Eighteenth Annual

Biotechnology Training Retreat

Christian Brothers Retreat & Conference Center
Napa, CA

Eighteenth Annual Biotechnology Training Retreat

Saturday, April 4, 2009

Christian Brothers Retreat & Conference Center
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

Table of Contents

2009 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 **2008-09 fellows and their preceptors**, as well as **our industry affiliates**. We also welcome the faculty and trainees associated with the NSF CREATE-IGERT Training Program (directed by Karen McDonald) as they are also members of the DEB program. It is hard to believe that we have been holding this retreat for the past 18 years!

The logistics of this retreat has been overseen by our stellar team: Linda Bates, our interim Program Assistant, Marianne Hunter, our Program Manager and our Associate Director, Dr. Denneal Jamison-McClung. Without their dedicated service, this annual event would not happen.

I would like to introduce our Biotechnology Fellows. Our **5 NIH Fellows** include: **Kristina Mahan,** Biochemistry & Molecular Biology (preceptor is Rebecca Parales); **Joseph Ramahi**, Cell and Developmental Biology (preceptor is Simon Chan); **David Sela**, Microbiology (preceptor is David Mills), **Sunny Shah**, Biomedical Engineering (preceptor is Alex Revzin), and **Erin Tapley**, Cell and Developmental Biology (preceptor is Daniel Starr). Our **4 Biotechnology Fellows** (industry and campus fellowships) include: **Matthew Hoopes,** Biophysics (preceptor is Marjorie Longo & Roland Faller); **Christina Takanishi,** Cell and Developmental Biology (preceptor is Matthew Wood); **Huilan Han,** Mechanical & Aeronautical Engineering (preceptor is Cristina Davis), and **Sarah Lockwood**, Biochemistry and Molecular Biology (preceptor is David Segal). The **2009 CREATE-IGERT Trainees** are **Lucas Arzola, Timothy Butterfield, Elenor Castillo, Dawn Chiniquy, Mitch Elmore, Tiffany Glavan, Rachel Kerwin, Ben Lindenmuth, Chris Simmons,** and **Mark Wolf.** Due to the limited time for oral presentations, we will showcase research performed by these students, as well as 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.

We will be selecting our **2009-10 NIH Fellows** in May. Nomination Forms are on the web at www.deb.ucdavis.edu. Application deadline is **Wednesday April, 22nd.** 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 170 and climbing.** Each of our students is showcased on the DEB website (www.deb.ucdavis.edu).

In regard to industrial internships for 2009, we placed many of our DEB students: Kevin Dietzel completed his internship with Amyris, Rita El-khouri interned with Amgen, Honglin Chen, Christina Takanishi and Jillian Silva completed their internships with Genentech, Nathanial Leachman interned with Innovation Access on the UC Davis Campus, Pradeepa Gunathilake finished her internship with Monsanto – Calgene Campus, Ting-Kuo Huang interned at Novartis, and Marina Meyerzon is presently interning with Novozymes.

We would like to thank all of our industry/government affiliates for their support of our training program. With the rapid growth of the DEB, we are going to need even more training sites in the near future.

A number of students graduated in 2008 and 2009 with their PhDs and a Designated Emphasis in Biotechnology: **Suzanne Barber, Craig Blackmore, Monica Britton, Ying Chen, Honglin Chen, Allison Dickey, Corey Dodge, Rita El-khouri, Wen-Ying Feng, Kristina Herzberg, Laura Higgins, Kevin Holden, T.K. Huang, Aminah Ikner, Artem Loukoianov, Robin Merod, Michael Plesha, Rowena Romano, Jillian Silva, and Alan Szmodis.**

Thank you so much for coming. Please enjoy the great presentations, the delicious food and wine and gorgeous scenery.

With warmest 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:

Roland Faller (Chemical Engineering)
Ian Kennedy (Mechanical & Aeronautical Engineering)
Tonya Kuhl (Chemical Engineering)
J. Clark Lagarias (Molecular & Cellular Biology)
Kit Lam (MED: Internal Medicine (Hemotology/Oncology)
Atul Parikh (Applied Science)
David Segal (Pharmacology/Genome Center)
Michael Wright (UC Davis Genome Center and Bioinformatics Program)

Industry:

Debbie Yaver, Novozymes, Inc.
Vishva Dixit (Genentech)
Kenneth Gruys, Monsanto, Calgene Campus

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

Designated Emphasis in Biotechnology (DEB) Graduate Program

www.deb.ucdavis.edu

Executive Committee

Abhaya Dandekar, Chair
Katayoon "Katie" Dehesh
Karen McDonald
David Rocke
Kou-San Ju, Student Member

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

UC Davis Biotechnology Program

www.biotech.ucdavis.edu

Judith A. Kjelstrom, Ph.D.
Director

Denneal Jamison-McClung, Ph.D.
Associate Director

Marianne Hunter; Program Manager
Linda Bates; Program Assistant

One Shields Ave
301 Life Sciences
Davis, CA 95616
biotechprogram@ucdavis.edu
(530) 752-3260
Fax: (530) 752-4125

UC Davis Eighteenth Annual Biotechnology Training Retreat
April 4, 2009
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** Martina Newell-McGloughlin Co-Director, NIH Training Grant in Biomolecular Technology
	Morning Session Karen McDonald Co-Director, NIH Training Grant in Biomolecular Technology
8:45 – 10:20 am	**Presentations** 8:45 am David Sela ..... *Mentor: David Mills* 9:10 am **Alberto Iandolino**..... **Monsanto, Calgene** 9:30 am Kristina Mahan ..... *Mentor: Rebecca Parales* 9:55 am Joseph Ramahi..... *Mentor: Simon Chan*
10:20 – 10:45 am	**Break / Poster Viewing**
10:45 – 12:15 pm	**Presentations** 10:45 am **Suchindra Maiyuran**.....**Novozymes, Inc.** 11:05 am Erin Tapley.....*Mentor: Daniel Starr* 11:30 am Sunny Shah.....*Mentor: Alex Revzin* 11:55 pm John Yoder .....Bioethics Question (Handout)
12:15 – 1:45 pm	**Lunch / Poster Viewing**
	Afternoon Session Chair Abhaya Dandekar Chair, DEB Executive Committee
1:45 – 3:40 pm	**Presentations** 1:45 pm John Yoder ..... Bioethics Question (Discussion) 2:20 pm Sarah Lockwood..... *Mentor: David Segal* 2:45 pm Matthew Hoopes ..... *Mentor: Marjorie Longo & Roland Faller* 3:20 pm **Caryle Vann**..... **Genentech**
3:40 - 3:50 pm	**Short Break (10 min)**
3:50 – 5:15 pm	**Presentations** 3:50 pm Christina Takanishi ..... *Mentor: Matthew Wood* 4:15 pm Huilan Han ..... *Mentor: Cristina Davis* 4:40 pm **Chandra Kilburn**..... **E&J Gallo Winery** 4:55 pm **Marie-Cecile van de Lavoir** ..... **Crystal Bioscience**
5:20 pm	**Closing Remarks** Martina Newell-McGloughlin Co-Director, NIH Training Grant in Biomolecular Technology

5:45 pm – Bus departs Napa

2009 Poster Titles

A. **"Chromosome Size-Dependent Control of Crossing-Over During Meiosis in *Saccharomyces cerevisiae*"**
Yi-Hwa (Patty) Hwang* and Neil Hunter
Department of Microbiology, University of California, Davis

B. **"Timely Septation Requires SNAD Dependent Spindle Pole Body Localization of the Septation Initiation Network Components in the Filamentous Fungus *Aspergillus nidulans*"**
Tracy Cui Zeng*[1], Jung-Mi Kim[1], Jean S. Tania Nayak[2] , Rongzhong Shao[1] , Angel Huang[1] , Berl R. Oakley[2] ,and Bo Liu[1]
[1]Department of Plant Biology, University of California, Davis
[2]Department of Molecular Biosciences, University of Kansas, Lawrence, Kansas

C. **"Design of a Disease Relevant RNA Editing Substrate For Use In High Throughput Screening"**
Rena Goodman*, Subhash Pokharel, and Peter Beal
Department of Chemistry, University of California, Davis

D. **"The Effects of Developmental Differences in CD4+T Cell Function On Viral Pathogenesis In Rhesus Macaques"**
Myra Grace A. dela Pena*[1], Peter Barry[1,2], and Kristina Abel[1]
[1]California National Primate Research Center, University of California, Davis
[2]Comparative Medicine, University of California, Davis

E. **"Investigating A Novel, Attenuated *Mycobacterium tuberculosis* Vaccine Vector To Enhance SIV Immunity In Infant Rhesus Macaques"**
Kara Jensen*[1], Michelle Larsen[2], Glenn Fennelly[2], and Kristina Abel[1]
[1]California National Primate Research Center, University of California, Davis
[2]Albert Einstein College of Medicine, New York

F. **"The 14-3-3 Protein Bmh1 Functions in Calorie Restriction and Nutrient-Sensing Pathways to Regulate Longevity"**
Chen Wang*, Craig Skinner, Erin Easlon and Su-Ju Lin
Department of Microbiology, University of California, Davis

G. **"Transient *In Planta* Expression of Cellulose-Degrading Enzymes: Plant Tissues as Bioreactors"**
Benjamin E. Lindenmuth*[1], Bryce W. Falk[2], Abhaya M. Dandekar[3], and Karen A. McDonald[1]
[1]Department of Chemical Engineering & Materials Science, University of California, Davis
[2]Department of Plant Pathology, University of California, Davis
[3]Department of Plant Sciences, University of California, Davis

H. **"qPCR Monitoring of T-Strand Populations in Agroinfiltrated Leaf Tissue"**
Christopher Simmons* and Jean VanderGheynst
Department of Biological and Agricultural Engineering, University of California, Davis

I. **"Identification and Characterization of Bacterial Effectors That Interact With the Plant Protein Folding Catalyst Cyclophilin"**
James M. Elmore* and Gitta Coaker
Department of Plant Pathology, University of California, Davis

J. **"Quantitative Simultaneous Determination of Fat Content and Fatty Acid Composition of Pig Tissues by Gas Chromatography in a High-throughput Manner"**
Chingying Li, Tim Hickman, and Martin Ruebelt*
Monsanto, Calgene Campus, Davis, California

K. **"Antibodies For Irreversible Capture"**
Prasad Gawande*, Amir Kalani, Mark McCoy, Vahid Eskandari, Jeff Day, Bernadette Marquez, and Claude Meares
Department of Chemistry, University of California, Davis

L **"Genomic Isolation of Alleles That Render Infertility in High Growth FVB/NJ Female Mice"**
Rashida Lathan*, Thomas E. Adams, and Juan Medrano
Department of Animal Science, University of California, Davis

M. **"Manipulation of Phytochrome-Mediated Signaling in Transgenic Plants"**
Timothy Butterfield*, Wei Hu, and J. Clark Lagarias
Department of Molecular and Cellular Biology, University of California, Davis

N. **"An eIF4E-Binding Protein Regulates Katanin Protein Levels in *C. elegans* embryos"**
Wei Li*, Leah DeBella, and Lesilee Rose
Department of Molecular and Cellular Biology, University of California, Davis

O. **"Transcriptomic Analysis of Transgenic Grape (*Vitis vinifera*) Plants Expressing PGIP"**
Yolanda Gogorcena*[1], Ana María Ibáñez[2], Cecilia Aguero[2], Russell L. Reagan[2], Sandie Uratsu[2], and Abhaya M. Dandekar[2]
[1]Department of Pomology, EEAD-CSIC, P.O. Box 13034, Zaragoza, Spain
[2]Department of Plant Sciences, University of California, Davis

P. **"Expression of the *Yersinia enterocolitica* Ysa Type III Secretion System is Anatomically Restricted to the Gastrointestinal Tissues During Infection"**
Zachary W. Bent*[1] and Glenn M. Young[1,2]
[1]Department of Microbiology, University of California, Davis
[2]Department of Food Science and Technology, University of California, Davis

Q. **"Novel Methods For the Capture and Detection of Nonvolatile Components of Human Breath"**

Melinda Simon*[1], Bruce Hammock[2], Nicholas Kenyon[3], and Cristina Davis[1]
[1]Department of Mechanical & Aeronautical Engineering, University of California, Davis
[2]University of California Davis Health System: MIND Institute
[3] University of California Davis Health System: Pulmonary & Critical Care Medicine

R. **"Topographies and Substrate Interactions of Model Cell Membranes"**

Matthew I. Hoopes*, Roland Faller, and Marjorie M. Longo
Department of Chemical Engineering and Materials Science, University of California, Davis

S. **"Swarm Intelligence Based Biomarker Detection for Fruit Disease Diagnosis"**

Weixiang Zhao*[1], Shankar Sankaran[1], Ana Maria Ibanez[2], Abhaya Dandekar[2], Cristina Davis[1]
[1]Department of Mechanical & Aeronautical Engineering, University of California, Davis
[2]Department of Plant Sciences, University of California, Davis

T. **"Volatile Compounds From Citrus Plants Measured Using Differential Mobility Spectrometry and Machine Learning Algorithms"**

Abhinav Bhushan*, Weixiang Zhao, Anthony Santamaria, Cristina Davis
Department of Mechanical & Aeronautical Engineering, University of California, Davis

U. **"CREATE-IGERT Summer Laboratory Short Courses"**

Lawrence D. Joh*[1], Karen A. McDonald[1], Pamela C. Ronald[2], David M. Tricoli[3], and Jean S. VanderGheynst[4]
[1]Department of Chemical Engineering & Materials Science, University of California, Davis
[2]Department of Plant Pathology, University of California, Davis
[3]Plant Transformation Facility, University of California, Davis
[4]Department of Biological and Agricultural Engineering, University of California, Davis

V. **"Development of Plant Cell Suspension Culture as a Bioproduction Platform of Recombinant Human Therapeutic Proteins"**

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

W. **"Catalytic Conversion of Bio-oil Components"**

Ron Runnebaum*
Department of Chemical Engineering & Materials Science, University of California, Davis

X. **"A Viral Amplicon Based Process For Production of Biopharmaceuticals"**

Karen A. McDonald[1], Michael A. Plesha[1], Kittipong Rattanaporn[1], Abhaya M. Dandekar[2], and Bryce W. Falk[3]
[1]Department of Chemical Engineering & Materials Science, University of California, Davis
[2]Department of Plant Sciences, University of California, Davis
[3]Department of Plant Pathology, University of California, Davis

Y. **"HPL-Derived Metabolites as a Vehicle For Production of Superior Stress-Tolerant Plants"**

Elenor Castillo* and Katayoon Dehesh
Department of Plant Biology, University of California, Davis

Z. **"*In vitro* Evolution For Engineering Cre Variants With Altered DNA Site Specificity"**

Roger Jesinghaus* and Michael Toney
Department of Chemistry, University of California, Davis

Aa. **"Elucidating the Metabolism of Nitrogen Use Efficient Plants"**

Gia C. Fazio*, George Theodoris, Zhongin Lu, and Jean C. Kridl
Arcadia Biosciences, Inc., Davis, California

Oral Presentation Abstracts

NIH FELLOW: David Sela

BIFIDOBACTERIUM LONGUM SUBSP. *INFANTIS* EMPLOYS TWO SIALIDASES TO UTILIZE ACIDIC MILK OLIGOSACCHARIDES

Presenter: David Sela*
Authors: **David A. Sela***, Larry A. Lerno, Yanhong Lin, Carlito B. Lebrilla and David A. Mills
Affiliations: Department of Microbiology, University of California, Davis
Preceptor: David Mills

Following birth, the breast-fed infant gastrointestinal tract is rapidly colonized by a microbial consortium often dominated by bifidobacteria. This numerical advantage confers a substantial health benefit to the neonate by hindering pathogen colonization through competitive exclusion. We have previously demonstrated that select bifidobacterial species utilize neutral oligosaccharides ubiquitous in human milk and secreted early in the lactation cycle. However the degree to which sialylated milk oligosaccharides are consumed by bifidobacteria remains obscure. Accordingly, the *Bifidobacterium longum* subsp. *infantis* genome reflects a competitive strategy fashioned under the influence of, and thus targeting, milk-borne molecules. *B. longum* subsp. *infantis* possesses catabolic loci that are predicted enable sialic acid utilization including two sialidases previously unknown in the bifidobacteria. These two sequences encode for functional sialidase enzymes that exhibit constitutive *in vivo* activity during growth on lactose or human milk oligosaccharides. Biochemical characterization of these two enzymes has confirmed that they are indeed active on milk oligosaccharide substrates. Moreover, temporal tracking of sialylated oligosaccharide consumption has revealed the specific compositions preferred by *B. longum* subsp. *infantis* during growth on milk oligosaccharides. These results indicate that *B. longum* subsp. *infantis* consumes acidic milk oligosaccharides and employs intracellular sialidases early in the catabolism of these molecules.

