested involving directly or indirectly in the pathogenesis of many neurological diseases and psychiatric disorders like epilepsy. It's mainly degraded by an enzyme, which is called γ-aminobutyrate aminotransferase (GABA-AT), a pyridoxal 5'-phosphate (PLP) dependent enzyme, and has long been a target for neuroactive drugs. GABA-AT is also found in plants and microorganism. Here we present the structure of GABA-AT from *E. coli* K-12, and its complex structure with aminooxyacetate, which is a potent inhibitor of GABA-AT in vivo and in vitro. The structures were refined to the resolutions of 2.4 Å for GABA-AT and 1.9 Å for its complex with aminooxyacetate. GABA-AT is α_4-tetramer. Each asymmetric unit contains four subunits. There is no structural asymmetry between four subunits, although four subunits were refined individually without non-crystallographic symmetry restriction. Two monomers related by a 2-fold non-crystallographic symmetry are tightly intertwined to form the dimer. The PLP cofactors are located close to the subunit interface of the dimer and very close to each other (the PLP phosphate atoms are 14.8 Å apart). Both active sites are formed from residues contributed by both monomers. The tetramer is formed from the symmetric association of two dimers. The structure of GABA-AT complex with aminooxyacetate was obtained by soaking GABA-AT crystals with ominooxyacetate. The electron density map at the active site clearly indicates aminooxyacetate inhibits the enzyme by covalently modifying the PLP cofactors.

*** Member of the DEB graduate group**

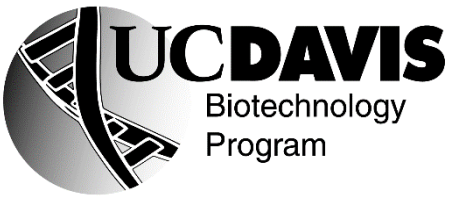
F. α-Tubulin Detyrosination: A Redox-Sensitive Regulatory Switch for Vascular Smooth Muscle Cell Growth

Anh Phung[1*], Lukas Kubala[1], Andrés Kamaid[1], Rebecca Arnold[2], J. David Lambeth[2], J. Chlöe Bulinski[3], and Jason Eiserich[1]

[1]Department of Internal Medicine, UC, Davis, [2]Pathology & Laboratory Medicine, Emory University, [3]Biological Sciences, Columbia University

Hyperproliferation of smooth muscle cells is a hallmark of vascular diseases such as atherosclerosis and is a prominent complication arising from restenosis following angioplasty. Whereas recent studies suggest that oxidants play a role in the hyperproliferative and hypertrophic responses of smooth muscle cells (SMCs), the mechanisms remain poorly characterized. Herein, we provide evidence that H2O2 produced by the nonphagocytic NAD(P)H oxidase Nox1 is an important redox mediator of SMC proliferation, and that this may be directly linked to posttranslational modifications of α-tubulin. While serum-starved rat aortic SMCs are essentially devoid of Nox1 expression, treatment with PDGF or AngII upregulates the expression of this NAD(P)H oxidase. In parallel, the levels of detyrosinated α-tubulin are markedly increased and temporally follow the cell cycle. Therefore, upregulated detyrosination of α-tubulin is a common feature of SMC proliferation and hypertrophy, potentially linked to the induced expression of Nox1 and H2O2 production. Supporting this notion, NIH 3T3 fibroblasts stably transfected with Nox1 reveal increased levels of detyrosinated α-tubulin, and co-expression of catalase reverses this effect. It was also found that 3-nitrotyrosine, which is irreversibly incorporated into the C-terminus of α-tubulin, blocked the proliferative response of Nox1 transfected cells, suggesting that α-tubulin detyrosination state may be an important factor in the proliferative response. Collectively, our data suggest that Nox1 expression is upregulated in PDGF- and AngII-activated smooth muscle cells, and that H2O2 derived from Nox1 induces characteristic posttranslational modifications to α-tubulin.

