Seventeenth Annual

# Biotechnology Training Retreat

Saturday,
March 29, 2008

*Christian Brothers Retreat & Conference Center*
*Napa, CA*

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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

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## *2008 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 **2007-08 fellows and their preceptors**, as well as **our industry affiliates**. It is hard to believe that we have been holding this retreat for the past 17 years. This year, we would like to welcome the faculty and trainees affiliated with the newly funded NSF CREATE-IGERT Training Program (directed by Karen McDonald). They will be joining this annual event, since they are also linked to the DEB.

The logistics of this retreat has been overseen by our stellar team: Madeline Osborn, our new event coordinator, Marianne Hunter, our program manager and our soon-to-be 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: **Don Barkauskas,** Biostatistics (preceptor is David Rocke); **Michael Howland**, Chemical Engineering (preceptor is Atul Parikh); **Joseph Ramahi**, Cell and Developmental Biology (preceptor is Simon Chan); **David Sela**, Microbiology (preceptor is David Mills) and **Erin Tapley**, Cell and Developmental Biology (preceptor is Daniel Starr). Our **5 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); **Kristina Mahan,** Biochemistry and Molecular Biology (preceptor is Rebecca Parales), **Scott Hamilton,** Biochemistry and Molecular Biology (preceptor is Noelle L'Etoile) and **Sarah Lockwood**, Biochemistry and Molecular Biology (preceptor is David Segal). The CREATE-IGERT Trainees are **Timothy Butterfield**, **Dawn Chiniquy**, **Tiffany Glavan**, **Ben Lindenmuth** and **Christopher Simmons**. 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 **2008-09 fellows** in May. Nomination Forms are on the web at www.deb.ucdavis.edu. Application deadline is **Monday April, 21.** 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 150 and climbing.** Each of our students is showcased on the DEB website (www.deb.ucdavis.edu).

In regard to industrial internships for 2008-09, we placed a record number of DEB students: **Andrew Wong** completed his internship at Aqua Bounty Technologies (a new site); **Gian Oddone** interned at AgraQuest (a new site); **Warren Place** and **Kou-San Ju** completed their internships with Amyris Biotechnologies (a new site); **Sandra Bennun-Serrano** spent six months at BioMarin Pharmaceuticals; **Jennifer Warren** interned with Carollo, an environmental engineering firm**; Laura Higgins** completed her internship with the Center for Biophotonics Science & Technology at UC Davis; **Kristina Herzberg** is interning with Hoffmann Eitle (patent attornies) in Munich Germany; **Xianxian (Janice) Liu** worked at Genencor (a new site); **Don Barkauskas, Craig Blackmore, Artem Loukoianov, Caroline Meloty-Kapella** and **James Stice** completed their 3-6 month internships at Genentech; **Ying Peng** spent the summer at Monsanto, Calgene campus

and now is employed there; **Andres Schwember** is currently at Calgene**; Ting-Kuo Huang, Vannarith Leang and Bei Xian** worked at Novartis (Vacaville and Emeryville); **Zachary Bent, Monica Britton and Kevin Holden** interned at Novozymes; **Riccardo LoCascio** completed a cross-college rotation with the Raybould lab, School of Veterinary Medicine; **Pavan Kumar** found a new company in Santa Cruz named Somagenics and secured his own internship, and **Robin GrayMerod** spent his time at State Water Control Resources Board in Sacramento. We are expanding our internship locations to Europe: **Suzanne Barber** is at Institut Charles Sadron in Strasbourg France and **Matthew Hoopes** finished his internship last summer with Unilever in the U.K. 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 2007 with their PhDs and a Designated Emphasis in Biotechnology**: James Evans; Ruixiao Lu, Carolyn Meloty-Kapella; Ying Peng; Esra Talu and Scott Wong.** Please see the latest edition of **Biotechnology Times** on the Biotechnology Program's website at http://www.biotech.ucdavis.edu/ for more information.

Thank you so much for coming. Please enjoy the great presentations, the delicious food and wine and gorgeous scenery. Mark your calendars for the 18th annual Biotechnology Training Retreat for **Saturday, April 5, 2009** (tentative date).

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

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Roland Faller (Chemical Engineering)
Ian Kennedy (Mechanical & Aeronautical Engineering)
Tonya Kuhl (Chemical Engineering)
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Atul Parikh (Applied Science)
David Segal (Pharmacology/Genome center)
Michael Wright (UC Davis Genome Center and Bioinformatics Program)

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


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

Judith A. Kjelstrom
Program Coordinator
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# UC Davis Biotechnology Program

www.biotech.ucdavis.edu

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# UC Davis Seventeenth Annual Biotechnology Training Retreat
# March 29, 2008
# 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**<br>Karen McDonald<br>Co-Director, NIH Training Grant in Biomolecular Technology | | |
| | **Morning Session**<br>Karen McDonald<br>Co-Director, NIH Training Grant in Biomolecular Technology | | |
| **8:45 – 10:20 am** | **Presentations** | | |
| | 8:45 am | Michael Howland | *Mentor: Atul Parikh* |
| | 9:10 am | **Henry Valentin** | **Monsanto, Calgene Campus** |
| | 9:35 am | David Sela | *Mentor: David Mills* |
| | 10:00 am | Joseph Ramahi | *Mentor: Simon Chan* |
| **10:20 – 10:45 am** | **Break / Poster Viewing** | | |
| **10:50 – 12:20 pm** | **Presentations** | | |
| | 10:45 am | **Caryl Vann** | **Genentech, Inc.** |
| | 11:10 am | Erin Tapley | *Mentor: Daniel Starr* |
| | 11:35 am | Don Barkauskas | *Mentor: David Rocke* |
| | 12:00 pm | John Yoder | Bioethics Question (Handout) |
| **12:20 – 2:00 pm** | **Lunch / Poster Viewing** | | |
| | **Afternoon Session Chair**<br>Abhaya Dandekar<br>Chair,DEB Executive Committee | | |
| **2:00 – 3:40 pm** | **Presentations** | | |
| | 2:00 pm | John Yoder | Bioethics Question (Discussion) |
| | 2:25 pm | Christina Takanishi | *Mentor: Matthew Wood* |
| | 2:50 pm | Matthew Hoopes | *Mentor: Marjorie Longo & Roland Faller* |
| | 3:15 pm | **Keith McCall** | **Novozymes, Inc.** |
| **3:40 - 3:50 pm** | **Short Break (10 min)** | | |
| **3:50 – 5:40 pm** | **Presentations** | | |
| | 3:50 pm | **Keith Waddell** | **Agilent** |
| | 4:15 pm | Kristina Mahan | *Mentor: Rebecca Parales* |
| | 4:40 pm | Sarah Lockwood | *Mentor: David Segal* |
| | 5:15 pm | Scott Hamilton | *Mentor: Noelle L'Etoile* |
| | 5:40 pm | **Eddie Moler** | **Tethys Bioscience, Inc.** |
| **6:05 pm** | **Closing Remarks**<br>Karen McDonald | | |

**6:30 pm – Bus departs Napa**

# 2008 Poster Titles

A. **"Multi-Modal Probes For the Integrated Assessment of Activated Microglia in Relation to Aβ Alzheimer Plaques"**
Erica Andreozzi*, Ben Jarrett, Angie Louie
Department of Biomedical Engineering, University of California, Davis

B. **"Developing Systems For Bioproduct Refining From Microalgae"**
Yu-Shen Cheng*[,1], John Labavitch[2] and Jean S. VanderGheynst[1]
[1] Biological Systems Engineering and [2] Plant Science, University of California, Davis, CA.

C. **"Impairment of the DNA Repair and Growth Arrest Pathways by p53R2 Silencing Enhances DNA Damage-Induced Apoptosis in p53-Dependent Manner in Prostate Cancer Cells"**
Hong-Lin Devlin*, Phillip C. Mack, Rebekah A. Burich Paul H. Gumerlock, Hsing-Jien Kung, Maria Mudryj and Ralph W. deVere White
Medical Microbiology and Immunology, Cancer Center
University of California, Davis

D. **"Using Ethanol Molecules to Disrupt Lipid?Ergosterol Interactions in Bilayers"**
Allison Dickey*, Wen-Sau Yim, Roland Faller
Chemical Engineering and Materials Science Department, University of California, Davis

E. **"PH-Responsive Surfaces For Preparing Bio-Mimetic Devices"**
Rita J. El-khouri[*], Daniel Bricarello[¶], Atul Parikh[¶], Timothy Patten[*]
University of California, Davis, Department of Chemistry[•] &
Department of Applied Science[¶]

F. **"Structural Analysis of the Catalytic Cycle of Heavy Riboflavin Synthase: Insights Into Quaternary Arrangement & Ligand-Induced Stability**
Dominik J. Green*, Li Xing, Rod Balhorn, & R Holland Cheng
University of California, Davis – Department of Molecular & Cellular Biology
Lawrence Livermore National Laboratory – CMLS Directorate

G. **"Nanofabrication Of Organometallic Structures For Biological Applications"**
Huilan Han*, Abhinav Bhushan*, Frank Yaghmaie, and Cristina Davis[†]
Department of Mechanical Engineering, University of California, Davis, CA, 95616

H. "Plant Cell Suspension Cultures As a Bioproduction Platform of Recombinant Human Therapeutic Proteins"

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

(1)Department of Chemical Engineering and Materials Science, University of California, Davis

(2)Department of Plant Pathology, University of California, Davis

(3)Department of Plant Sciences, University of California, Davis

I. "Laboratory Evolution Of A Novel Pathway For 4-Nitrotoluene Degradation"

Kou-San Ju* and Rebecca E. Parales

Section of Microbiology, University of California, Davis, CA

J. "Infertility In High Growth Mice: C57BL/6, FVB, and A/J Strains

Rashida Lathan*, Thomas E. Adams, Juan F. Medrano

Department of Animal Science, University of California, Davis

K. "Evidence For Paternal Allele Specific Chromatin Extension and Looping of the *SNRPN* To *UBE3A* Locus In Mature Neurons by Fluorescence In Situ Hybridization"

Karen N. Leung*, Roxanne O. Vallero, Janine M. LaSalle.

Dept. of Medical Microbiology and Immunology, Rowe Program in Human Genetics, School of Medicine, University of California, Davis, CA

L. "A Plant-Based Expression System For In Planta Production and Localization of a Cellulose Degrading Enzyme"

Ben Lindenmuth*[1], Mike Plesha, Bryce Falk[1], Abhaya Dandekar[3], and Karen McDonald[1]

(1)Department of Chemical Engineering and Materials Science, University of California, Davis

(2)Department of Plant Pathology, University of California, Davis

(3)Department of Plant Sciences, University of California, Davis

M. "Oxidant Specificity of the ORP1 THIOL Peroxidase

Li-Hua Ma*, Christina L. Takanishi, and Matthew J. Wood

Department of Environmental Toxicology, University of California, Davis, CA, 95616

N. "The *Caenorhabditis Elegans* Conventional Kinesin Light Chain, KLC-2, Functions In Nuclear Migration"

Marina Meyerzon*, Daniel A Starr

Molecular and Cellular Biology, UC Davis, Davis, CA

O. "Structure Determination of HIV-1 gp140 Envelope Protein By Single Particle Reconstruction"

Carlos G. Moscoso*, Dominik J. Green, and R Holland Cheng
Department of Molecular and Cellular Biology, University of California, Davis, CA 95616

P. "Predicting *L. Lactis* Strain Improvements Using Metabolic Flux Balancing

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

Q. "Intersurface Measurements of Liquid Phase Supported Membranes Coated With PEG2000"

Raquel Orozco-Alcaraz* and Tonya Kuhl
Department of Chemical Engineering and Materials Science, University of Californ1ia, Davis

R. "Bacterial Nanoglue For Self-Assembly of Microstructures"

Stephanie Pulford* and Cristina Davis
Department of Mechanical Engineering, University of California, Davis, CA, 95616

S. "The Role of the MUS81-MMS4 Endonuclease in Reinitiation and Repair of Stalled Replication Forks"

Erin K. Schwartz* and Wolf-Dietrich Heyer
Department of Microbiology, University of California, Davis

T. "Developing An Allosteric Regulatory Mechanism For Engineered Zinc Finger Proteins"

Sarah Lockwood* and David Segal
Genome Center, University of California, Davis, CA, 95616

U. "Exercising Spatiotemporal Control of Cell Adhesion To Optically Transparent Microelectyrodes"

Sunny Shah*[1], Ji Youn Lee[1], Nazgul Tuleuova[1], Mark Zern[2] and Alexander Revzin[1]
1. Department of Biomedical Engineering, University of California, Davis
2. Department of Medicine, Transplant Research Institute, University of California, Davis

*V.* "A Kinetic Model of the T-DNA Secretion Pathway of *Agrobacterium Tumefaciens"*

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

W. "Crystal Structure Based Mutagenesis of RecBCD Enzyme Reveals Residues That Are Responsible to the Recognition of the Regulatory Sequence, χ"

Liang Yang[1*], Naofumi Handa[1,2], Mark S. Dillingham[1,3], Dale B. Wigley[4] and Stephen C. Kowalczykowski[1]

1: Sections of Microbiology and of Molecular and Cellular Biology, University of California, Davis

2: Department of Medical Genome Sciences, Graduate School of Frontier Science and Institute of Medical Science, University of Tokyo, Shirokanedai, Tokyo 108-8639 Japan. 3: DNA-protein Interactions Group, Dept. of Biochemistry, School of Medical Sciences, University of Bristol, Bristol BS8 1TD, UK.

