Sixteenth Annual

Biotechnology Training Retreat

Saturday,
March 31, 2007

Christian Brothers Retreat & Conference Center
Napa, CA

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Napa, CA

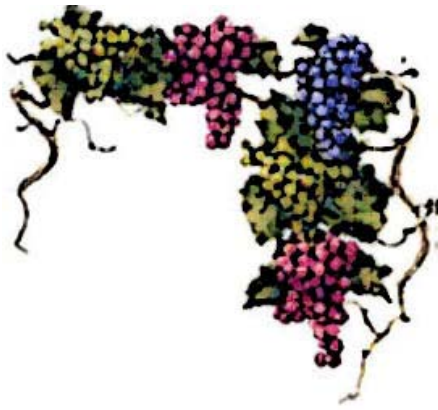
Co-sponsored by:

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

UC Davis Designated Emphasis in Biotechnology
Graduate Program (DEB)

UC Davis Biotechnology Program





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Welcome

On behalf of the UC Davis 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 **2006-07 fellows and their preceptors**, as well as **our industry affiliates**. The logistics of this retreat has been graciously overseen by our assistant director, Dr. Denneal Jamison-McClung and our event manager, Marianne Hunter. Please enjoy the great presentations, the delicious food and wine and magical scenery.

I would like to introduce our Biotechnology Fellows. Our **5 NIH Fellows** include: **Suzanne Barber,** Chemical Engineering (preceptor is Tonya Kuhl); **Allison Dickey**, Chemical Engineering (preceptor is Roland Faller); **Corey Dodge**, Chemical Engineering (preceptor is Karen McDonald); **Dominik Green**, Biochemistry & Molecular Biology (preceptor is R. Holland Cheng) and **Jennifer Warren**, Civil and Environmental Engineering (preceptor is Stefan Wuertz). Our **4 Biotechnology Fellows** (industry and campus fellowships) include: **Vannarith "Van" Leang,** Chemical Engineering (preceptor is Robert "Bob" Powell); **Riccardo LoCascio,** Microbiology (preceptor is David Mills); **Michael Howland,** Chemical Engineering (preceptor is Atul Parikh) and **Vu Bao Trinh,** Biochemistry & Molecular Biology (preceptor is Yohei Yokobayashi). We would also like to recognize our **First Year Biotechnology Fellows: Ben Lindenmuth** (Chemical Engineering); **Sarah Statt** (Biochemistry & Molecular Biology) and **Elianna Goldstein** (Plant Biology). Ben and Elianna have already become members of the DEB. 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 are very proud of all of them.

Pending renewed funding of the Training Grant, we will select our **2007-08 fellows** in May. Nomination Forms will be on the web at www.deb.ucdavis.edu). Remember, you must be a member of the DEB to be eligible for funding. The DEB graduate program is the formal training program for the NIH training grant and the number of **DEB students is currently up to 114 and climbing.** Each of our students is showcased on the newly revised DEB website (www.deb.ucdavis.edu).

In regard to industrial internships for 2006-7, we placed many students: **Ying Chen** completed her internship at Advanced Micro Devices (AMD); **Corey Dodge** interned for 6 months with BioMarin Pharmaceuticals; **Anh Phung, Li Peng** and **Craig Blackmore** chose Genentech while **Michael Plesha, Brad Niles** and **Juan Pedro-Sanchez** went with Monsanto, Calgene Campus. **Aminah Ikner** completed her internship at Novozymes and is now a post-doc at Genentech; while **Rowena Romano** is currently at Novozymes, Inc. **Jessica Bohonowych** interned with Scios and is now doing a post-doc at the Medical University of South Carolina. We are busy placing students in various companies for the summer of 2007. A couple of new locations are Tethys and Novartis in Vacaville. We would like to thank all of our industry affiliates for their support of our training program. A number of students graduated in 2006 with their PhDs with a Designated Emphasis in Biotechnology: **Susanne Berglund; Jessica Bohonowych; Aminah Ikner, Anh Phung; Daniel Scott; Jennifer Taylor and Melinda Zaragoza.** Please see the latest edition of **Biotechnology Times** on the Biotechnology Program's website at http://www.biotech.ucdavis.edu/ for more information.

Thanks for coming. Please Come Again on **April 5, 2008** (tentative date).

With warm regards,

Judy Kjelstrom,
Director, UC Davis Biotechnology Program

NIH Training Program in Biomolecular Technology

(NIH-1-T32-GM08799)

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

Executive Committee

Faculty:

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

Industry:

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

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

Designated Emphasis in Biotechnology (DEB) Graduate Program

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UC Davis Biotechnology Program

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UC Davis Sixteenth Annual Biotechnology Training Retreat
March 31, 2007
Christian Brothers Retreat & Conference Center

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

8:00 – 8:30 am	**Registration/Continental Breakfast**		
8:30 – 8:45 am	**Welcome** Bruce Hammock Director, NIH Training Grant in Biomolecular Technology		
	Morning Session Chair Martina Newell McGloughlin Co-Director, NIH Training Grant in Biomolecular Technology		
8:45 – 10:20 am	**Presentations**		
	8:45 am	Suzanne Barber	*Mentor: Tonya Kuhl*
	9:10 am	**Kathy Lardizabal**	**Monsanto, Calgene Campus**
	9:35 am	Jennifer Warren	*Mentor: Stefan Wuertz*
	10:00 am	Dominik Green	*Mentor: R. Holland Cheng*
10:20 – 10:50 am	**Break / Poster Viewing**		
10:50 am – 12:20 pm	**Presentations**		
	10:50 am	**Amit Chaudhuri**	**Genentech, Inc.**
	11:15 am	Allison Dickey	*Mentor: Roland Faller*
	11:35 am	Corey Dodge	*Mentor: Karen McDonald*
	12:00 pm	Martina Newell-McGloughlin	Bioethics Question (Handout)
12:20 – 2:15 pm	**Lunch / Poster Viewing**		
	Afternoon Session Chair Abhaya Dandekar Chair,DEB Executive Committee		
2:15 – 4:00 pm	**Presentations**		
	2:15 pm	Martina Newell-McGloughlin	Bioethics Question (Discussion)
	2:40 pm	**Sandy Merino**	**Novozymes, Inc.**
	3:05 pm	Riccardo LoCascio	*Mentor: David Mills* *Mentor: Robert Powell*
	3:30 pm	Vannarith Leang	
4:00 pm	**Short Break (10 min)**		
4:10 – 5:30 pm	**Presentations**		
	4:10 pm	Vu Bao Trinh	*Mentor: Yohei Yokobayashi*
	4:50 pm	Michael Howland	*Mentor: Atul Parikh* **Amyris**
	5:15 pm	**Jack Newman**	**Amgen, Inc.**
	5:40 pm	**Shawn Jeffries**	
6:00 pm	**Closing Remarks** Bruce Hammock / Martina Newell McGloughlin		

6:30 pm – Bus departs Napa

2007 Poster Titles

A. **"Characterization of Adult Cardiac Stem Cells"**
Astra I. Chang*[£], Jennifer Moore[§¥], Qian Zhang[£], Valeriy Timofevey[£], J. Nilas Young[#], Ronald A. Li[§¥] and Nipavan Chiamvimonvat[£]
[£]Division of Cardiovascular Medicine, [§]Department of Cell Biology & Human Anatomy, [¥]Stem Cell Program, [#]Division of Cardiothoracic Surgery, University of California Davis

B. **"Bacterial Chemotaxis To *S*-Triazines and Pyrimidines"**
Xianxian Liu* and Rebecca E. Parales
Section of Microbiology, University of California, Davis, CA 95616

C. **"Identification and Characterization of Longevity Regulation Genes in *S. Cerevisiae*"**
Chen Wang* and Su-ju Lin
Section of Microbiology, University of California, Davis, 95616

D. **"Transcriptional Control of 2-Nitroluene Degradation Genes in *Acidovorax* SP. Strain JS42"**
Kou-San Ju*, Juan V. Parales, and Rebecca E. Parales
Section of Microbiology, University of California, Davis, CA, 95616

E. **"The Complete Genome Sequence of *Bifidobacterium longum* bv. *infantis*"**
David A. Sela[1*], Samara L. Freeman[2], Paul M. Richardson[3], J. Bruce German[2], and David A. M ills[1]
[1] Dept. of Viticulture and Enology, University of California, Davis, CA, 95616
[2] Dept. of Food Science & Technology, University of California, Davis, CA, 95616
[3]Joint Genome Institute Production Genomics Facility, Walnut Creek, CA, 94598

F. **"Identification and Characterization of Longevity Regulation Genes in *S. Cerevisiae*"**
Chen Wang* and Su-ju Lin
Section of Microbiology, University of California, Davis, CA, 95616

G. **"XB15 Is a Negative Regulator of XA21-Mediated Disease Resistance"**
Ying Peng[1*], Chang Jin Park[1], Christopher Dardick[2], Randy Ruan[1] and Pamela Rona ld[1]
[1]Department of Plant Pathology, University of California, Davis, CA 95616
[2]USDA-ARS, Appalachian Fruit Research Station, Kearneysville, WV

H. "Strategies for Improving the Production of Functional Recombinant Human Therapeutics in Transgenic Tobacco Cell Cultures"

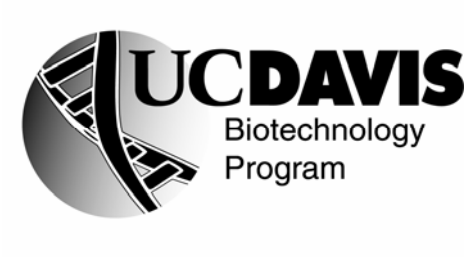
Ting-Kuo Huang[1]*, Michael A. Plesha[1], Bryce W. Falk[2], Abhaya M. Dandekar[3] and Karen McDonald[1]
[1]Department of Chemical Engineering and Materials Science,
[2]Department of Plant Pathology, ,
[3]Department of Plant Sciences,
University of California, Davis, 1 Shields Ave., Davis, CA 95616

I. A Metabolic Modeling Approach to Optimizing Recombinant Protein Production in *L. Lactis* Fermentations

Gian Oddone[1]*, David A. Mills[2] and David E. Block[1,2]
[1]Department of Chemical Engineering and Materials Science,
[2]Department of Viticulture and Enology
University of California Davis, 1 Shields Ave, Davis, CA 95616

See pages 30 - 39 for poster abstracts.