*** Member of the DEB graduate program**

COMPANY AFFILIATE: Monsanto, Calgene Campus

AGRICULTURAL BIOTECHNOLOGY: MONSANTO'S APPROACH TO INCREASE CROP YIELD AND FARMING PRODUCTIVITY

Presenter:	Alberto Iandolino*, PhD
Authors:	**Alberto Iandolino*, PhD**
Affiliations:	Monsanto, Calgene Campus 1920 Fifth Street Davis, CA 95616
Email:	alberto.b.iandolino@monsanto.com

Monsanto is a global company focused on providing solutions to improve agricultural productivity. The company's core business includes crop protection, seed and biotech products. The unique synergistic combination of molecular and conventional breeding and biotechnology allowed Monsanto to build a robust R&D pipeline and establish leading positions in the large and small acreage crop seed and trait business. Monsanto's sustainable yield initiative is to double current yields of corn, soybean and cotton by 2030 while at the same time reducing by 1/3 the cumulative amount of input resources per unit crop output and improve the lives of farmers. Yield traits underlying this gain in agricultural productivity and resource use efficiency are associated with genes functional in a multiplicity of developmental and stress response pathways. Monsanto's unique approach to identify and test a large array of genes affecting specific yield traits will be reviewed together with examples of yield genes in advanced stages of development.

* DEB Graduate

NIH FELLOW: Kristina Mahan

OXIDATION AND DETOXIFICATION OF MAN-MADE CHEMICALS BY NITROBENZENE DIOXYGENASE

Presenter: Kristina Mahan*
Authors: **Kristina Mahan***, Tiffany S. Louie, Juan V. Parales, and Rebecca E. Parales
Affiliations: Department of Microbiology, University of California, Davis
Preceptor: Rebecca E. Parales

Industrialization has resulted in the development of many new chemicals and products in the last century. The production, use, and disposal of these novel compounds have introduced significant amounts of toxic contaminants into the environment. Among the most damaging are the nitroaromatic compounds commonly used in the production of pesticides, dyes, plastics, and explosives. These synthetic compounds are resistant to biological and chemical degradation, and therefore they persist in the environment for long periods of time. While humans have been trying to develop methods to clean up contaminated areas, some microorganisms have evolved new metabolic pathways that utilize these man-made compounds as their sole carbon, nitrogen, and energy sources. One such microbe is *Comamonas* sp. JS765, a strain capable of completely mineralizing the toxic nitroaromatic compound nitrobenzene. We are interested in characterizing nitrobenzene 1,2-dioxygenase (NBDO), the initial enzyme in the nitrobenzene degradation pathway. This enzyme oxidizes toxic nitrobenzene to the easily degraded product catechol. NBDO requires specific electron transfer proteins (reductase and ferredoxin) to transfer electrons from NADH to the catalytic oxygenase component. Using structural data we identified residues on the surface of the oxygenase that may be involved in protein-protein interactions between the oxygenase and ferredoxin components. Site-directed mutagenesis was used to make amino acid substitutions in the oxygenase component at sites predicted to interfere with electron transfer. Using whole cell biotransformation assays, we found that amino acid substitutions at position 98 (changing Val 98 to Asp, Glu, or Phe) of the oxygenase resulted in severely reduced enzymatic activity. We also developed a strategy to identify mutant ferredoxins with compensatory mutations that restore wild-type activity to the Val 98 oxygenase mutants. Purification strategies for all three proteins have been developed and we are working to purify mutant oxygenases. These studies will identify residues on the surface of the oxygenase and ferredoxin that are involved in direct protein-protein interactions and electron transfer and will help to elucidate the mechanism of action of this key detoxification enzyme.

*** Member of the DEB graduate program**

NIH FELLOW: Joseph Ramahi

QUANTITATIVE CHARACTERIZATION OF CENH3 CHROMATIN IN THE MEGABASE ARABIDOPSIS CENTROMERE

Presenter: Joseph Ramahi*
Authors: **Joseph Ramahi***, Ravi Maruthachalam, Pak Ning Kwong, and Simon Chan
Affiliations: Department of Plant Biology, University of California, Davis
Preceptor: Simon Chan

The centromere is the chromosomal location of kinetochore assembly and is essential for proper cell division in mitosis and meiosis. The kinetochore itself is where chromosomes are attached to machinery that physically segregates a duplicated genome into two daughter cells. Many organisms have "regional" centromeric DNA sequences spanning megabases of tandem repeats and kinetochore localization is determined by the loading of the centromere specific histone H3 variant CENH3. While CENH3 is known to be required for kinetochore nucleation, the amount of CENH3 loaded into a regional kinetochore has been difficult to determine due to the fact that only a subset of repetitive centromere DNA is loaded with CENH3.

We are developing a fluorescence microscopy method to count CENH3 molecules in the megabase-scale *Arabidopsis thaliana* plant centromere. We are using GFP-CENH3 in *Saccharomyces cerevisiae* as a fluorescence standard for calculating the amount of GFP-CENH3 molecules in *Arabidopsis* kinetochores. *S. cerevisiae* kinetochores contain a single CENH3 nucleosome, and there are thus a known number of GFP-CENH3 molecules in a budding yeast kinetochore cluster. In *Arabidopsis*, the recent isolation of a *cenh3* null allele allows complementation with a GFP-CENH3 transgene. Comparing fluorescence intensity from yeast to plants allows the quantification of GFP signal from *Arabidopsis* kinetochores to calculate the amount of GFP-CENH3 loaded into individual *Arabidopsis* kinetochores. This amount is found to be ~120 molecules or ~60 specialized nucleosomes, a surprisingly low value given that there are megabases of centromere DNA. We have GFP-tagged several other *Arabidopsis* kinetochore proteins, and are using these lines together with GFP-CENH3 to compare the stoichiometry of complex plant centromeres to the simple ones of budding yeast. We are also examining ways to genetically reduce the amount of CENH3, and test how much CENH3 is required for proper kinetochore function. These experiments will allow us to better understand the mechanism that cells use to segregate their chromosomes.

*** Member of the DEB graduate program**

COMPANY AFFILIATE: Novozymes, Inc.

DEVELOPMENT OF A RECOMBINANT *TRICHODERMA* STRAIN FOR IMPROVED HYDROLYSIS OF PRETREATED CORN STOVER

Presenter:	Suchindra Maiyuran, PhD
Authors:	**Suchindra Maiyuran, PhD**
Affiliations:	Novozymes, Inc. 1445 Drew Avenue Davis, CA 95616
Email:	SMAI@novozymes.com

A majority of currently available commercial enzyme products for biomass hydrolysis are produced by the saprophytic mesophilic fungus *Trichoderma reesei*. *Trichoderma* produces two cellobiohydrolases (CBHI and CBHII), five endoglucanases (EGs), and two β-glucosidases (BGs). Although this mix is relatively efficient at cellulose degradation and large quantities of these proteins are secreted from the fungus, improvements in the total enzyme specific activity and secretion yield may further enhance this product. A primary factor in the high cost of enzymes for biomass hydrolysis is the quantity of enzyme that must be applied for efficient cellulose conversion to glucose. Compared with starch hydrolysis, a 15-100-fold additional enzyme is required to produce an equivalent amount of ethanol, depending on specific process conditions. It is well known that efficient cellulose hydrolysis requires a complex, interacting mix of cellulose degrading proteins. To significantly reduce the enzyme loading required, one may replace *Trichoderma* components with more efficient candidates, or augment the enzyme system with additional components to improve the overall enzyme performance. In this study, identification of new genes that improve specific performance in hydrolysis of pretreated corn stover, and their expression in *Trichoderma* will be discussed.

NIH FELLOW: Erin Tapley

BUILDING A NUCLEAR ENVELOPE BRIDGE: A STRUCTURE/FUNCTION ANALYSIS OF AN INNER NUCLEAR MEMBRANE SUN PROTEIN

Presenter: Erin Tapley*

Authors: **Erin Tapley*[1]**, Nina Ly[1], Brooks Hayes[2], and Daniel Starr[1]

Affiliations: [1]Department of Molecular and Cellular Biology, University of California, Davis

[2]Expression Systems, Biotechnology Company, Woodland, CA

Preceptor: Daniel Starr

Inner nuclear membrane SUN proteins are conserved across eukaryotes and function in a wide variety of processes by recruiting outer nuclear membrane KASH proteins to the nuclear envelope (NE). The KASH/SUN interaction in the perinuclear space establishes a bridge across the NE that allows forces to be transferred from the cytoskeleton to the nuclear lamina. In *C. elegans,* a nuclear envelope bridge between UNC-84 and UNC-83 functions during nuclear migration. Attempts to better understand how KASH and SUN proteins interact with one another have been thwarted by an incomplete knowledge of SUN protein topology. Additionally, the mechanisms by which SUN proteins are targeted to the INM remain to be elucidated.

To better understand how SUN and KASH proteins function to bridge the NE, we performed a structure function analysis of UNC-84. To determine the topology of UNC-84, each of UNC-84's five putative transmembrane domains were deleted from our *unc-84* rescuing construct. Deletion constructs were injected into *unc-84* null animals and the ability to rescue the nuclear migration defect was examined. Only deletion of putative transmembrane domain two was unable to rescue the nuclear migration defect. These results suggest UNC-84 has one transmembrane domain located at residues 512-532. Understanding of the KASH/SUN interaction will ultimately require a structural analysis. The cellular environment in which the SUN/KASH interaction occurs suggests that protein modifications within the ER lumen may be important for proper SUN protein folding. We are currently expressing the lumenal region of UNC-84 fused to a signal sequence in baculovirus transfected insect cells. Our goal is to purify UNC-84 from the tissue culture media for use in *in vitro* binding assays and structural studies.

While determining UNC-84's topology we also began another project to gain insight into how UNC-84 is targeted to the INM. Based on the localization of UNC-84 GFP::LacZ fusion proteins in *C. elegans,* which are too large to enter the nucleus unless actively

imported, we have determined that UNC-84 contains a non-canonical nuclear localization signal between residues 118 and 370. Interestingly, when we deleted this region in a membrane bound construct, it was still able to localize to the NE. This suggests that UNC-84 has multiple determinants in its nucleoplasmic domain that may play a role in its active import. We are actively trying to identify all determinants involved in this process.

The mechanism(s) by which INM proteins are trafficked is unclear. However, recent evidence suggests that some INM proteins may be actively shuttled toward the nuclear envelope and across the nuclear pore complex. This facilitated trafficking is mediated by protein-protein interactions between the nucleoplasmic domain of the INM protein and members of the karyopherin family, who recognize nuclear localization signals (NLSs) and/or INM-sorting motifs in the cargo to be imported into the nucleus.

To better understand how INM SUN proteins are trafficked within the cell, we have examined the *in vivo* localization of various UNC-84 fusion proteins. UNC-84 has one transmembrane domain located at residues 512-532. Consistent with models that describe the facilitated trafficking of INM proteins into the nucleus, the N-terminal 535 residues of UNC-84 are sufficient for NE localization. To test whether UNC-84 is actively imported, we have expressed various UNC-84 GFP-LacZ fusion proteins *in vivo.* All GFP-LacZ fusions are too large to enter the nucleus unless actively imported. UNC-84$^{1\text{-}370}$ is sufficient for NE localization. To test whether either of UNC-84's putative NLSs that reside in UNC-84$^{1\text{-}370}$ are functional, site directed mutagenesis was used to mutate both of these NLSs in our *unc-84* rescuing construct. The double NLS mutant localizes to the NE and has the ability to recruit UNC-83. These results suggest that UNC-84 is actively imported into the nucleus and that neither putative NLS is required for its localization. *In vivo* localization studies of other GFP-LacZ fusions suggest UNC-84 contains an unidentified NLS between residues 118 and 370. To address which regions of UNC-84's N-terminus are required for NE localization, we made four N-terminal deletions constructs: UNC-84$^{1\text{-}535}$ Δ 1-208, Δ118-244, Δ239-361 and Δ 347-467. All membrane bound deletions localized to the NE to at least some extent. The presented data suggests that multiple determinants in UNC-84's nucleoplasmic domain may mediate its INM localization. We are actively searching for all determinants involved in this process.

* Member of the DEB graduate program

NIH FELLOW: Sunny Shah

USING SWITCHABLE SURFACES TO FORM MICROPATTERNED CO-CULTURES

Presenter: Sunny Shah*
Authors: **Sunny Shah*[1]**, Ji Youn Lee[1], Mark Zern[2], and Alexander Revzin[1]
Affiliations: [1]Department of Biomedical Engineering, University of California, Davis
[2]Department of Medicine, Transplant Research Institute, University of California, Davis
Preceptor: Alex Revzin

The local microenvironment consisting of neighboring cells, extracellular matrix (ECM) components, and soluble factors acts as a regulator of tissue differentiation and morphogenesis. The ability to exercise precise spatial and temporal control over cell-surface and cell-microenvironment interactions is an important prerequisite to the assembly of multi-cellular constructs serving as *in vitro* mimics of native tissues. In this study, photolithography and wet etching techniques were used to fabricate individually addressable indium tin oxide (ITO) electrodes on glass substrates. The glass substrates containing ITO microelectrodes were modified with poly(ethylene glycol) (PEG) silane to make them protein and cell resistive. Application of reductive potential caused desorption of the PEG layer which was characterized using cyclic voltammetry, time-of-flight secondary ion mass spectrometry (TOF-SIMS), and protein patterning. Electrochemical stripping of PEG-silane layer from ITO microelectrodes allowed for cell adhesion to take place in a spatially defined fashion, with cellular patterns corresponding closely to electrode patterns. Micropatterning of several cell types was demonstrated on these substrates. The technique was also used to assemble a micropatterned co-culture of fibroblasts and hepatic cells by sequential stripping of PEG silane and attachment of cells. In the future, such combinatorial cell culture systems will be used to expedite discovery of the microenvironment niche required for guided differentiation of stem cells towards specific lineage. This technique can be used to develop complex cell cultures comprised of mature hepatocytes, non-parenchymal or supporting liver cells as well as immature hepatic cells or stem cells. The presence of mature liver cells in the co-culture might provide the "instructive" environment for the immature cells to grow and proliferate. The precise location of the stem cells will enable analysis of cell function using immunostaining, and liver-specific gene expression.

*** Member of the DEB graduate program**

BIOTECHNOLOGY FELLOW: Sarah Lockwood

DEVELOPING AN ALLOSTERIC REGULATORY MECHANISM FOR ENGINEERED ZINC FINGER PROTEINS

Presenter: Sarah Lockwood*
Authors: **Sarah Lockwood***, and David J. Segal
Affiliations: Genome Center, University of California, Davis
Preceptor: David J. Segal

The Cys_2His_2 zinc finger motif offers a stable and versatile framework for designing polyfinger proteins that can target sequences of interest. Attaching protein functional domains to the zinc finger modules furthers this technology, in that the chimeric proteins are capable of sequence specific and sequence dependent activity. Engineering these proteins has many practical applications, including sequence imaging and detection. We have developed a system entitled SEquence Enabled Reassembly, or SEER, using β-Lactamase. The enzyme was effectually cut into halves, each half then attached to a set of zinc fingers. Having both chimeric constructs bound to DNA via the zinc finger domains to their respective neighboring sequences brings the β-lactamase halves in close enough proximity for them to reassemble into an active enzyme. However, one complication with this system is β-lactamase reassembly in solution without having bound to the target DNA, resulting in false positive or background signal. The development of an allosteric regulator, or modular control switch would significantly reduce this issue by allowing reassembly only when the constructs are bound to DNA. It's been shown that zinc finger proteins are highly flexible in solution, attributed to a pentapeptide linker sequence between fingers. Upon binding to DNA, the linkers become structured and the fingers wrap around the DNA helix. Using this information, we plan to attach complimentary but catalytic inhibitory β-lactamase halves to the existing constructs. Therefore, in the absence of DNA there will be reassembly of halves on the same construct, but no signal due to the inhibitory domain. In the presence of target DNA, the zinc fingers will tightly bind and physically separate these two halves. This frees the "activatable" half to reassemble with the complimentary "activatable" half from the neighboring construct, which was also exposed upon zinc finger binding to its target sequence. We anticipate a significant improvement in assay sensitivity.