4: Clare Hall Laboratories, Cancer Research UK, London Research Institute, Blanche Lane, South Mimms Potters Bar, Herts EN6 3LD, UK

X. "Adaptation of Machine Learning Algorithms for Spectrometer Data Analysis"

Weixiang Zhao[1*], Abhinav Bhushan[1*], Shankar Sankaran[1], Susan Ayer[1], Ana Maria[2], Abhaya Dandekar[2], and Cristina Davis [†,1]

1: Department of Mechanical Engineering, University of California, Davis, CA 95616

2: Department of Pomology, University of California, Davis, CA 95616

See pages 37 - 67 for poster abstracts.

*Member of DEB graduate group

UCDAVIS Biotechnology Program

# Oral Presentation Abstracts

## NIH FELLOW: Michael C. Howland

# WETTABILITY-BASED PATTERNING OF SUPPORTED LIPID BILAYERS: IMPLICATIONS FOR DETERGENT AND RESISTANCE DEHYDRATION STUDIES


Presenter: Michael C. Howland*

Authors: **Michael C. Howland**[1]*, Ann E. Oliver[2], and Atul N. Parikh[2]

Affiliations: [1]Dept of Chemical Engineering and Materials Science, [2]Dept. of Applied Science, UC Davis

Preceptor: Atul N. Parikh, PhD



Supported lipid membranes, single bilayers at solid liquid interfaces, remain a popular technology for a variety of studies. These systems have shown promise in biosensing, biocompatibility, and drug delivery and for conducting model membrane studies. In our current research, we combine supported lipid membrane technology with photolithography and wettability based patterning to provide higher levels of function. To that end, we use these processes, borrowed from the microelectronics industry, to direct the placement and environment of lipid bilayers. We have previously shown the ability to spatially control membrane morphology by this approach. Now using these spatially controlled membrane morphologies, we have investigated the interaction of supported membranes with detergents in order to explore the mechanism of detergent resistance, a phenomenom central to the 'raft' hypothesis. It is well known that composition and packing density are key players in detergent resistance. However, we show that substrate coupling can also play a major role. In many ways, this substrate coupling mimics the adhesion and support of the cytoskeleton. This coupling may then play a role in biological detergent resistance. In addition to studying detergent resistance, wettability based patterning also holds promise for building dehydration tolerant membranes. Using a disaccharide, trehalose, to provide psuedo-hydration in the absence of water, supported membranes can be dried and rehydrated without major damage to the membrane integrity. Using patterns of wettability, we are working towards spatially arrayed patches of trehalose-supported membranes, with a goal of allowing for the dehydration and storage of arrays of functional lipid bilayers. Such bilayer arrays could be used for high throughput assays or other multiplexed arrays applications.


*** Member of the DEB graduate program**

## COMPANY AFFILIATE: Monsanto, Calgene Campus

# NOVEL VEGETABLE OILS: THE LONG AND WINDY PATH TO COMMERCIALIZATION


Presenter: Henry Valentin, PhD

Authors: **Henry Valentin**

Affiliations: Monsanto, Calgene Campus
1920 Fifth Street
Davis, CA 95616

Email:



Worldwide, about 140 million tons of vegetable oils are produced annually, a major source of calories for humans. Vegetable oils are extracted from fruit (olive, oil palm) or seeds (soy, rapeseed, sunflower). The fatty acid composition is dependent on the source species, and compositions vary in the levels of saturated, monounsaturated or polyunsaturated fatty acids. The particular fatty acid composition gives each vegetable oil its physical properties (melting point), nutritional value (omega3, saturated) and determines its utility for food applications (salad dressing, frying, baking). Often, the natural composition of a vegetable oil is not optimal for certain uses. For example, native soybean oil is too unsaturated to be used in frying operations, therefore it was chemically hydrogenated. Alternatively, the fatty acid composition of seed oils can be altered by either mutations or transgenic alterations of the oil biosynthesis pathway, leading to custom oils. I will discuss aspects of the development of several novel soybean oils, covering nutritional studies, regulatory requirements and food application research.

## NIH FELLOW: David Sela

# THE COMPLETE GENOME SEQUENCE OF *Bifidobacterium longum* ssp. *infantis* REVEALS ADAPTATION FOR MILK UTILIZATION WITHIN THE INFANT GUT


| | |
|---|---|
| Presenter: | David A. Sela* |
| Authors: | **David A. Sela**, Jarrod Chapman, Dan S. Rokhsar, Carlito B. Lebrilla, J. Bruce German, Paul M. Richardson, and David A. Mills |
| Affiliations: | Microbiology Graduate Group and Designated Emphasis in Biotechnology, University of California, Davis, CA 95616 |
| Preceptor: | David A. Mills, PhD |



Following birth, the gastrointestinal tract is rapidly colonized by a microbial consortium often dominated by bifidobacteria in breast-fed infants. This numerical advantage confers a substantial health benefit to the neonate by hindering pathogen colonization through competitive exclusion.

We have previously demonstrated a capacity for select bifidobacterial species to utilize specific oligosaccharides ubiquitous in human milk and secreted early in the lactation cycle. Accordingly, the complete genome sequence of the milk oligosaccharide utilizing *Bifidobacterium longum* ssp. *infantis* reflects a competitive strategy fashioned under the influence of, and thus targeting, milk-borne molecules that do not possess nutritive value to the neonate. Specifically, several chromosomal loci reflect host adaptation including a 40 kbp cluster encoding catabolic genes, extracellular solute binding proteins, and permeases predicted to be active on milk oligosaccharides. Sequencing of two additional *B. longum* ssp. *infantis* strains supports the proposed genomic mechanism underlying oligosaccharide utilization through conservation of predicted milk-related loci.


* Member of the DEB graduate program

## NIH FELLOW: Joseph Ramahi

# HETEROCHROMATIN AND CENTROMERE FUNCTION IN ARABIDOPSIS


| | |
|---|---|
| Presenter: | Joseph S. Ramahi* |
| Authors: | **Joseph S. Ramahi**, Simon W.L. Chan |
| Affiliations: | Cell and Developmental Biology Graduate Group and Designated Emphasis in Biotechnology<br>University of California, Davis, CA 95616 |
| Preceptor: | Simon W. L. Chan, PhD |



The centromere and its associated protein complex are essential for chromosome segregation during cell division. However, the requirements for centromeric identity and function remain to be understood. Centromere identity in higher eukaryotes is thought to be epigenetically determined by localization of centromere-specific H3 variant histone (CENH3). While the centromere is a region of heterochromatic DNA, it is not clear whether heterochromatin is important for proper centromere function. The *Arabidopsis* centromere has proven to be an ideal model to study centromere dynamics, with a megabase-scale tandem repeat array of centromeric DNA sequence. Also, much of the gene silencing machinery, namely DNA methylation and histone modifications, in *Arabidopsis* is orthologous to vertebrate systems. Deletion of the DNA methyltransferase MET1 results in loss of almost all CG DNA methylation, and in mammalian cells mitotic catastrophe and cell death. met1 null plants are viable, providing a system to study the role of heterochromatin at the centromere. We hypothesize that heterochromatin is important for proper centromere function. Using a CenH3-GFP transgene to visualize centromeres *in vivo*, centromere dynamics can be quantitatively analyzed. Using deconvolution microscopy to image mitotic root cells, we can compare mitotic progression of several heterochromatin mutants to wild type CenH3-GFP plants, to observe any possible effects on centromere function. By measuring amount of CenH3 loaded into the centromere, length of time for mitotic progression, and other centromere dynamics the role of heterochromatin in centromere function can be better understood.


*** Member of the DEB graduate program**

## COMPANY AFFILIATE: Genentech

# SCIENCE INTERSECTS BUSINESS: CHALLENGES FOR 2008 AND BEYOND


| | |
|---|---|
| Presenter: | Caryle S. Vann* |
| Authors: | **Caryle S. Vann** |
| Affiliations: | Genentech<br>Vacaville, CA |
| Email: | vann.caryle@gene.com |


Genentech has successfully transitioned from a small startup science-based research organization to a large world class biopharmaceutical manufacturing company. What are some of biggest challenges facing Genentech today and in the coming years, at this intersection of science and business?

## NIH FELLOW: Erin Tapley

# CHARACTERIZATION OF UNC-84, A *CAENORHABDITIS ELEGANS* INNER NUCLEAR MEMBRANE PROTEIN THAT FUNCTIONS IN NUCLEAR POSITIONING


| | |
|---|---|
| Presenter: | Erin Tapley* |
| Authors: | **Erin Tapley**, Nina Ly, and Dan Starr |
| Affiliations: | Department of Molecular and Cellular Biology Group<br>University of California, Davis, CA 95616 |
| Preceptor: | Dan Starr, PhD |



Nuclear positioning is important to a wide variety of eukaryotes. Defects in this process have been linked to human diseases such as muscular dystrophy, cerebellar ataxia and lissencephaly. Using *C. elegans* genetics, we have identified UNC-84, an inner nuclear membrane (INM) protein with a C-terminal SUN domain. *In vivo* we have shown that UNC-84 is required to specify the localization of KASH domain containing proteins to the outer nuclear membrane (ONM) and that both the SUN and KASH domains are essential for nuclear migration. SUN and KASH proteins are conserved from yeast to humans. We propose that the SUN/KASH interaction between these proteins creates a structural bridge across the nuclear envelope (NE) that allows force to be transferred from the cytoskeleton to the nuclear matrix during nuclear positioning. Central to this model is the SUN/KASH interaction. There are two independent KASH interaction domains in UNC-84 and its mammalian homolog, Sun1. Attempts to characterize an *in vitro* KASH/SUN interaction were unsuccessful, presumably due to UNC-84's poorly defined topology. Therefore, to define the topology I am performing cell free microsomal targeting experiments and *in vivo* cell fractionation experiments, both of which will be followed by protease protection assays. In conjunction with these experiments, UNC-84's putative transmembrane domains are being deleted from our *unc-84* rescuing construct and assayed for rescue *in vivo.* Using the strength of *C. elegans* we have found that the first 535 residues of UNC-84 are sufficient for NE localization. To further narrow down the NE retention and/or localization domains we are performing deletion mapping experiments and testing whether either of UNC-84's two putative nuclear localization signals are necessary and sufficient for *in vivo* localization. Future work is aimed at identifying UNC-84 nucleoplasmic binding partners, measuring the strength of the SUN/KASH interaction, and determining the structure of UNC-84.


*** Member of the DEB graduate program**

## NIH FELLOW: Erin Tapley

# DETECTING BIOMARKERS FOR PROSTATE CANCER USING MASS SPECTROMETRY DATA


Presenter: Erin Tapley*

Authors: **Donald A. Barkauskas**[1,*], Crystal Kirmiz[2], Maria Lorna de Leoz[2], Carlito Lebrilla[2], and David M. Rocke[3]

Affiliations: University of California, Davis. [1]Graduate Group in Biostatistics with a Designated Emphasis in Biotechnology, [2]Department of Chemistry, [3]Division of Biostatistics, School of Medicine

Preceptor: David M. Rocke, PhD


The development of better tests to detect cancer in its earliest stages is one of the most sought-after goals in medicine. Especially important are minimally invasive tests that require only a blood or urine sample. By profiling oligosaccharides adducted to proteins shed by cells into the blood stream, we hope to determine glycoprotein profiles that will help identify cancer patients using a simple blood test. The data is being generated by using matrix-assisted laser desorption/ionization Fourier transform ion cyclotron resonance mass spectrometry, and we have developed methods to analyze the data and determine the profiles that are associated with prostate cancer patients.

We have data from 20 subjects: 10 human patients diagnosed with prostate cancer under active surveillance with a prostate specific antigen (PSA) score of at least 5.0, and 10 human control subjects who have had their prostates removed and have a negative PSA. Although this project is specifically working with prostate cancer patients, we expect that the computational techniques we have developed will be applicable to the detection of any sort of biomarkers in samples, including other types of cancer, other diseases, or even exposure to toxic chemicals.

In this presentation, I will share the progress we have made toward the automation of the data analysis as well as some of the difficulties we've encountered along the way. I will also present a preliminary analysis of the data set, which shows several possible compounds which are significantly different in the two groups. I will also attempt to answer the two burning questions "What exactly do statisticians do, anyway?" and "Why should I always consult a statistician *before* I collect my data?"

*** Member of the DEB graduate program**

## BIOTECHNOLOGY FELLOW: Christina L. Takanishi

# A GENETICALLY ENCODED PROBE FOR DETECTING PROTEINS THAT RESPOND TO OXIDATIVE STRESS IN VIVO


| | |
|---|---|
| Presenter: | Christina L. Takanishi* |
| Authors: | **Christina L. Takanishi***, Matthew J. Wood |
| Affiliations: | Department of Environmental Toxicology, University of California, Davis, CA, 95616 |
| Preceptor: | Matthew J. Wood, PhD |


Although it is known that reactive oxidative species (ROS) play a major role in oxidative damage, increasing evidence reveals that ROS have wider cellular effects through their role in signal transduction pathways, transcription factors, and gene expression in a variety of prokaryotic and eukaryotic organisms. Therefore, it is of great interest to determine the specific protein targets of ROS. The overall goal of my research is to understand the molecular mechanisms by which oxidative stress regulates the function of biological molecules and signal transduction pathways. In *Saccharomyces cerevisiae*, the conserved Orp1-Yap1 cysteine thiol-based sensor is the master regulator of oxidative stress. 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) (*1*). 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. We are currently adapting the redox-regulated domain from the Yap1 transcription factor in S. cerevisiae for use as a general trap for proteins that form Cys-SOH in vivo with the goal of developing genetically encoded proteomic tools to specifically identify transient Cys-SOH formation and apply them to *S. cerevisiae* and human keratinocytes to determine the effects of ROS on protein Cys-SOH formation (*2*).