***Member of DEB graduate group**



Oral Presentation Abstracts

NIH FELLOW: Suzanne Barber

ENGINEERING INTERACTIONS BETWEEN BIOLOGICAL MATERIALS: FROM BIOSENSORS TO MEMBRANE FUSION

Presenter:	Suzanne Barber*
Authors:	**Suzanne Barber***, Philip J. Costanzo, Jarek Majewski, Chad E. Miller, Vishal Trivedi, Walter Stockinger, Timothy E. Patten, Tonya L. Kuhl and Axel Nohturfft
Affiliations:	Department of Chemical Engineering and Materials Science University of California-Davis, One Shields Ave, Davis, CA 95616 Weapons and Multifunctional Materials Branch, Army Research Laboratory, 9804 Georgia Ave. #302, Silver Springs, MD 20902 Los Alamos National Lab, Manuel Lujan Neutron Scattering Center, Los Alamos, NM 87545 Harvard University, Department of Molecular & Cellular Biology, Cambridge, MA 02138 Department of Chemistry, University of California at Davis, One Shields Ave, Davis, CA 95616
Preceptor:	Tonya Kuhl, PhD

Rarely in Nature are single molecule interactions used for cell adhesion. Rather, several different types of molecules or structures interact in concert to build effective adhesion. One important role of these multivalent interactions that form adhesion is the key step in fusion between cell membranes. To understand how multivalency is utilized by biological systems, we are working to develop a tailorable, nanoparticle-based biosensor that can probe the range of interactions from the single molecule level to the ensemble average of multiple interactions. In parallel, we are studying the composition and behavior of cell membranes, both *in vitro* and *in vivo*. In this way, we aim to devise an improved model cell membrane system, thus allowing a wider range of techniques to be utilized in the study of critical biological processes, such as adhesion and fusion.

*** Member of the DEB graduate program**

COMPANY AFFILIATE: Monsanto, Calgene Campus

PRODUCTION OF WAX ESTERS IN SEEDS OF TRANSGENIC BRASSICA

Presenter:	Kathryn Lardizabal, PhD
Authors:	**Kathyryn Lardizabal**
Affiliations:	Monsanto, Calgene Campus Davis, CA 95616
Email:	kathy.lardizabal@monsanto.com

Jojoba (*Simmondsia chinensis*) produces long-chain linear wax esters as a seed storage lipid rather than the triacylglycerols found in all other oilseed crops. Three genes have been identified in jojoba, which encode enzymes involved in wax biosynthesis: beta-ketoacyl-CoA synthase (responsible for elongation of fatty acids outside the plastid), long chain acyl-CoA reductase (responsible for formation of primary alcohols), and wax synthase (which combines an acyl-CoA and a primary alcohol to form wax esters). Using genetic technology the genes were introduced into a model oilseed crop, *Arabidopsis thaliana*. Wax levels of R1 seed pools were quantitated using 13C-NMR. Data indicate up to 49.2 mole% of the acyl lipids are present in wax. Single seed analyses of plants with the two highest phenotypes were analyzed by gas chromatography and showed wax levels up to 70% (by weight) of the seed oil. The genes were introduced into *Brassica napus*, a crop that has more favorable agronomic properties, and similar levels of wax production were achieved. Providing a stable supply of long-chain liquid wax at lower cost should make this valuable lipid more attractive for large-scale commercial purposes.

NIH FELLOW: Jennifer Warren

EFFECT OF EPS AND BIOFILM ARCHITECTURE ON CONJUGATIVE GENE TRANSFER IN *VIBRIO CHOLERAE* BIOFILMS

Presenter: Jennifer Warren*

Authors: **Jennifer Warren*,** and Stefan Wuertz

Affiliations: Department of Civil and Environmental Engineering, University of California, Davis, CA 95616

Preceptor: Stefan Wuertz, PhD

Bacteria acquire genes that enable them to adapt and survive in the environment via conjugative gene transfer (HGT). Dissemination of certain genes can present a threat to humans, such as the spread of antibiotic resistance among pathogenic organisms. However, conjugative gene transfer also holds promise as a bioremediation scheme through the transfer of catabolic genes. There is a need to understand conjugative HGT in order to either effectively combat or promote its occurrence. However, many questions persist about conjugation in microbial aggregates. For instance, there is conflicting information on the distribution of transconjugants within biofilms, and the role extracellular polymers play on the dissemination of plasmids is unknown. The main objective of this research is to determine the effect of extracellular polymers and biofilm architecture on conjugative HGT using *Vibrio cholerae* as a model organism. *V. cholerae* can undergo phase variation between two morphologically different variants, termed smooth and rugose, which differ in the extent of EPS production. The rugose variant is defined by increased production of an extracellular polysaccharide, termed Vibrio-polysaccharide (VPS), which leads to enhanced biofilm formation. In contrast, the smooth variant does not produce EPS. Biofilms of rugose and smooth variants chromosomally labeled with the *gfp* were grown in flow cells. For controls, a rugose mutant (RΔ*vps*) and smooth mutant (SΔ*vps)*, with a deletion in the *vps* gene operon causing a constitutively smooth colony type were also utilized. Donor *Pseudomonas putida* cells containing the *rfp* labeled plasmid, pWDL7, which confers resistance to kanamycin were then added. Transconjugants were identified by dual fluorescence of *gfp* and *rfp* using a Confocal Laser Scanning Microscope (CLSM). A novel EPS stain, Solophenyl Flavine, was utilized to quantify EPS. Results show that the rugose, RΔ*vps,* and SΔ*vps* strains all produced different biofilm architectures. The RΔ*vps* and SΔ*vps* biofilms contained similar amounts of EPS, while the rugose biofilm had an order of magnitude higher amount of EPS than either mutant strain. Further, all three strains varied in the percent of transconjugants, with RΔ*vps* having 6.14%, rugose with 1.12%, and SΔ*vps* with 0.6%. It can be seen that both biofilm architecture and EPS have an effect on conjugative horizontal gene transfer.

*** Member of the DEB graduate program**

NIH FELLOW: Dominik Green

STRUCTURAL ANALYSIS OF HEAVY RIBOFLAVIN SYNTHASE FROM *Bacillus subtilis* – TECHNIQUES IN IDENTIFYING AND CLASSIFYING CONFORMATIONAL HETEROGENITY

Presenter:	Dominik J. Green*
Authors:	**Dominik J. Green**, **Li Xing, & R Holland Cheng**
Affiliations:	Biochemistry and Molecular Biology Graduate Group and Section of Molecular & Cellular Biology
Preceptor:	R. Holland Cheng, PhD

Throughout the past decade, cryo-electron microscopy (cryoEM) and single particle reconstruction (SPR) techniques have emerged as powerful tools for use in studying the three-dimensional (3D) structures of large-molecular weight, multi-protein complexes. Advantages of cryoEM and SPR in structural determination include the ability to: 1) study proteins within their native, hydrated environments; 2) subject the proteins to varying buffers, pHs, and substrate/ligand conditions; and 3) perform time-dependent experiments to within millisecond timescales. With these advantages in mind, our lab has sought to study the catalytic cycle of heavy riboflavin synthase (HRFS) from *Bacillus subtilis* using cryoEM and SPR with the goals of determining the specific protein-protein interactions and rearrangements that occur throughout catalysis. Early physical studies on HRFS have shown that it exists as a capsid of 60 subunits of lumazine synthase (LS) arranged as an icosahedron around a trimer core of riboflavin synthase (RS). Our preliminary studies of weakly-liganded LS capsids (LS in presence of only a single substrate analog) have revealed that the LS structures experience thermally-driven expansions and contractions, generating projections with varying diameters, along with capsid distortions that generate projections which deviate from circularity. Additionally, at least two populations of particles have been found: one population mimicking the native HRFS; the other, novel in structure, appears to reveal decreased contact between associating pentamers. We hypothesize that the LS capsid is greatly destabilized without the presence of the RS trimer core and/or without the presence of both substrate ligands. In order to solve a stable yet weakly-liganded LS structure, multivariate statistical analysis (MSA) has been utilized to classify particles according to their size variations. Our early results have shown that differences in diameter of less than 1% can be accurately classified with MSA. Future work will concentrate on the identification and exclusion of distorted particles by using edge- and ellipse-detection methods.

*** Member of the DEB graduate program**

COMPANY AFFILIATE: Genentech, Inc.

Presenter:	Amitabha Chaudhuri,Ph.D.
Authors:	**AmitabhaChaudhuri**
Affiliations:	Department of Molecular Oncology, 1 DNA Way, South San Francisco, CA 94080
Email:	chaudhuri.amitabha@gene.com

Receptor tyrosine kinases are central mediators of many aspects of cellular homeostasis, including cell proliferation, survival, differentiation and migration. The signaling pathways downstream to receptor tyrosine kinases are commonly dysregulated in various types of cancers making them attractive targets of cancer therapy. Our understanding of various types of genetic and epigenetic alterations in receptor tyrosine kinases have led to the discovery of novel therapies that have been effectively translated into medicines improving the lives of cancer patients' significantly.

NIH FELLOW: Allison Dickey

GLOBAL AND LOCAL CHANGES IN THE ENVIRONMENT: PERSEPECTIVES FROM A TRANSMEMBRANE PROTEIN

Presenter:	Allison Dickey*
Authors:	**Allison Dickey, Roland Faller**
Affiliations:	Departments of Chemical Engineering and Material Science, University of California, Davis, CA 95616
Preceptor:	Roland Faller, PhD

Prescribing anesthetics to relieve pain during medical procedures has long been a common practice. However, it is still widely debated how these compounds interact with the cellular membrane and cause anesthesia. One theory is that anesthetic molecules diffuse into the lipid bilayer, increasing lateral pressure on neighboring transmembrane proteins. This results in slight alterations in receptor conformation, rendering the proteins non-functional. Currently, we use molecular dynamics simulations to study this hypothesis in conjunction with the nicotinic acetylcholine receptor (nAChR) and ethanol, a general anesthetic.