*** Member of the DEB graduate program**

BIOTECHNOLOGY FELLOW: Matthew Hoopes

TOPOLOGIES AND SUBSTRATE INTERACTIONS OF MODEL CELL MEMBRANES

Presenter: Matthew Hoopes*
Authors: **Matthew Hoopes***[1], Roland Faller[1,2], and Marjorie M. Longo[1,2]
Affiliations: [1]Biophysics Graduate Group, University of California, Davis
[2]Chemical and Material Science, University of California, Dav
Preceptor: Roland Faller, and Marjorie L. Longo

Bionanotechnology relies on the understanding and control of materials at the molecular level. Substrate interactions with adsorbed membranes modify the intrinsic mechanics of supported lipid bilayers. Fluorescence Interference Contrast microscopy provides one of many techniques for resolving spatial information below the diffraction limit of conventional microscopy. Supported lipid bilayers (SLB) continue to be an important means of measuring the thermodynamic and mechanical properties of phospholipid membranes, which are the basis of compartmentalization in living cells. Biotechnology relies on knowledge of these properties for engineering lipid based products such as immunological assays, non-viral gene delivery, and hybrid membrane chemical sensors. Understanding SLB systems with respect to their substrates enhances the understanding of the measurements taken thereon and promotes design of new substrates to expand the usefulness of these systems.

*** Member of the DEB graduate program**

COMPANY AFFILIATE: Genentech

LIFE AFTER DISSERTATION: DERIVING MAXIMUM VALUE FROM CAREER INVESTMENTS

Presenter:	Caryle Vann, PE, PMP
Authors:	**Caryle Vann, PE, PMP**
Affiliations:	Genentech 1000 New Horizons Way Vacaville, CA 95688
Email:	vann.caryle@gene.com

After your hood, robe and parchment are safely stored away, life AD (after dissertation) begins. How sure are you that you will be satisfied with the results? What is "success", and how will you measure it? Regardless of the job offer that you accept, how can you be assured that you derive maximum value from your career investments?

BIOTECHNOLOGY FELLOW: Christina L. Takanishi

A GENETICALLY ENCODED PROBE FOR THE IDENTIFICATION OF PROTEINS THAT RESPOND TO OXIDATIVE STRESS

Presenter: Christina L. Takanishi*
Authors: **Christina L. Takanishi*** and Matthew J. Wood
Affiliations: Department of Environmental Toxicology, University of California, Davis
Preceptor: Matthew J. Wood

Reactive oxygen species (ROS), such as free radicals and peroxides, cause a wide variety of cellular effects through their roles in signal transduction pathways, transcription factors, and gene expression. The overall goal of my research is to understand the molecular mechanisms by which ROS contribute to oxidative stress and how oxidative stress regulates the function of biological molecules. In *Saccharomyces cerevisiae*, the conserved Orp1-Yap1 cysteine thiol-based sensor can be thought of as an archetypical oxidative stress signaling module. The oxidant receptor protein, Orp1, perceives hydrogen peroxide (H_2O_2) through the reaction of H_2O_2 and an active site cysteine residue, resulting in the formation of a cysteine sulfenic acid (Cys-SOH). Cys598 in the Yap1-cCRD domain reacts with the Cys-SOH on Orp1, resulting in an intermolecular disulfide bond between Orp1 and Yap1, ultimately activating the Yap1 transcription factor via an intramolecular disulfide bond. Although there is increasing evidence that organisms have conserved molecular mechanisms to perceive and respond to oxidative stress using Cys-SOH biochemistry and cysteine thiol-based regulatory switches, there are currently no general tools to detect the proteins that form Cys-SOH in live organisms. The Yap1 transcription factor was successfully engineered for use as a general trap for proteins that form Cys-SOH in vivo and was used to identify proteins that transiently form Cys-SOH in *Escherichia coli*. We are currently working to develop organelle specific probes to identify proteins that form Cys-SOH and apply them to *S. cerevisiae* and human keratinocytes to determine the effects of ROS on protein Cys-SOH formation.

*** Member of the DEB graduate program**

BIOTECHNOLOGY FELLOW: Huilan Han

ADVANCESIN CHIP-BASED ELECTROPHYSIOLOGY

Presenter: Huilan Han*
Authors: **Huilan Han*** and Cristina Davis
Affiliations: Department of Environmental Toxicology, University of California, Davis
Preceptor: Cristina Davis

Ion channels, which are transmembrane proteins, play important roles in both physiology and disease processes. The patch-clamp technique is considered the gold standard to assess ion channel function across cell membrane. In a traditional patch-clamp experiment, typical throughput is very low and requires doctoral-level expertise to operate the instrument. Both the functional analysis of ion-channels and the screening of pharmaceutical compounds require much higher-throughput assays, making chip-based automation very attractive. Although these chip-based devices are geometrically equal to the traditional patch-clamp method, gigaseal (>10^9 □) formation is rarely observed and average seals is still in the MOhm (~10^6 □) range. We hypothesize that that surface roughness affects both the magnitude of the seal resistance as well as the percentage of gigaseal successes. To test our hypothesis, we proposed two experimental methods to produce more uniform surface roughness surrounding the chip aperture: organometallic hybrid film synthesis and special glass deposition. At the final stage of the device fabrication, a self-developing hybrid film is deposited onto the substrate and the material is then reflowed to reduce roughness. Subsequent test of seal strength and seal formation rates on both modified and unmodified patch-clamp chips will determine the affect of reduced roughness. The final phase of my research will focus on the integration of a microfluidic platform, aperture arrays and recording electrodes onto a single chip. Together, all of these innovations will reduce the complexity of planar patch-clamp manufacturing and increase the range of applications for this technology.

*** Member of the DEB graduate program**

COMPANY AFFILIATE: E & J Gallo Winery

WINE, YEAST AND GENETICS

Presenter:	Chandra Kilburn PhD
Authors:	**Chandra Kilburn, PhD**
Affiliations:	E & J Gallo 600 Yosemite Blvd. Modesto, CA 95354
Email:	chandra.kilburn@ejgallo.com

Wine, the fermented juice of grapes, has been made by man for thousands of years. Louis Pasteur and other microbiologists in the mid-1800s described the scientific basis for fermentation as being attributed to micro-organisms, such as yeast, sipping sugars in the grape juice and excreting alcohol. As the importance of yeast as an ingredient in the winemaking process became more appreciated, companies all over the world began to collect and market specific yeast strains promised to enhance positive attributes and minimize negative attributes in wine. At E&J Gallo, we are committed to creating excellent, world-class wines. To make the best wine possible ingredients are carefully selected; this includes selecting the appropriate yeast strain for each wine-style. In order to select the best yeast strain for the each wine we must better understand how yeast, through metabolic processes, impact flavor and aroma. We are currently employing modern molecular and cellular biology techniques to identify how genetic differences between natural isolates of yeast create unique flavor profiles in wine.

COMPANY AFFILIATE: Crystal Bioscience

HIGH VALUE ANTIBODIES FROM UNCONVENTIONAL SOURCES

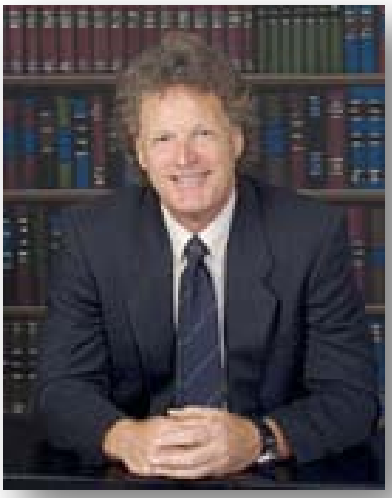
Presenter: Marie-Cecile van de Lavoir, PhD

Authors: **Marie-Cecile van de Lavoir, PhD**

Affiliations: Crystal Bioscience, Inc.
2105 Woodside Road
Woodside, CA 94062-1153

Email: lavoir@crystalbioscience.com

Monoclonal antibodies (MAb) are the largest class of therapeutics currently being developed by the pharmaceutical industry and form the backbone of most diagnostic tests. However, the traditional process of isolating antibodies using hybridomas is time- consuming, costly and scans only a very small proportion of the entire array of monoclonal antibodies that are produced following immunization. Furthermore, traditional methods of producing MAb use mammals rather than birds. Birds would be the preferred species since they recognize more epitopes because they are phylogenetically less related to humans from which antigens are frequently derived. We are developing a technology for directly isolating MAb from B cells recovered from immunized chickens to (1) obviate the need for making hybridomas and, therefore, scan the entire array of monoclonal antibodies that are produced in response to immunization and (2) to increase the production of novel antibodies that would not be generated in the traditional mammals (i.e. rats, rabbits, guinea pigs and mice). This goal will be accomplished by developing a culture system to clonally propagate small colonies of chicken B cells and a rapid technology to detect their production of antigen-specific antibody. Combined, these technologies will provide access to novel antibodies against epitopes that have not yet been identified. These MAb can be used to develop new therapeutics and to create new diagnostic tests with greater sensitivity, specificity and precision.



Bioethics

ETHICS QUESTION

What You (Think You) Know About Mentoring

Written by:
Martina Newell-McGloughlin
Co-Director of NIH Training Program
In Biomolecular Technology (NIH-1-T32-GM08799)

Presented by:
John I. Yoder
Faculty Trainer of NIH Training Program
In Biomolecular Technology (NIH-1-T32-GM08799)

What You (Think You) Know About Mentoring

Case Study

Marley Neville is a fourth-year biology graduate student at Legend University. She is conducting her research in the lab of Dr. Alice Krippin, a well-respected lab director whose research focuses on RNA interference. Marley's work has been conscientious but unproductive. She feels stuck and has tried to discuss this with Dr. Krippin, but she tells her to just keep working. "You'll get results eventually" is all Dr. Krippin ever tells Marley.

Recognizing that mentoring is of the utmost importance in the training of graduate students, the Biology Department at Legend University has a policy that lab directors are to act as formal mentors for their trainees. Marley has therefore relied on Dr. Krippin and has not formed a personal relationship with anyone else in the department. She thinks that Dr. Krippin is not giving her the attention she needs because of her other activities. Dr. Krippin has a personal interest in bioinformatics and computer programming. As the instructor for the department's molecular-biology course, she develops a computer program that generates a video demonstration of RNAi (iRNA) and uses it to teach the class about this phenomenon and its many potential biotech applications. iRNA is a hit with the students and with other faculty. Realizing that the program has broad appeal, and that she has a talent for programming, Dr. Krippin sets up her own business, iRNation. She markets the program, and others she develops, commercially to faculty at other universities via the Web, but she shares the programs with Legend faculty pro bono.

In addition to Marley 's concern that Dr. Krippin is not providing her with the guidance she needs, she often ends up answering calls to the lab about iRNation and troubleshooting programs for Dr. Krippin's business. Along with research, exams, and work on her projected thesis, these activities have left Marley feeling overwhelmed. But she doesn't want to appear unwilling to help. Marley knows that Dr. Krippin, owing to her excellent reputation and her extensive contacts in the field, can be very helpful to her in securing a postdoctoral appointment. She also hopes that in the next year Dr. Krippin will arrange for her to make presentations within the department as well as at a national meeting.

In Marley's department, comprehensive examinations are given in part on a take-home basis. She has completed two drafts for one of her examinations, but it is being held up before approval by a particularly exacting member of the review committee, who has a reputation for unreasonable demands. She has shown her most recent draft to specialists in the field, who believe that her exam has earned well beyond a passing grade and cannot understand why it is being held up. When Marley discusses the exam with Dr. Krippin, in the hope that she will intercede in some way with the difficult faculty member, she refuses to get involved. "It is not my responsibility," she says.

To add to her feelings of neglect, Marley has not had a committee meeting to discuss her research in more than a year, and Dr. Krippin shows no signs of calling one anytime soon. Marley is quite frustrated and has thought of talking to Dr. Samantha Sheppard (Dr. Sam), a more senior faculty member in the department and another member of her committee. Marley has seen Dr. Sam work with other graduate students, and Dr. Sam seems to take an active part in fostering their graduate work and careers.

Marley decides to talk to Dr. Sam, who suggests that Marley should have a committee meeting and initiates the scheduling of one. At the meeting, the other members of Marley's committee express concern about her progress; they believe that she is not likely to finish by the end of her fifth year, her expected completion date. Marley is upset, because she believes that she has been doing exactly what was asked of her by Dr. Krippin, assuming that her work would eventually lead to a thesis. Dr. Krippin points out to the committee that she never asked Marley to answer the phone or troubleshoot the programs, that Marley did those things by her own choice and in doing so drew time away from her thesis and exam work.

Marley decides that even at this point in her graduate education she is better off starting over in another lab. She asks Dr. Krippin for a letter of recommendation. She tells Marley that she can't write a strong letter, but she would be willing to describe her accomplishments, the coursework she completed, her time in the lab, etc. Marley schedules an appointment with the dean to discuss her graduate-student career and her timetable in working toward her degree.

QUESTIONS:
1: It appears early on that Dr. Krippin may have low expectations of Marley, or that she is, for other reasons, relatively passive with regard to Marley's progress. What is Marley's responsibility in this situation?

2: Dr. Krippin has many responsibilities as a professor, and she is also running a business. What is her responsibility as Marley's supervisor and mentor?

3: Marley's work on behalf of Dr. Krippin' business is diverting her attention from meeting her own academic needs. Whose responsibility is it to insure that this does not happen? Is it ever appropriate for a graduate student to perform, on behalf of a faculty member, work that is not related to the student's own academic work?

4: Is it appropriate for a lab director to advocate for a graduate student who is in a difficult academic situation? If so, what form should that advocacy take?

5: Whose responsibility is it to call committee meetings? What are the committee members' responsibilities in this situation? Should anyone monitor the supervisor-trainee relationship?

6: Does Dr. Sam have any responsibility after Marley comes to talk to her?

7: Should Marley take any further actions with regard to Dr. Krippin and her lab before she decides to transfer?

8: Is Dr. Krippin acting reasonably in response to Marley's request for a letter of recommendation? What other options did Marley have in attempting to handle this situation?

9: What departmental policies might prevent, or help address, such a situation?

General

1: What can be done to understand mentoring better? What quantitative and/or qualitative studies might be undertaken?

2: If a trainee believes that he or she has been seriously injured by something a mentor has done, how can the trainee seek redress? How should he or she proceed?

4: To what extent is empathy necessary on the part of the mentor? What about cultural or other differences when they interfere with understanding?

Poster Abstracts

A. CHROMOSOME SIZE-DEPENDENT CONTROL OF CROSSING OVER DURING MEIOSIS IN *SACCHAROMYCES CEREVISIAE*

Patty Yi-Hwa Hwang* and Neil Hunter
Department of Microbiology, University of California, Davis

I am studying chromosome size-dependent control of crossing-over during meiosis using *Saccharomyces cerevisiae* as a research model. Crossover formation is a highly regulated process, and unregulated crossovers can lead to pregnancy loss or Down's syndrome in humans. **Chromosome size-effect** describes the observation that small chromosomes crossover at a higher density (cM/Kbp) than long chromosomes; this phenomenon is thought to effect **crossover assurance** (The observation that all chromosomes make at least one crossover, even when the chromosome length is smaller than the average distance between the crossovers in long chromosomes). My research aims to understand the function, nature and mechanism of the chromosome-size effect in budding yeast. To this end, I shortened chromosome III by half and found a 1.3 -fold increase in recombination density. The "extra" crossovers are spread out along the entire length of chromosome III and do not facilitate crossover assurance. On the contrary, the "extra" crossovers are on a population of shortened chromosomes that already have one or more crossovers. I am currently testing the idea that a greater fraction of initiated recombination events result in crossing-over when chromosome III is shortened. I am also investigating genetic requirements for the extra crossovers.