*** Member of the DEB graduate group**



Company Affiliates

Company Affiliates** Support Biotech at UC Davis

- Berlex Biosciences
- Chiron Corporation
- Genentech
- Monsanto, Calgene Campus
- Novozymes Biotech, Inc
- Scios, Inc.

**These Biotechnology companies have donated at least $15,000 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 programs depend on the continued support of our affiliates and the Biotechnology Program would like to thank them for their continued support.

Berlex Biosciences
Contact: Gabor Rubanyi (not in attendance)
2600 Hilltop Drive
Richmond, CA 94806
http://www.berlex.com/

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.

Chiron Corporation
Contact: Eddie Moler
4560 Horton Street
Emeryville, CA 94608-2916
http://www.chiron.com/

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.

Genentech
Contact: Melody Trexler (not in attendance)
1 DNA Way
South San Francisco, CA 94080-4990
http://www.gene.com/

Our Mission:
Our mission is to be the leading biotechnology company, using human genetic information to discover, develop, manufacture and commercialize biotherapeutics that address significant unmet medical needs. We commit ourselves to high standards of integrity in contributing to the best interests of patients, the medical profession, our employees and our communities, and to seeking significant returns to our stockholders, based on the continual pursuit of scientific and operational excellence.

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 13 protein-based products for serious or life-threatening medical conditions -- giving Genentech one of the leading product portfolios in the biotech industry.

Product Pipeline:
Genentech's expertise runs wide and deep, resulting in a robust product pipeline. With projects in several different disease categories and in different stages of development, Genentech is working hard to continue creating breakthrough medicines for patients in need.

Mosanto-Calgene Campus
Contact: Nordine Cheikh
Site Manager
1920 Fifth Street
Davis, CA 95616
http://www.monsanto.com/

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.

Novozymes Biotech, Inc
Contact: Glenn Nedwin, President
Debbie Yaver, Research Manager
Joel Cherry, Research Manager, BioEnergy Group
1445 Drew Ave.
Davis, CA 95616
http://www.novozymesbiotech.com/

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.

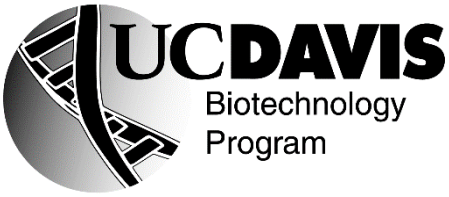
Novozymes has introduced, with few exceptions, every new enzyme to the industry, from lipases, which remove grease stains during washing, to amylases, which are used to manufacture sweeteners. In our work we use the following technologies: microbiology, bioinformatics, gene technology, protein chemistry,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

Scios, Inc.
Contact: Linda Higgins (not in attendance)
2450 Bayshore Parkway
Mountain View, CA 94043
http://www.sciosinc.com/

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.



Invited Companies (prospective affiliates)

Agilent Technologies
Contact: David Hirschberg
3500 Deer Creek Road
Palo Alto, CA 94304
650-485-2120
david_hirschberg@agilent.com

"An Update on Protein Arrays"

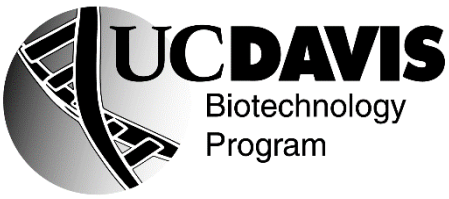
Protein arrays have begun to demonstrate great potential in the detection and quantitation of protein from biological samples and should eventually be able to leverage all the advantages of DNA array technology. A protein array is a planer, solid phase assay where molecules that can bind or in some way affect protein function are confined in defined areas by spotting, or in wells. The surface can be made of glass, plastic, membranes, or gold and can be flat, wells, beads or other types of particles. The assays are organized in a highly parallel format and often miniaturized. They share many of the same advantages with gene arrays in that the assays are, rapid, capable of automation, have very high sensitivity, use very small amounts are reagents and yield a tremendous amount of data at a low cost.