(1) Ma, L. H., Takanishi, C. L., and Wood, M. J. (2007) Molecular mechanism of oxidative stress perception by the Orp1 protein. *J Biol Chem 282*, 31429-36.

(2) Takanishi, C. L., Ma, L. H., and Wood, M. J. (2007) A genetically encoded probe for cysteine sulfenic Acid protein modification in vivo. *Biochemistry 46*, 14725-32.

* Member of the DEB graduate program

## BIOTECHNOLOGY FELLOW: Matthew I. Hoopes

# COARSE-GRAIN SUPPORTED LIPID BILAYERS ON PATTEREND SURFACES


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| Presenter: | Matthew I. Hoopes* |
| Authors: | **Matthew I. Hoopes***, Marjorie M. Longo, and Roland Faller |
| Affiliations: | Biophysics Graduate Group, University of California, Davis<br>Department Chemical Engineering and Material Science, University of California, Davis |
| Preceptor: | Marjorie M. Longo, PhD, and Roland Faller, PhD |



Model membranes on supports of well defined geometries are very useful to determine mechanical properties of lipid bilayers. Yet, questions of substrate choice and its influence on the bilayer create additional complexity when analyzing bilayer systems. Coarse-grained solvent-free molecular dynamic models of supported lipid bilayers [Cooke, I. R. and M. Deserno (2005)] allow for studies at longer length scales and time scales than are available with atomistic models. We present results using such models with particle based surfaces for calculations of bending, density profile, area per lipid, tension, and variation in the normal component of the pressure tensor.


*** Member of the DEB graduate program**

## COMPANY AFFILIATE: Novozymes, Inc.

# ENZYMES ENABLING A NEW INDUSTRY-CELLULOSIC ETHANOL


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Novozymes is a world leader in industrial enzyme production and development and has been helping to make cellulosic ethanol a reality since 2001. Our work has been in collaboration with the DOE as well as many other governmental and academic organizations. This talk is a progress update of the talk given last year and covers the many approaches being used to move cellulosic ethanol from the realm of theory to practical application.

Current corn starch ethanol plants produce a yield of ~114 gallons ethanol per dry ton of corn grain, at an enzyme usage of only 1 g protein per gallon ethanol produced. Current pilot plants utilizing crop waste produce a yield of ~72 gallons ethanol per dry ton of corn stover, but at an economically non-viable requirement of ~ 100 g enzyme protein per gallon ethanol produced.
Despite current costs, cellulosic ethanol has a suite of benefits, including relieving pressure on grain prices, more efficient utilization of resources, and the ability to convert wastes (crop waste, newsprint, mill discards) to fuel.

Research is being conducted on all possible fronts for improvement, with efforts being made to reduce enzyme production costs by: utilization of reduced cost feed-stocks, increasing fermentation yield of enzyme, and reducing enzyme recovery costs as well as efforts being made to increase enzyme efficiency by: creating more thermostable enzymes, selection of enzymes with higher specific activity, selection of enzymes with resistance to inhibitors, and optimization of cellulase enzyme mix.

Many of these efforts have demonstrated the power of classic techniques, including broth fractionation and combination studies and random mutagenesis and screening. These techniques have increased enzyme yield and increased the efficiency of the enzyme mixture by greater than 6-fold under industrially relevant conditions.

## COMPANY AFFILIATE: Agilent


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| Presenter: | Keith Waddell*, PhD |
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## BIOTECHNOLOGY FELLOW: Kristina M. Mahan

# PROTEIN-PROTEIN INTERACTIONS OF NITROBENZENE DIOXYGENASE


Presenter: Kristina M. Mahan*

Authors: **Kristina M. Mahan***, Tiffany S. Louie, Juan V. Parales, and Rebecca E. Parales

Affiliations: Section of Microbiology
University of California, Davis

Preceptor: Rebecca E. Parales, PhD


The production of compounds like pesticides, dyes, and explosives has resulted in the introduction of significant amounts of nitroaromatic contaminants into the environment. These degradation-resistant compounds are of varying risk to the ecosystem as well as human health. Recently, microorganisms have evolved pathways for the utilization of these toxic man-made compounds as sole carbon, nitrogen, and energy sources. We are interested in characterizing nitrobenzene dioxygenase (NBDO), the initial enzyme in the nitrobenzene degradation pathway of *Comamonas* sp. strain JS765. NBDO catalyzes the conversion of the synthetic nitroaromatic compound nitrobenzene to the easily degraded natural product, catechol. NBDO is a member of a large family of multicomponent Rieske non-heme iron oxygenases that require specific electron transfer proteins (reductase and ferredoxin) to transfer electrons from NADH to the catalytic oxygenase component. The structure of the NBDO oxygenase component and the precise location of the Rieske iron-sulfur centers that function as electron carriers in the protein are known. Using this 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 generate amino acid substitutions in the oxygenase component at sites predicted to interfere with electron transfer between the oxygenase and ferredoxin (Val 98 and Gln113). Using whole cell biotransformation assays, we found that Gln113 mutants had slightly reduced activity, while V98 mutants had severely reduced enzymatic activity compared to wild type. We report here the identification of several amino acid substitutions (changing Val 98 to Asp, Glu, or Phe) that resulted in reduced enzymatic activity. Activity was restored when the mutant oxygenases were artificially reduced in the presence of dithionite, indicating that the mutations specifically affect electron transfer between the ferredoxin and oxygenase components. We also report a strategy to identify mutant ferredoxins with compensatory mutations that restore wild-type activity to the V98 oxygenase mutants. These studies will identify amino acid residues on the two

proteins that are involved in direct protein-protein interactions and electron transfer and help to elucidate the mechanism of action of this key detoxification enzyme.

* Member of the DEB graduate program

## BIOTECHNOLOGY FELLOW: Sarah Lockwood

# DEVELOPING AN ALLOSTERIC REGULATORY MECHANISM FOR ENGINEERED ZINC FINGER PROTEINS


Presenter: Sarah Lockwood*

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Preceptor: David Segal, PhD



The Segal Lab designs chimeric zinc finger DNA binding proteins. Engineering these proteins has many practical applications, including imaging/sequence detection. This can be achieved by attaching various proteins and/or enzyme functional domains to produce a desired activity at zinc finger-specified sequences. 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 complex. However, one complication with this system is β-lactamase reassembly in solution without having bound to 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 target. Using this information, we plan to attach catalytic inhibitory and complimentary 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 one being inhibitory. In the presence of DNA, the zinc fingers will tightly bind to their target sequence 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 the target sequence. We anticipate a significant improvement in assay sensitivity.


*** Member of the DEB graduate program**

## BIOTECHNOLOGY FELLOW: O. Scott Hamilton

# GENETICALLY MALLEABLE *C. ELEGANS* NEURAL CIRCUITS


Presenter: O. Scott Hamilton*

Authors: **O. Scott Hamilton***, Damien O'Halloran and Noelle L.'Etoile

Affiliations: Center for Neuroscience
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Preceptor: Noelle L'Etoile, PhD



The L'Etoile lab's research includes the use of genetics and molecular biology in the nematode *C. elegans* to address the problem of attention and adaptation. While neural circuits underpin all behaviors and we are beginning to understand how individual neurons process information, it is still unclear how even two neurons work in a simple circuit. We are coupling neurobiological techniques with bioengineering technologies to construct a neuronal cell culture system in which individual neural circuits can be activated, modified and examined. Simple neuronal circuits of *C. elegans* neurons will be cultured within a microfluidic device. These circuits are designed to simultaneously excite one population of neurons in the circuit and record activity from a second. Progress to date includes the creation of transgenic lines of *C. elegans* animals that have specific *in vitro* neural readouts and, with our collaborators at the Georgia Institute of Technology, we have designed and tested a first generation microfluidic device. The goal of this project is to examine how complex properties emerge from a simple array of *C. elegans* sensory and downstream interneurons by using these in vitro circuits derived from genetically malleable neurons. This technique will enable us to determine how architecture, individual neuron properties and genes influence circuit behavior.


*** Member of the DEB graduate program**

## COMPANY AFFILIATE: Tethys Bioscience, Inc.

# PERSONALIZED MEDICINE, BIOMARKERS, AND THE PREDICTION OF DISEASE PROGRESSION


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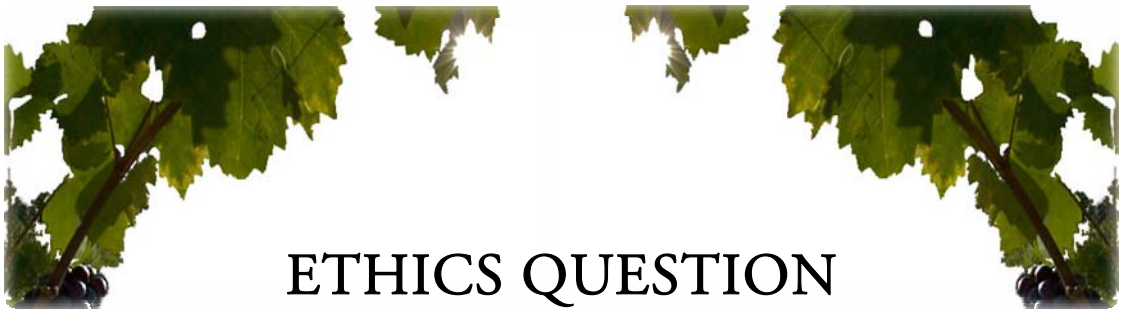
Tethys Bioscience is dedicated to the discovery, development and commercialization of novel biological markers – biomarkers – that provide a practical tool to address the growing global challenge of chronic metabolic diseases such as diabetes.

Our research strategies lead to sets of biomarkers that can be used to quantify the level of an individual's risk. 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.

Tethys is using novel, ultra-sensitive proteomics technology to discover, validate, and commercialize new predictive biomarkers. The technology platform, called Molecular Counting Technology (MCT), is based on counting individual fluorescently labeled proteins. It requires less than 1 uL of serum per assay and has a sensitivity limit 10-100 times better than conventional quantitative protein assays.

Studies on retrospective serum sample banks utilizing this MCT technology have led to the discovery of a panel of biomarkers that predict 5-year risk of developing Type 2 Diabetes. The Tethys Diabetes PreDx™ test, currently in development, involves a simple to administer blood test which fits easily into current clinical practice and provides clinically important, personalized risk information -- while matching or outperforming traditional clinical risk scores and measures of glucose dysregulation or insulin resistance.

# Bioethics



# ETHICS QUESTION

## Peter Parker Picked a Problematic Partner

by

John I. Yoder
Faculty Trainer of NIH Training Grant
in Biomolecular Technology

(NIH-1-T32-GM08799)

## Peter Parker Picked a Problematic Partner (Ad astra per aspera!)

Peter Parker and Mary Jane Watson are both graduate students working with Dr. Norman Osborn, an eminent environmental chemist branching into molecular biology. Although both are fourth year students, neither has published a manuscript. Both are beginning to worry that if they do not publish soon they will not be able to obtain good postdoc positions.

Finally, Peter's project starts to look promising. After many months of high throughput screening, he has honed in on a bug isolated near a plastics factory which he believes has the potential to degrade some hithertofore "non-biodegradable" plastics in an environmentally sound way. However it had low activity so he has it modified through random mutagenesis and selected a candidate in another round of screening. Peter now has to scale up to make sufficient carotherase so that he can perform a series of analyses on the product to verify some of its properties. The candidate bug is a notoriously recalcitrant fungus that just does not want to grow in culture conditions so he sets about isolating and cloning the gene. Dr. Osborn is very excited about Peter's progress, and tells him to begin to write up the results, because isolation and properties of the modified enzyme are unique enough to be published in a high profile journal, such as Nature Biotech, even before cloning the gene.

Although only small amounts of carotherase are available, Peter and Dr. Osborn agree that they must push ahead and work quickly. In order to help Peter as he works on isolating the gene and increasing expression of the enzyme, Dr. Osborn recruits Mary Jane to assist Peter in some analyses. Mary Jane has not been very successful with her project, which involves biotransformation of PCBs into a non-toxic compound, and Dr. Osborn feels that performing the analyses will teach her some skills that she could apply to her own project. Dr. Osborn promises her a second authorship on the paper if the results of her analytic studies pan out. Although Peter does not think highly of Mary Jane, believing her to be sloppy, he wants to move ahead with his research. He gives her the carotherase in two batches for the analytic studies.

Mary Jane completes the first set of analyses on the first batch and is excited by the results, which identify some novel characteristics. On the day she is doing the first experiment on the second batch of carotherase she phones Peter from the mass spec facility and asks him if a contaminant might have gotten mixed up, since the spectral pattern is not consistent. Peter asks Mary Jane to save the remaining material, telling her that he will perform the second round of analyses. But when Mary Jane comes back to the lab a few hours later, she does not give him the leftover carotherase. She tells Peter that she obtained positive results and that her mistake in the original interpretation was due to low blood glucose and to the fact that she had focused inadvertently on a reference sample, not on carotherase. There is no way for Peter to validate her findings,

since there is not enough carotherase left to do another run. Mary Jane tried to reassure Peter by showing him the readout from the LC/MS/MS on the second batch.

Dr. Osborn is ecstatic about the findings, and tells Peter to quickly write up a manuscript. Peter doesn't want to accuse Mary Jane of manipulating research results, but later in the day he looks through her research notebook and sees a written procedure and data for the first batch of experiments. For the second batch, he sees that she has put only the readout in the notebook, which looks too clean to him. It also has no accompanying text. He wonders what might have happened. Perhaps she used a reference sample and some mechanical manipulation to make the peaks appear so clean.