* Member of the DEB graduate program

B. TIMELY SEPTATION REQUIRES SNAD-DEPENDENT SPINDLE POLE BODY LOCALIZATION OF THE SEPTATION INITIATION NETWORK COMPONENTS IN THE FILAMENTOUS FUNGUS *ASPERGILLUS NIDULANS*

Cui Jing Tracy Zeng [1*], Jung-Mi Kim[1], Tania Nayak[2], Rongzhong Shao[1], Angel Huang[1], Berl R. Oakley[2], and Bo Liu[1]

[1]Department of Plant Biology, University of California, Davis, CA, 95616

[2]Department of Molecular Biosciences, University of Kansas, Lawrence, KS, 66045

In the filamentous fungus *Aspergillus nidulans*, cytokinesis/septation is triggered by the kinase cascade of the septation initiation network (SIN) which first appears at the spindle pole body (SPB) during mitosis. The novel coiled-coil protein SNAD is associated with the SPB, and is required for timely septation, and conidiation. We have determined that SNAD acts as a scaffold protein that is required for the localization of the SIN proteins of SIDB and MOBA to the SPB. Another scaffold protein SEPK/SNAE, whose localization at SPB was dependent on SNAD, was also required for SIDB and MOBA localization to the SPB. In the absence of either SEPK/SNAE or SNAD, SIDB/MOBA successfully localized to the septation site, indicating that their earlier localization at SPB was not essential for their later appearance at the division site. Our results suggested that through SEPK/SNAE, SNAD mediates the interaction between SIN components and cell cycle regulators at the SPB. Unlike their functional counterparts in fission yeast, SEPK/SNAE and SNAD were not required for vegetative growth except for timely septation. Furthermore, hyperactivation of the SIN pathway by downregulation of negative regulators of the SIN suppressed the phenotype of aborted conidiation due to the loss of SNAD. Therefore, we conclude that SPB localization of SIN components is not essential for septation *per se*, but critical for septation to take place in a timely fashion. In addition, we conclude that timely execution of septation is a prerequisite for conidiation.

* Member of the DEB graduate program

C. DESIGN OF A DISEASE RELEVANT RNA EDITING SUBSTRATE FOR USE IN HIGH THROUGHPUT SCREENING

Rena Goodman*, Subhash Pokharel and Peter Beal
Department of Chemistry, University of California, Davis, CA, 95616

Deamination of adenosine to produce inosine in mRNA is one example of RNA editing. Inosine is translated as guanosine, so editing can result in codon changes including extension of a protein if a stop codon is involved. These differences in protein structural diversity caused by editing are necessary for a properly functioning nervous system in metazoa. The Beal lab has developed a high-throughput screen in yeast to test for RNA editing activity of ADAR2, an adenosine deaminase acting on RNA. The screen uses two plasmids, one containing a gene for ADAR2 and one containing a gene encoding the sequence of an mRNA substrate followed by a reporter gene, α-galactosidase. The mRNA substrate contains a stop codon that, upon editing, will be translated as a tryptophan codon. This results in read-through of the downstream reporter gene, which in turn causes the yeast colonies to change color from white to green. Mutations can be made in either gene and these mutants can be rapidly screened to determine whether the substrate/enzyme pair is competent for editing. Currently, the screen uses the RNA sequence from the GluR-B (human glutamate receptor-B) R/G site. The serotonin $5HT_{2C}$ receptor mRNA is also edited by ADAR2 *in vivo*, and over-editing of this mRNA may be a cause of Prader-Willi syndrome. We propose to adapt this high-throughput screen to use an mRNA substrate based on the serotonin $5HT_{2C}$ receptor sequence, so that we can better explore the interactions between ADAR2 and this substrate, as well as test potential inhibitors of this reaction.

* Member of the DEB graduate program

D. THE EFFECTS OF DEVELOPMENTAL DIFFERENCES IN CD4+ T CELL FUNCTION ON VIRAL PATHOGENESIS IN RHESUS MACAQUES

Myra Grace A. dela Pena[1*], Peter Barry[1, 2], and Kristina Abel[1]
[1]California National Primate Research Center, University of California, Davis
[2]Center for Comparative Medicine, University of California, Davis

Background: Human cytomegalovirus (HCMV) generally establishes a lifelong infection without clinical symptoms in immunocompetent individuals. The immune systems of infants undergo many developmental changes after birth and these changes may affect their ability to respond to viral pathogens. Interestingly, HCMV-infected children shed the virus longer and in higher titers than adults.
Hypothesis: We hypothesize that the decreased ability to produce IFN-γ and the higher frequency of regulatory T cells in the infant immune system will interfere with CD4+ T cell differentiation, contributing to the inefficiency of the infant immune system to control viral shedding.
Methods: We inoculate Specific Pathogen Free (SPF) infant and adult rhesus macaques orally with rhesus CMV (RhCMV) to study the mechanisms responsible for the differences in immunological response and virological outcome in these animals. Blood samples are collected from these monkeys longitudinally and peripheral blood mononuclear cells are isolated and analyzed by multi-parameter flow cytometry to examine their T cell response including frequency, cytokine levels, cytotoxicity and regulatory function. We measure antibody titers to RhCMV by ELISA and collect plasma, saliva, and urine to determine viral load by PCR.
Results: As predicted, infant rhesus macaques are rapidly infected via the oral route when compared to adults. No RhCMV -specific T cell responses are observed in these infants despite early seroconversion while T cell responses are evident in the adult macaques. Further, more CD8 T cell activation are observed in the adults. We anticipate that the infant macaques will have prolonged high viral shedding in their saliva and urine when compared to the adult macaques.
Conclusion: Developing this nonhuman primate model of infant RhCMV will facilitate in our understanding of the temporal development and differences of the infant immune system's response to viral pathogens and potentially provide the knowledge to design effective vaccines for children.

* Member of the DEB graduate program

E. INVESTIGATING A NOVEL, ATTENUATED *MYCOBACTERIUM TUBERCULOSIS* VACCINE VECTOR TO ENHANCE SIV IMMUNITY IN INFANT RHESUS MACAQUES

Kara Jensen[1*], Michelle Larsen[2], Glenn Fennelly[2] and Kristina Abel[1]
[1]California National Primate Research Center, University of California, Davis
[2]Albert Einstein College of Medicine, NY

HIV-1 mother-to-child transmission via breastfeeding continues to be a major killer of children despite improved antiretroviral therapies, viral screening and formula feeding. Vaccination with *Mycobacterium bovis bacilli Calmette-Guérin* (BCG) is known to elicit a strong T helper 1 response in human infants. Therefore, we hypothesize that the use of a highly attenuated *M. tuberculosis* vaccine vector harboring HIV-1 genes will induce a robust antiviral immune response in infants leading to protection against oral HIV-1 infection. To ensure the safety of our vector (rA*Mtb*) we vaccinated healthy (n=3) and SIV-infected (n=3) infant rhesus macaques with rA*Mtb* orally (10^9 cfu) and intradermally (10^6 cfu). We measured lymphocyte phenotypes and antigen-specific T cell responses longitudinally in peripheral blood and in tissues at necropsy. We also assessed rA*Mtb* dissemination in tissues via acid-fast staining. We have shown that rA*Mtb* does not cause disseminated tuberculosis in healthy or SIV-infected infant rhesus macaques. Importantly, vaccination with rA*Mtb* induced robust T cell responses to BCG antigens. Our results suggest that rA*Mtb* may be an effective and safe vaccine vector for SIV antigens. Our upcoming studies will evaluate the efficacy of oral versus intradermal immunization at eliciting viral immunity and examine the dosage of rA*Mtb* that best induces both cell-mediated and humoral immune responses.

* Member of the DEB graduate program

F. THE 14-3-3 PROTEIN Bmh1 FUNCTIONS IN CALORIE RESTRICTION AND NUTRIENT-SENSING PATHWAYS TO REGULATE LONGEVITY

Chen Wang, Craig Skinner, Erin Easlon* and Su-Ju Lin
Department of Microbiology, University of California, Davis

Calorie restriction (CR) has been suggested to extend life span by reducing the activities of conserved nutrient-sensing pathways. Here we report the yeast 14-3-3 protein, Bmh1, as a common down stream target of CR and the TOR and PKA pathways. Our data show that Bmh1 elicits both beneficial and adverse effects in life span regulation and it differentially regulates the life span of cells in different metabolic states. Bmh1 over-expression increases life span primarily by increasing mitochondrial respiration. Deletions of Bmh1 extend life span mainly through eliminating the adverse effects of Bmh1. Our data support that phosphorylated Bmh1 is a major source of the adverse effects. The level of phosphorylated Ser238 on Bmh1 increases during chronological aging, which is delayed by CR or by reduced TOR and PKA activities. We demonstrate that PKA can directly phosphorylate Bmh1-Ser238. In addition, phosphorylation of Bmh1 specifically prevents *tor1Δ*-induced chronological life span extension and heat resistance suggesting Bmh1 plays a more specific role in the TOR pathway.

* Member of the DEB graduate program

G. TRANSIENT IN PLANTA EXPRESSION OF CELLULOSE-DEGRADING ENZYMES: PLANT TISSUES AS BIOREACTORS

Benjamin E. Lindenmuth*[1], Bryce W. Falk[1], Abhaya M. Dandekar[3], and Karen A. McDonald[1]

[1]Department of Chemical Engineering & Materials Science, University of California, Davis
[2]Department of Plant Pathology, University of California, Davis
[3]Department of Plant Sciences, University of California, Davis

Biofuels such as ethanol are fermented from glucose, and the cellulose in biomass is a potential source of this sugar. However, a synergistic set of enzymes is needed to degrade the cellulose into glucose. Currently, these enzymes are produced by fungal cell culture. As an alternative way to reduce capital costs, energy consumption and net CO_2 emissions, we propose to use agroinfiltration of harvested plant tissues to produce these enzymes. In this research, we have shown that harvested tissues can produce as much enzyme as can be produced in intact plants.

Agrobacterium tumefaciens can transfer a specific gene into plant cells. This gene is then expressed using the plant cell transcription and translation mechanisms. In this project, the gene for a cellulose-degrading enzyme – the endoglucanase from the thermophilic bacteria *A. cellulolyticus* – was transferred to and expressed by the plant tissue. Agroinfiltration involves bringing *Agrobacteria* in contact with plant cells by applying and releasing a vacuum. Enzyme production is monitored over time as intact plants and harvested leaves are stored in different environments.

Future work will involve monitoring the subcellular location of the enzyme, utilizing a viral replicase expression system for increasing enzyme production, assessing production in tissues from different plant species being considered as bioenergy crops, and optimizing infiltration and incubation conditions.

* Member of the DEB graduate program

H. qPCR MONITORING OF T-STRAND POPULATIONS IN AGROINFILTRATED LEAF TISSUE

Christopher Simmons* and Jean VanderGheynst
Department of Biological and Agricultural Engineering, University of California, Davis

Agrobacterium tumefaciens-mediated gene transfer, or agroinfiltration, is a common plant transformation technique. However, the efficacy of agroinfiltration varies widely between plant species. We are interested in studying whether populations of T-strands, the genetic material transferred from *Agrobacteria* to plant cells, change over time as plant cells are transfected by the bacteria. The number of T-strand copies within plant cells is related to the ultimate *in planta* expression level of recombinant genes housed on the T-strand. Changes in T-strand levels within plant tissue may yield clues as to why transgene expression varies between plant species following agroinfiltration. Moreover, the behavior of T-strand populations in agroinfiltrated plant tissue may suggest targets for improving agroinfiltration. Quantitative PCR (qPCR) was used to quantify the densities of T-strands in lysates from agroinfiltrated leaf tissue. Furthermore, qPCR was used to monitor the concentrations of the plasmid pTFS40, from which T-strands are synthesized in the bacteria, in agroinfiltrated leaf tissue. T-strand levels were normalized against pTFS40 levels to determine changes in T-strand concentrations within agroinfiltrated leaf tissue.

* Member of the DEB graduate program

I. IDENTIFICATION AND CHARACTERIZATION OF BACTERIAL EFFECTORS THAT INTERACT WITH THE PLANT PROTEIN FOLDING CATALYST CYCLOPHILIN

Mitch Elmore* and Gitta Coaker
Department of Plant Pathology, University of California, Davis

Effector proteins are essential virulence determinants for many Gram-negative bacterial plant pathogens. These proteins are delivered into the host cell cytoplasm via the Type III Secretion System during infection and collectively contribute to pathogen fitness on host plants. Due to size constraints of the Type III Secretion System, effectors are delivered as either partially or completely unfolded proteins and it is hypothesized that many exploit plant folding catalysts for activation. One such folding catalyst, cyclophilin, has been identified. Cyclophilins are molecular chaperones that catalyze the *cis/trans* isomerization of peptidyl-prolyl bonds, a rate-limiting step during protein folding. We have designed and implemented a targeted, high-throughput protein interaction screen to identify effectors that interact with the *Arabidopsis* cyclophilin ROC1. To date, eight effectors from different species of phytopathogenic bacteria have been identified in this screen. Functional analysis of effectors that require cyclophilin for activation is underway. Identification of the host activators of bacterial effectors will enable the production of enzymatically active effector proteins *in vitro* and facilitate investigations into their functions during the infection process.

* Member of the DEB graduate program

J. CLUSTER ANALYSIS OF MULTI-DIMENSIONAL EXPRESSION DATA

Chingying Li, Tim Hickman, and Martin Ruebelt*
Monsanto, Calgene Campus, Davis, California

As part of an effort to produce healthier oils, soybean oil containing stearidonic acid (SDA) was produced by overexpressing a delta-15 and a delta-6 desaturase in developing seed. The □-3 fatty acid SDA is a precursor of EPA with the advantage of being more oxidatively stable. SDA soybean oil may offer a more sustainable alternative to fish oil. In order to explore additional applications for such a product, Monsanto examined in an animal feeding study the effects of dietary SDA supplementation on fat quality, sensory quality, and fatty acid composition of pork. Therefore, a reliable method was needed for the quantitative determination of fat content and fatty acid composition (FAC) of the various pig tissues, including loin, belly, ham and skin. Here we report the development and validation of a high-throughput method. The described method is based on an acid-catalyzed direct transesterification of the sample without a lipid extraction step. Producing a homogeneously ground sample powder was essential to developing this high-throughput method. Therefore, special attention was paid to optimization of the sample preparation process. Per week, one person can analyze more than 600 samples with the described method compared to 40 samples per week with traditional methods.

K. ANTIBODIES FOR IRREVERSIBLE CAPTURE

Prasad Gawande*, Amir Kalani, Mark McCoy, Vahid Eskandari, Jeff Day, Bernadette Marquez and Claude Meares
Department of Chemistry, University of California, Davis

In the past, our lab has developed a new class of irreversible ligand-receptor systems, which we also call as antibodies with infinite affinity. We want this antibody to attach its specific target irreversibly and not dissociate. A permanent covalent bond should be formed to achieve this irreversible binding. We have successfully developed systems like CHA255 and Benzyl-EDTA, 2D12.5 antibody and Benzyl-DOTA. For the imaging purposes, antibody targets are the lysine residues on the antigen. This poster will entail a novel approach for achieving this using 2D12.5 G54K fab protein as a model system and the experiments with different set of electrophiles (ligands) with this protein. Our results have shown that this 2D12.5 G54K fab protein binds covalently with DITC (DOTA analog) when the reaction was done at 37^0C and at physiological pH. The increase in the yield of the reaction was also seen when the pH was increased. From various control experiments, we have also shown that DITC is tagging the engineered lysine only and not any other lysine from the protein. Now, we can apply the similar scheme with the lysines on antigen and the antibody specific for that to form a covalent bond between them using a bifunctional linker. The methods of making the anti-CD20 fusion proteins used in Non-Hodgkin's Lymphoma Pretargeting and Cancer Therapy techniques are also shown. It will also deal with the experiments we have performed for making antibody fragments (scFv) bind to their targets covalently. The results of the activity assays for these proteins using Flow Cytometry will be also presented.