We have been investigating several types of content and use models for protein arrays. We are currently evaluating an antibody panel of markers for cardiac inflammatory disease that has been printed down on coated glass slides. Our first printing consisted of 45 antibodies printed in quadruplicate in 3 dilutions for a total of 540 features per array (600 with controls). Eight arrays were printed per slide and 384 slides were printed for a total of 3072 arrays. The assay consisted of serum samples (8 per slide) added on to the slide followed by biotinylated antibody is added to complete the sandwich. Avidin conjugated to cyanine 3 is then added and the slide is read in a fluorescence scanner. Initial evaluation shows that about 50 % of the antibodies are able to detect purified antigen at levels comparable to those seen in ELIZA. We are currently evaluating patient serum to look for possible reactivity patterns that would lead to more effective diagnosis and disease monitoring. We are currently looking to into what other classes of content will expand our portfolio of capture agents.

AMGEN, Inc.
Contact: Timothy D. Osslund
Pharmaceutics Division
One Amgen Center Drive
Thousand Oaks, CA
91320-1799
805-447-1000
http://www.amgen.com/

"The Role of Structure in the Design of Human Therapeutics"

Over two decades ago the Biotechnology Industry was founded on providing novel biological drugs, which for the most part were naturally occurring ligands for extracellular receptors. The goal was to produce proteins, which were as similar as the native protein as possible. Today the most promising protein biologicals are fusion proteins, antibodies, peptibodies or proteins, which have been truncated or modified with pegylation or glycosylation to improve their pharmaceutical properties. These types of biological therapeutics pose a new series of technological problems including stability, formulation and antigenicity issues. Typically these proteins may need to be formulated at concentrations that are hundreds of milligrams per milliliter. An understanding of the atomic structure of protein biologics aids in the design of the next generation of products, which may have superior pharmaceutical properties.



Participants

Participants

NIH Fellows (2003-2004)	Department/Organization
Craig Blanchette	Biophysics
Chad Green	Biomedical Engineering
Lawrence Joh	Biological and Agricultural Engineering
Scott Wong	Med: Pathology

Biotech Fellows (2003-2004)	Department/Organization
Amanda Ellsmore	Molecular & Cellular Biology
Robert Ward	Food Science & Technology

Graduate students/post docs

Michael Cabbage	Plant Biology
Katherine Chang	Biological & Agricultural Engineering
Honglin Chen	Genetics
Allison Dickey	Chemical Engineering
Corey Dodge	Chemical Engineering & Materials Science
Chris Dupont	UC San Diego graduate student
Ze He	Chemistry
Alberto Inadolino	Plant Biology
Aminah Ikner	Microbiology
Benjamin Jarrett	Biomedical Engineering
Bill Johnson	Chemical Engineering & Materials Science
Kou-San Ju	Microbiology
Michaels Kareta	Genetics
Wan-Chen Lin	Biophysics
Wenshe Liu	Chemistry
Caroline Meloty-Kapella	Cell & Developmental Biology
Ryann Muir	Pomology
Tamara Peoples	Molecular & Cellular Biology

Ahn Phung	Med: Internal Medicine
Michael Plesha	Chemical Engineering & Materials Science
Russell Reagan	Vegetable Crops
Wade Reh	Animal Science
James Ross	Biomedical Engineering
Dong Shin	Vegetable Crops
Masaru Shiratori	Chemical Engineering & Materials Science
Alexey Tomilov	Vegetable Crops
Natalia Tomilova	Vegetable Crops
Jennifer Weidhaas	Civil & Environmental Engineering
Qing Xie	Chemical Engineering & Materials Science
Abigail Yip	Molecular & Cellular Biology
Susan Youens	Biomedical Engineering
Melinda Zaragoza	Med: Microbiology & Immunology