When constructing a lipid bilayer for nAChR solvation, it is important that the model bilayer accurately portray the composition of a cellular lipid membrane. Experimentally, it has been found that the nAChR will exist in a functional state that conducts ions only when the receptor is surrounded by the anionic lipid, phosphatidic acid [1]. To determine how the interactions between the nAChR and phosphatidic acid might differ from those of other lipids, we compare the mechanical and structural properties of a lipid bilayer composed of phosphatidic acid with those from a bilayer composed of the neutral lipid phosphatidylcholine and a bilayer composed of the anionic lipid phosphatidylglycerol.

After having determined the structure of the nAChR, Unwin et. al. reported that the activation energy required to switch between the open and resting states is very small and that only a minor structural perturbation is required to convert the ion channel from one state to the other [2]. Because the state of the nAChR is very sensitive to its surroundings, we examine which nAChR residues are the most responsive to changes in local environment through a self-consistent mean theory approach [3]. In using this method, we hope to identify those residues whose conformations are the most easily altered. We compare these results with those from a simulation where a global change in the nAChR environment is introduced in the form of an ethanol solution.

1. Sunshine, C., McNamee, M., 1992. Lipid modulation of nicotinic acetylcholine receptor function: the role of neutral and negatively charged lipids. *BBAMEM 1108*: 240-246.

2. Unwin, N., 2005. Refined Structure of the Nicotinic Acetylcholine Receptor at 4 Å Resolution. *J.Mol.Biol. 346*: 967-989.
3. Koehl, P., Delarue, M., 1994. Application of a Self-consistent Mean Field Theory to Predict Protein Side-chains Conformation and Estimate Their Conformational Entropy. *J. Mol. Biol.* 239: 249-275.

*** Member of the DEB graduate program**

NIH FELLOW: Corey Dodge

EXPRESSION OF RECOMBINANT GELATIN IN TRANSGENIC RICE CELL CULTURES

Presenter: Corey Dodge*

Authors: **Corey Dodge***[1], Julio Baez[2] and Karen A. McDonald[1]

Affiliations: [1]Department of Chemical Engineering and Materials Science, University of California at Davis, Davis, CA 95616
[2]Fibrogen, South San Francisco, CA 94080

Preceptor: Karen McDonald, PhD

Animal-derived gelatin is used extensively in the manufacturing of pharmaceutical capsules. However the intrinsic variability and potential for contamination of animal-derived gelatin have prompted the development of novel production technologies for recombinant gelatin (rGelatin). Genetically-modified yeast and plants have been developed as attractive technologies for the production of low cost/high volume industrial proteins such as gelatin. We are developing plant cell culture as a complementary technology to transgenic plants for the fast evaluation of plant-derived industrial recombinant proteins. Previously, our laboratory successfully demonstrated the ability of transgenic rice (*Oryza sativa*) cell culture to express and secrete a 100kDa fragment of rGelatin. Here we present the results of efforts to improve the productivity of the system through the inhibition of protease activity and improvement of the growth media, which have resulted in a significant improvement in batch culture productivity. Further studies have been performed to investigate continuous perfusion cell culture as means to optimize the volumetric productivity. We have conducted trials with several types of cell retention devices, which are crucial to the operation of a robust perfusion process, and have identified two, an acoustic filter and an impeller shaft spin filter, as promising alternatives.

*** Member of the DEB graduate program**

COMPANY AFFILIATE: Novozymes, Inc.

ENZYME IMPROVEMENT FOR BIOMAS UTILIZATION

Presenter: Sandy T. Merino, PhD
Authors: **Sandy T. Merino**
Affiliations: Novozymes, Inc., 1445 Drew Ave., Davis, CA 95616
Email: SAME@novozymes.com

The fungus, *Trichoderma reesei*, secretes numerous enzymes involved in the metabolism of plant polysaccharides such as xylan, starch, pectin, and cellulose. These enzymes play a critical role in the conversion of cellulosic waste into fuels, by breaking down polymeric sugars to fermentable monomers. Recently, there has been a significant effort to reduce the cost of enzymes required for biofuels production. New enzymes have been identified, the efficiency of enzymes has been improved, and new enzyme mixes are being created based on substrate type. This presentation will discuss recent advances in enzyme technology for conversion of biomass to fermentable sugars.

BIOTECH FELLOW: Riccardo LoCascio

CHARACTERIZATION OF HUMAN BREAST MILK OLIGOSACCHARIDES AND PLANT FRUCTOLIGOSACCHARIDES CONSUMPTION BY INFANT-BORN BIFIDOBACTERIA

Presenter: Riccardo LoCascio*

Authors: **Riccardo G. LoCascio[1-4]***, Milady Ninonuevo[2], Mariana Barboza[2], J. Bruce German[3], Carlito B. Lebrilla[2] and David A. Mills[1]

Affiliations: [1]Department of Viticulture & Enology, University of California, Davis, 95616
[2]Department of Chemistry, University of California, Davis, 95616
[3]Department of Food Science & Technology, University of California, Davis, 95616
[4]Microbiology Graduate Group, University of California, Davis, 95616

Preceptor: David Mills, PhD

The molecular basis by which human breast milk supports the development of a protective intestinal microbiota in infants is unknown. Human Milk Oligosaccharides (HMOs) are believed to provide a range of benefits to the developing infant including protection against pathogens and prebiotic enrichment of beneficial commensals such as bifidobacteria. To date, the mechanistic detail for the prebiotic effect of these oligosaccharides on bifidobacteria remains unknown. In this work, glycomic profiling of HMO consumption by bifidobacteria reveals that one species, *Bifidobacterium longum* biovar *infantis*, an isolate from the infant gut, specifically consumes four small mass milk oligosaccharides. These four small mass oligosaccharides (DP < 7) represent nearly 70% of all HMOs present in pooled breast milk. Lactation glycoprofiles have confirmed that during the first 30 days of lactation these HMOs are secreted in breast milk. In contrast, other tested bifidobacteria consumed minimally one HMO. In contrast fructo-oligosaccharides are widely and non-specifically consumed among all the tested strains. This approach is currently being replicated for a large scale profiling of oligosaccharide consumption patterns of other bifidobacteria, with an emphasis of infant-borne isolates.

*** Member of the DEB graduate program**

BIOTECH FELLOW: Vannarith Leang

USING NMR TECHNIQUES TO DETECT COALESCENCE OF EMULSIONS

Presenter:	Vannarith M. Leang*
Authors:	**Vannarith M. Leang***, Jeffery H. Walton, Robert L. Powell, Stephanie R. Dungan, and Ronald J. Phillips
Affiliations:	Department of Chemical Engineering, University of California, Davis, CA 95616
Preceptors:	Robert Powell, PhD & Stephanie R. Dungan, PhD

An emulsion is a thermodynamically unstable mixture of two immiscible fluids with one fluid being dispersed in the other. Coalescence, which is the fusion of two similarly sized drops forming a larger drop, is one of several emulsion breakdown methods. The coalescence mechanism can be broken into four distinct steps: Collision, Film Drainage, Film Rupture, and Confluence. These four steps happen sequentially, each step with its own time scale. Our research focuses on the first two steps, collision and film drainage, which are dominated by hydrodynamic forces. We are able to study hydrodynamic forces in the coalescence process by shearing the emulsion. The rate of coalescence will be directly related to the change in drop size of the system, which will be measured by MRI Techniques through the use of the restricted diffusion theory. MRI is a non-invasive and insensitive technique that allows us to measure drop sizes and distinguish the difference between a cluster of small drops and one big drop. Preliminary results using a mixture of octane, water, and Tween 20 show that coalescence happens to a small volume percent of the oil, which leaves the rest of the emulsion mixture unchanged. Furthermore, this small population of drops becomes so big that they cream out of the emulsion affecting the flow field. These results will help in the development of emulsion systems that coalesces more homogeneously.

*** Member of the DEB graduate program**

BIOTECH FELLOW: Vu Bao Trinh

GENE REGULATION WITH RNAi-BASED GENETIC SWITCHES CONTROLLED BY AN APTAMER

Presenter: Vu Bao Trinh*

Authors: **Vu B. Trinh***, Chung-Il An, and Yohei Yokobayashi

Affiliations: Biochemistry and Molecular Biology Graduate Group and Department of Biochemistry and Molecular Biology and Department of Biomedical Engineering, University of California, Davis, California 95616, USA

Preceptor: Yohei Yokobayashi, PhD

RNA interference (RNAi) has been used as a powerful tool to silence gene expression. We developed a strategy for post-transcriptional gene regulation in mammalian cells by modulating RNAi with a small molecule. Using a theophylline aptamer-fused short hairpin RNAs (shRNAs), Dicer-mediated cleavage of the shRNA is inhibited upon binding theophylline, resulting in theophylline-induced expression of an exogenous gene. We originally used artificial expression of enhanced green fluorescent protein to prove the functionality of the genetic switch. To show the potential for control of endogenous proteins, the aptamer-fused shRNA was redesigned to silence Lamin A/C, non-essential proteins that make up part of the inner nuclear membrane in mammalian cells. We are also establishing a stable cell line to examine the reversibility of the theophylline regulated genetic switch. In addition to the theophylline aptamer, we are also examining the possibility of combining the shRNA with other aptamers, such as the HIV-1 Rev protein aptamer. These ligand-responsive genetic switches based on RNAi may provide new insights into the functionality of RNA molecules as well as its applications.