* Member of the DEB graduate program

L. GENOMIC ISOLATION OF ALLELES THAT RENDER INFERTILITY IN HIGH GROWTH FVB/NJ FEMALE MICE

Rashida Lathan*, Thomas E. Adams, and Juan F. Medrano
Department of Animal Science, University of California, Davis

Our lab is studying a startling phenotype of infertility in the FVB/NJ line of high growth (*hg*) female mice (FVB/NJ-*hghg*). These mice when paired with fertile male breeders produce no progeny. High growth (*hg)* is a mutation in mouse chromosome 10 that results in a 40% increased growth in mice and is due to deletion that encompasses 3 genes (Raidd/Cradd, PlexinC1 and suppressor of cytokine signaling-2, Socs2). It appears that complex genetic interactions between the homozygous *hg* deletion and the FVB/NJ strain background has a direct influence on female fertility. This project is designed to survey the FVB/NJ genome and to incorporate data from functional assays to identify candidate genes responsible for the infertility phenotype. To isolate possible causative loci we are producing a population for genome-wide association analysis, in which a fertile C57BL/6J-*hghg* female was crossed to a fertile FVB/NJ male. The resulting females are being recurrently backcrossed to FVB/NJ-*hghg* males to introgress the FVB/NJ background onto the C57BL/6J. Continued selection of fertile females as progenitors of the next generation will create fertile backcrossed FVB/NJ females, where C57BL/6J DNA will remain in those regions that impact fertility in the original infertile FVB/NJ females. In order to isolate these fertility regions, fertile females will be genotyped with a high density SNP chip capable of differentiating C57BL/6J and FVB/NJ SNP markers. Integral to the discovery of candidate genes is the understanding of the biological processes that result in the fertility defect and the ability to associate a refined phenotype for genomic analysis. Since it has been reported that Socs2 disruption can interfere with reproductive hormone, prolactin, we are investigating with special interest the interaction of these metabolic regulator in fertile and infertile FVB/NJ females. Our experimental data indicate normal coital plug rate, normal estrous cyclicity, an ovulatory-stage dysfunction in ooctye release, normal structural histology of ovary and oviduct and to date normal hypothalamic mRNA expression of prolactin in the FVB/NJ-*hghg*. Our aims are to 1) continue the recurrent backcross population for five to nine generations and to 2) characterize the infertility phenotype in the FVB/NJ-*hghg* female by examining a larger sample size.

*** Member of the DEB graduate program**

M. MANIPULATION OF PHYTOCHROME-MEDIATED SIGNALING IN TRANSGENIC PLANTS

Timothy Butterfield*, Wei Hu, and J. Clark Lagarias
Department of Molecular and Cellular Biology, University of California, Davis

As a consequence of their sessile nature, plants must maximize the limited resources available to them. For plants, an incredibly important resource and signal is light – particularly the red region of the spectrum that is optimal for photosynthesis. The phytochromes, a family of red/far-red light-responsive proteins possessing non-protein bilin chromophore adducts, have evolved to perceive this region and initiate signal transduction cascades resulting in optimized light harvesting and effective energy conversion. Phytochrome activation-coupled signaling networks include altered protein-protein interactions, release of second messengers and changes in gene expression impacting nearly every stage of plant growth and development. Our understanding of phytochrome-regulated signaling networks has grown dramatically in recent years; however, we lack a thorough appreciation of the early steps in phytochrome signaling. A more complete understanding of the biochemistry of phytochrome-mediated signaling is expected to enable novel, intelligently designed light-mediated plant growth and development. Our studies exploit a dominant, gain-of-function phytochrome mutation rendering the holoprotein constitutively activated, independent of light input. We have recently shown that transgenic Arabidopsis plants expressing a tyrosine to histidine mutation in phytochrome B (YHB) exhibit altered seed germination, seedling establishment, shade sensing and flowering phenotypes (Su and Lagarias, 2007) due to a light-independent misregulation of the phytochrome B-mediated gene network normally modulated by red/far-red light (Hu et al., 2008). My research aims to address the following questions: Does phytochrome A regulate the same signaling network as phytochrome B? Can the activities of wildtype and mutant phytochromes be altered and regulated by modifications to the chromophore structure and regulation of synthesis? Is is feasible to selectively regulate photomorphogenic traits of an agronomically important crop species with altered chromophore and YH alleles of phytochromes to generate robust, environmentally sustainable crops of value to biofuels and plant-made products applications? Research to answer these questions will include phenotypic, molecular genetic and biochemical analyses of available and novel transgenic Arabidopsis and selected crop plant species via regulated expression of epitope-tagged YH alleles and chromophore biosynthesis genes together with transcriptomic, proteomic and metabolomic analyses.

Su Y-S. and Lagarias J.C. (2007) Light-Independent Phytochrome Signaling Mediated by Dominant GAF Domain Tyrosine Mutants of Arabidopsis Phytochromes in Transgenic Plants. *Plant Cell* 19:2124-2139.

Hu W., Su Y-S. and Lagarias J.C. (2009) A light-independent allele of phytochrome B faithfully recapitulates photomorphogenic transcriptional networks. *Molecular Plant* 2, 166-182.

* Member of the DEB graduate program

N. AN Eif4E-BINDING PROTEIN REGULATES KATANIN PROTEIN LEVELS IN *C. ELEGANS* EMBRYOS

Wei Li*, Leah DeBella, and Lesilee Rose
Department of Molecular and Cellular Biology, University of California, Davis

In *C. elegans*, the MEI-1/katanin microtubule-severing complex is required for meiosis, but must be down-regulated during the transition to embryogenesis to prevent defects in mitosis. A cullin dependent degradation pathway for MEI-1 protein has been well documented. Here we report that translational repression may also play a role in MEI-1 down-regulation. Mutations in the *spn-2* gene result in spindle orientation defects due to ectopic MEI-1 during mitosis. However, MEL-26, which is both required for MEI-1 degradation and is itself a target of the cullin degradation pathway, is present at normal levels in *spn-2* mutants, suggesting that the degradation pathway is functional. We cloned *spn-2* and find it encodes an eIF4E-binding protein that binds to 4 of the 5 *C. elegans* eIF4E isoforms. SPN-2 protein localizes to the cytoplasm and to P granules, ribonucleoprotein complexes thought to be involved in translational regulation. Our results suggest that SPN-2 functions as an eIF4E-BP to negatively regulate MEI-1 protein levels.

* Member of the DEB graduate program

O. TRANSCRIPTOMIC ANALYSIS OF TRANSGENIC GRAPE (*VITIS VINIFERA*) PLANTS EXPRESSING PGIP

Yolanda Gogorcena[1], Ana María Ibáñez[2], Cecilia Aguero[2], Russell L. Reagan[2], Sandie Uratsu[2], Abhaya M. Dandekar[2]

[1]Department of Pomology, EEAD-CSIC, Zaragoza, Spain

[2]Department of Plant Sciences, University of California, Davis

To prevent and control *Xylella fastidiosa,* the causative agent of Pierce's disease (PD), grapevines of *Vitis vinifera* cv 'Thompson Seedless' (TS) were transformed with the pear polygalacturonase inhibiting protein (pPGIP), a stimulator of plant innate immunity[1]. Transgenic lines were obtained using *Agrobacterium*-mediated transformation. Transgenic plants expressing the PGIP protein show decreased symptoms in leaves after infection with *X. fastidiosa* and with *Botrytis cinerea*. Microarray (Affymetrix) analysis of leaves from a PGIP expressing line TS-50 and non-transgenic line TS showed that 3007 genes were significantly up- or down-regulated (FDR-adjusted p-value cut-off $p < 0.05$) in the transgenic line. These genes were further examined for function using the MapMan program that permits visualization of metabolic pathways based on over 900 functional classifications in *Arabidopsis* (TAIR 7). Many of the differentially regulated grapevine genes are homologous to *Arabidopsis* proteins from the cell wall or from secondary metabolic pathways related to plant defense. Additional gene annotation with the Gene Ontology vocabulary will be conducted using BLAST2GO. Transcription of pPGIP and other differentially expressed transcripts will be validated using RT-qPCR with TaqMan probes to identify the most important affected pathways. Leaf extracts from transformed and wild type TS plants were tested for polygalacturonase-inhibiting activity using polygalacturonase obtained from *B. cinerea* isolated from grape. Selected transformed lines have been bench grafted with wild type TS scions. Preliminary results showed that the PGIP protein moves from the rootstock up into the xylem sap of the wild type scion. Since pPGIP activity was found in the xylem sap of the untransformed scion when transgenic lines were used as rootstocks, we expect pPGIP will confer resistance to xylem-specific infections such as PD and assist in control of *X. fastidiosa* infections.

1) Dandekar, A. M.; Labavitch, J.; Almeida, R.; Ibanez A. M.; Uratsu, S. L.; Aguero, C.; McFarland, S. *In Planta* Testing of Signal Peptides and Anti-Microbial Proteins for Rapid Clearance of *Xylella*. 2008 California Department of Food and Agriculture. *Pierce's disease Research Symposium Proceedings* 2008 pp. 149-155.

P. EXPRESSION OF THE *YERSINIA ENTEROCOLITICA* YSA TYPE III SECRETION SYSTEM IS ANATOMICALLY RESTRICTED TO THE GASTROINTESTINAL TISSUES DURING INFECTION

Zachary W. Bent*[1], and Glenn M. Young[1,2]
[1]Department of Food Science and Technology, University of California, Davis

Infection with the bacterium *Yersinia enterocolitica* typically leads to a self-limiting gastroenteritis in immuno-competent individuals. In immuno-compromised patients, especially infants, however the bacterium is able to exit the gut and cause an often fatal systemic infection. This systemic infection can be recapitulated in mice, making the mouse an effective animal model to study infantile yersiniosis. *Y. enterocolitica* Biovar 1B possesses two Type III Secretion (T3S) systems that play a role in virulence, the plasmid encoded Ysc T3S system and the chromosomally encoded Ysa T3S system. Our previous analysis supports the hypothesis that the Ysa T3S system plays an important role during the gastrointestinal phase of infection. Ysa mutants have a defect in their ability to colonize a variety of gastrointestinal tissues including the terminal ileum, Peyer's patches, and mesenteric lymph nodes. However, *In vitro* the Ysa T3S system can only be induced by growth at 26°C in a high salt (290mM NaCl) medium, conditions which would seem to preclude expression during the infection of a mammalian host. To resolve this apparent set of contradictory observations, we examined the expression of Ysa T3S genes during an infection using GFP (green fluorescent protein) reporters. The reporters were generated by transcriptionally fusing the promoters of several Ysa genes to *gfp*. Two-color flow cytometry was then used to analyze the tissues of mice infected with *Y. enterocolitica* for expression of GFP from the Ysa promoters. Mice were infected for 2 or 5 days at which point gastrointestinal and systemic organs were harvested, homogenized, and analyzed for the presence of bacteria expressing GFP. We demonstrate that while the Ysc T3S system is expressed during all stages of infection, expression of the Ysa T3S system is restricted to the gastrointestinal tissues including the terminal ileum, Peyer's patches, and mesenteric lymph nodes. GFP expression from the Ysa promoters was not seen in any of the systemic organs that were analyzed. Based on these results we conclude that the Ysa T3S system is expressed during an infection in response to specific conditions encountered in the gastrointestinal environment.

* Member of the DEB graduate program

Q. NOVEL METHODS FOR THE CAPTURE AND DETECTION OF NONVOLATILE COMPONENTS OF HUMAN BREATH

Melinda Simon*[1], Bruce Hammock[2], Nicholas Kenyon[3], Cristina Davis[1]
[1]Department of Mechanical & Aeronautical Engineering, University of California, Davis
[2]University of California, Davis Health System: MIND Institute
[3]University of California, Davis Health System; Pulmonary & Critical Care Medicine

Along with the many volatile components that are released during expiration, nonvolatile components, such as proteins, are released in the form of an aerosol in human breath. Although these components are present in very low abundance, the ability to capture and detect them could provide a low-cost and noninvasive technique for monitoring or diagnosing pulmonary diseases such as asthma, chronic obstructive pulmonary disease, gastrointestinal reflux disease, and cystic fibrosis. Several methods are being developed to detect eicosanoids (fatty acid metabolites) and cytokines in exhaled human breath samples. In one method, a new coating material for breath collection devices was investigated for the specific capture of eicosanoid compounds. In order to detect the presence of cytokine molecules in the breath, a novel antibody microarray technique will be investigated, to allow for the simultaneous assessment of the concentration of various cytokines in the breath sample. As biomarkers of disease, the detection of these cytokines or eicosanoids will quickly and reliably determine the presence and progression of the disease state. The end goal of this research is toward the miniaturization of diagnostic platforms, which may enable portable and faster diagnosis of disease. In addition, breath analysis provides a cost-effective and noninvasive means of obtaining samples, and is tolerated well with repeated sampling.

* Member of the DEB graduate program

R. TOPOLOGIES AND SUBSTRATE INTERACTIONS OF MODEL CELL MEMBRANES

Matthew I. Hoopes*, Roland Faller, and Marjorie L. Longo
Department of Chemical Engineering and Materials Science, University of California, Davis

Bionanotechnology relies on the understanding and control of materials at the molecular level. Substrate interactions with adsorbed membranes modify the intrinsic mechanics of supported lipid bilayers. Fluorescence Interference Contrast microscopy provides one of many techniques for resolving spatial information below the diffraction limit of conventional microscopy. Supported lipid bilayers (SLB) continue to be an important means of measuring the thermodynamic and mechanical properties of phospholipid membranes, which are the basis of compartmentalization in living cells. Biotechnology relies on knowledge of these properties for engineering lipid based products such as immunological assays, non-viral gene delivery, and hybrid membrane chemical sensors. Understanding SLB systems with respect to their substrates enhances the understanding of the measurements taken thereon and promotes design of new substrates to expand the usefulness of these systems.

* Member of the DEB graduate program

S. SWARM INTELLIGENCE BASED BIOMARKER DETECTION FOR FRUIT DISEASE DIAGNOSIS

Weixiang Zhao*[1], Shankar Sankaran[1], Ana Maria Ibanez[2], Abhaya Dandekar[2], Cristina Davis[1]

[1]Department of Mechanical & Aeronautical Engineering, University of California, Davis
[2]Department of Plant Sciences, University of California, Davis

This poster introduces ant colony algorithms (ACA), a novel swarm intelligence optimization method, to detect discernable biomarkers from raw gas chromatography/differential mobility spectrometry (GC/DMS) data. Partial least squares (PLS) regression was embedded into the searching process to evaluate the classification effect of selected biomarkers. GC/DMS data from sixteen disordered and twenty-two control fruit samples were employed for this study. Yielding a high classification accuracy (>= 93%) from a three-fold cross validating process, this study demonstrated the feasibility of using ACA coupled with a classification model to detect discernable biomarkers for the characterization and classification of 3-D GC/DMS data system. The detected biomarkers can not only significantly expedite sample analysis and recognition, but also provide pertinent information for pathology studies of fruit disease.

* Member of the DEB graduate program

T. VOLATILE COMPOUNDS FROM CITRUS PLANTS MEASURED USING DIFFERENTIAL MOBILITY SPECTROMETRY AND MACHINE LEARNING ALGORITHMS

Abhinav Bhushan*, Weixiang Zhao*, Anthony Santamaria, and Cristina Davis
Department of Mechanical Engineering, University of California, Davis

In addition to exchanging non-volatile organic volatiles during photosynthesis and respiration, plants emit volatile organic compounds from different organs such as flowers, leaves, stems, and fruits. These compounds may reflect an image of the physiochemical processes taking place in the plant body. Many of these chemicals are emitted in response to stress, tissue damage, and microbial growth. We are interested in characterizing volatile chemical biomarkers of citrus plants to disease and infection. As a high value fruit crop with over 10 billion dollars at risk, the citrus crops are highly susceptible to diseases caused by introduced pests and pathogens. Currently, disease detection relies on scouting orchards for visible symptoms followed by suspect tree removal, sanitation, and disease diagnosis in the laboratory. Measuring the volatile compounds presents an opportunity to use novel sensor such as a differential mobility spectrometer to perform a multidimensional chemical analysis that can detect low concentrations of these chemicals. This poster will include preliminary results from our study on speciation of citrus varietals and will include a discussion of machine learning algorithms that we have used to analyze the data.