Faculty

George Bruening	Plant Pathology
Daniel Chang	Civil & Environmental Engineering
Gussie Curran	UC Systemwide Biotechnology Research and Education Program
Abhaya Dandekar	Pomology
Jason Eiserich	Med: Nephrology
Bruce German	Food Science & Technology
Thomas Jue	Med: Biological Chemistry
Clark Lagarias	Plant Biology
Marjorie Longo	Chemical Engineering & Materials Science
Angelique Louie	Biomedical Engineering
Karen McDonald	Chemical Engineering & Materials Science
Martina Newell-McGloughlin	UC Systemwide Biotechnology Research and Education Program/Plant Pathology
Rebecca Parales	Microbiology
Earl Sawai	Med: Pathology

Scott Simon	Biomedical Engineering
Jean VanderGheynst	Biological & Agricultural Engineering
Tilahun Yilma	Vet Med: ILMB
John Yoder	Vegetable Crops

Affiliated Companies

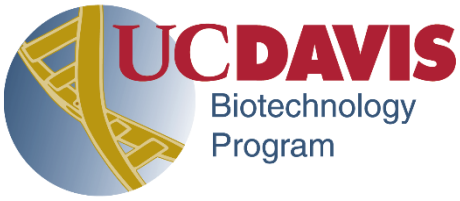
Berlex Biosciences	(not in Attendance)
Chiron Corporation	Eddie Moler
Genentech	(not in attendance)
Monsanto Company	Nordine Cheikh, Byron Froman, Ken Gruys, John Purcell
Novozymes Biotech, Inc.	Stephen Brown
Scios, Inc.	(not in attendance)

Guests

Agilent Technologies	Petula D'Andrade, David Hirschberg, Xiaohua Huang, Khanh Nguyen
AMGEN Inc.	Timothy Osslund
Business Development Consulting	John Callahan
CIFAR	Sharon Shoemaker
Division of Infectious Diseases & Immunity, Modesto Community College	Dallas Baehs, Paul Cordova, Elfida Cojdill, Stephanie Graves, Shanna Iudice, Jenessa Jame, Doug Kain, Levera Mejia, Christiane Pailo, Juan Silva
UC Davis Biotechnology Undergraduate	Tzita Horning

UC Davis Biotechnology Program (Coordinators of the Retreat)

Judith Kjelstrom	Acting Director
Erica Seitz Chédin	Assistant Director
Jennifer Lee	Event Manager



www.biotech.ucdavis.edu

The Mission of the Biotechnology Program:

To assist in the organization of University activities related to biotechnology and to coordinate such activities with other efforts on the Davis campus, a Biotechnology Program was created. 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.

Biotechnology Program Office:

Dr. Judith Kjelstrom, Acting Director, and the staff run the program from the offices in 301 Life Sciences Addition.

Telephone: (530) 752-3260
FAX: (530) 752-4125
Email: biotechprogram@ucdavis.edu

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. **2004-05 Fellowship Nominations are due on April 19, 2004 .**

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 (MCB/Chemistry)
Craig Benham (Mathematics/Biomedical Engineering)
George Bruening (Plant Pathology)
Alan Buckpitt (Vet Med: Molecular Biosciences)
Kenneth Burtis (MCB-Molecular & Cellular Biology)
Daniel Chang (Civil & Environmental Engineering)
Abhaya Dandekar (Pomology) [also DEB chair]
Michael Denison (Environmental Toxicology)
Bryce Falk (Plant Pathology)
Katherine Ferrara (Biomedical Engineering)
Andrew Fisher (MCB/Chemistry)
J. Bruce German (Food Science & Technology)
Jeff Gregg (MED: Pathology)
Daniel Gusfield (Computer Science)
Alan Jackman (Chem Engineering & Materials Science
Ian Kennedy (Mechanical & Aeronautical Engineering)
Hsing-Jien Kung (MED: Internal Medicine)
J. Clark Lagarias (MCB)
Kit Lam (MED: Internal Medincine (Hem/Onc)
K. C. Kent Lloyd (Vet Med: Anatomy, Physiology & Cell Biology)
Marjorie Longo (Chemical Engineering & Materials Science)
Karen McDonald (Chemical Engineering & Materials Science)
Claude Meares (Chemistry)
Juan Medrano (Animal Science)
Richard Michelmore (Vegetable Crops)
James Murray (Animal Science)
Martin Privalsky (Microbiology)
Robert Rice (Environmental Toxicology)
David Rocke (Applied Science. MED: Epidemiology & Preventative Medicine)
Kate Scow (Land, Air & Water Resources)
Scott Simon (Biomedical Engineering)
Jean VanderGheynst (Biological Systems Engineering)
Craig Warden (NPB/ MED: Pediatrics)
David Wilson (MCB)
John Yoder (Vegetable Crops)