Peter is unsure about whether he can trust Mary Jane's findings, but he proceeds to write up the manuscript about his mutagenesis, isolation and characterization of carotherase and its analysis by Mary Jane. The article is published in Nature Biotech, but in the next several months other scientists who repeat his characterization find anomalies with his published data. During that time, Peter has been able to clone the gene and express the enzyme in a high expression fungal system. So it is very upsetting to him that this clearly promising system may be tainted by the appearance of impropriety. In addition industry has come calling with clear interest in carotherase's commercial capabilities. When he repeats the analysis of carotherase, he finds a rather different outcome than that obtained by Mary Jane and which they had published. He believes that she must have manipulated the data.

## QUESTIONS

1: How can the pressure to publish influence the conduct of research?

2: Was it appropriate for Dr. Osborn to promise Mary Jane second authorship based on performing some assays?

3: Trust is one of the central issues in science. What might Peter have done to feel better about working with Mary Jane if he didn't think highly of her?

4: At this point, it remains unclear whether Mary Jane has done anything wrong, even though she did not follow Peter's instructions to let him do the second analytic experiment. What action should Peter take?

5: Data collection and management are important issues in the responsible conduct of research. Independent of the possibility that Mary Jane might have engaged in manipulating data, what is the major problem in the way she kept her lab notebook?

6: What is misconduct? If it is found that Mary Jane engaged in misconduct, is Peter also guilty of misconduct, because he did not report his concerns earlier?

7: If science is self-correcting why do we need federal laws and regulations against misconduct?

8: It seems clear that there was a problem with Mary Jane's data. What should Peter do? Should industry's interest have any bearing on this decision?

Questions for Further Reflection
1: Have you ever taken shortcuts to produce results under pressure-filled conditions?
2: How do you think you would feel about accusing a colleague of misconduct?
3: Do you know whom you would speak to in case you had suspicions of misconduct by a graduate student, postdoctoral fellow, laboratory head, or department head?

## Possible Answers

1: How can the pressure to publish influence the conduct of research?

As graduate students, Peter and Mary Jane are worried that they need to publish a paper in order to help them get a good job after they graduate. Some studies have found that people might engage in misconduct if they are feeling career pressure and believe that they can take a shortcut to get a research answer.

2: Was it appropriate for Dr. Osborn to promise Mary Jane second authorship based on performing some assays?

Most publication guidelines to ethical practices in authorship say that an author is someone who has made a significant scientific contribution to a paper and will share responsibility for the accountability of results. All others should be listed in the acknowledgments. Do you think that Mary Jane has fulfilled the requirements? Also, do you think that Dr. Osborn exerted undue pressure on Mary Jane by tying authorship to her ability to get certain results?

3: Trust is one of the central issues in science. What might Peter have done to feel better about working with Mary Jane if he didn't think highly of her?

If Peter didn't feel comfortable with Mary Jane performing the analytic experiments, he probably should have said something to Dr. Osborn about his concerns. Even though there was some pressure to move the analysis along, he could have insisted on doing the experiments himself or supervised Mary Jane to ensure that they were done correctly.

4: At this point, it remains unclear whether Mary Jane has done anything wrong, even though she did not follow Peter's instructions to let him do the second analytic experiment. What action should Peter take?

Rather than continuing along as if nothing has happened, Peter should probably talk to Mary Jane about what might have occurred and to Dr. Osborn about concerns that he has about Mary Jane's findings.

5: Data collection and management are important issues in the responsible conduct of research. Independent of the possibility that Mary Jane might have engaged in manipulating data, what is the major problem in the way she kept her lab notebook?

Clearly, after four years as a graduate student, she should have known to clearly document all relevant information in her laboratory notebook. Maintaining a laboratory notebook, which includes writing down procedures and results, is part of the practice of the responsible conduct of research. But, in this case, Mary Jane was probably concerned about putting anything down in writing about her experience with the second experiment, committing the sin of omission rather than the sin of commission.

6: What is misconduct? If it is found that Mary Jane engaged in misconduct, is Peter also guilty of misconduct, because he did not report his concerns earlier?

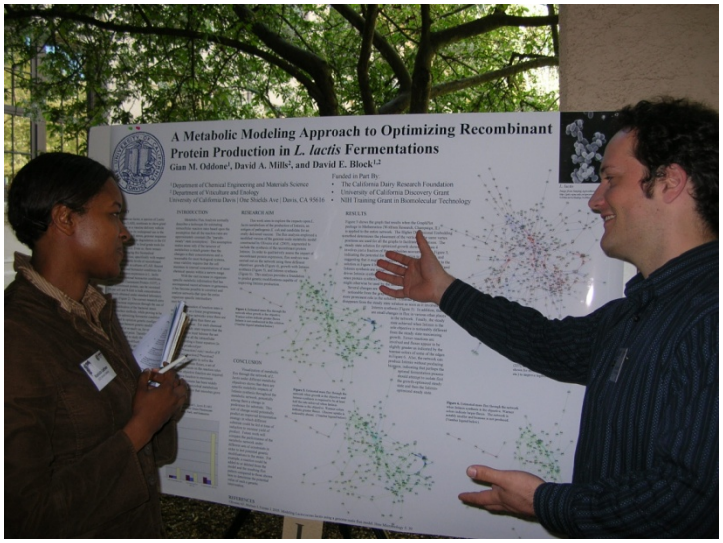
Research as performed in this laboratory was probably funded by a federal agency such as the National Science Foundation. According to the NSF, "Research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. Fabrication is making up results and recording or reporting them. Falsification is manipulating research materials, equipment, or processes or changing or omitting data or results such that the research is not accurately represented in the research record. Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit". Research misconduct does not include honest error or differences of opinion." In 1995, the National Academy of Sciences said that scientists are advised that "someone who has witnessed misconduct has an unmistaken obligation to act." UC Davis policy says this, too. Government regulations require that institutions have systems in place so that individuals are able to report misconduct. Although Peter probably should have spoken to Dr. Osborn when he had initial concerns, there is no evidence of misconduct at this point.

7: If science is self-correcting why are there laws and regulations against misconduct?

In the 80s/90s, several high-profile cases of misconduct became the subject of congressional investigations. Since the Feds fund research with taxpayer dollars, agencies felt that they had to develop regulations addressing how research institutions should deal with misconduct allegations and how oversight departments within federal agencies should monitor the actions of research institutions to investigate accusations.

8: It seems clear that there was a problem with Mary Jane's data. What should Peter do? Should industry's interest have any bearing on this decision?

Peter has several options for how to proceed. First, he should document any allegations that he might have about Mary Jane's findings. Then he should probably relay his concerns to Dr. Osborn, who might follow up with the research- integrity office in his institution. Universities that receive federal funding for research have an office or administrator that addresses allegations of misconduct. When such a situation arises people should bring concerns initially to their departments and, if not resolved at that level, then to OVCR. These offices follow guidelines set by the federal government about various phases in a misconduct allegation, including inquiry, investigation, and adjudication. Sanctions against those who are found guilty of misconduct might range from a reprimand to being barred from obtaining research funding for a period of time. In this case, if misconduct were determined to have occurred, the researcher would also have to contact the journal to retract the false results from the published paper about the enzyme analysis. While industry's interest is irrelevant per se, the commercial potential of carotherase means that it is even more likely any data tampering will come to light and, a fortiori, will call into question the integrity of not just Peter's work but also Dr. Osborn's and the institution's as a whole.




# Poster Abstracts

# A. MULTI-MODAL PROBES FOR THE INTEGRATED ASSESSMENT OF ACTIVATED MICROGLIA IN RELATION TO Aβ ALZHEIMER PLAQUES

**Erica Andreozzi*, Ben Jarrett, Angie Louie**
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Activated microglia have been implicated to have an important role in the neuroinflammatory response associated with disease states such as stroke and Alzheimer's disease (AD). The ability to non-invasively monitor activated microglia during disease progression and therapeutic response is critically important for patient monitoring and also to assess effectiveness of new therapies. Studies have shown that microglia are activated in the presence of senile plaques--currently used for the absolute diagnosis of AD--and that this activation appears to be mediated by macrophage scavenger receptors. Since microglia have been identified as a target for anti-inflammatory drugs as a possible treatment for AD, there is currently great interest for *in vivo* methods to identify senile plaques in order to confirm diagnoses of AD. Our hypothesis is that by targeting novel imaging probes to a type of scavenger receptor (SR-A) that is highly expressed by microglia in AD but not by normal microglia, we will be able to identify activated microglia associated with AD in mouse models. SR-A is upregulated in AD and is believed to be responsible for mediating the interaction of microglia with amyloid β (Aβ) fibrils in plaques. Therefore we propose that SR-A can be used as a target to load microglia with imaging probes to allow *in vivo* visualization of activated microglia associated with senile plaques.

We have generated SRA probes that are based on iron oxide nanoparticles coated with the SR-A ligand dextran sulfate. These are negative contrast agents (reduce signal) which exploit a different MR contrast mechanism and can produce better images where positive contrast fails. We conjugated the dextran sulfate coated iron oxides with the $^{64}$Cu chelating agent *p*-SCN-Bn-DOTA so that $^{64}$Cu can be incorporated to allow imaging with Positron Emission Tomography (PET). While PET will utilized to assess general probe biodistribution, Magnetic Resonance Imagine (MRI) will be investigated for labeling plaques too small to resolve by PET. Probes will be introduced in the presence of mannitol or by intraventricular injection to bypass the blood brain barrier (BBB), but future work will consist of conjugating a synthetic peptide to the probe that facilitates receptor mediated endocytosis across the BBB. Overall, this multimodal imaging approach will allow for the integrated assessment of activated microglia in relation to Aβ plaques in mouse models of AD using MRI and PET. In this way, we can attempt to correlate activated microglia with both senile

plaque location and degree of neurotoxicity. In the future, these probes hold great promise for monitoring activated microglia in AD during disease progression as well as during therapeutic intervention.

* Member of the DEB graduate program

# B. DEVELOPING SYSTEMS FOR BIOPRODUCT REFINING FROM MICROALGAE

**Yu-Shen Cheng*[,1], John Labavitch[2] and Jean S. VanderGheynst[1]**
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Microalgae have remarkable potential for producing biofuels and bioproducts and for sequestering $CO_2$ from industrial flue gases. These features have been considered independent from one another making each use of algae economically impractical. An important goal of our research is to facilitate the harvesting of algal cellular constituents by engineering the timed activation of cell wall polysaccharide auto-disassembly, a process that would make both the sugars and lipids in algae available for conversion to biofuels. The objective of this preliminary study was to examine the effect of light and dark incubation conditions on the polysaccharide composition of *Chlorella vulgaris*. The non-cellulosic neutral sugars (NCNS) in these cultures were identified by gas chromatographic analysis following acid hydrolysis and derivatization. The analysis identified a substantial relative decrease in the NCNS glucose content in the dark-grown cultures, presumably representing starch reserves that were utilized under light-starved conditions. The other NCNS sugars showed a relative increase in the dark cultures, presumably reflecting the decreasing starch content of the wall preparations. Data suggest that the starch content of cultures could account for 75% or more of the NCNS glucose content of wall preparations. Alpha cellulose content was approximately 7% of the cell wall dry weight. The glucose content of the starch in the light-grown culture represented as much neutral sugar as was present in the cellulose and all other non-cellulosic wall polysaccharides combined, suggesting that one benefit from optimization of cell wall deconstruction would be the resulting access of the alga's starch reserves to starch-degrading enzymes for conversion to glucose and fermentation to biofuels.

*** Member of the DEB graduate program**

# C. IMPAIRMENT OF THE DNA REPAIR AND GROWTH ARREST PATHWAYS BY p53R2 SILENCING ENHANCES DNA DAMAGE-INDUCED APOPTOSIS IN p53-DEPENDENT MANNER IN PROSTATE CANCER CELLS

**Hong-Lin Devlin*, Phillip C. Mack, Rebekah A. Burich Paul H. Gumerlock, Hsing-Jien Kung, Maria Mudryj and Ralph W. deVere White**
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**Introduction and objective:** p53R2 is a p53-inducible ribonucleotide reductase that contributes to DNA repair by supplying dNTP pools in response to DNA damage. The purpose of this study was to determine whether silencing p53R2 sensitizes prostate cancer (CaP) cells to ionizing radiation (IR) or to doxorubicin (Dox). **Methods:** LNCaP, its sublines expressing dominant-negative p53 mutant alleles (R273H, R248W, G245S and P151S), CWR22rv1, DU145 and PC3 were studied. Cells were treated with IR or Dox. Gene silencing of p53R2 was achieved using siRNA. Biological effects were investigated by Western blot, flow cytometry, clonogenic assays and DNA repair assays. **Results:** p53R2 was over-expressed in prostate tumor cell lines compared to immortalized prostatic epithelial cells and that the protein was induced upon DNA damage. In LNCaP cells, silencing p53R2 combined with 10Gy IR or 0.5ug/ml Dox enhanced sub-G1 content 5-fold (24.08% ± 1.66%, 48r) post-IR and 2-fold (55.29% ± 4.31%, 48hr) post-Dox. Clonogenic assays showed at least 50% reduction in colony formation following combined p53R2 silencing and different doses of IR (2 and 4Gy) or Dox (0.01 and 0.05ug/ml). This sensitizing effect was specific to DNA damaging agents. Comet assay and γ-H2AX phosphorylation status showed that the decreased p53R2 levels inhibited DNA repair. Silencing p53R2 also reduced the levels of $p21^{WAF1/CIP1}$ at the post-transcriptional level, suggesting links between the p53-dependent DNA repair and the cell cycle arrest pathways. Using LNCaP sublines, we found that the sensitizing effect of p53R2 silencing is mediated by p53-dependent apoptosis pathways. In the sublines R273H, R248W and G245S that have defects in inducing p53-dependent apoptosis, p53R2 silencing did not potentiate DNA damage-induced apoptosis, whereas p53R2 silencing was effective in the subline P151S which retains the ability to induce p53-dependent apoptosis. **Conclusions:** p53R2 is over-expressed in CaP cells. p53R2 silencing sensitizes CaP cells to DNA damaging agents. The mechanism includes retardation of DNA damage repair, elimination of p53-mediated growth arrest induced by p21 and activation of p53-dependent apoptosis. This study demonstrates that p53R2 is a potential therapeutic target to enhance the effectiveness of IR or DNA damaging chemotherapy in a subset of prostate cancer patients.