*** Member of the DEB graduate program**

BIOTECH FELLOW: Michael Howland

UNDERSTANDING SUBSTRATE EFFECTS IN SUPPORTED LIPID MEMBRANES

Presenter: Michael C. Howland*

Authors: **Michael C. Howland*** and Atul N. Parikh

Affiliations: Department of Chemical Engineering and Materials Science, University of California – Davis

Preceptor: Atul Parikh, PhD

Supported membranes, single lipid bilayers on solid surfaces, hold promise in a wide range of applications from biocompatibility and biosensing to protein crystallization and drug discovery. However, many unanswered fundamental questions hamper their practical applications. Many of these questions relate to the perturbations experienced by the bilayer because of the proximity of and interactions with the substrate. In particular, the substrate gives rise to both the geometry and morphology of the supported systems and can also interact with the membranes, effecting properties such as mobility and leaflet composition. We have investigated a number of aspects of the substrate-membrane interaction. In our initial studies, we examined the role of the substrate hydrophobicity in templating membrane morphologies. Lipid vesicles were introduced to substrates of varying hydrophobicity and the resulting structures were investigated. As expected, the hydrophobicity of the substrate greatly influences the resultant morphology of the supported membrane. In the limiting cases, a bilayer is formed on hydrophilic substrates while single leaflet monolayers form on hydrophobic substrates. Using these results in combination with photolithography, we have constructed templated arrays of varied membrane composition. These arrays allow us to investigate the electrostatic influence of the substrate on the adherent membrane by providing a reference of the original SUB composition. The negative charge of the substrate interacts with molecules within the membrane and affects the transverse distribution of charged constituents. We have begun to measure the leaflet specific distributions of a commonly used fluorescent probe, Texas Red DHPE, as well as ganglioside protein receptor, GMI. Both molecules carry a negative charge at typical pH values. We aim to quantitatively establish the leaflet distribution propensities of these and other molecules to aid in the development of supported membrane applications.

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COMPANY AFFILIATE: AMYRIS BIOTECHNOLOGIES

AMYRIS: TOWARDS BUILDING AN IMPACTFUL COMMUNITY

Presenter: Jack D. Newman, PhD
Authors: **Jack D. Newman**.
Affiliations: Amyris Biotechnologies, Emeryville, CA 94608
Email: Newman@amyrisbiotech.com

Amyris was formed by scientists and engineers with a desire to build a high-impact company based on innovative science. Our first project is synthesizing anti-malarial drugs for a fraction of the current production cost. The funding for this project comes through the Institute for One World Health with a $43M grant from the Bill and Melinda Gates Foundation. In this arrangement, Amyris has agreed to take no profit in supplying this cutting edge technology to solve a developing world problem in Africa and Asia. We estimate that our production costs would be significantly lower than current costs of extracting the drug from a plant source. Amyris is collaborating on this project with UC Berkeley, staying ahead of our three year target deadline. The heart of the technology relies on re-engineering the "pipes" in microbes such as yeast, manipulating the cells to produce a target molecule. Our next project, funded by outside investors, further manipulates yeast to make next-generation biofuels that burn more efficiently than ethanol and function in today's cars without modification.

COMPANY AFFILIATE: Amgen Inc.

AMGEN: A WORLD LEADER IN BIOTECHNOLOGY

Presenter: Shawn Jeffries, Ph.D.

Authors: **Shawn Jeffries**

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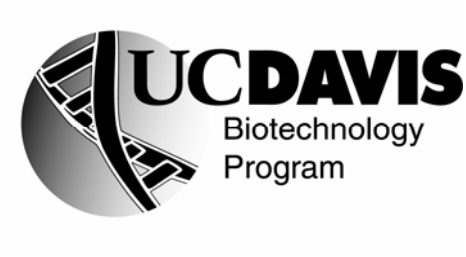
Amgen is a leading human therapeutics company in the biotechnology industry. For more than 25 years, the company has tapped the power of scientific discovery and innovation to advance the practice of medicine and dramatically improve the quality of people's lives.

Amgen pioneered the development of novel products based on advances in recombinant DNA and molecular biology and launched the biotechnology industry's first blockbuster medicines. Today, as a *Fortune* 500 company serving millions of patients, Amgen continues to be an entrepreneurial, science-driven enterprise dedicated to helping people fight serious illness.

Our mission in the Hematology/Oncology therapeutic area is to discover new therapies to treat cancer and hematological malignancies. We employ a modality-independent approach to identify and target key proteins involved in the genesis and progression of cancer.



Bioethics

ETHICS QUESTION

Can You Tell If a Science Publication Isn't Authentic?

by

Martina Newell-McGloughlin
Co-Director of NIH Training Grant
in Biomolecular Technology

(NIH-1-T32-GM08799)

Peer Review, Purview or Purloin?

Prof Jean Luc Borg is one of very few molecular biologists working in a particular field. Dr. Borg receives a paper to review, about a protein called existencin, which he and a graduate student in his laboratory are researching. The article was submitted by Dr. Paul Murky to *Protein Connections*, a medium-impact journal, and the editor asked Dr. Borg and two other experts in the field to review the paper. The article suggests a new interaction between existencin and the protein PS3 and provides evidence for the fact that both proteins are necessary for the full survival-promoting function of existencin in a cell. The article also demonstrates, though, that if there is too much existencin inside cells they cease to exist.

But the paper is fraught with problems: poor controls, inconsistent data in figures, and alternative explanations are not considered and claims are overstated. Dr. Borg gives the paper to his graduate student Marge Innovera, who gives it a detailed critique and recommends significant revisions. Ms. Innovera has never reviewed an article before, and Dr. Borg thinks that doing so would be a good educational experience for her. Ms. Innovera notes the finding about too much existencin being toxic to cells, a problem she has had working with the protein, and discusses it with Dr. Borg. Both agree that they should lower the dosage of existencin in her experiments; the cells actually survive for a week, longer than her experience before, and then they die.

Dr. Borg submits Ms. Innovera's and his own comments about the research to the editor, suggesting that the paper be accepted only after a few more experiments are performed to validate some of the conclusions. One of the other reviewers has comments similar to Dr. Borg's, and the editor asks Dr. Murky, the author, to make the revisions before he will accept the paper.

But in the next few weeks the interaction between PS3 and existencin that is discussed in the paper remains in Dr. Borg's mind. PS3 was not a line of inquiry that Dr. Borg and Ms. Innovera were following in their research. They were focusing on other stimulatory proteins, but unsuccessfully. Dr. Borg suggests to Ms. Innovera that she add a compound to the cell culture system that stimulates the cell to produce its own PS3, a method that is somewhat different from what was in the paper by Dr. Murky that is under review. The enhancement method works. The cells live for a month.

Ms. Innovera and Dr. Borg draft a paper based on the results, which includes appropriate controls. *Science*, a prestigious journal, accepts the paper. Several months later, *Protein Connections* publishes a revised paper from the laboratory of Dr. Murky. But after Dr. Murky sees the article in *Science* he suspects that Dr. Borg, who was an anonymous peer reviewer on the paper, might have taken some of the ideas for the *Science* article from his paper under review. Dr. Murky knows that Dr. Borg hadn't been working on PS3 because it was hard to purify, and deduces that he used material in the unpublished manuscript to stimulate PS3 activity (he ground it up and added it to the media!!).

What is responsible peer review?

1: What types of conflict of interest might arise when someone is asked to review a paper or grant application?

2: Is it ever appropriate for a peer reviewer to give a paper to a graduate student for review? If so, how should the reviewer do so?

3: Is it appropriate for a peer reviewer to use ideas from an article under review to stop unfruitful research in the reviewer's laboratory?

4: Is it ever appropriate for a reviewer to use ideas from a paper under review, even if the reviewer's method to achieve a result is different from that used in the paper under review? If so, how should the reviewer proceed?

5: What are some of the challenges in the current peer-review process, in which the peer reviewer is anonymous but the author is known to the reviewer?

6: What recourse is there for Dr. Murky if he suspects that his ideas were plagiarized?

Other thoughts

1: How can one separate oneself from the content of a paper or grant application under review?

2: What are some ways in which the process of peer review might be improved?

Poster Abstracts

A. CHARACTERIZATION OF ADULT CARDIAC STEM CELLS

Astra I. Chang*[£], Jennifer Moore[§¥], Qian Zhang[£], Valeriy Timofevey[£], J. Nilas Young[#], Ronald A. Li[§¥] and Nipavan Chiamvimonvat[£]
Division of Cardiovascular Medicine[£], Department of Cell Biology & Human Anatomy[§], Stem Cell Program[¥], Division of Cardiothoracic Surgery[#], University of California Davis

Despite numerous pharmacological and other treatments, cardiovascular disease (CVD) remains the most common cause of death in the United States, emphasizing the need for new and more effective therapies. One novel approach to treat heart disease involves the repopulation of malfunctioning and dying cardiomyocytes in patients with ischemic heart disease by cell transplantation. The beneficial effects from transplantation of various cell types (e.g. neonatal cardiomyocytes, embryonic stem cells, bone marrow progenitors, and myoblasts) remain uncertain due to lack of integration with the myocardium and loss of transplanted cells. Recent identification of cardiac stem cells (CSCs) resident in the adult heart provides evidence that challenges the paradigm of the non-regenerating heart. Cardiac stem cells represent an enormously promising donor source for transplantation, circumventing many of the concerns surrounding the use of other stem cell types. However, much remains to be understood and elucidated about CSCs including whether CSCs can be optimally grown *in vitro* when isolated from a small fragment of adult cardiac tissue, whether they can be autologously administered to patients with heart failure, and whether they can successfully improve cardiac health. The goal of this project is to systematically identify the biological, functional, and biochemical properties of CSCs. Central to our hypothesis is that CSCs are multipotent cells which can differentiate into multiple lineages. It is further hypothesized that CSCs can be specifically and optimally proliferated and differentiated *in vitro* for direct cardiac transplantation. We have successfully isolated CSCs using stem cell surface markers and are currently conducting a robust characterization of CSCs using cellular, biophotonic, genomic and proteomic, and electrophysiological approaches, as well as how these change over time as CSCs differentiate. In so doing, new insights gained will enable the identification and circumvention of obstacles currently impinging upon the therapeutic applications of CSCs. It is of utmost importance that the biology of these cells is more fully understood. Only then can beneficial therapeutic use be obtained.