* Member of the DEB graduate program

U. CREATE-IGERT SUMMER LABORATORY SHORT COURSES

Lawrence D. Joh*[1], Karen A. McDonald[1], Pamela C. Ronald[2], David M. Tricoli[3], and Jean S. VanderGheynst[4]

[1]Department of Chemical Engineering & Materials Science, University of California, Davis
[2]Department of Plant Pathology, University of California, Davis
[3]Plant Transformation Facility, University of California, Davis
[4]Department of Biological and Agricultural Engineering, University of California, Davis

Two summer laboratory short courses will be offered for CREATE IGERT students in 2009-2012. The courses will emphasize participation in multi-disciplinary teams, communication, safety, and proper handling of recombinant materials.

The Plant Transformation Methods Course will provide students hands-on experience with the equipment and broad exposure to the methods involved with stable transformation and transient gene expression in representative monocot and dicot plants and cell suspension culture. Students will explore alternative plant-based systems to produce recombinant protein and measure expression levels using qualitative and quantitative techniques. The Recovery and Purification of Plant-Derived Products Course will cover extraction, concentration, purification, and characterization of protein produced in transgenic plants and *in vitro* plant systems. Through a combination of pilot-scale demonstrations and lab-scale experiments, students will design a bioprocess to recover and purify recombinant protein expressed in the Plant Transformation Methods Course.

UC Davis students must be enrolled in the Designated Emphasis in Biotechnology program to be eligible for CREATE IGERT traineeships. The multi-institutional National Science Foundation (NSF) funded Integrative Graduate Education and Research Traineeship (IGERT) program, entitled Collaborative Research and Education in Agricultural Technologies and Engineering (CREATE), provides a structured, well-integrated graduate research and educational training program that focuses on the use of transgenic plants and *in vitro* plant systems for the production of industrial non-food products and biopharmaceuticals.

*** DEB Graduate**

V. DEVELOPMENT OF PLANT CELL SUSPENSION CULTURE AS A BIOPRODUCTION PLATFORM OF RECOMBINANT HUMAN THERAPEUTIC PROTEINS

Ting-Kuo Huang*[1]; Michael A. Plesha*[1]; Bryce Falk[2], Abhaya M. Dandekar[3], and Karen A. McDonald[1]

[1]Department of Chemical Engineering & Materials Science, University of California, Davis
[2]Department of Plant Pathology, University of California, Davis
[3]Department of Plant Sciences, University of California, Davis

Plant cell suspension culture production of recombinant human therapeutic proteins provides unique advantages over traditional suspended prokaryotic (e.g. *Escherichia coli*) and eukaryotic (e.g. yeast, insect and mammalian cells) host expression cells in terms of product safety (plant cells and culture medium are not sourced from animals and do not harbor and propagate mammalian viruses), production cost (lower medium, production and downstream costs) and product quality (capability for protein post-translation modification). In this study, we investigated various strategies for improving the expression yield and functionality of a recombinant human blood protein, alpha-1-antitrypsin (AAT), using our novel *Cucumber mosaic virus* (CMV) inducible viral amplicon (CMViva) expression system in transgenic tobacco (*Nicotiana benthamiana*) cell suspension cultures in a stirred-tank bioreactor.

For a chemically inducible plant viral vector system, the timing of induction (TOI) and concentration of inducer (COI) are two critical parameters for regulating the transgene expression in a chemically inducible cell culture process in bioreactor. We applied OUR (oxygen uptake rate) of plant cell cultures as a physiology indicator for determining the optimal TOI and developed a semicontinuous culture process for optimizing the COI effects. Total and functional recombinant AAT production yield, protease activity, total phenolics content, inducer (estradiol) concentration, OUR and biomass concentration were monitored as important parameters for bioreactor operation optimization.

A bioreactor semicontinous culture process, which was optimized from the above investigations, was further developed for maximizing the recombinant AAT productivity yield and functionality. These results lay for a foundation for developing plant cell cultures as a platform of biopharmaceuticals production in industry.

*** Member of the DEB graduate program**

W. CATALYTIC CONVERSION OF BIO-OIL COMPONENTS

Ron Runnebaum*, Bruce Gates
Department of Chemical Engineering & Materials Science, University of California, Davis

Biomass-derived oxygen-containing compounds such as phenolics, ethers, carboxylic acids, ketones, and aldehydes can be converted into high-quality fuels by catalytic processing. The reaction products, besides water, include CO, CO2, aromatics, light alkanes, water-soluble organics, oil-soluble organics, and coke. We will investigate the conversion of prototypical oxygen-containing organic compounds with products analyzed by GC-TCD, TC-FID, and GC-MS. The objectives of our project are to deliver a thorough, quantitative understanding of important reaction networks for the conversion of biomass-derived compounds. This understanding is expected to be valuable in guiding the selection of improved catalysts and process conditions for conversion of renewable biomass-derived oxygen-containing compounds to biofuels.

* Member of the DEB graduate program

X. A VIRAL AMPLICON BASED PROCESS FOR PRODUCTION OF BIOPHARMACEUTICALS

Karen A. McDonald[1], Michael A. Plesha[1], Kittipong Rattanaporn*[1], Abhaya M. Dandekar,[2] and Bryce W. Falk[3]

[1]Department of Chemical Engineering & Materials Science, University of California, Davis
[2]Department of Plant Sciences, University of California, Davis
[3]Department of Plant Pathology, University of California, Davis

Plants offer a number of advantages for large-scale production of recombinant proteins compared with current biomanufacturing methods that utilize mammalian or microbial cultures. These advantages include lower capital equipment and production costs, green manufacturing technology with lower net energy requirements, CO_2 consumption, scalability, low risk of product contamination by mammalian viruses, blood-borne pathogens, prions and bacterial toxins, and eukaryotic posttranslational modification capabilities. However, recombinant protein production using stable transgenic plants suffer from a number of challenges including the long time frame required to establish stably transformed plants, environmental concerns related to the deployment of transgenic plants in the field, low expression levels, and challenges associated with product recovery and purification. For many applications, such as rapid vaccine production in the case of a global pandemic or bioterrorism event, speed (as well as scalability) will be key issues that cannot be met with current manufacturing platforms.

Our group has developed a novel expression system and an efficient, scalable production strategy, based on transient agroinfiltration in harvested (nontransgenic) living (i.e. green) plant tissues that addresses these problems. In this process, plant cells within the plant tissues provide the biosynthetic machinery for transcription, translation, post-translational modifications, folding and intracellular targeting/secretion of the product, while the soil bacterium, *Agrobacterium tumefaciens*, is used to propagate the genetic instructions and efficiently transfer them to the plant cells.

We have developed a chemically-inducible plant viral amplicon (self-replicating viral RNA containing a foreign gene) expression system that allows controllable, high level expression of foreign genes in plant hosts that we refer to as **CMViva** (**CMV i**nducible **v**iral **a**mplicon). Because CMV has one of the widest host ranges of all known plant viruses and infects both dicots and monocots, the CMViva system can potentially be used in a wide variety of hosts to rapidly and efficiently produce a wide variety of recombinant proteins. In this study we demonstrate the rapid, efficient production of a labile human blood protein, alpha-1-antitrypsin (AAT), in harvested leaves of *Nicotiana benthamiana*.

*** Member of the DEB graduate program**

Y. HPL-DERIVED METABOLITES AS A VEHICLE FOR PRODUCTION OF SUPERIOR STRESS-TOLERANT PLANTS

Elenor Castillo* and Katayoon Dehesh
Department of Plant Biology, University of California, Davis

Plants are sessile organisms that have developed sophisticated signaling mechanisms to defend themselves against biotic and abiotic stresses. One of the primary signaling mechanisms involved is the oxylipin pathway. This pathway is comprised of several competing branches among them the Hydroperoxide Lyase (HPL) branch which, catalyzes the cleavage of fatty acid hydroperoxides into aldehydes and oxoacids. The HPL-derived metabolites are known to promote the aromas of fruits and vegetables, and function as signals in intra- and inter-plant crosstalk.

The focus of this research is to elucidate the regulatory role of HPL- derived metabolites in mediating plant responses to environmental and developmental cues. The outcome of this research has potential for exciting applications towards improvement of aroma, and identification of a key master switch involved in plant responses to biotic and abiotic stresses thus providing new targets for biotechnologically-based interventions aimed at producing crops with superior stress-tolerance and insect-resistance characteristics. In addition, this work will provide insight into the potential value of using the HPL pathway to provide inter-plant induced enhanced stress tolerance by generating non-crop GMO "guardian" plants engineered to emit high levels of volatiles. Planting of these non-crop GMOs interspaced with non-GMO crop plants would be intended to provide inductive signals to improve tolerance of neighboring crop plants to biotic and abiotic stresses. This approach will eliminate the necessity for pesticides while providing optimal growth and viability.

* Member of the DEB graduate program

Z. IN VITRO EVOLUTION FOR ENGINEERING CRE VARIANTS WITH ALTERED DNA SITE SPECIFICITY

Roger Jesinghaus* and Michael Toney
Department of Chemistry, University of California, Davis

The Cre protein derived from the P1 phage is a tyrosine site-specific recombinase that generates precise cross-over between DNA strands containing the 34bp LoxP recognition sequence. Cre-Lox recombination has been utilized to add insertions, deletions and translocations to the genomes of a variety of agriculturally and medicinally important plants and animals. These transgenic organisms are of great utility for medicine and biotechnology. The Baldwin laboratory is striving to increase the utility of the Cre-Lox system by using in vitro evolution to engineer Cre Variants with altered DNA site specificity, while either maintaining or enhancing the catalytic rate of DNA crossover. Our goal is to create a library of mutant Cre genes by error prone pcr and subsequent DNA shuffling. This library is then ligated to our novel LoxX site and a biotin group. We then plan on using the method of in vitro compartmentalization (IVC) developed by Griffiths and Tawfiks to introduce our gene library of about 10^9 variants with s30 extract into water in oil emulsion. Each water "bubble" within the oil emulsion will ideally contain one gene and after subsequent translation and transcription by the included s30 extract the mutant Cre proteins will be selected by efficiency of recombination of the LoxX site. Thus, the IVC emulsion serves to directly maintain the linkage between genotype to phenotype, allowing the selection of successful Cre mutants, collected on magnetic streptavidin coated beads. The selected genes are then amplified, and after further DNA shuffling are iteratively subjected to further rounds of selection by the IVC emulsion method.

* Member of the DEB graduate program

Aa. ELUCIDATING THE METABOLISM OF NITROGEN USE EFFICIENT PLANTS

Gia C. Fazio *, George Theodoris, Zhongin Lu, and Jean C. Kridl
Arcadia Bioscience, Inc., Davis, California

Nitrogen is essential to plant growth and its application in the form of fertilizers improves yield in crop plants. Unfortunately, as much as 50% of applied nitrogen is lost to leaching and volatilization. In addition to being costly to farmers, fertilizer loss due to inefficient use of nitrogen by plants leads to deleterious environmental consequences including dead zones in oceans, nitrous oxide release into the air and groundwater contamination. Enhancing a plant's ability to utilize nitrogen reduces the negative environmental impact as well as lowers farming costs. We have demonstrated increased nitrogen use efficiency (NUE) in canola (*Brassica napus*) expressing a barley (*Hordeum vulgare*) alanine aminotransferase (AlaAT); an enzyme involved in nitrogen utilization. Canola plants expressing AlaAT have been tested in more than seven field trials and consistently show yields equivalent to control plants, yet use as much as 50% less fertilizer. A greenhouse test system was established to screen new events and analyze NUE phenotypes. It was shown that during early development NUE plants accumulate as much as 15% more biomass. To elucidate potential gene expression and metabolic differences, plant samples are collected at various times during early development and vegetative growth. Preliminary results from gas chromatography mass spectrometry (GC-MS) suggest key pathways are altered in transgenic plants.

Company Affiliates

*Company Affiliates ** Support Biotech at UC Davis*

- Agilent Technologies
- AgraQuest
- Amgen, Inc.
- Amyris Biotechnologies
- Bayer
- BioMarin Pharmaceutical, Inc.
- Genencor
- Genentech, Inc.**
- Monsanto, Calgene Campus**
- Novartis AG (formerly Chiron)
- Novozymes, Inc.**
- Tethys Bioscience, Inc.
- Ventria Biosciences, Inc.

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

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

Agilent Technologies

Contact:
Jim Hollenhorst, Ph.D., Director, Molecular Technology Lab
Rudolf Grimm, Ph.D., Development Manager, Worldwide Proteomics Market & Metabolomics

3500 Deer Creek Road
Palo Alto, CA 94304
(650) 485-4327
www.agilent.com
jim_hollenhorst@agilent.com
rudolf_grimm@agilent.com

Agilent delivers critical tools and technologies that sense, measure and interpret the physical and biological world. Our innovative solutions enable a wide range of customers in communications, electronics, life sciences and chemical analysis to make technological advancements that drive productivity and improve the way people live and work.

Our life sciences and chemical analysis business provides application-focused solutions that include instruments, software, consumables and services that enable customers to identify, quantify and analyze the physical and biological properties of substances and products.

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

AgraQuest, Inc.

Contact:
Magalie Guilhabert, Ph.D., Scientist

1540 Drew Ave.
Davis, CA 95616
(530) 750-0150
www.agraquest.com
mguilhabert@agraquest.com

AgraQuest is a biotechnology company that focuses on, discovering, developing, manufacturing and marketing effective, safe and environmentally friendly natural pest management products for the agricultural, institutional and home & garden markets

Fast. Nimble. Small. Competitive. These words not only describe a hummingbird, the symbol on AgraQuest's logo, but also embody the company's style and culture. And, like the hummingbird searches for nectar from a flower, AgraQuest searches for pesticidal products from naturally occurring microorganisms.

The founders of AgraQuest believed that the natural world was fertile ground for the search and discovery of new products for pest management. More than 50% of human drugs are derived from natural sources like plants and microorganisms; but only 7% of all pesticides are derived from these sources. Since 1995, AgraQuest has proven that the natural world is an untapped source of new, and natural, pesticidal products. After discovering and screening over 20,000 microorganisms, AgraQuest has developed and commercialized a line of innovative, effective, natural products for pest management.

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., Vice President; 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.

Amyris Biotechnologies

Contact:
Jack D. Newman, Ph.D., Co-founder & V.P. Research

5980 Horton St., Suite 450
Emeryville, CA 94608
(510) 450-0761
www.amyrisbiotech.com
Newman@amyrisbiotech.com

Amyris Biotechnologies is focused on translating the promise of synthetic biology into solutions for real-world problems. Applying advances in molecular biology and chemistry, we have engineered microbes capable of cost-effectively producing high-value, complex molecules that are currently available only in small quantities through extraction from natural resources. We are employing these living microbial chemical factories to produce new pharmaceuticals, specialty chemicals, and biofuels.

Bayer HealthCare Pharmaceuticals, Inc

Contact:
Rick Harkins, Ph.D., Principal Scientist; Novel Technologies, Protein Therapeutics Research

2600 Hilltop Drive
Richmond, CA 94804
(510) 669-4066
http://www.bayerhealthcare.com
rick.harkins@bayer.com

Bayer HealthCare is a globally active company with sites on all five continents. The Company markets products from its four divisions: Animal Health, Bayer Schering Pharma, Consumer Care, and Diabetes Care via regional and national distribution companies. More than 50,000 people are employed by Bayer HealthCare worldwide.

Our aim is to discover and manufacture innovative products that will improve human and animal health worldwide. Our products enhance well-being and quality of life by diagnosing, preventing and treating disease.