* Member of the DEB graduate program

# D. USING ETHANOL MOLECULES TO DISRUPT LIPID/ERGOSTEROL INTERACTIONS IN BILAYERS

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Cholesterol, the main sterol component in higher eukaryotes, has a counterpart sterol, ergosterol, that is found in lower eukaryotes (such as yeast). As with cholesterol, ergosterol molecules are important in maintaining the fluidity of plasma membranes and it is interesting to examine changes in the lipid/ergosterol phase diagram resulting from an ergosterol concentration change. Formation of an intedigitated phase, characterized by the intertwining of lipid molecules from opposing bilayer leaflets, may play a role in "stuck fermentations". A stuck fermentation is the wine industry term for a premature stoppage in ethanol production due to unknown metabolic changes in yeast. Yeast membranes consist of 10-25 mol% ergosterol and in a micropipette aspiration experiment conducted at an enological relevant temperature and ~12-16 vol% ethanol, interdigitation between leaflets that contained ~10-25 mol% ergosterol was visible [1]. Hence, induction of this phase may lead to reduced yeast productivity [1]. In this study, we use atomistic Molecular Dynamics simulations to examine the mechanical properties of lipid bilayers that contain ergosterol concentrations of 10, 20, 25 mol% with ethanol concentrations of 0, 10, 15 vol%. We find that the most probable distance between ergosterol and ethanol molecules is 0.75-1.0 nm and this region appears to serve as a buffer between lipid/ergosterol and bulk lipid/lipid interactions.

1.) Biophys. J. 89: 2481-2493.

*** Member of the DEB graduate program**

# E. PH-RESPONSIVE SURFACES FOR PREPARING BIO-MIMETIC DEVICES

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Department of Applied Science[¶]

Plasma membrane bilayers that are found at the cellular surface have the inherent quality of being orthogonally *dynamic*. The *horizontal* fluidity of these membranes are well understood, and mimicked in self-assembled biodevices.[1] The *vertical* dynamics is largely due to the cytosolic side of the membrane interface that is constantly reorganizing its cytoskeletal polymer (e.g., actin). The coupling between membrane and cytoskeleton dynamics gives rise to an impressive set of time-dependent functions, including transport, recognition, and energy transduction. Although many self-assembled biomimetic functional materials have been developed, they are vertically *static*. Examples of systems that are orthogonal dynamic are rare, but it appears may provide a substantial new advance in designing novel biodevices. The following project provides a new class of interfacial structures comprised of two-dimensionally fluid phospholipid bilayer supported on an active substrate capable of undergoing large-scale structural changes via small environmental perturbations. Atom Transfer Radical Polymerization method is employed for the polymerization of pH-responsive poly(methyacrylic acid) brushes off of silicon wafers. [2] Membrane bilayers, with or without transmembrane proteins, are placed on top of these substrates using vesicle fusion technique, figure 1. These types of biodevices can serve as simple templates for understanding individual complications that occur during specific cellular processes.

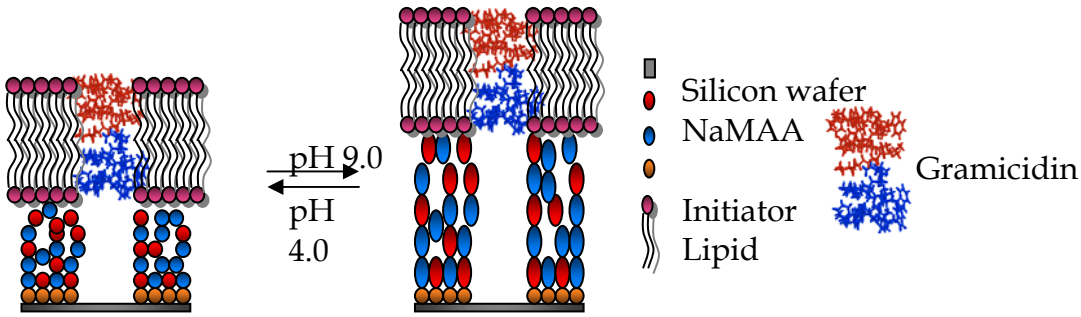


**Figure 1:** Design of pH responsive biomimetic device. Membrane bilayer is impregnated with Gramicidin A proton ion channel, and can be manipulated to vary pH in aqueous region beneath the membrane causing for the polyelectrolyte cushion to increase in height.

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[2] Pucker, O.; Ruhe, J.; Macromolecules, 31, 1998, 592.

# F. STRUCTURAL ANALYSIS OF THE CATALYTIC CYCLE OF HEAVY RIBOFLAVIN SYNTHASE: INSIGHTS INTO QUATERNARY ARRANGEMENT & LIGAND-INDUCED STABILITY

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Throughout the past decade, cryo-electron microscopy (cryoEM) and single particle reconstruction (SPR) techniques have emerged as powerful tools for use in studying the three-dimensional (3D) structures of large-molecular weight, multi-protein complexes. Advantages of cryoEM and SPR in structural determination include the ability to: 1) study proteins within their native, hydrated environments; 2) subject the proteins to varying buffers, pHs, and substrate/ligand conditions; and 3) perform time-dependent experiments with millisecond timescales. With these advantages in mind, our lab has sought to study the catalytic cycle of heavy riboflavin synthase (HRFS) from *Bacillus subtilis* using cryoEM and SPR with the goals of determining the specific protein-protein interactions and rearrangements that occur throughout catalysis. Early physical studies on HRFS have shown that it exists as a capsid of 60 subunits of lumazine synthase (LS) arranged as an icosahedron around a trimer core of riboflavin synthase (RS). Our preliminary studies of weakly-liganded LS capsids (LS in presence of only a single substrate analog) reveal capsids that are heterogeneous in nature, containing projections of varying diameters and degrees of distortion. We hypothesize that the LS capsid is greatly destabilized without the presence of the RS trimer core and/or without the presence of both substrate ligands. In order to solve a stable yet weakly-liganded LS structure, multivariate statistical analysis (MSA) has been utilized to classify particles according to their size variations. Early results using model data have shown that differences in diameter of less than 1% can be accurately classified using MSA. Application of this MSA-based sized sorting technique has now been applied to actual datasets of LSAQ-IDEA insertion mutants and of various quaternary arrangements of sapovirus, and has been found to be capable of successfully sorting particles of varying diameter into unique size classes. Future work will concentrate on the identification and exclusion of distorted particles by using a modified MSA-based protocol.

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# G. NANOFABRICATION OF ORGANOMETALLIC STRUCTURES FOR BIOLOGICAL APPLICATIONS

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With current medical and biological science advances, there is an increasing need for the development and processing of advanced materials that can be used in interdisciplinary biological, electronic and photonic research applications. Hybrid organometallic films have recently attracted considerable attention due to its advantages of both organic materials and inorganic materials, which include the ease in processing, superior resistance to chemicals, and excellent mechanical and optical properties. We have developed a novel methodology to synthesize photo-patternable orgnaometallic thin films. In this technique, a metal-containing polymer thin film is patterned directly on a silicon wafer, and the material can be directly patterned by UV light exposure due to the photoactive compounds contained in the polymer mixture. This process can produce small metal-containing structures down to 1 m in size. In addition to this microprocessing capability, we can also use nanoimprint lithography (NIL) to create nanometer sized features and structures into the coated films – in sizes down to ~50 nm or less in size. As we make advances in the fabrication methods, we hope to reduce this further down to ~10 nm in size. One last characteristic of the film that is attractive, is the ability to remove the organic phase of the polymer through exposure to a simple oxygen plasma. This will leave behind the metal film embedded in a polymer framework.

This approach has the following benefits. First, more than one kind of metal (or organic, metal salt, etc) can be incorporated into the film. These heterogeneous materials can thus be tailored to a wide variety of physical and chemical properties which would otherwise be unobtainable. Second, there is no special equipment required to deposit this hybrid film due to film photosensitive property, and we tremendously simplify fabrication process for devices made from these materials. Finally, the films have excellent chemical resistance to even strong acids and bases, and they can be incorporated into a wide variety of devices.

A wide variety of application areas in the biomedical and biological device industry can make use of these micro- and nano-structured materials and take advantage of their novel properties. We are currently investigating several different lines of research including: (1) chip-based high-throughput screening devices for automated electrophysiology and patch clamp experiments, (2) high-throughput chip-based nano-chemical factories for synthesis of challenging to manufacture compounds of interest to the pharmaceutical industry, (3) fabrication of tagged nano-particles for cellular

imaging contrast agents, (4) miniature chip-based biochemical reaction chambers for diagnostic platforms.

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# H. PLANT CELL SUSPENSION CULTURES AS A BIOPRODUCTION PLATFORM OF RECOMBINANT HUMAN THERAPEUTIC PROTEINS

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Plant cell cultures have been investigated for developing as a potential bioproduction platform of recombinant protein, and especially for human therapeutics due to their intrinsic safety, cost-effective bioprocessing that leads to lower production and downstream costs, and the capacity for post-translation modifications. Plant cell cultures in bioreactors have advantages over whole plant systems for sustained biopharmaceutical production including 1) simplified purification particularly for secreted products; 2) consistency in product yield, quality and homogeneity; 3) ease of compliance with cGMP requirements; 4) easy use of inducible promoter systems; and 5) reduced potential for endotoxin and mycotoxin contamination derived from the plant source or soil bacterium.

To realize using plant cell suspension cultures as alternative to traditional prokaryotic and eukaryotic systems for producing biopharmaceuticals in industry, in this study, we investigated various factors which may affect the expression yield and functionality of a recombinant human blood protein, alpha-1-antitrypsin (AAT), in transgenic tobacco cell suspension cultures. First, we demonstrated that the productivity and functionality of rAAT could be enhanced by using our novel Cucumber mosaic virus (CMV) inducible viral amplicon (CMViva) expression system while comparing with a Cauliflower mosaic virus (CaMV) 35S constitutive promoter expression system or a chemically inducible promoter expression system. Second, to decrease the proteolytic degradation effects and increase the stability of rAAT during plant cell cultures, a rational induction strategy combining medium exchange and pH control was proposed in bioreactor. Third, the timing of induction (TOI) is a critical parameter for chemically inducible plant cell cultures in bioreactor. We applied OUR (oxygen uptake rate) of plant cell cultures as physiology indicator for determining the optimal TOI. Last but not least, amino acids supplied in cultivation medium have been proven that could affect mammalian cells growth and recombinant product yield and quality. We studied the effects of amino acid supplementation on the rAAT production in plant cell cultures using design of experiments (DOE). All of our results have been

investigated and further play a foundation for developing plant cell cultures as a platform of biopharmaceuticals production in industry.

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

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

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

In this study, we showed that the novel chemically inducible viral amplicon system (CMViva) resulted in higher yield of functional extracellular rAAT and higher ratio of functional rAAT to total rAAT (20%~40%) in transgenic *Nicotiana benthamiana* suspension cultures. Furthermore, the pH effect of bioreactor strategy could reduce the

protease activity as well as stabilize the conformation and/or structure of human protein that allow execute its biological function. These results lay the foundation for developing scaleable transgenic plant cell cultures in bioreactors for production of human therapeutics.

* Members of the DEB graduate program

# I. LABORATORY EVOLUTION OF A NOVEL PATHWAY FOR 4-NITROTOLUENE DEGRADATION

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*Acidovorax* sp. strain JS42 utilizes nitrobenzene (NB) and 2-nitrotoluene (2NT) as sole sources of carbon, nitrogen, and energy. Metabolism of both NB and 2NT is initiated by 2-nitrotoluene dioxygenase (2NTDO), which catalyzes the formation of (3-methyl)catechol and the release of nitrite. In a similar reaction, 2NTDO converts 4-nitrotoluene (4NT) into 4-methylcatechol, a growth substrate for JS42. However, the activity of this reaction is over 50-fold less compared to 2NT, and may account for the inability of JS42 to grow on 4NT. To test this hypothesis, spontaneous mutants of JS42 that utilize 4NT as sole source of carbon and energy were obtained by an initial enrichment in liquid culture, followed by continued selection of individual isolates on solid medium. These 4NT+ mutants retained the ability to grow on NB and 2NT. Regulation of the genes encoding 2NTDO was analyzed by growing strains with salicylate, NB, 2NT, 3NT, or 4NT as potential inducers, and quantifying nitrite formation from NB. 2NTDO activity was induced to comparable levels by all five compounds in wild-type JS42 and 4NT+ mutants except for slightly increased induction by 2NT or 3NT in certain mutants. 2NTDO activity was then assayed by providing NB, 2NT, 3NT, or 4NT as biotransformation substrates to induced cultures, and measuring nitrite formation. Dioxygenase activity with 4NT increased 4- to 5-fold in the mutant strains compared to wild-type JS42, while activity with NB, 2NT, and 3NT was largely unchanged. Sequence analysis of the 2NTDO genes from the mutant strains revealed a conserved missense mutation encoding the substitution of methionine 248 by isoleucine. While additional mutations were identified at positions 238 or 242 in some of the 4NT+ mutants, the single M248I change was sufficient to increase 4NT oxidation by 2NTDO. The residue at position 248 is located near the predicted active site of the enzyme; corresponding residues in related enzymes have not been reported to affect substrate specificity or activity. This study expands the range of nitroarene growth substrates for JS42 and reports the first example of a dioxygenase-mediated pathway for 4NT degradation.