NIH Training Program in Biomolecular Technology

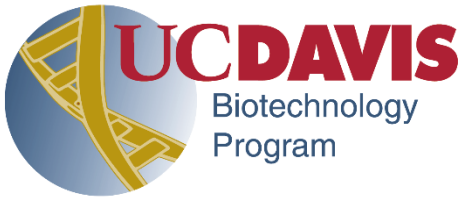
- The DEB is a **formal training program** for the NIH Training Grant.

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

- The DEB provide 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. It is based on: **academic merit; quality of the research; interdisciplinary nature of research; and 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 2002-2003

Last Name	First Name	Department
Bao	Tian	Chemical Engineering
Blanchette	Craig	Biophysics
Boonyaratanakornkit	Jerry	Chemical Engineering
Britton	Monica	Pomology
Chai	Yongping	Biochemistry & Molecular Biology
Chan	Kenneth	VET MED: PMI/ILMB
Chang	Katherine	Biological & Agricultural Engineering
Diaz	Jerome	Food Science & Technology
Do	An	Biochemistry & Molecular Biology
Easlon	Hsien Ming	Plant Biology
Ellsmore-Fisher	Amanda	Plant Biology
Enstrom	Amanda	MED:Hematology & Oncology
Evans	James	Biochemistry & Molecular Biology
Feng	Wen-Ying	Statistics
Gades	Matthew	Nutrition
Gierhart	Brian	Electrical Engineering
Green	Chad	Biomedical Engineering
Guadalupe	Moraima	MED: Microbiology & Immunology
Haghnazari	Edwin	Microbiology
He	Ze	Chemistry
Higgins	Laura	Molecular, Cellular and Integrative Physiology
Holden	Kevin	Microbiology
Horner	Jennifer	Biochemistry & Molecular Biology
Hwang	Yi-Hwa (Patty)	TBD
Iandolino	Alberto	Viticulture & Enology
Ikner	Aminah	Microbiology
Joh	Larry	Biological & Agricultural Engineering
Ju	Kou-San	Microbiology
Kang	Kyung-Don	Entomology
Kareta	Michael	Biochemistry & Molecular Biology
Kuhlman	Susanne	MED: Microbiology
Kunathigan	Viyada	Viticulture & Enology
Lee	Young	MED:Hematology & Oncology
Liu	Wenshe	Chemistry
LoCascio	Riccardo	Viticulture & Enology
Loukoianov	Artem	Agronomy and Range Sciences
McHale	Leah	Vegetable Crops
Meloty-Kapella	Caroline	Cellular & Developmental Biology
Muir	Ryann	Pomology
Peng	Ying	Plant Pathology
Peoples	Tamara	Molecular & Cellular Biology