*** Member of the DEB graduate program**

B. BACTERIAL CHEMOTAXIS TO *S*-TRIAZINES AND PYRIMIDINES

Xianxian Liu* and Rebecca E. Parales
Section of Microbiology, University of California, Davis, CA 95616

Atrazine, a man-made *s*-triazine compound, is used world wide as an herbicide and has been reported to be toxic to animals. The atrazine-degrading bacterium *Pseudomonas* sp. ADP utilizes atrazine as its sole nitrogen source and mineralizes it in the process. We are interested in investigating the chemotactic response of this strain towards atrazine and related *s*-triazines. We demonstrated that atrazine and atrazine degradation intermediates are chemoattractants for strain ADP using quantitative capillary assays. The chemotactic response to these *s*-triazines was constitutively expressed, and atrazine metabolism was not required. Two other *Pseudomonas* strains, *P. putida* F1 and *P. putida* PRS2000, neither of which is able to utilize atrazine, were tested for chemotaxis and shown to be attracted to some of the *s*-triazines. These results suggest that *s*-triazines may be detected by similar chromosomally-encoded chemoreceptor(s) in all three strains. Because pyrimidines are the closest natural structural analogs to *s*-triazines, the three strains were also tested for chemotaxis to pyrimidines. All three *Pseudomonas* strains responded to pyrimidines. We propose that *s*-triazines may be recognized by a pyrimidine chemoreceptor. To test this hypothesis, we first studied *E. coli* chemotaxis to pyrimidines and *s*-triazines. Wild-type *E. coli* was attracted to all three pyrimidines and some *s*-triazines. A Tap^- mutant showed no response to pyrimidines or *s*-triazines, indicating that Tap, which is known to be involved in dipeptide chemotaxis, is also required for chemotaxis to pyrimidines. We constructed chimeric chemoreceptors (Tapsr and Tsrap), in which the periplasmic and cytoplasmic domains of Tap and Tsr were switched. Tapsr and Tsrap were individually expressed in an MCP^- strain and chemotaxis was analyzed. Tapsr mediated chemotaxis towards dipeptides, pyrimidines, and the *s*-triazine compound cyanuric acid. In contrast, the reciprocal chimeric receptor Tsrap did not complement the chemotaxis defect. Our results indicate that the periplasmic domain of Tap is responsible for detecting pyrimidines and *s*-triazines, and the Tsr signaling domain confers Tapsr with the ability to mediate efficient chemotaxis. We are working to identify the *s*-triazine chemoreceptor in pseudomonads and will test whether the same chemoreceptor is also responsible for pyrimidine chemotaxis.

*** Member of the DEB graduate program**

C. IDENTIFICATION AND CHARACTERIZATION OF LONGEVITY REGULATION GENES IN *S. CEREVISIAE*

Chen Wang* and Su-ju Lin
Section of Microbiology, University of California, Davis, CA, 95616

We are interested in exploring the mechanism of longevity regulation. Calorie restriction (CR) has been shown to extend life span in virtually all the model systems examined. However, the mechanism by which CR extend life span is still uncertain. Here, we have conducted a genetic screen to identify new components that regulate chronological lifespan, the length of time cell remains viable in a non-dividing state (stationary phase). We accelerated the screen process by utilizing temperature sensitive mutant *cdc25-10* which exhibit phenotypes similar to stationary phase cells at non-permissive temperature. In this screen, we got three genes: *BMH2*, *WSC3*, and *ERG6*, which can extend chronological lifespan when overexpressed. *WSC3* is one of the four family members involved in cell integrity and stress response. *BMH2* is a 14-3-3 protein which is involved in signal transduction, cell cycle regulation, apoptosis and stress response. *EGR6* is a sterol methyltransferase, an enzyme in the ergosterol synthesis pathway. Here we mainly described how the 14-3-3 proteins function to affect life span. Our results showed that overexpressing Bmh1 and Bmh2 also extend replicative life span which refers to the number of divisions an individual cell undergoes before senescence. Stress resistance studies showed that cells overexpressing 14-3-3 proteins may have increased stress tolerance to some challenges such as oxidative drug H_2O_2. We further investigated whether 14-3-3 proteins function in CR-dependent pathway. The preliminary data showed that 14-3-3 proteins are partially required for some CR genetic mimics. How the phosphorylation of 14-3-3 proteins affects life span is still in progress, and we will further determine whether CR will change 14-3-3 proteins' phosphorylation status.

D. TRANSCRIPTIONAL CONTROL OF 2-NITROTOLUENE DEGRADATON GENES IN *ACIDOVORAX* SP. STRAIN JS42

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

Acidovorax sp. strain JS42 is unique in its ability to utilize 2-nitrotoluene (2NT), an environmental pollutant from the production of the explosive 2,4,6-trinitrotoluene (TNT), as a sole carbon and energy source for growth. The genes for 2NT degradation in JS42 are closely related to the naphthalene degradation genes of *Ralstonia* sp. strain U2, suggesting an evolutionary connection between the two pathways. Expression of the dioxygenase gene cluster responsible for the initial oxidation of 2NT in JS42 and for naphthalene degradation in U2 is under the direct control of a divergently transcribed LysR-type transcriptional regulator (LTTR). Despite differing in sequence by only five amino acids, NtdR, the regulator in JS42, responds to a wide range of nitroaromatic compounds and aromatic acids, while NagR from strain U2 recognizes only four compounds, including salicylate and gentisate, which are key intermediates in naphthalene degradation. To determine which of the five residues (positions 74, 169, 189, 227, 232) controls inducer specificity, rational mutagenesis of *ntdR* and *nagR* was performed. Transcription in response to 56 potential inducers was quantified by measuring activity of 2NT dioxygenase and a chromosomal *ntd-lacZ* reporter fusion in a JS42 background. Tested inducers included benzoic acid and benzene derivatives with hydroxyl-, nitro-, chloro-, amino-, methyl- or *iso*-propyl functional groups at the 2-, 3-, or 4-positions of the aromatic ring. Substrate specificity and transcriptional activity was tunable by single and multiple amino acid substitutions at positions 169, 189, 227, and 232 of the LTTRs, with the residues at 227 and 232 playing the most important roles. The greatest change in inducer specificity resulted from changing proline 227 to a serine, where NagR P227S gained the ability to recognize a wide range of nitroarene compounds including nitrobenzene, mono- and di-nitrotoluenes, and mono- and di-nitrophenols. A double mutant of NagR containing both P227S and I232V mutations was able to induce expression in the presence of nitrochlorobenzenes, whereas the variants containing the individual changes did not. Homology modeling of NtdR locates residues 227 and 232 to a predicted inducer binding pocket, where they may act synergistically to bind inducer molecules.

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E. THE COMPLETE GENOME SEQUENCE OF *BIFIDOBACTERIUM LONGUM* BY *INFANTIS*

David A. Sela[1*], Samara L. Freeman[2], Paul M. Richardson[3], J. Bruce German[2], and David A. Mills[1]

[1] Dept. of Viticulture and Enology, University of California, Davis, CA, 95616 [2] Dept. of Food Science and Technology, University of California, Davis, CA, 95616
[3]Joint Genome Institute Production Genomics Facility, Walnut Creek, CA, 94598

Bifidobacterium longum bv. *infantis* is one of the early colonizers of the breast-fed infant colon and subsequently dominates the lower gastrointestinal tract prior to weaning. We have characterized the *B. longum* bv. *infantis* isolate UCD272 which exhibits strong growth on human milk oligosaccharides (HMO) as a sole carbon source. UCD272 also exhibits fucosidase and sialidase activities which are believed to contribute to degradation of the complex HMO polymer. In collaboration with the Department of Energy's Joint Genome Institute, we have completely sequenced the genome of this microorganism. UCD272 represents the largest bifidobacterial genome reported to date (2.8 Mbp), and is predicted to contain >500 additional ORFs compared to previously sequenced genomes. Accordingly, the UCD272 genome possesses a large number of two-component regulatory systems, transport proteins, and selfish elements, by comparison to other sequenced bifidobacteria. Furthermore, the UCD272 genome sequence reveals a number of genes associated with utilization of mammalian-derived oligosaccharides and glycoconjugates which are unique to this strain. Characterization of the *B. longum* bv. *infantis* genome helps define the role for this important member of the infant gut consortium.

*** Member of the DEB graduate program**

F. IDENTIFICATION AND CHARACTERIZATION OF LONGEVITY REGULATION GENES IN *S. CEREVISIAE*

Chen Wang* and Su-ju Lin
Section of Microbiology, University of California, Davis, CA, 95616

We are interested in exploring the mechanism of longevity regulation. Calorie restriction (CR) has been shown to extend life span in virtually all the model systems examined. However, the mechanism by which CR extend life span is still uncertain. Here, we have conducted a genetic screen to identify new components that regulate chronological lifespan, the length of time cell remains viable in a non-dividing state (stationary phase). We accelerated the screen process by utilizing temperature sensitive mutant *cdc25-10* which exhibit phenotypes similar to stationary phase cells at non-permissive temperature. In this screen, we got three genes: *BMH2*, *WSC3*, and *ERG6*, which can extend chronological lifespan when overexpressed. *WSC3* is one of the four family members involved in cell integrity and stress response. *BMH2* is a 14-3-3 protein which is involved in signal transduction, cell cycle regulation, apoptosis and stress response. *EGR6* is a sterol methyltransferase, an enzyme in the ergosterol synthesis pathway. Here we mainly described how the 14-3-3 proteins function to affect life span. Our results showed that overexpressing Bmh1 and Bmh2 also extend replicative life span which refers to the number of divisions an individual cell undergoes before senescence. Stress resistance studies showed that cells overexpressing 14-3-3 proteins may have increased stress tolerance to some challenges such as oxidative drug H_2O_2. We further investigated whether 14-3-3 proteins function in CR-dependent pathway. The preliminary data showed that 14-3-3 proteins are partially required for some CR genetic mimics. How the phosphorylation of 14-3-3 proteins affects life span is still in progress, and we will further determine whether CR will change 14-3-3 proteins' phosphorylation status.

G. XB15 IS A NEGATIVE REGULATOR OF XA21-MEDIATED DISEASE RESISTANCE

Ying Peng[1*], Chang Jin Park[1], Christopher Dardick[2], Randy Ruan[1] and Pamela Ronald[1]

[1]Department of Plant Pathology, University of California, Davis, CA, USA.

[2]USDA-ARS, Appalachian Fruit Research Station, Kearneysville, WV, USA.