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# J. INFERTILITY IN HIGH GROWTH MICE: C57BL/6, FVB, AND A/J STRAINS

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Our laboratory previously discovered that female C57BL/6J high growth (hg) mice produce 40% less offspring than controls due to an inability to form corpora lutea, possibly due to deregulation at the hypothalamic-pituitary axis involving prolactin[1]. To examine the effects on reproduction on a high fecundity genetic background the hg mutation was introgressed into the FVB strain. When FVB-hghg mice were mated with proven breeders, males produced normal, viable pups. Females despite the presence of coital plugs bore no offspring. Dissection of mated female FVB-hghg at 12 weeks revealed no fetal development. Heterozygous +/hg FVB females reproduced normally. A similar female infertility problem was also observed in homozygous A/J-hghg strain females. The high growth mutation includes a deletion of growth and developmental genes *Socs2, Raidd/Cradd* and *Plexin C1*. We hypothesize that complex genetic interactions between the homozygous high growth deletion and the background strain influences fertility. Since it is reported that suppressor of cytokine signaling-2 (*Socs2*) disruption can interfere with prolactin signaling,[3,4] we will investigate the possible interaction of these two metabolic regulators. Our specific aims are to determine: 1) the reproduction stage where FVB-hghg and A/J-hghg mice suffer infertility; 2.) the hormonal differences between wildtype and hghg strains; 3.) the genetic region that plays a role in the infertility phenotype. Currently we are using +hg FVB mice to produce an F2 female population that are hghg and that are recombinants for the FVB and C57BL/6J backgrounds. Metabolic and structural analysis of hghg FVB and A/J strains, and quantitative trait loci analysis of the recombinants will help determine the key processes that contribute to infertility in the high growth mouse model.

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# K EVIDENCE FOR PATERNAL ALLELE-SPECIFIC CHROMATIN EXTENSION AND LOOPING OF THE *SNRPN* TO *UBE3A* LOCUS IN MATURE NEURONS BY FLUORESCENCE IN SITU HYBRIDIZATION

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The human imprinted region 15q11-13, and its murine syntenic counterpart 7qB5, contains a cluster of both paternally and maternally imprinted genes whose complex developmental and tissue specific expression are regulated by small imprinting control regions (ICR) within the cluster. The highly active paternal allele expresses genes up- and down-stream of the IC including a neuron-specific polycistronic transcript containing ~148 exons over ~1Mb, including: the coding sequence for a splicesomal protein (*SNRPN*), clusters of small nucleolar RNAs (*HBII/MBII-13,85,52*), and the antisense transcript to a maternally expressed ubiquitin ligase (*UBE3A -AS*). Several neurodevelopmental disorders are associated with deletions, mutations or aberrant gene expression in this region including Angelman syndrome, Prader-Willi syndrome, autism, and Rett syndrome. It has been proposed that chromatin looping in this region may allow the paternal ICR to bi-directionally regulate gene expression. Utilizing DNA FISH we have found visual evidence for paternal allele-specific chromatin extension and looping of *SNRPN* through *UBE3A* in both human and mouse post-mortem brain. In neurons, the paternal allele was highly extended and looped into the euchromatin while the maternal allele was observed as a single spot found primarily near heterochromatin. The allele-specific chromatin extension increased with brain age and neuronal maturity (~0.5μ at 1d mouse to ~4μ at 10wk), while the maternal allele remained small and compact (~0.5μ at all ages). High concentrations of RNAse A used pre- or post-hybridization did not affect the size of the chromatin structures, demonstrating that the extended signal was due to DNA not RNA. Extended paternal chromatin loops were specific to neurons as they were not found in glial cells, thymus, kidney, liver or spleen. These results suggest dynamic changes in chromatin conformation of the paternal *SNRPN-UBE3A* locus in neurons that may serve to regulate gene expression and imprinting in this region.

* Member of the DEB graduate program

# K. A PLANT-BASED EXPRESSION SYSTEM FOR IN PLANTA PRODUCTION AND LOCALIZATION OF A CELLULOSE-DEGRADING ENZYME

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A high-payoff opportunity for conversion of lignocellulosic materials to biofuels is simplifying the bioconversion process by understanding cell-wall deconstruction enzymes expressed directly in plants. In this project, we propose to use *Agrobacterium* infection to transiently express a cellulase in tobacco leaf cells. The CMViva system has been developed at UC Davis for this purpose, and produces high expression levels of the gene-of-interest. The cellulase will be constructed as a fusion protein with the N-terminal rice a-amylase signal peptide, which targets the enzyme to the cell wall. The cellulase is an endoglucanase from the extremophilic bacteria *Acidothermus cellulolyticus*, and is only active at high temperatures and mildly acidic conditions.

Once expressed and localized, the leaf tissue can be heated and the rate of cellulose degradation can be measured. The impact of constraining the enzyme within the plant cells' apoplastic space and targeting the intracellular side of the cell wall can then be deduced. This work will give us a better understanding of how cellulose-degrading enzymes function within the apoplastic space, and may lead to more efficient generation of fermentable sugars for biofuel production.

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# L OXIDANT SPECIFICITY OF THE ORP1 THIOL PEROXIDASE

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Oxidative stress has been defined as a cellular disturbance in the prooxidant-antioxidant balance in favor of prooxidants. An enormous body of evidence suggests that the production of reactive oxygen species (ROS) induces cellular damage and contributes to the etiology of degenerative diseases such as cancer. Recent studies have demonstrated that ROS, such as hydrogen peroxide and alkyl hydroperoxides, can regulate signal transduction pathways, transcription factors, and gene expression in a variety of prokaryotic and eukaryotic organisms. An enzyme's ability to detoxify various peroxides and regulate peroxide signaling is influenced by its substrate specificity and redox potential, as is the case for the peroxiredoxin family of proteins (1). It is known that cysteine sulfenic acid (S-OH), an important reactive intermediate in redox catalysis and regulation, was detected in the Orp1 oxidation by the chemical 4-nitrobenzo-2-oxa-1,3-diazole (NBD) after exposure to hydrogen peroxide ($H_2O_2$) (2). In the present study, this assay was carried out with *t*-butyl hydroperoxide (t-BOOH) and cumene hydroperoxide (CHP) to assess the substrate specificity of wild-type Orp1, as well as Orp1 containing mutations in key residues (F38A, Q70A, W125A, N126A and F127A). The results indicate that (I) wild-type Orp1 has the similar ability to form S-OH in response to different types of peroxides; (II) Orp1 (F38A) can form S-OH, but formation is dependent on its substrate, with the order of $H_2O_2$>t-BOOH>CHP; and (III) Q70A, N126A and F127A cannot form S-OH in the presence of the three oxidants.

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# M. THE *CAENORHABDITIS ELEGANS* CONVENTIONAL KINESIN LIGHT CHAIN, KLC-2, FUNCTIONS IN NUCLEAR MIGRATION

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Nuclear migration and anchorage are essential cellular processes that affect a number of developmental events and have been linked to human disease. In *C. elegans*, the migration of P-cell nuclei and hyp7 nuclei is dependent on the function of two proteins, UNC-83 and UNC-84. These proteins bridge the nuclear envelope and allow nuclear migration to occur by presumably connecting the cytoskeleton with the nuclear matrix. UNC-83 is recruited to the outer nuclear envelope by the SUN domain of UNC-84. A C-terminal region of UNC-83, known as the KASH domain, is required for its localization, while the N-terminal region of the protein extends into the cytosol. To elucidate the role of the N-terminal portion of UNC-83 in nuclear migration, I performed a yeast-two-hybrid screen for proteins interacting with the N-terminal region of the protein. A portion of the UNC-83 N-terminal domain (aa137-554) was placed into the Invitrogen ProQuest system bait vector and was used to screen a C. elegans cDNA library in the complimentary prey vector. The screen resulted in the identification of 45 potential UNC-83 interacting partners, including KLC-2. KLC-2 interacts with the kinesin heavy chain protein UNC-116 to form a homologue of the mammalian conventional kinesin, or kinesin I. Two mutant alleles of KLC-2, the null *km28* and the hypomorphic *km11*, display defects in hyp7 nuclear migration but not in P-cell nuclear migration. A rabbit polyclonal antibody to KLC-2 is expressed in wild type and the *km11* mutant hyp7 cells in a pattern indicative of exclusion from the nucleus and at least some co-expression with UNC-83. Expression in *km11* mutants is fainter and more punctate compared to wild type. The KLC-2/UNC-83 interaction was mapped using a directed yeast-two-hybrid approach. Amino acids 137-362 of UNC-83 were sufficient to interact with N-terminal portion (aa1-176) of KLC-2. These results will be confirmed by pull-down experiments. These data suggest a model in which UNC-83 functions as a cargo specific adapter to recruit kinesin to the nuclear envelope. Future work to test this model includes characterization of the *km11* allele as well as the construction of a KLC-2-KASH construct and analysis of its ability to rescue nuclear migration in UNC-83 mutants.

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# N. STRUCTURE DETERMINATION OF HIV-1 gp140 ENVELOPE PROTEIN BY SINGLE PARTICLE RECONSTRUCTION

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Human immunodeficiency virus (HIV) has affected over 40 million people worldwide with more than 20 million having perished due to its debilitating effects on the immune system. A promising research target for vaccination is the Env protein: the envelope spike gp120 and the transmembrane protein and linker gp41. Upon binding of HIV to T-cell lymphocyte CD4 receptors and chemokine coreceptors, these proteins mediate membrane fusion via conformational rearrangement, enabling the insertion of the RNA genome into the host cell. The aim of this project is to elucidate the tertiary fold and quaternary arrangement of Env in its native, unbound state by single particle reconstruction. A successful structure would greatly aid in vaccine research toward developing neutralizing antibodies against conformational epitopes that are discovered. The capability of cryoelectron microscopy (cryoEM) to keep samples hydrated in their native conformational state will allow for an accurate representation of the envelope proteins, which can be compared to the existing X-ray crystallography model of unbound monomeric gp120 for validation. Single particle reconstruction entails combining electron microscopy images of a biological specimen obtained from many different orientations to generate a three-dimensional model using computer-based algorithms. Using deep salt-stained samples of gp140, a non-covalent construct comprised of gp120 and the ectodomain of gp41, a low resolution model (~2.3 nm) has been achieved using ~19000 particle images. The model displays a trimeric arrangement and obvious handedness, and can be used as a suitable starting model for cryoEM, where images have poorer contrast but contain higher resolution information.

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# O. PREDICTING *L. LACTIS* STRAIN IMPROVEMENTS USING METABOLIC FLUX BALANCING

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*Lactococcus lactis*, a species of Lactic Acid Bacteria (LAB), continues to show great promise for use as a vaccine delivery vehicle thanks to its widespread use in the dairy industry, GRAS status, genome sequence availability, resistance to degradation in the GI tract, and susceptibility to food grade tools for genetic modification. Even so, there remain obstacles on the path that will bring this biomedical application to fruition. The currently attainable level of recombinant protein per cell severely undershoots the levels typical of production organisms such as *E. coli* and has been suggested to be a crucial parameter in studies of vaccine efficacy and specificity. Metabolic flux balancing is a powerful analytic tool that has been used successfully both to measure rates of intracellular biochemical reactions and to predict the consequences of genetic modifications affecting the central metabolism. In this work, a predictive computational model of fermentation performance has been constructed by applying time-stepped metabolic flux balancing to the genome-scale metabolic network of *L. lactis.* This metabolic model permits the visualization of intracellular carbon flux under different cellular objectives and the prediction of fermentation performance under different environmental or genetic conditions. The fermentation performance of genetically modified strains of *L. lactis* expressing the model Green Fluorescent Protein will be evaluated in order to test the ability of the metabolic model to drive strain improvement.

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# P. INTERSURFACE MEASUREMENTS OF LIQUID PHASE SUPPORTED MEMBRANES COATED WITH PEG2000

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The interaction between bilayers coated with PEG polymers is important for drug delivery applications as PEG functionalized bilayers are commonly used to extend the circulation time of liposomes. The Surface Force Apparatus was used to measure the intersurface forces between liquid phase bilayers coated with PEG-polymer. The force-distance profiles show the presence of electrostatic and steric repulsions that arise from the presence of the polymer chains, a similar behavior to experiments carried out with solid phase lipids. Liquid-phase bilayers have high lateral diffusion relative to gel phase bilayers, thus a quantitative comparison demonstrates a greatly reduced rate of diffusion for the liquid-phase lipids. It is believed that at a much slower intersurface rate of approach, the force profile between the PEGylated liquid-phase bilayers should be similar to the force-profile between two bare bilayers. Our results demonstrate that the diffusion of PEG-lipids is substantially reduced and suggests that lateral friction between the polymer chains is significant.