Phung	Anh	MED: Internal Medicine
Place	Warren	Viticulture & Enology
Reh	Wade	Animal Science
Silva	Jillian	Biochemistry & Molecular Biology
Singh	Sheetal	Food Science & Technology
Southworth	Jesse	Chemical Engineering & Materials Science
Talu	Esra	Chemical Engineering & Materials Science
Taylor	Jennifer	MED: Internal Medicine
Torres	Manuel	Vegetable Crops
Wan	Wei	VET MED:PMI
Ward	Robert	Food Science and Technology
Weidhaas	Jennifer	Civil and Environmental Engineering
Wise	Emily	Biochemistry & Molecular Biology
Wong	Marisa	Animal Science
Wong	Andrew	Animal Science
Wong	Scott	MED:Pathology
Wu	Jing	Microbiology
Xie	Qing	Chemical Engineering & Materials Science
Zaragoza	Melinda	Microbiology
Zumstein	Erin	Biochemistry & Molecular Biology

DEB Participating Faculty

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

Biochemistry & Molecular Biology
Everett Bandman
Alan Bennett
Linda Bisson
Sean Burgess
Ronald Chuang
Michael Denison
Charles Gasser
Bruce Hammock
Thomas Jue
Clarence Kado
Stephen Kowalczykowski
Hsing-Jien Kung
J. Clark Lagarias
Kit Lam
Janine LaSalle
Paul Luciw
Claude Meares
Marty Privalsky
Robert Rice
Pam Ronald
Robert Rucker
Dewey Ryu
Earl Sawai
Kazuhiro Shiozaki
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
Katherine Ferrara
Ian Kennedy
Tonya Kuhl
Kit Lam
Marjorie Longo
Claude Meares
Dewey Ryu
Scott Simon

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

Cell & Developmental Biology
Gary Anderson
Everett Bandman
Ron Baskin
Paul FitzGerald
Robert Rice
Reen Wu

Chemical Engineering & Materials Science Engineering
Stephanie Dungan
Tonya Kuhl
Marjorie Longo
Karen McDonald
Ron Phillips
Robert Powell
Subhash Risbud
Dewey Ryu

Chemistry
Matthew Augustine

DEB Participating Faculty

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
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

Environmental Toxicology
Michael Denison
Fumio Matsumura
Barry Wilson

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

Genetics
Alan Bennett
Linda Bisson
George Bruening
Sean Burgess
Abhaya Dandekar
Charles Gasser
David Gilchrist
Clarence Kado
Stephen Kowalczykowski
Janine LaSalle
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

Mechanical & Aeronautical Engineering

Abdul Barakat
Ian Kennedy

Microbiology
Blaine Beaman
Linda Bisson
Richard Bostock
George Bruening
Sean Burgess
Ronald Chuang
Satya Dandekar
Bruce Hammock
Paul Luciw
Clarence Kado
Karen McDonald
David Ogrydziak
Rebecca Parales
Marty Privalsky
Dewey Ryu

DEB Participating Faculty

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
Dewey Ryu
Judith Stern
Alice Tarantal
Barry Wilson
Reen Wu

Nutrition
Christopher Calvert
Andrew Clifford
J. Bruce German
Judith Stern

Pharmacology & Toxicology
Ronald Chuang
Bruce Hammock
Hsing-Jien Kung
Jerold Last
Robert Rice
Robert Rucker
Barry Wilson
Reen Wu

Plant Biology
Diane Barrett
Alan Bennett
Richard Bostock
Abhaya Dandekar
Katayoon "Katy" Dehesh
Don Durzan
Charles Gasser
Tom Gradziel
J. Clark Lagarias
Terence Murphy
Michael Reid
Pam Ronald
Valerie Williamson
John Yoder

Plant Pathology
Richard Bostock
George Bruening
David Gilchrist
Clarence Kado
Richard Michelmore
Pam Ronald

Statistics
Andrew Clifford
Shu Geng
David Rocke

The Value of Internships

Over the last 10 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:

Bayer;
Berlex Biosciences;
Celera AgGen;
Chiron;
DuPont
Exelixis;
Genentech;
ICOS
Maxygen;
Monsanto, Calgene Campus;
Novozymes Biotech, Inc (aka Novo Nordisk);
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

With over 60 students currently enrolled, we need more Academic-Industry Partnerships