BioMarin Pharmaceutical, Inc.

Contact:
Eric Fouts, Ph.D., Associate Director; Manufacturing Sciences

105 Digital Drive
Novato, CA 94949
(415) 506.6700
http://www.biomarinpharm.com/
EFouts@bmrn.com

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.

Genencor (A Danisco Division)

Contact:
Colin Mitchinson, Ph.D., Director; Biomass Applications

925 Page Mill Road
Palo Alto, CA 94304
(650) 846-5853
www.genencor.com
colin.mitchinson@danisco.com

A Danisco Division, Genencor is amongst the largest developers and manufacturers of industrial enzymes and the second largest biotechnology company in the world.

Reaching diverse industries
Genencor discovers, develops, manufactures, and delivers eco-friendly, efficient enzyme product solutions for the agri processing, cleaning and textiles, food and feed, consumer, and industrial markets. We also develop innovative advancements for the biofuels, biodefense, and biosafety industries.

A technology leader
We are a recognized leader in protein and pathway engineering. No other biotechnology company offers the breadth of skills and experience that we do to deliver total solutions to a broad array of markets.

A catalyst for change
As a Catalyst of the Biobased Economy[sm], Genencor is committed to contributing to a sustainable industrial system that relies on renewable resources to produce effective, environmentally friendly products. Our focus on research and development and sustainability is making this happen by driving the application of biotechnology into new areas.

Genentech, Inc.

Contacts:
Ellen Filvaroff, PhD, Senior Scientist, Molecular Oncology
Melody Trexler Schmidt, Ph.D., Scientist (DEB Graduate)

1 DNA Way
South San Francisco, CA 94080-4990
(650) 225-1000

Caryle Vann, Senior Project Manager & Engineer
1000 New Horizons Way
Vacaville, CA 95688
(707) 454-2843
www.gene.com
filvarof@gene.com
schmidt.melody@gene.com
vann.caryle@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.

Monsanto Company – Calgene Campus

Contacts:
Kenneth Gruys, Ph.D., Site Manager
Kristen Bennett*, Ph.D., Senior Scientist, Project Leader

1920 Fifth Street
Davis, CA 95616
(530) 753-6313
www.monsanto.com
kenneth.j.gruys@monsanto.com
kristen.a.bennett@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.

*** DEB Graduate**

Novartis AG (formerly Chiron Corporation)

Contacts:
John Donnelly, Ph.D., Senior Director

4560 Horton Street
Emeryville, CA 94608-2916
(510) 655-8730

Robert Carter, Ph.D., Site Head – Vacaville

2010 Cessna Drive
Vacaville, CA 95688
(707) 453-2200
www.chiron.com
john_donnelly@chiron.com
robert.carter@novartis.com

Mission

Novartis 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 Novartis 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

Contact:
Debbie Yaver, Ph.D., Director

1445 Drew Ave.
Davis, CA 95616
(530) 757-8100
www.novozymesbiotech.com
dsy@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.

Tethys Bioscience, Inc.

Contact:
Edward J. Moler, Ph.D., Associate Director; Biostatistics and Informatics

5858 Horton Street, Suite 550
Emeryville, CA 94608
(510) 724-3260
www.tethysbio.com/index.html
emoler@tethysbio.com

Tethys Bioscience is dedicated to the discovery, development and commercialization of novel biological markers — biomarkers — that provide a practical tool to address the growing global challenge of chronic metabolic diseases such as diabetes.

By developing new tests that use protein and other bloodborne biomarkers to identify people at high risk for devastating and preventable diseases, we can arm patients and physicians with knowledge they can use to help prevent disease progression. These biomarkers give a snapshot of an individual's current risk, which may be modifiable. Our goal is to provide clinicians with an objective and convenient means to risk-stratify their patients and help them focus appropriate intervention strategies on those most likely to benefit. Our research strategies lead to sets of biomarkers that can be used to quantify the level of an individual's risk.

We approach the market with a unique combination of strengths:

- A research, management and commercialization team with extensive experience in diagnostic innovation
- Alliances with world-class researchers and partners
- A solid financial foundation

The company has become a pioneer in the discovery, development and value creation of novel biological markers for the clinical diagnostics marketplace: ***Biomarkers***. The company believes there is a large unmet need in both the discovery of potentially important biomarkers and the eventual use of them in routine clinical practice for many significant diseases.

Tethys Bioscience has built expertise, created significant intellectual property, and is executing its business plan around three key areas: ***Biomarker Discovery, Clinical Validation***

and ValueCreation. Tethys is focused upon introducing products that yield significant savings to the health care system and improve the quality of life for patients.

- Biomarker discovery efforts are focused on applying advanced research tools to identify important biomarkers associated with diseases that affect many people and are very costly to health care systems throughout the world today.
- Clinical validation involves a complex process that results in defining a set of new biomarkers and the application of the resulting test to enhance current clinical practice.
- Value creation encompasses the use of sophisticated health economic analyses to define appropriate performance criteria for new biomarkers and the execution of market development strategies to drive the adoption of new biomarkers in clinical practice.

Ventria Biosciences

Contact:
Scott Deeter, MBA, MSc., President & CEO

4110 N. Freeway Blvd.
Sacramento, CA 95834
(916) 921-6148
www.ventriabio.com
sdeeter@ventria.com

Ventria Bioscience is uniquely positioned to become a scientific leader in the biopharmaceutical industry. We are dedicated to developing and producing innovative, high value products that enhance and save lives.

We have achieved scientific excellence through internal research and development and collaborations with world-renowned biotech and industry leaders. Together we have created a rich product pipeline with innovative products in human nutrition and human therapeutics. The market for these products exceeds $2 billion annually.

In 1997, Ventria's scientists developed a breakthrough protein expression technology with unrivaled efficiency. This proprietary technology platform is called ExpressTec. ExpressTec's cost-efficiency and proven commercial scalability make it possible for Ventria to address unmet and underserved needs in human and animal health by delivering affordable treatments on a global scale.

Participants

Retreat Participants

NIH Fellows 2008 - 2009	
Kristina Mahan	Molecular Cellular Biology
Joseph Ramahi	Plant Biology
David Sela	Microbiology
Sunny Shah	Biomedical Engineering
Erin Tapley	Molecular Cellular Biology
Biotech Fellows 2008 - 2009	
Huilan Han	Mechanical & Aeronautical Engineering
Matthew Hoopes	Biophysics
Sarah Lockwood	Pharmacology & Toxicology
Christina Takanishi	Environmental Toxicology
CREATE-IGERT Fellows, Cohort 1	
Timothy Butterfield	Plant Biology
Dawn Chiniquy	Plant Biology
Tiffany Glavan	Microbiology
Ben Lindenmuth	Chemical Engineering
Christopher Simmons	Biological Systems Engineering
CREATE-IGERT Fellows, Cohort 2	
Lucas Arzola	Chemical Engineering
Elenor Castillo	Plant Biology
Mitch Elmore	Plant Pathology
Rachel Kerwin	Plant Biology
Mark Wolf	Biochemistry & Molecular Biology
Graduate Students/Post-docs	
Zachary Bent	DEB, Microbiology
Abhinav Bhushan	Post-doc, Mechanical & Aeronautical Engineering
Heather Bolstad	Environmental Toxicology
Patricia Castillo	DEB, Immunology
Pauline (JoJo) Chang	DEB, Electrical & Computer Engineering
Michelle Lozada Contreras	Chemical Engineering
David Dallas	DEB, Nutritional Biology
Myra de la Pena	DEB, Immunology
Daniel Garrido	DEB, Viticulture & Enology
Prasad Gawande	DEB, Chemistry
Yolanda Gogorcena	Plant Science
Rena Goodman	DEB, Chemistry
Dominik Green	DEB, Biochemistry & Molecular Biology

Michael Howland	DEB, Chemical Engineering
Ting-Kuo Huang	DEB, Chemical Engineering
Patty Yi-Hwa Hwang	DEB, Biochemistry & Molecular Biology
Kara Jensen	DEB, Comparative Pathology
Roger Jesinghaus	DEB, Chemistry
Geetika Joshi	DEB, Soils & Biogeochemistry
Sang-Kyu Jung	Chemical Engineering
Nate Kingsbury	DEB, Chemical Engineering
Katarzyna Koscielska	DEB, Biochemistry & Molecular Biology
Rashida Lathan	DEB, Animal Science
ChengYuk Lee	DEB, Chemical Engineering
Wei Li	Molecular & Cellular Biology
Kinjal Maniar	DEB, Immunology
Marina Meyerzon	DEB, Genetics
Raquel Orozco-Alcaraz	DEB, Chemical Engineering
Kittipong Rattanaporn	DEB, Chemical Engineering
Ana Riveros	Environmental Toxicology
Ron Runnebaum	DEB, Chemical Engineering
Mindy Simon	DEB, Biomedical Engineering
Zane Starkewolf	DEB, Chemistry
Vu Trinh	DEB, Biochemistry & Molecular Biology
Chen Wang	Microbiology
Ambrose Williams	DEB, Biochemistry & Molecular Biology
Tracy Cui Zeng	Plant Biology
Weixiang Zhao	Post-doc, Mechanical & Aeronautical Engineering
UC Davis Faculty	
Kristina Able	DEB, Med: Internal Medicine, Infectious Diseases
Simon Chan	DEB, Plant Biology
Abhaya Dandekar	DEB, Pomology
Cristina Davis	DEB, Mechanical Engineering
Roland Faller	DEB, Chemical Engineering & Materials Science
J. Clark Lagarias	DEB, Molecular & Cellular Biology
Marjorie Longo	DEB, Chemical Engineering & Materials Science
Karen McDonald	DEB, Chemical Engineering & Materials Science
Rebecca Parales	DEB, Microbiology
Alexander Revzin	DEB, Biomedical Engineering
David Segal	DEB, Pharmacology
Sharon Shoemaker	Food Science & Technology, CIFAR
Dan Starr	DEB, Molecular and Cellular Biology
John Yoder	DEB, Plant Biology

Industry	
Chandra Kilburn	E & J Gallo
Suchindra Maiyuran	Novozymes, Inc.
Marie Cecile van de Lavoir	Crystal Bioscience
Alberto Iandolino	Monsanto, Calgene Campus
Martin Ruebelt	Monsanto, Calgene Campus
Guests	
Jason Brennan	Sheldon High School Instructor
Stephanie Faldwell	Sheldon High School Student
Rebecca Faulds	Dixon High School Instructor
Shaun Martins	Enochs High School Instructor
Carol Schutt	Enochs High School Instructor
Aaron Simmons	Sheldon High School Student
UC Davis Staff	
Cheryl Guadagna	Internal Medicine
Larry Joh	Chemical Engineering & Material Science (DEB Graduate)
Biotechnology Program & UC BREP	
Linda Bates	Biotechnology Program, Program Assistant
Marianne Hunter	Biotechnology Program, Program Manager
Denneal Jamison-McClung	Biotechnology Program, Associate Director
Judy Kjelstrom	Biotechnology Program, Director
Martina Newell-McGloughlin	UC Biotechnology Research & Ed. Program, Director
Natalie Merchant	Biotechnology Program Aid

www.biotech.ucdavis.edu

The Mission of the Biotechnology Program:

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

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

The Program serves as the **Administrative Home** for 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 – Associate Director
Marianne Hunter – Program Manager
Linda Bates – Program Assistant
Office location: 0301 Life Sciences
Telephone: (530) 752-3260 (main line) FAX: (530) 752-4125
Email: biotechprogram@ucdavis.edu

NIH Training Grant in Biomolecular Technology
July 1, 2007- June 30, 2012

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 and subsequently renewed for an additional 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	
Director: Bruce Hammock	
Co-Directors: Karen McDonald and Martina Newell-McGloughlin	
Enoch Baldwin	Molecular & Cellular Biology
Craig Benham	Biomedical Engineering/Genome Center
David Block	Chemical Engineering
Alan Buckpitt	VM: Molecular Biosciences
Simon Chan	Plant Biology
R. Holland Cheng	Molecular & Cellular Biology
Abhaya Dandekar	Plant Sciences-Pomology
Michael Denison	Environmental Toxicology
Yong Duan	Applied Science
Bryce Falk	Plant Pathology
Roland Faller	Chemical Engineering & Materials Science
Peggy Farnham	Pharmacology
Katherine Ferrara	Biomedical Engineering
Richard Michelmore	Plant Sciences – Vegetable Crops
David Mills	Viticulture & Enology
Atul Parikh	Applied Science
Martin Privalsky	Microbiology
Robert Rice	Environmental Toxicology
David Rocke	Applied Science
David Segal	Pharmacology
Simon Scott	Biomedical Engineering
Henning Stahlberg	Molecular & Cellular Biology
Oliver Fiehn	Genome Center & Bioinformatics Program
Andrew Fisher	Chemistry
J. Bruce German	Food Science & Technology
Ian Kennedy	Mechanical & Aeronautical Engineering
Patrice Koehl	Computer Science
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
Julie Leary	Molecular & Cellular Biology
Marjorie Longo	Chemical Engineering & Materials Sciences
Claude Meares	Chemistry
Juan Medrano	Animal Science
Daniel Starr	Molecular & Cellular Biology
Michael Toney	Chemistry
Jean VanderGheynst	Biological & Agricultural Engineering
David Wilson	Molecular & Cellular Biology
Michael Wright	Genome Center & Bioinformatics Program

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 dynamic 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 **27 programs**: Agricultural and Environmental Chemistry; Animal Biology; 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; Electrical and Computer Engineering; 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; Soils & Biogeochemistry; 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, 2007 - June 30, 2012). 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 2008 the DEB has 27 affiliated graduate groups or departmentally based graduate programs. The number of students in the Designated Emphasis in Biotechnology has increased dramatically over the last two years and now boasts 160 members, with many being first year students. We have graduated over 60 students with a DEB notation on their diplomas as of December of 2002.