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# R. BACTERIAL NANOGLUE FOR SELF-ASEEMBLY OF MICROSTRUCTURES

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As the development of minimally-invasive implants and shape-specific porous scaffolds increases, micro- and nanoscale fabrication become attractive methods for creating controlled microscopic structures. Microfabrication, as developed for semiconductor technology, is limited for several reasons: it is difficult to create complex nonplanar 3D architecture, and the limited palette of compatible materials constrains the use of many biocompatible materials. A promising solution to these limitations lies in the field of self-assembly, the spontaneous ordering of small systems to minimize their surface energy. This tendency can be observed on a molecular level in the assembly of biological macromolecule complexes, and in other biochemistry molecular self-assembly. On the microscale, ordered and complex three-dimensional structures can be self assembled by designing compatibly-shaped parts and applying a randomizing energy. An additional mechanical stabilizing force is required on the microscale to make the structures permanent. Few biocompatible methods of microscale stabilization have been explored in the literature.

In the current work, we test the hypothesis that the secretions of micro-organisms can be used as an adhesive to stabilize self-assembled structures. Our proof of concept uses the polysaccharide secretion of the ubiquitous and nontoxic bacteria *Caulobacter crescentus* as a method of affixing a simple self-assembled system of two interlocking PDMS pieces. This work lays the foundation for future exploration of hands-off bottom-up assembly of complex microarchitectures of biocompatible material, suitable for *in vivo* assembly and direct mechanical interaction with existing tissue and regenerative cells.

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# S. THE ROLE OF THE MUS81-MMS4 ENDONUCLEASE IN REINITIATION AND REPAIR OF STALLED REPLICATION FORKS

**Erin K. Schwartz* and Wolf-Dietrich Heyer**
Department of Microbiology, University of California, Davis

Stabilization and reinitiation of stalled replication forks are critical for maintaining genomic stability. The structure-selective endonuclease, Mus81, and its partner, Mms4 (Eme1), has been suggested to be involved in stalled replication fork processing. A physical interaction between Mus81 and the recombination-mediated DNA repair enzyme, Rad54, lead to its original discovery in the laboratory of Dr. Wolf-Dietrich Heyer and suggests that Mus81-Mms4 could be recruited to stalled replication forks to process DNA-joint molecules involved in recombination-mediated repair. In the fission yeast *Schizosaccharomyces pombe*, Mus81 also physically interacts with the checkpoint protein, Cds1, which leads to a checkpoint-dependent phosphorylation shift of both Mus81 and Mms4 subunits upon treatment with methyl methanesulfonate (MMS) and hydroxyurea (HU). This checkpoint dependent phosphorylation is not observed to significantly affect Mus81-Mms4 activity on DNA substrates *in vitro* and alternatively may regulate Mus81 localization to its substrates. I hypothesize that Mus81-Mms4 is recruited to the sites of stalled replication forks in a checkpoint- and Rad54- dependent manner to facilitate homologous recombination-mediated replication fork restart by cleaving specific branched structures involved in the repair. To test this hypothesis, I will use *S. cerevisiae* as a model system to (1) directly test for Mus81 association with the replication fork and determine the regulatory mechanisms controlling its association, (2) develop a mechanism for substrate specificity by determining Mus81's in vitro protein structure and in vivo oligomeric association and (3) dissect the potential early and late roles of Mus81 activity relative to the initiation of recombination during the repair of stalled replication forks.

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# T. DEVELOPING AN ALLOSTERIC REGULATORY MECHANISM FOR ENGINEERED ZINC FINGER PROTEINS

**Sarah Lockwood* and David Segal**
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The Segal Lab designs chimeric zinc finger DNA binding proteins. Engineering these proteins has many practical applications, including imaging/sequence detection. This can be achieved by attaching various proteins and/or enzyme functional domains to produce a desired activity at zinc finger-specified sequences. 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 complex. However, one complication with this system is β-lactamase reassembly in solution without having bound to 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 target. Using this information, we plan to attach catalytic inhibitory and complimentary 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 one being inhibitory. In the presence of DNA, the zinc fingers will tightly bind to their target sequence 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 the target sequence. We anticipate a significant improvement in assay sensitivity.

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# U. EXERCISING SPATIOTEMPORAL CONTROL OF CELL ADHESION TO OPTICALLY TRANSPARENT MICROELECTRODES

**Sunny Shah*[1], Ji Youn Lee[1], Nazgul Tuleuova[1], Mark Zern[2] and Alexander Revzin[1]**

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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 hESC. 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.

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# V. A KINETIC MODEL OF THE T-DNA SECRETION PATHWAY OF *AGROBACTERIUM TUMEFACIENS*

**Chris 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 the kinetics of gene transfer from *A. tumefaciens* to plant cells. In the process, we plan to create a methodology for identifying the rate limiting steps in the gene secretion pathway that act to reduce transformation efficiency in various plants. During agroinfiltration, genetic material from *Agrobacterium*, the transferred strand (T-strand), is exported from the bacteria into plant cells. Ultimately, genes housed on the T-strand may be expressed by the infected plant cells via transient expression. A variety of virulence (Vir) proteins encoded by *Agrobacterium* facilitate this DNA secretion pathway. Unique Vir proteins form complexes with the T-strand at distinct steps in the pathway. Immunoprecipitation will be used to isolate T-strands at key pathway steps from extracts of agroinfiltrated plant tissue based on their associations with certain Vir proteins. Once isolated, quantitative PCR will be used to determine the concentration of T-strands at each pathway step. We will collect T-strand concentration data over time for each pathway step. This data will be used to fit parameters in a power-law mass balance describing the flux of T-strands through each step of the agroinfiltration pathway. This model will allow us to determine which stage of the pathway is rate-limiting with regards to T-strand insertion into plant cells. As a result, the model will be a powerful tool for optimizing *in planta* transient expression of agroinfiltrated genes and will have implications for many industries, including the biopharmaceutical and biofuel industries, where plant-based transient expression may be desirable.

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# W. CRYSTAL STRUCTURE BASED MUTAGENESIS OF RecBCD ENZYME REVEALS RESIDUES THAT ARE RESPONSIBLE TO THE RECOGNITION OF THE REGULATORY SEQUENCE, χ

**Liang Yang[1*], Naofumi Handa[1,2], Mark S. Dillingham[1,3], Dale B. Wigley[4] and Stephen C. Kowalczykowski[1]**

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The RecBCD enzyme is a complex heterotrimeric helicase/nuclease that initiates homologous recombination at double-stranded DNA breaks in *Escherichia coli*. Several of its activities are regulated by the DNA sequence χ (5′-GCTGGTGG-3′), which is recognized in *cis* by the translocating enzyme. Upon recognition of χ, the nuclease polarity of RecBCD is switched, the translocation rate is reduced, most importantly, RecBCD gains the ability to load RecA onto the χ-containing, unwound single-stranded DNA. Previous studies argue that RecC subunit recognizes χ. Recent published crystal structure revealed that after duplex DNA is split by the helicase function, the two nascent ssDNA strands are fed into two tunnels that propagate right through the RecBCD duplex, and then presented to the nuclease domain at the rear of the enzyme. The channel that is passed through by the 3'ssDNA has a putative "Chi-scanning site" which searches for a correctly oriented recombination spot. Here we did site-directed experiments to identify the residues responsible for the nucleotide sequence recognition. Based on the crystal structure, thirty-seven residues on the channel surface were substituted with alanine one at a time. Genetic analyses were applied to screen for mutations that cannot recognize χ sequence, but retain recombination proficiency and the nuclease activity. The mutants were characterized *in vitro* with purified proteins to confirm the phenotype. Our work verified that seven residues on the RecC channel are essential for χ recognition. These findings accompanied with the position at the structure provide a new insight into how the enzyme recognizes the specific sequence and induces conformational/functional alterations.

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# X. ADAPTATION OF MACHINE LEARNING ALGORITHMS FOR SPECTROMETER DATA ANALYSIS

**Weixiang Zhao[1]*, Abhinav Bhushan[1]*, Shankar Sankaran[1], Susan Ayer[1], Ana Maria[2], Abhaya Dandekar[2], and Cristina Davis [†,1]**
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Metabolomics is becoming a core and attractive field of modern bioscience studies. The development of complex biological instrumentation and chemical sensors allow us to generate large amounts of complex data. Metabolomics is increasingly reliant on powerful information processing tools, and we often refer to these methods as "data mining" techniques. This poster aims to introduce some novel data mining or machine learning methods and illustrate their applications to spectrometer data analysis in the bioscience field.

First, auto-regressive (AR) model has been introduced to the feature extraction of chromatogram data. In this study, four types of bacteria were characterized by applying gas chromatography/mass spectrometer (GC/MS) to their headspace gas above the proliferating cell culture samples. The successful application of this method to the classification of the four types of bacteria (with the accuracy being over 95%) demonstrates: (1) this feature extraction method is able to free us from time alignment in signal processing, which is the most significant advantage of this method; (2) this feature extraction method does not need to be coupled with specific classification models, which would ensure the wide application of this method; (3) this method shows its robustness in terms of modeling parameters and resistance of possible noise.

Second, genetic algorithm and swarm intelligence approaches were coupled with neural network models. We have shown feasibility to distinguish virus from protein (94% accuracy) through detecting discernable biomarkers from their original three dimensional pyrolysis/gas chromatography/differential mobility spectrometry (pyrolysis/GC/DMS) data. The success of this study provides a promising strategy to detect discernable biomarkers for the complex bio-systems, especially those with noise contamination.

Third, wavelet analysis has been successfully applied to the classification of the fruit samples analyzed via GC/DMS. This study suggests: (1) wavelets are an effective image analysis tool, and are also feasible to process three dimensional GC/DMS data; and (2) wavelet analysis not only significantly reduces sample data dimensions but also shows an even better classification effects than conventional methods. Essentially different from conventional feature extraction methods like principal component analysis (PCA), these novel methods will be greatly beneficial to the mining of

complex and high dimensional spectrometry data in the bioscience field. Our group continues to apply and develop more advanced machine learning methods for metabolomics studies.

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UCDAVIS Biotechnology Program

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Novozymes, Inc

**These Biotechnology companies have donated at least $20,000 per year for a Biotechnology fellowship and/or 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 educational programs.

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

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- 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.

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

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

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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

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

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

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### Mission

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

### Leadership Strategy

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

### Ethical Standards

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

### Values

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

### Quality

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

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

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## The Mission of the Biotechnology Program:

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

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

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- NIH Training Program in Biomolecular Technology for PhD students
- **BioTech SYSTEM** – K-14 educational consortium

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## *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*

**Directorship of Bruce Hammock**
**Co-Directors are 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**

**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**

Plant Sciences – Vegetable Crops

**David Mills**
Viticulture & Enology

**Atul Parikh**
Applied Scienc

**Katherine Pollard**
Statistics

**Martin Privalsaky**
Microbiology

**Robert Rice**
Environmental Toxicology

**David Rocke**
Applied Science

**David Segal**
Pharmacology

**Simon Scott**
Biomedical Engineering

**Henning Stahlberg**
Molecular & Cellular Biology

Molecular & Cellular Biology

**Michael Toney**
Chemistry

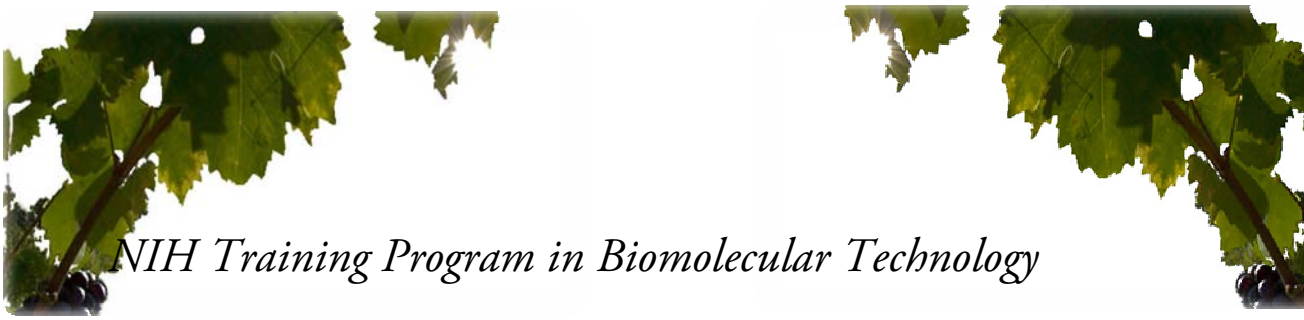
**Jean VanderGheynst**
Biological & Agricultural Engineering

**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 nurturing interactive environment to promote integration of multiple disciplinary approaches to the conduct of research and to promote learning in biotechnology. The mission is to prepare well-educated students to approach problems with creativity and flexibility. The program will provide tools for the students to be leaders, visionaries, entrepreneurs, researchers and teachers in the broad area of biomolecular technology.

### DEB Mission:

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

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

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

Students come from a wide array of disciplines: Participating graduate programs currently include **25 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; Entomology; Genetics; Immunology; Materials Science and Engineering; Mechanical and Aeronautical Engineering; Food Science; Microbiology ; Molecular, Cellular and Integrative Physiology (formerly Physiology); Nutrition; Pharmacology & Toxicology; Plant Biology; Plant Pathology; and Statistics. The DEB program supplements a student's Ph.D. curriculum and those completing the

program will obtain an official designation on their diploma & transcript indicating a qualification in biotechnology. Example: **Doctoral Degree in Microbiology with a Designated Emphasis in Biotechnology**

## Brief History:

The DEB was formally established in 1997 as an outgrowth of the first NIH Training Grant in Biotechnology (funded in the early 1990s). The DEB became the formal training program for the current NIH Training Grant in Biomolecular Technology (1-T32-GM08799: July 1, 2002-June 30, 2007). The DEB provides a very effective multidisciplinary biotechnology concentration, which includes exposure to bioethics, business and legal aspects of biotechnology as well as a 3-6 month internship in a biotechnology company or research laboratory in another college or national laboratory. As of March 2007 the DEB has 24 affiliated graduate groups or departmentally based graduate programs and we are in the process of adding Electrical & Computer Engineering. The number of students in the Designated Emphasis in Biotechnology has increased dramatically over the last two years and now boasts 114 members, with many being first year students. We have graduated 38 students with a DEB notation on their diplomas as of December of 2003.