Receptor kinases are an important class of molecules that can detect extracellular signals and initiate signal transduction through phosphorylation events. The rice *XA21* gene, which confers resistance to the bacterial pathogen *Xanthomonas oryzae* pv. *oryzae* race 6 (*Xoo*), encodes a receptor serine/threonine kinase (RSTK) consisting of leucine-rich repeats in the extracellular domain and a serine/threonine kinase in the putative intracellular domain. To identify components involved in *XA21*-mediated signal transduction pathway, we used the XA21 cytoplasmic kinase domain as bait in yeast two-hybrid screens of rice cDNA libraries. XA21 binding (XB) protein XB15 was identified. *XB15* encodes a protein phosphatase 2C (PP2C). Phosphatase activity was observed for both full length XB15 protein and partial XB15 protein without its unique N-terminal domain. Interaction between XA21 and XB15 was confirmed by *in vitro* pull down assay. One *XB15* knockout mutant line was identified, showing a programmed cell death (PCD) phenotype. The *XB15* insertion mutation co-segregates with the PCD phenotype. Over-expression of *XB15* in kitaake plants containing the *XA21* gene causes compromised resistance to *Xoo*. These results indicate that XB15 functions as a negative regulator of cell death and XA21-mediated defense response.

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H. STRATEGIES FOR IMPROVING THE PRODUCTION OF FUNCTIONAL RECOMBINANT HUMAN THERAPEUTICS IN TRANSGENIC TOBACCO CELL CULTURES

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Plant cell cultures are entering a new phase of application and playing an important role in production of human therapeutics. However, utilizing plant cell cultures for recombinant human protein production faces two major challenges including lack of efficient gene expression system and proteolytic degradation of recombinant protein during the cell cultures. For evaluating an efficient expression system, we developed and compared three different gene expression systems, including a *Cauliflower mosaic virus* (CaMV) 35S constitutive promoter expression system, a chemically inducible promoter expression system (an estrogen receptor-based, estradiol-inducible promoter system), and a novel *Cucumber mosaic virus* (CMV) inducible viral amplicon (CMViva) expression system for production of a recombinant human protein, alpha-1-antitrypsin (AAT), in transgenic *Nicotiana benthamiana* suspension cell cultures.

Another important bottleneck is recombinant target protein degradation, which can reduce levels of "functional" product in plant cell cultures. Target proteins secreted into the culture medium are commonly degraded by the action of proteases that are simultaneously produced during the culture period. To prevent the proteolytic degradation of recombinant protein, studies applying protease inhibitors and stabilizing agents have been investigated. Although these applications have shown good results, protease inhibitors have short-life and are expensive for use in large-scale production. In addition, the use of stabilizing agents in cell cultures could produce harmful effects on cell growth and cause trouble in downstream processing. To address above issues, we proposed a bioreactor strategy for improving functional human protein production by pH control strategy during cell cultures.

In this study, we showed that the novel chemically inducible viral amplicon system (CMViva) resulted in higher yield of functional extracellular rAAT and higher ratio of functional rAAT to total rAAT (20%~40%) in transgenic *Nicotiana benthamiana* suspension cultures. Furthermore, the pH effect of bioreactor strategy could reduce the protease activity as well as stabilize the conformation and/or structure of human protein that allow execute its biological function. These results

lay the foundation for developing scaleable transgenic plant cell cultures in bioreactors for production of human therapeutics.

*** Members of the DEB graduate program**

I. A METABOLIC MODELING APPROACH TO OPTIMIZING RECOMBINANT PROTEIN PRODUCTION IN *L. LACTIS* FERMENTATIONS

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Lactococcus lactis, a species of Lactic Acid Bacteria (LAB), continues to show great promise for use as a vaccine delivery vehicle (Figure 1) thanks to its widespread use in the dairy industry, GRAS status, genome sequence availability, resistance to degradation in the GI tract, and susceptibility to food grade tools for genetic modification. Even so, there remain challenges in bringing this biomedical application to fruition, specifically with respect to currently attainable levels of recombinant protein expression in cultures of LAB. Recent work has optimized bioreactor conditions for recombinant protein expression in L. lactis IL1403. Under optimal bioreactor conditions, levels of Green Fluorescent Protein (GFP), a model recombinant protein, can be increased 50% per cell and 8-fold in bulk concentration over levels obtained under standard laboratory conditions (Figure 2). The current research aims to further increase expression through the use of genetic modification of the bacterial strain. Response surface methods, while proving to be very useful in optimizing bioreactor conditions, cannot be used to optimize genetic configuration of the host strain because genetic modifications cannot be dialed in so easily as, for example, a new temperature set point. Therefore, metabolic modeling is required to study the potential impact of plausible genetic modifications. Metabolic flux analysis (MFA) of a genome-scale L. lactis metabolic network leverages the vast available information on reaction stoichiometry to estimate the rates of all intracellular reactions, among them the reaction producing the recombinant protein. The desirability of a particular genetic modification can be estimated by using MFA to analyze the metabolic model that results from that modification. This procedure provides a basis to target particular genes for modification in progressing toward the goal of maximal recombinant protein expression.

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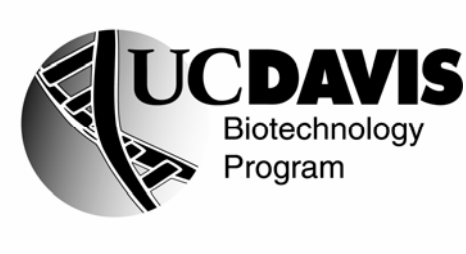

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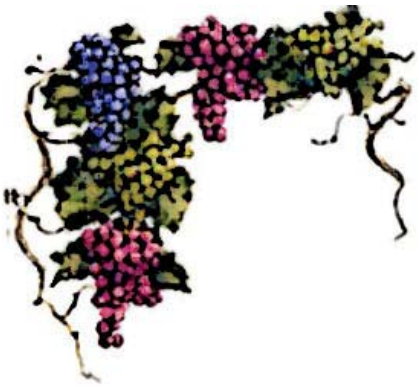

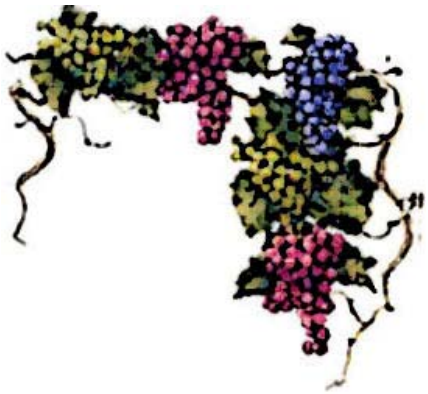

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BioMarin develops and commercializes innovative biopharmaceuticals for serious diseases and medical conditions, focusing on product candidates that:

- Address currently unmet medical needs
- Suggest a clear-cut development profile
- Provide an opportunity to be first-to-market

Approval of Aldurazyme® (laronidase), the first specific therapy approved for the treatment of mucopolysaccharidosis I (MPS I), reflects the company's commitment and ability to execute its business strategy. Today, with two approved products on the market and a fully-integrated infrastructure in place, BioMarin is positioned to realize continued success in providing patients with innovative therapeutics for serious diseases.

Amgen, Inc

Contacts:
Bruce Kerwin, Ph.D, Scientific Director; Protein Pharmaceutics
One Amgen Center Drive
Thousand Oaks, CA 91320-1799
(805) 447-1000
Dave Lacey, M.D., Basic Research, Metabolic Disorders
1120 Veterans Boulevard
S. San Francisco, CA 94080
www.amgen.com
bkerwin@amgen.com
dlacey@amgen.com

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

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

Genentech, Inc.

Contact:
Vishva Dixit, Ph.D., Vice President, Molecular Oncology
Ellen Filvaroff, PhD, Senior Scientist, Molecular Oncology
Melody Trexler Schmidt, Ph.D., Scientist (DEB Graduate)
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South San Francisco, CA 94080-4990
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filvarof@gene.com
schmidt.melody@gene.com

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

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

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

Development Pipeline:
As a biotechnology leader, Genentech has a long-standing tradition of reinvesting a significant percentage of revenues back into research and development — a practice that has proved successful in transforming promising candidates into important new products. With the projects below under way, Genentech's

development pipeline has never been more robust and promising. More than half of Genentech's pipeline is composed of potential antibody therapies.

Mosanto Company – Calgene Campus

Contact:
Kenneth Gruys, Ph.D., Site Manager
1920 Fifth Street
Davis, CA 95616
(530) 753-6313
www.monsanto.com
kenneth.j.gruys@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.

Novartis AG (formerly Chiron Corporation)

Contacts:
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Indresh Srivastava, Ph.D., Assoc. Dir., Imm. & Cell Biology; Vaccines Research
4560 Horton Street
Emeryville, CA 94608-2916
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Vacaville, CA 95688
(707) 453-2200
www.chiron.com
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Indresh_Srivastava@chiron.com
robert.carter@novartis.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.

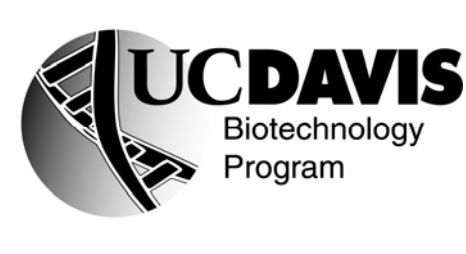
Quality
Our goal at Chiron is to deliver quality products and services on time to all customers, internal and external. We provide employees with training and resources to meet or exceed customer requirements. We monitor processes and products to identify opportunities for continuous improvement.

Novozymes Inc

Contacts:
Debbie Yaver, Ph.D., Research Manager
Joel Cherry, Ph.D., Research Manager, BioEnergy Group
1445 Drew Ave.
Davis, CA 95616
(530) 757-8100
www.novozymesbiotech.com
dsy@novozymes.com
jroc@novozymes.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.