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 27 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 BIM298 (Scientific Ethics and Inquiry – formerly BIM289), ECL 290 (Responsible Conduct of Research for Environmental Scientists), PLP 298 (Scientific Ethics in Biotech Research), and PMI 250 (Philosophy and Ethics of Biomedical Science)**

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 2009	
Danielle Aldredge	Chemistry
Erica Andreozzi	Biomedical Engineering
Lucas Arzola	Chemical Engineering
Roberto Barrozo	Immunology
Zachary Bent	Microbiology
Crystal Berger	Biochemistry & Molecular Biology
Jennifer Bratt	Biochemistry & Molecular Biology
Timothy Butterfield	Plant Biology
Milo Careaga	Immunology
Anna Cartier	Plant Biology
Jennifer Cash	Chemistry
Elenor Castillo	Plant Biology
Patricia Castillo	Immunology
Shannon Ceballos	Cellular & Developmental Biology
Jeffrey Chan	Immunology
Astra Chang	Comparative Pathology
Pauline (JoJo) Chang	Electrical & Computer Engineering
Chao-Yu Chen	Pharmacology & Toxicology
Honglin Chen	Genetics
Yu-Shen Cheng	Biological Systems Engineering
Dawn Chiniquy	Plant Biology
Stephanie Crockett	Comparative Pathology
David Dallas	Nutrition
Ryan Davis	Chemistry
Kevin Dietzel	Microbiology
Neha Dixit	Immunology
Matthew Doherty	Microbiology
Collin Ellis	Nutritional Biology
James Elmore	Plant Pathology
Brett Fite	Biophysics
Erik Fostvedt	Biochemistry and Molecular Biology
Paula Garay	Biochemistry & Molecular Biology
Daniel Garrido	Food Science
Prasad Gawande	Chemistry
Laura Gillies	Food Science Technology
Tiffany Glavan	Microbiology
Barbara Gluvers	Chemical Engineering
Felipe Godinez	Biomedical Engineering
Elianna Goldstein	Plant Biology
Rena Goodman	Chemistry
Myra Grace dela Pena	Immunology
Dmitry Grapov	Agricultural & Environmental Chemistry
Dominik Green	Biochemistry & Molecular Biology

Pradeepa Gunathilake	Plant Biology
Brian Hamilton	Biochemistry & Molecular Biology
Oldham (Scott) Hamilton	Biochemistry & Molecular Biology
Huilan Han	Mechanical & Aeronautical Engineering
Victor Haroldsen	Biochemistry & Molecular Biology
Jason Harrison	Chemistry
Christine Hastey	Microbiology
Thomas Hill III	Pharmacology & Toxicology
Laura Ho	Pharmacology & Toxicology
Reef Holland	Microbiology
Matthew Hoopes	Biophysics
Jessica Houghton	Pharmacology & Toxicology
Michael Howland	Chemical Engineering
Ting-Kuo Huang	Chemical Engineering
Tu Anh Huynh	Food Science Technology
Yi-Hwa (Patty) Hwang	Biochemistry & Molecular Biology
Darren Hwee	Molecular, Cellular & Integrative Physiology
Connie Jen	Biochemistry & Molecular Biology
Kara Jensen	Comparative Pathology
Roger Jesinghaus	Chemistry
Rogelio Jimenez Espinoza	Chemical Engineering
Geetika Joshi	Soils and Biogeochemistry
Yun Joon Jung	Biomedical Engineering
Kavya Katipally	Biomedical Engineering
Robert Kauffman	Microbiology
Rachel Kerwin	Plant Biology
Saeed Khazaie	Chemistry
Zahra Khedri	Chemistry
Nathiel Kingsbury	Chemical Engineering
Katarzyna Koscielska	Biochemistry & Molecular Biology
Rashida Lathan	Animal Biology
Nathaniel Leachman	Cellular & Developmental Biology
Vannarith Leang	Chemical Engineering
ChengYuk Lee	Chemical Engineering
Karen Leung (nee Thatcher)	Genetics
Ben Lindenmuth	Chemical Engineering
Riccardo LoCascio	Microbiology
Sarah Lockwood	Biochemistry & Molecular Biology
Michelle Lozada-Contreras	Chemical Engineering
Thomas Luu	Biochemistry & Molecular Biology
Kristina Mahan	Biochemistry & Molecular Biology
Hamed Malekan	Chemistry
Kinjal Maniar	Immunology
Philip Matern	Molecular, Cellular & Integrative Physiology

Daniël Melters	Cell & Developmental Biology
Robin Merod	Civil & Environmental Engineering
Marina Meyerzon	Genetics
Mary Moore	Biochemistry & Molecular Biology
Diana Morales-Hernandez	Biomedical Engineering
Thuc Nghi Nguyen	Biomedical Engineering
Tarit Nimmanwudipong	Chemical Engineering
Charles Nwosu	Chemistry
Maria Olubunmi Ogunyankin Marquez	Chemical Engineering
Alanna O'Leary	Immunology
Patricia Oliveira	Comparative Pathology
David Olivos	Comparative Pathology
Charity Onore	Immunology
Raquel Orozco-Alcaraz	Chemical Engineering
Richard Osibanjo	Chemistry
Cecilia Osorio	Plant Biology
Emily Pfeiffer	Biomedical Engineering
Jonathan Pham	Microbiology
Stephanie Pulford	Mechanical & Aeronautical Engineering
Jingyao Qu	Chemistry
Alina Rabinovich	Cell & Developmental Biology
Joseph Ramahi	Cell and Developmental Biology
Kittipong Rattanaporn	Chemical Engineering
Patrick Rogers	Chemistry
Meghan Rosen (nee Dukerich)	Biochemistry & Molecular Biology
Shailise Ross	Chemistry
Ron Runnebaum	Chemical Engineering
Juan Pedro Sanchez	Plant Biology
Mary Saunders	Comparative Pathology
Erin Schwartz	Biochemistry & Molecular Biology
Andres Schwember	Plant Biology
Gail Sckisel	Immunology
David Sela	Microbiology
Sunny Shah	Biomedical Engineering
Laura Shih	Biomedical Engineering
Christopher Simmons	Biological Systems Engineering
Melinda (Mindy) Simon	Biomedical Engineering
Padmini Sirish	Molecular Cellular Integrative Physiology
Zane Starkewolfe	Chemistry
Sarah Statt	Biochemistry & Molecular Biology
John Strum	Chemistry
Wesley Sughrue	Biochemistry & Molecular Biology
Grace Sunil	Chemistry
Anandkumar Surendrarao	Plant Biology

Mimi Swe	Nutritional Biology
Christina Takanishi	Cellular & Developmental Biology
Erin Tapley	Cellular & Developmental Biology
Jared Townsend	Biochemistry & Molecular Biology
Vu Trinh	Biochemistry & Molecular Biology
Michelle Tu	Cell & Developmental Biology
Breanna Wallace	Molecular, Cellular and Integrative Physiology
Don-Hong Wang	Genetics
Jennifer Warren	Civil & Environmental Engineering
Monica Watson	Molecular, Cellular and Integrative Physiology
Alan Wilder	Biophysics
Ambrose Williams	Biochemistry & Molecular Biology
Kelly Williams	Biological Systems Engineering
David Woessner	Microbiology
Mark Wolf	Biochemistry & Molecular Biology
Andrew Wong	Genetics
Rebecca Wright	Microbiology
Chun-Yi (Jimmy) Wu	Pharmacology & Toxicology
Shuai Wu	Chemistry
Zhaoju (Daisy) Wu	Pharmacology & Toxicology
Fei Yian Yoon	Plant Biology
Chao Wei Yu	Biological System Engineering
Kseniya Zakharyevich	Microbiology
Cui Jing (Tracy) Zeng	Microbiology

DEB Program Faculty Participants	
Kristina Abel	Internal Medicine, Division of Infectious Diseases: MED
Steffen Abel	Vegetable Crops & Weed Science
Venkatesh Akella	Electrical & Computer Engineering
Rajeevan Amirtharajah	Electrical & Computer Engineering
Gary Anderson	Animal Science
Matthew Augustine	Chemistry
Alan Balch	Chemistry
Enoch Baldwin	Molecular and Cellular Biology
Everett Bandman	Food Science & Technology
Abdul Barakat	Mechanical & Aeronautical Engineering
Diane Barrett	Food Science & Technology
Peter Barry	Center for Comparative Medicine
Stephen Barthold	Pathology, Microbiology & Immunology
Ronald Baskin	Biophysics, MCB
Nicole Baumgarth	Dept. Pathology, Microbiology &Immunology; CCM, VetMed
Peter Beal	Chemistry
Blaine Beaman	MED: Micro & Immunology
Craig Benham	Biomedical Engineering / Genome Center
Alan Bennett	Vegetable Crops (Plant Science)
Charles L. Bevins	Microbiology & Immunology
Linda Bisson	Viticulture & Enology
Caroline Bledsoe	Soils and Biogeochemistry
David Block	Viticulture & Enology
Sue Bodine	Neurobiology, Physiology and Behavior (NPB)
Richard Bostock	Plant Pathology
Kent Bradford	Vegetable Crops
George Bruening	Plant Pathology, CEPRAP
Christine Bruhn	Food Science & Technology
Alan Buckpitt	VM: Molecular Biosciences
Sean Burgess	Molecular & Cellular Biology
Christopher Calvert	Animal Science
Simon Chan	Plant Biology
Daniel Chang	Civil & Environmental Engineering
Frederic Chédin	Molecular & Cellular Biology
Xi Chen	Chemistry
Xinbin Chen	Comparative Oncology
Holland Cheng	Molecular & Cellular Biology
Nipavan Chiamvimonvat	Internal Medicine; Div of Cardiovascular Medicine
Andrew Clifford	Nutritional Biology
Gitta Coaker	Plant Pathology

Luca Comai	Plant Biology
Douglas Cook	Plant Pathology
Gino Cortopassi	Vet Med Molecular Biosciences
John Crowe	Molecular & Cellular Biology
Abhaya Dandekar	Pomology
Satya Dandekar	MED: Medical Microbiology & Immunology
Sheila David	Chemistry
Cristina Davis	Mechanical and Aeronautical Engineering
Scott Dawson	Microbiology
Katayoon (Katy) Dehesh	Plant Biology
Wenbin Deng	Cell Biology and Human Anatomy:MED
Michael Denison	Environmental Toxicology
Thorsten Dieckmann	Chemistry
Zhi Ding	Electrical & Computer Engineering
Stephanie Dungan	Food Science & Technology; Chem Engineering & Material Science
Don Durzan	Environmental Horticulture
Jason Eiserich	Nephrology: INT MED
Nael El-Farra	Chemical Engineering & Material Science
Robert Fairclough	Neurology: MED
Bryce Falk	Plant Pathology
Roland Faller	Chemical Engineering & Material Sciences
Zhiliang (Julia) Fan	Biological & Agricultural Engineering
Peggy Farnham	Department of Medical Pharmacology and Toxicology: MED
Katherine Ferrara	Biomedical Engineering
Oliver Fiehn	Genome Center
Andrew Fisher	Chemistry
Paul Fitzgerald	MED: Cell Biology & Human Anatomy
Ching Yao Fong	Physics
Annaliese Franz	Chemistry
David Furlow	Section of Neurobiology, Physiology, and Behavior
Charles Gasser	Molecular & Cellular Biology
Shu Geng	Agronomy & Range Science
J. Bruce German	Food Science & Technology
Jacquelyn Gervay-Hague	Chemistry
Soheil Ghiasi	Electrical & Computer Engineering
David Gilchrist	Plant Pathology
Tom Gradziel	Pomology
Jeffrey Gregg	MED: Pathology
Paul Gumerlock	MED: Hematology/Oncology
Ting Guo	Chemistry
Bruce Hammock	Entomology & Cancer Center

Stacy Harmer	Plant Biology
Richart W. Harper	Division of Pulmonary/Critical Care Medicine
Volkmar Heinrich	Biomedical Engineering
Wolf-Dietrich Heyer	Microbiology
Krassi Hristova	Soils and Biogeochemistry
You-Lo Hsieh	Textiles & Clothing
Neil Hunter	Microbiology
Kentaro Inoue	Plant Sciences
M. Saif Islam	Electrical & Computer Engineering
Roslyn-Rivkah Isseroff	MED: Dermatology
Thomas Jue	MED: Biochemistry
Clarence Kado	Plant Pathology
Carl Keen	Nutrition
Ian Kennedy	Mechanical & Aeronautical Engineering
Richard Kiehl	Electrical & Computer Engineering
Dan Kliebenstein	Vegetable Crops & Weed Science
Anne Knowlton	Cardiovascular Div, Dept. Med Pharmacology & Toxicology
Patrice Koehl	Computer Science
Stephen Kowalczykowski	Microbiology
Tonya Kuhl	Chemical Engineering & Material Science
Hsing-Jien Kung	MED: Biochemistry / UC Davis Cancer Center
J. Clark Lagarias	Molecular & Cellular Biology
Kit Lam	MED: Hematology & Oncology
Delmar Larsen	Chemistry
Janine LaSalle	MED: Microbiology & Immunology
Jerold Last	Pulmonary / Critical Care Medicine
Kent Leach	Biomedical Engineering
Carlito Lebrilla	Chemistry
Noelle L'Etoile	Center for Neuroscience & Dept. of Psychiatry & Behavioral Sciences
Ronald Li	Cell Biology and Human Anatomy - MED
Su-Ju Lin	Center for Genetics & Development - UCD Cancer Center
Bo Liu	Plant Biology
Gang-yu Liu	Chemistry
Marjorie Longo	Chemical Engineering & Material Sciences
Angelique Louie	Biomedical Engineering
Paul Luciw	MED: Pathology
Neville Luhmann, Jr.	Electrical & Computer Engineering
Laura Marcu	Biomedical Engineering
Fumio Matsumura	Environmental Toxicology
Karen McDonald	Chemical Engineering & Material Sciences
Claude Meares	Chemistry

Juan Medrano	Animal Science
Richard Michelmore	Vegetable Crops
Lisa Miller	Department of Anatomy, Physiology and Cell Biology, CNPRC, School of Veterinary Medicine
Marion Miller-Sears	Environmental Toxicology
David Mills	Viticulture & Enology
Terence Murphy	Plant Biology
James Murray	Animal Science / Genetic Engineering Large Animals
Krishnan Nambiar	Chemistry
John Newman	Nutrition - USDA, ARS, WHNRC
Thomas North	Center for Comparative Medicine
Martha O'Donnell	Physiology & membrane Biology; School of Medicine
David Ogrydziak	Food Science & Technology
Tingrui Pan	Biomedical Engineering
Rebecca Parales	Microbiology
Atul Parikh	Biomedical Engineering
Anthony Passerini	Dept. of Biomedical Engineering
Timothy Patten	Chemistry
Niels Pedersen	Department of Medicine and Epidemiology
Ronald Phillips	Chemical Engineering & Material Science
Jerry Powell	Hematology & Oncology: Med
Robert Powell	Chemical Engineering & Material Science
Martin Privalsky	Microbiology
Jinyi Qi	Biomedical Engineering
Subhadip Raychaudhuri	Biomedical Engineering
David Reid	Food Science & Technology
Michael Reid	Environmental Horticulture
Alexander Revzin	Biomedical Engineering
Robert Rice	Environmental Toxicology
Subhash Risbud	Chemical Engineering & Material Science
William Ristenpart	Chem. Engineering & Materials Science & Dept. Food Science
David Rocke	Inst. For Data Analysis & Visualization
Ray Rodriguez	Molecular & Cellular Biology
Pamela Ronald	Plant Pathology
Robert Rucker	Nutritional Biology
John Rutledge	MED: Endocrinology
Dewey Ryu	Chemical Engineering & Material Sciences
Earl Sawai	Pathology & Laboratory Medicine
Kate Scow	Land, Air & Water Resources
David Segal	Pharmacology

Kazuhiro Shiozaki	Microbiology
Wendy Silk	Soils and Biogeochemistry
Scott Simon	Biomedical Engineering
David Slaughter	Biological & Agricultural Engineering
Jay Solnick	MED: Infectious & Immunological Diseases
Henning Stallberg	Molecular & Cellular Biology
Daniel Starr	Center for Genetics and Development
Francene Steinberg	Dept. of Nutrition
Pieter Stroeve	Chemical Engineering & Material Science
Gang Sun	Textiles & Clothing
Dean Tantillo	Chemistry
Alice Tarantal	Pediatrics, School of Medicine, CNPRC
Steven Theg	Plant Biology
Li Tian	Plant Sciences
Michael Toney	Chemistry
Jose Torres	MED: Medical Microbiology & Immunology
Renee Tsolis	Med Microbiology & Immunology: MED
Richard Tucker	Cell Biology & Human Anatomy
Jamal Tuqan	Electrical & Computer Engineering
Alison Van Eenennaam	Animal Science
Jean VanderGheynst	Biological & Agricultural Engineering
Patricia Wakenell	Population Health & Reproduction: Vet Med
Robert Weiss	Internal Medicine: Division of Nephrology, MED
Valerie Williamson	Nematology
Barry Wilson	Animal Science & Environmental Toxicology
David Wilson	Molecular & Cellular Biology
Matthew Wood	Environmental Toxicology
Reen Wu	MED: Pulmonary / Critical Care Medicine
Stefan Wuertz	Civil & Environmental Engineering
Soichiro Yamada	Biomedical Engineering
Yin Yeh	Applied Science
Tilahun Yilma	VM: Pathology, Microbiology & Immunology
John Yoder	Vegetable Crops
Yohei Yokobayashi	Biomedical Engineering
Glenn Young	Food Science & Technology
Ruihong Zhang	Biological & Agricultural Engineering

The Value of Internships

Over the last 16 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
AgraQuest
Alza
Amgen
Amyris
Aqua Bounty
Bayer
Berlex Biosciences
BioMarin Pharmaceuticals
Carollo
Celera AgGen
DuPont
Exelixis
Genencor
Genentech
Hoffmann Eitle
ICOS
Institut Charles Sadron,
Maxygen
Monsanto, Calgene Campus;
Novartis (formerly Chiron)
Novozymes Biotech
Scios
Somagenics
Syntex
Recovery Sciences
Roche Biosciences
State Water Control Resources Board
Unilever
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 160 students enrolled, so we need more Academic-Industry Partnerships.