Participants

Retreat Participants

NIH Fellows 2006 – 2007

Suzanne (Balko) Barber
Chemical Engineering

Allison Dickey
Chemical Engineering

Corey Dodge
Chemical Engineering

Dominik Green
Biochemistry & Molecular Biology

Jennifer Warren
Civil & Environmental Engineering

Biotech Fellows 2006 - 2007

Michael Howland
Chemical Engineering

Vannarith Leang
Chemical Engineering

Riccardo LoCascio
Microbiology

Vu Bao Trinh
Biochemistry & Molecular Biology

First Year Fellows 2006 - 2007

Elianna Goldstein
Plant Biology

Ben Lindenmuth
Chemical Engineering

Sarah Statt
Biochemistry & Molecular Biology

Graduate Students / Post Docs

Susan Ayer
Mechanical & Aeronautical Engineering

Monica Britton
Genetics

Astra Chang
Molecular, Cellular & Integrative Physiology

Meghan Dukerich
Biochemistry & Molecular Biology

Laura Gillies
Food Science Technology

Ivan Godinez
Microbiology

Scott Hamilton
Biochemistry & Molecular Biology

Huilan Han
Mechanical & Aeronautical Engineering

Kevin Holden
Microbiology

Ting-Kuo Huang
Chemical Engineering

Yi-Hwa (Patty) Hwang
Biochemistry & Molecular Biology

AnaMaria Ibanez
Plant Sciences

Aminah Ikner
Biochemistry & Molecular Biology

Kou-San Ju
Microbiology

Rashida Lathan
Animal Science

Ben Lindenmuth
Chemical Engineering

Xianxian Liu
Microbiology

Artem Loukoianov
Genetics

Kristina Mahan
Biochemistry & Molecular Biology

Marina Meyerzon
Genetics

Thuc Nguyen
Mechanical & Aeronautical Engineering

Gian Oddone
Chemical Engineering

Ying Peng
Genetics

Michael Plesha
Chemical Engineering

Stephanie Pulford
Mechanical & Aeronautical Engineering

Jose Antonio Rocha-Valadez
Chemical Engineering

Benjamin Rosen
Plant Pathology

Sagayamary Sagayaradj
Plant Biology

Juan Sanchez
Plant Biology

Andres Schwember
Plant Biology

Dave Sela
Microbiology

Laura Shih
Biomedical Engineering

Zane Starkewolfe
Chemistry

James Stice
Molecular, Cellular & Integrative Physiology

Erin Tapley
Cellular & Developmental Biology

Chen Wang
Microbiology

Kelly Williams
Biological Systems Engineering

Dave Woessner
Microbiology

Faculty

Kent Bradford
Plant Sciences

R. Holland Cheng
Molecular & Cellular Biology

Abhaya Dandekar
Pomology

Cristina Davis
Mechanical & Aeronautical Engineering

Scott Dawson
Microbiology

Roland Faller
Chemical Engineering

Bruce Hammock
Entomology

Tonya Kuhl
Chemical Engineering

David Mills
Viticulture & Enology

Martina Newell-McGloughlin
UC Biotechnology Research & Education Program (BREP)

Rebecca Parales
Microbiology

Atul Parik
Biomedical Engineering

Ronald Phillips
Chemical Engineering & Materials Science

Stefan Wuertz
Civil & Environmental Engineering

Industry

Julio Baez
FibroGen

Amitabha Chaudhuri
Genentech

Subhra Chaudhuri
Genentech

Kenneth Gruys
Monsanto, Calgene Campus

Shawn Jeffries
Amgen

Kathy Lardizabal
Monsanto, Calgene Campus

Lisa Marshall
Amgen

Sandy Merino
Novozymes, Inc.

Priya Mitty
Amgen

Eddie Moler
Tethys Bioscience, Inc.

Jack Newman
Amyris Biotechnologies

Guests

Russell Reagan
Plant Sciences

Janice Morand
UCD Internship & Career Center

Mario Tinoco
Plant Sciences

UC Davis Biotechnology Program Staff

Judy Kjelstrom
Director

Denneal Jamison McClung
Assistant Director

Marianne Hunter
Event Manager

www.biotech.ucdavis.edu

The Mission of the Biotechnology Program:

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

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

The Program serves as the **Administrative Home** for educational programs:

- Designated Emphasis in Biotechnology (**DEB**) graduate program
  - www.deb.ucdavis.edu
- Advanced Degree Program (**ADP**) for corporate employees
  - A PhD program for the working professional
- NIH Training Program in Biomolecular Technology for PhD students
- **BioTech SYSTEM** – K-14 educational consortium

Biotechnology Program Office:

Dr. Judith Kjelstrom - Director
Dr. Denneal Jamison-McClung – Assistant Director
Cathy Miller – Budget Analyst
Marianne Hunter – Event Manager
Office location: 0301 Life Sciences
Telephone: (530) 752-3260 (main line) FAX: (530) 752-4125
Email: biotechprogram@ucdavis.edu

July 1, 2002- June 30, 2007 (Renewal Pending)

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.

NIH Training Grant Faculty

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

Gary Anderson
Animal Science

Matthew Augustine
Chemistry

Enoch Baldwin
Molecular & Cellular Biology

Craig Benham
Biomedical Engineering/Genome Center

David Block
Chemical Engineering

George Bruening
Plant Pathology

Alan Buckpitt
VM: Molecular Biosciences

Kenneth Burtis
Molecular & Cellular Biology/Genome Center

Daniel Chang
Molecular & Cellular Biology

Abhaya Dandekar
Plant Sciences-Pomology

Michael Denison
Environmental Toxicology

Bryce Falk
Plant Pathology

Roland Faller
Chemical Engineering & Materials Science

Katherine Ferrara
Biomedical Engineering

Andrew Fisher
Chemistry

J. Bruce German
Food Science & Technology

Jeffrey Gregg
MED: Pathology

Daniel Gusfield
Computer Science

Bruce Hammock
Entomology/UCD Cancer Center

Alan Jackman
Chemical Engineering & Materials Science

Ian Kennedy
Mechanical & Aeronautical Engineering

Tonya Kuhl
Chemical Engineering & Materials Science

Hsing-Jien Kung
MED: Biochemistry/UCD Cancer Center

J. Clark Lagarias
Molecular & Cellular Biology

Kit Lam
MED: Hematology & Oncology/Chemistry

Kent Lloyd
VM: Anatomy Physiology & Cell Biology

Marjorie Longo
Chemical Engineering & Materials Sciences

Karen McDonald
Chemical Engineering & Materials Sciences

Claude Meares
Chemistry

Juan Medrano
Animal Science

Richard Michelmore
Plant Sciences – Vegetable Crops

James Murray
Animal Science/Genetic Engineering, Large Animals

Atul Parikh
Applied Science

Martin Privalsaky
Microbiology

Kate Scow
Land, Air & Water Resources

Simon Scott
Biomedical Engineering

Michael Toney
Chemistry

Robert Rice
Environmental Toxicology

David Rocke
Applied Science

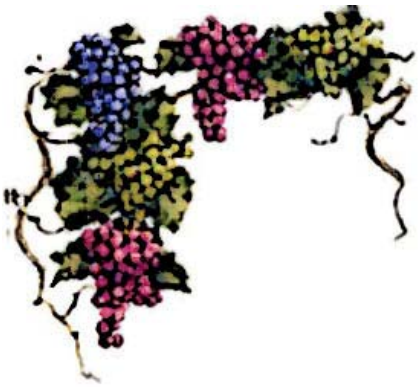
Jean VanderGheynst
Biological & Agricultural Engineering

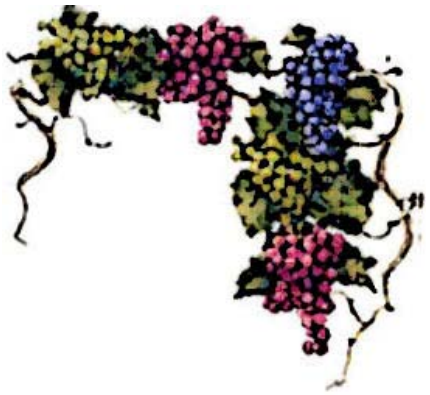
Craig Warden
Neurobiology, Physiology & Behavior

David Wilson
Molecular & Cellular Biology

Stefan Wuertz
Civil & Environmental Engineering

John Yoder
Plant Sciences – Vegetable Crops





NIH Training Program in Biomolecular Technology

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

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

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

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

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

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

Designated Emphasis in Biotechnology Program (DEB)

Goals and Mission of the DEB

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

DEB Mission:

> To provide well-coordinated, cross-disciplinary training of graduate students in critical areas of biomolecular technology research.
>
> To promote interdisciplinary research environments that integrate basic biological science, engineering and computational disciplines.
>
> To allow cross-disciplinary training and trainee experience in a biotechnology company or cross-college laboratory.

Students come from a wide array of disciplines: Participating graduate programs currently include **24 programs**: Agricultural and Environmental Chemistry; Applied Science;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 March 2007 the DEB has 24 affiliated graduate groups or departmentally based graduate programs and we are in the process of adding Electrical & Computer Engineering. The number of students in the Designated Emphasis in Biotechnology has increased dramatically over the last two years and now boasts 114 members, with many being first year students. We have graduated 38 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), Katayoon Dehesh (Plant Biology) 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/pharmaceutical company, government lab 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 24 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, every year)

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, 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 required. Approved substitutes for GGG 296 are BIM289A (Scientific Ethics and Inquiry) and ECL 290 (Responsible Conduct of Research for Environmental Scientists)**

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. The syllabus for the MCB 263 course can be used as a guide for questioning.

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 as of March 2007

Sean Adams
Microbiology

Suzanne (Balko) Barber
Chemical Engineering

Don Barkauskas
Statistics

Sandra Bennun Serrano
Chemical Engineering

Zachary Bent
Food Science

Craig Blackmore
Comparative Pathology

Craig Blanchette
Biophysics

Jessica Bohonowych
Environmental & Toxicology

Jennifer Bratt
Biochemistry & Molecular Biology

Monica Britton
Genetics

Anna Cartier
Plant Biology

Jennifer Cash
Chemistry

Shannon Ceballos
Cellular & Developmental Biology

Astra Chang
Plant Biology

Ying Chen
Statistics

Honglin Chen
Genetics

Li-Kuan (Alex) Chen
Biomedical Engineering

Yu-Shen Cheng
Biological & Agricultural Engineering

John (Wes) Cline
Pharmacology & Toxicology

Noah Decker
Nutritional Biology

Allison Dickey
Chemical Engineering

Kevin Dietzel
Microbiology

Corey Dodge
Chemical Engineering

Mathew Doherty
Microbiology

Meghan Dukerich
Biochemistry & Molecular Biology

Rita El-khouri
Chemistry

James Evans
Biochemistry & Molecular Biology

Xin Fei
Agricultural & Environmental Chemistry

Wen-Ying Feng
Statistics

Prasad Gawande
Chemistry

Laura Gillies
Food Science Technology

Ivan Godinez
Microbiology

Elianna Goldstein
Plant Biology

Robin GrayMerod
Civil & Environmental Engineering

Dominik Green
Biochemistry & Molecular Biology

Oldham (Scott) Hamilton
Bochemistry & Molecular Biology

Victor Haroldsen
Biochemistry & Molecular Biology

Christine Hastey
Microbiology

Kristina Herzberg
Biochemistry & Molecular Biology

Laura Higgins
Molecular, Cellular & Integrative Physiology

Thomas Hill III
Pharmacology & Toxicology

Kevin Holden
Microbiology

Ben Lindenmuth
Chemical Engineering

Matthew Hoopes
Biophysics

Jennifer Horner
Biochemistry & Molecular Biology

Jessica Houghton
Pharmacology & Toxicology

Michael Howland
Chemical Engineering

Ting-Kuo Huang
Chemical Engineering

Yi-Hwa (Patty) Hwang
Biochemistry & Molecular Biology

Connie Jen
Biochemistry & Molecular Biology

Kou-San Ju
Microbiology

Michael Kareta
Biochemistry & Molecular Biology

Saeed Khazaie
Chemistry

Pavan Kumar
Plant Biology

Nathaniel Leachman
Cell & Developmental Biology

Vannarith Leang
Chemical Engineering

Young (Lauren) Lee
Biochemistry & Molecular Biology

Raquel Orozco-Alcaraz
Chemical Engineering

Song Liu
Agricultural & Environmental Chemistry

Xianxian (Janice) Liu
Microbiology

Riccardo LoCascio
Microbiology

George Lomidze
Biomedical Engineering

Artem Loukoianov
Genetics

Ruixiao Lu
Statistics

Thomas Luu
Biochemistry & Molecular Biology

Kristina Mahan
Biochemistry & Molecular Biology

Caroline Meloty-Kapella
Cell & Developmental Biology

Marina Meyerzon
Genetics

Brad Niles
Nutrition

Gian Odonne
Chemical Engineering

David Olivos
Comparative Pathology

Christopher Simmons
Biological Systems Engineering

Cheng Song
Cell & Developmental Biology

Ying Peng
Genetics

Warren Place
Microbiology

Michael Plesha
Chemical Engineering

Wade Reh
Genetics

Rowena Romano
Biological Systems Engineering

Ahmad Rushdi
Electrical & Computer Engineering

Juan Pedro Sanchez
Plant Biology

Mary Saunders
Comparative Pathology

Erin Schwartz
Biochemistry & Molecular Biology

Andres Schwember
Plant Biology

David Sela
Food Science

Laura Shih
Biomedical Engineering

Jillian Silva
Biochemistry & Molecular Biology

Don-Hong Wang
Genetics

Dong Wang
Agricultural & Environmental Chemistry

Zane Starkewolfe
Chemistry

James Stice
Molecular, Cellular & Integrative Physiology

Wesley Sughrue
Biochemistry & Molecular Biology

Qi Sun
Chemical Engineering

Anandkumar Surendrarao
Plant Biology

Alan Szmodis
Biophysics

Christina Takanishi
Cellular & Developmental Biology

Esra Talu
Chemical Engineering

Erin Tapley
Cellular & Developmental Biology

Karen Thatcher
Genetics

Jared Townsend
Biochemistry & Molecular Biology

Vu Trinh
Biochemistry & Molecular Biology

Erin Zumstein
Biochemistry & Molecular Biology

Jennifer Warren
Civil & Environmental Engineering

Kelly Williams
Biological Systems Engineering

David Woessner
Microbiology

Andrew Wong
Genetics

Scott Wong
Biochemistry & Molecular Biology

Chun-Yi (Jimmy) Wu
Pharmacology & Toxicology

Zhaoju (Daisy) Wu
Pharmacology & Toxicology

Fred (Yuanxin) Xi
Applied Science Engineering

Bei Xiang
Chemical Engineering

Liang Yang
Biochemistry & Molecular Biology

Kseniya Zakharyevich
Microbiology

He (James) Zhu
Biomedical Engineering

DEB Faculty Participants

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

Biochemistry & Molecular Biology
Steffen Abel
Everett Bandman
Alan Bennett
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Sue Bodine
Sean Burgess
R. Holland Cheng
Ronald Chuang
Gino Cortopassi
Michael Denison
Peggy Farnham
Charles Gasser
Bruce Hammock
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Kentaro Inoue
Thomas Jue
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Stephen Kowalczykowski
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Kit Lam
Janine LaSalle
Su-Ju Lin
Paul Luciw
Claude Meares
Jerry Powell
Marty Privalsky
Robert Rice
Pam Ronald
Robert Rucker
Dewey Ryu
Earl Sawai
Kazuhiro Shiozaki
Henning Stahlberg
Daniel Starr
Steven Theg
Valerie Williamson
David Wilson
Matthew Wood
Reen Wu
John Yoder
Glenn Young

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

Biomedical Engineering
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Volkmar Heinrich
Ian Kennedy
Tonya Kuhl
Kit Lam
Marjorie Longo
Angelique Louie
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Alice Tarantal
Yohei Yokobayashi

Biophysics
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Thorsten Dieckmann
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Gang-yu Liu
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Atul Parikh
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Steven Theg
Michael D. Toney
David Wilson
Yin Yeh

Cell & Developmental Biology
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Everett Bandman
Ron Baskin
Frederic Chédin
Jason Eiserich
Peggy Farnham

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Neil Hunter
Anne Knowlton
Su-Ju Lin
Bo Liu
Robert Rice
Daniel Starr
Alice Tarantal
Richard Tucker
Matthew Wood
Reen Wu

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

Chemistry
Matthew Augustine
Alan Balch
Thorsten Dieckman
Andrew Fisher
Bruce Hammock
J. Clark Lagarias
Carlito Lebrilla
Gang-yu Liu
Claude Meares
Krishnan Nambiar
Timothy Patten
Michael Toney

Civil & Environmental Engineering
Daniel Chang
Stefan Wuertz

Comparative Pathology
Peter Barry
Stephen Barthold
Satya Dandekar
Jeff Gregg
Rivkah Isseroff
Kit Lam
Thomas North
Jerry Powell
Earl Sawai
Jay Solnick
Alice Tarantal
Jose Torres
Patricia Wakenell
Reen Wu
Tilahun Yilma

Entomology
Bruce Hammock

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

Genetics
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Frederic Chédin
Douglas Cook
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Abhaya Dandekar
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Peggy Farnham
Charles Gasser
David Gilchrist
Tom Gradziel
Paul Gumerlock
Stacy Harmer
Neil Hunter
Clarence Kado
Dan Kliebenstein
Stephen Kowalczykowski
Janine LaSalle
Su-Ju Lin
Juan Medrano
Richard Michelmore
James Murray
Marty Privalsky
Ray Rodriguez
Pam Ronald
Earl Sawai
Daniel Starr
Alison Van Eenennaam
Valerie Williamson
Reen Wu
John Yoder

Immunology
Satya Dandekar
Kit Lam
Jose Torres
Tilahun Yilma

Material Science & Engineering
Subhash Risbud

Mechanical & Aeronautical Engineering
Abdul Barakat
Cristina Davis
Ian Kennedy

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

Molecular, Cellular and Integrative Physiology
(formerly "Physiology")
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Sue Bodine
Christopher Calvert
Nipavan Chiamvimonvat
Jason Eiserich
Anne Knowlton
Ray Rodriguez
John Rutledge
Dewey Ryu
Alice Tarantal
Barry Wilson
Reen Wu

Nutritional Biology
Christopher Calvert
Andrew Clifford
J. Bruce German
Carl Keen

Pharmacology & Toxicology
Alan Buckpitt
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Gino Cortopassi
Michael Denison
Jason Eiserich
Bruce Hammock
Carl Keen
Anne Knowlton
Hsing-Jien Kung
Jerold Last
Fumio Matsumura
Marion Miller-Sears
Robert Rice
Robert Rucker
Barry Wilson
Matthew Wood
Reen Wu

Plant Biology
Steffen Able
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Richard Bostock
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Katayoon "Katy" Dehesh
Don Durzan
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Charles Gasser
Tom Gradziel
Stacy Harmer
Kentaro Inoue
Dan Kliebenstein
J. Clark Lagarias
Bo Liu
Terence Murphy
Michael Reid
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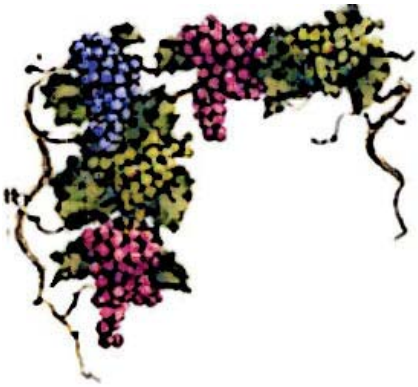
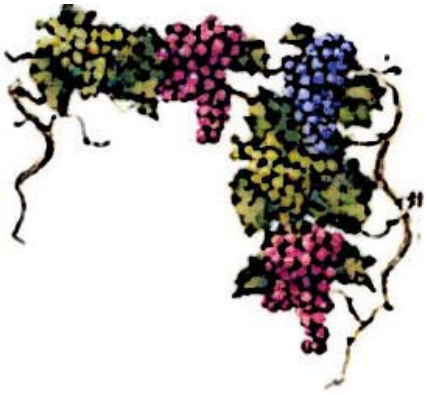
John Yoder

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

Statistics
Andrew Clifford
Shu Geng
Katherine Pollard
David Rocke





The Value of Internships

Over the last 14 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:

Advanced Micro Devices (AMD)
Agilent Technologies
Alza
Amgen
Amyris
Bayer
Berlex Biosciences
BioMarin Pharmaceuticals
Celera AgGen
DuPont
Exelixis
Genentech
ICOS
Maxygen
Monsanto, Calgene Campus;
Novartis (formerly Chiron)
Novozymes Biotech
Scios
Syntex
Recovery Sciences
Roche Biosciences
Ventria Biosciences
and others

Industry Partners gain many things from internships:

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

Students gain much from internships:

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

Currently, there are 114 students enrolled, so we need more Academic-Industry Partnerships.