## Program Administration:

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

## Course Work:

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

We have created a website for the Designated Emphasis in Biotechnology (http://www.deb.ucdavis.edu/) to advertise the program as well as the NIH Training Grant. The announcement of the grant is on the site. Program information, forms, pictures and other pertinent information is listed on the site. We have linked the website to graduate home pages of most of the 24 DEB program affiliates in the Division of Biological Sciences, College of Engineering, College of Letters and Science and the College of Agriculture and Environmental Sciences.

1. Course Requirements:

a. MCB 263 (2 units): Biotechnology Fundamentals and Application (winter quarter, every year)

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

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

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

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

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

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

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

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

The course will allow the student to become familiar with their roles and responsibilities as a professional scientist and/or instructor. While some standards of acceptable scientific behavior will be presented in class, most of the time will be spent discussing various "gray zone" scenarios, in which proper conduct is unclear. Grading: S/U grading; active class participation in class discussions is required. **This course is required. Approved substitutes for GGG 296 are 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 2008*

**Erica Andreozzi**
Biomedical Engineering

**Lucas Arzola**
Chemical Engineering

**Suzanne Barber**
Chemical Engineering

**Don Barkauskas**
Biostatistics

**Sandra Bennun Serrano**
Chemical Engineering

**Zachary Bent**
Microbiology

**Crystal Berger**
Biochemistry & Molecular Biology

**Craig Blackmore**
Comparative Pathology

**Jennifer Bratt**
Biochemistry & Molecular Biology

**Monica Britton**
Genetics

**Timothy Butterfield**
Plant Biology

**Milo Careaga**
Immunology

**Anna Cartier**
Plant Biology

**Jennifer Cash**
Chemistry

**Shannon Ceballos**
Cellular & Developmental Biology

**Jeffrey Chan**
Immunology

**Astra Chang**
Molecular, Cell. & Integrative Physiology

**Chao Yu Chen**
Pharmacology & Toxicology

**Honglin Chen**
Genetics

**Ying Chen**
Statistics

**Yu-Shen Cheng**
Biological Systems Engineering

**Dawn Chiniquy**
Plant Biology

**Ryan Davis**
Chemistry

**Noah Decker**
Nutritional Biology

**Allison Dickey**
Chemical Engineering

**Kevin Dietzel**
Microbiology

**Corey Dodge**
Chemical Engineering

**Matthew Doherty**
Microbiology

**Meghan Dukerich**
Biochemistry & Molecular Biology

**Erin Easlon**
Biochemistry & Molecular Biology

**Rita El-khouri**
Chemistry

**James Elmore**
Plant Pathology

**Xin Fei**
Agricultural & Environmental Chemistry

**Wen-Ying Feng**
Biostatistics

**Erik Fostvedt**
Biochemistry & Molecular Biology

**Paula Garay**
Biochemistry & Molecular Biology

**Prasad Gawande**
Chemistry

**Laura Gillies**
Food Science& Technology

**Tiffany Glavan**
Microbiology

**Elianna Goldstein**
Plant Biology

**Dmitry Grapov**
Agricultural & Env. Chemistry

**Robin GrayMerod**
Civil & Environmental Engineering

**Dominik Green**
Biochemistry & Molecular Biology

**Pradeepa Gunathilake**
Plant Biology

**Brian Hamilton**
Biochemistry & Molecular Biology

**Scott Hamilton**
Biochemistry & Molecular Biology

**Huilan Han**
Mechanical & Aeronautical Engineering

**Victor Haroldsen**
Biochemistry & Molecular Biology

**Christine Hastey**
Microbiology

**Kristina Herzberg**
Biochemistry & Molecular Biology

**Laura Higgins**
Molecular, Cell. & Integrative Phys.

**Thomas Hill III**
Pharmacology & Toxicology

**Laura Ho**
Pharmacology & Toxicology

**Kevin Holden**
Microbiology

**Reef Holland**
Microbiology

**Matthew Hoopes**
Biophysics

**Jessica Houghton**
Pharmacology & Toxicology

**Michael Howland**
Chemical Engineering

**Ting-Kuo Huang**
Chemical Engineering

**Patty Hwang**
Biochemistry & Molecular Biology

**Darren Hwee**
Molecular, Cell. & Integrative Phys.

**Tatz Ishimaru**
Cell & Developmental Biology

**Connie Jen**
Biochemistry & Molecular Biology

**Roger Jesinghaus**
Chemistry

**Geetika Joshi**
Soils Biochemistry

**Kou-San Ju**
Microbiology

**Yun Joon Jung**
Biomedical Engineering

**Michael Kareta**
Biochemistry & Molecular Biology

**Kavya Katipally**
Biomedical Engineering

**Robert Kauffman**
Microbiology

**Rachel Kerwin**
Plant Biology

**Saeed Khazaie**
Chemistry

**Pavan Kumar**
Plant Biology

**Rashida Lathan**
Animal Biology

**Nathaniel Leachman**
Cell & Developmental Biology

**Vannarith Leang**
Chemical Engineering

**Cheng-Yuk Lee**
Chemical Engineering

**Karen Leung**
Genetics

**Ben Lindenmuth**
Chemical Engineering

**Song Liu**
Agricultural & Environ. Chemistry

**Xianxian Liu**
Microbiology

**Riccardo LoCascio**
Microbiology

**Sarah Lockwood**
Biochemistry & Molecular Biology

**Artem Loukoianov**
Genetics

**Thomas Luu**
Biochemistry & Molecular Biology

**Kristina Mahan**
Biochemistry & Molecular Biology

**Phillip Matern**
Molecular, Cell. & Integrative Phys.

**Marina Meyerzon**
Genetics

**Mary Moore**
Biochemistry & Molecular Biology

**Jeffrey Myers**
Genetics

**Gian Oddone**
Chemical Engineering

**David Olivos**
Comparative Pathology

**Raquel Orozco-Alcaraz**
Chemical Engineering

**Cecilia Osorio**
Plant Biology

**Emily Pfeiffer**
Biomedical Engineering

**Jennifer Phipps**
Biomedical Engineering

**Warren Place**
Microbiology

**Dante Placido**
Microbiology

**Michael Plesha**
Chemical Engineering

**Stephanie Pulford**
Mechanical & Aeronautical Engin.

**Joseph Ramahi**
Cell & Developmental Biology

**Kittipong Rattanporn**
Chemical Engineering

**Wade Reh**
Genetics

**Ron Runnebaum**
Chemical Engineering

**Juan Pedro Sanchez**
Plant Biology

**Mary Saunders**
Comparative Pathology

**Erin Schwartz**
Biochemistry & Molecular Biology

**Andres Schwember**
Plant Biology

**David Sela**
Microbiology

**Sunny Shah**
Biomedical Engineering

**Laura Shih**
Biomedical Engineering

**Jillian Silva**
Biochemistry & Molecular Biology

**Chris Simmons**
Biological Systems Engineering

**Padmini Sirish**
Molecular Cell. Integrative Phys.

**Cheng Song**
Cellular & Developmental Biology

**Zane Starkewolfe**
Chemistry

**Sarah Statt**
Biochemistry & Molecular Biology

**James Stice**
Molecular Cell. & Integrative Phys.

**Wesley Sughrue**
Biochemistry & Molecular Biology

**Anandkumar Surendrarao**
Plant Biology

**Mimi Swe**
Nutritional Biology

**Christina Takanishi**
Cell & Developmental Biology

**Erin Tapley**
Cell & Developmental Biology

**Jared Townsend**
Biochemistry & Molecular Biology

**Vu Trinh**
Biochemistry & Molecular Biology

**Breanna Wallace**
Molecular Cell. & Integrative Phys.

**Don-Hong Wang**
Genetics

**Jennifer Warren**
Civil & Environmental Engineering

**Monica Watson**
Molecular Cell. & Integrative Phys.

**Ambrose Williams**
Biochemistry & Molecular Biology

**Kelly Williams**
Biological & Agricultural Engineering

**David Woessner**
Microbiology

**Andrew Wong**
Genetics

**Jimmy Wu**
Pharmacology & Toxicology

**Daisy Wu**
Pharmacology & Toxicology

**Bei Xiang**
Chemical Engineering

**Liang Yang**
Biochemistry & Molecular Biology

**Long Ye**
Chemistry

**Chao Wei Yu**
Biological Systems Engineering

**Kseniya Zakharyevich**
Microbiology

**Tracy Zeng**
Microbiology

**James Zhu**
Biomedical Engineering

## *DEB Faculty Participants*

**Steffen Abel**
Vegetable Crops& Weed Science

**Gary Anderson**
Animal Science

**Matthew Augustine**
Chemistry

**Alan Balch**
Chemistry

**Enoch Baldwin**
Molecular & Cellular Biology

**Everett Bandman**
Food Science & Techonology

**Abdul Barakat**
Mechanical & Aeronautical Engineering

**Diane Barrett**
Food Science & Technology

**Peter Barry**
Center for Comparative Medicine

**Stephen Barthold**
Pathology, Microbiology & Immunology

**Ronald Baskin**
Biophysics,

**Nicole Baumgarth**
Pathology, Microbiology & Immunology

**Blaine Beaman**
Microbiology & Immunology

**Craig Benham**
Biomedical Engineering/Genome Center

**Alan Bennett**
Plant Science

**Linda Bisson**
Viticulture & Enology

**David Block**
Viticulture & Enology

**Sue Bodine**
Neurology, Physiology & Behavior

**Richard Bostock**
Plant Pathology

**Kent Bradford**
Vegetable Crops

**George Bruening**
Plant Pathology

**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

**Xinbin Chen**
Comparative Oncology

**Holland Cheng**
Molecular & Cellular Biology

**Nipavan Chiamvimonvat**
Internal Medicine

**Andrew Clifford**
Nutritional Biology

**Gitta Coaker**
Plant Pathology

**Douglas Cook**

Plant Pathology

**Gino Cortopassi**
VM: Molecular Biosciences

**John Crowe**
Molecular & Cellular Biology

**Abhaya Dandekar**
Pomology

**Satya Dandekar**
Medical Microbiology & Immunology

**Cristina Davis**
Mechanical & Aeronautical Engineering

**Scott Dawson**
Microbiology

**Katayoon Dehesh**
Plant Biology

**Wenbin Deng**
Cell Biology & Human Anatomy

**Michael Denison**
Environmental Toxicology

**Thorsten Dieckmann**
Chemistry

**Stephanie Dungan**
Food Science & Technology

**Don Durzan**
Environmental Horticulture

**Jason Eiserich**
Internal Medicine

**Nael El-Farra**
Chemical Engineering & Material Science

**Bryce Falk**
Plant Pathology

**Roland Faller**
Chemical Engineering & Material Science

**Peggy Farnham**
Medical Pharmacology & Toxicology

**Katherine Ferrara**
Biomedical Engineering

**Oliver Fiehn**
Genome Center

**Andrew Fisher**
Chemistry

**Paul Fitzgerald**
Cell Biology & Human Anatomy

**Ching Yao Fong**
Physics

**David Furlow**
Neurobiology, Physiology & Behavior

**Charles Gasser**
Molecular & Cellular Biology

**Shu Geng**
Agronomy & Range Science

**Bruce German**
Food Science & Technology

**Jacquelyn Gervay-Hague**
Chemistry

**David Gilchrist**
Plant Pathology

**Tom Gradziel**
Pomology

**Jeffrey Gregg**
Pathology

**Paul Gumerlock**
Hematology & Oncology

**Bruce Hammock**
Entomology

**Stacy Harmer**
Plant Biology

**Richart Harper**
Pulmonary/Critical Care Medicine

**Volkmar Heinrich**
Biomedical Engineering

**Wolf-Dietrich Heyer**
Microbiology

**You-Lo Hsieh**
Textiles & Clothing

**Neil Hunter**
Microbiology

**Kentaro Inoue**
Plant Sciences

**Roslyn-Rivkah Isseroff**
Dermatology

**Thomas Jue**
Biochemistry

**Clarence Kado**
Plant Pathology

**Carl Keen**
Nutrition

**Ian Kennedy**
Mechanical & Aeronautical Engineering

**Dan Kliebenstein**
Vegetable Crops & Weed Science

**Anne Knowlton**
Cardiovascular Medicine

**Patrice Koehl**
Computer Science

**Stephen Kowalczykowski**
Microbiology

**Tonya Kuhl**
Chemical Engineering & Materials Science

**Hsing-Jien Kung**
Biochemistry

**Clark Lagarias**
Molecular & Cellular Biology

**Kit Lam**
Hematology & Oncology

**Janine LaSalle**
Microbiology & Immunology

**Jerold Last**
Internal Medicine

**Carlito Lebrilla**
Chemistry

**Noelle L'Etoile**
Center for Neuroscience

**Ronald Li**
Cell Biology & Human Anatomy

**Su-Ju Lin**
Center for Genetics & Devlopment

**Bo Liu**
Plant Biology

**Gang-Yu Liu**
Chemistry

**Marjorie Longo**
Chemical Engin. & Material Sciences

**Angelique Louie**
Biomedical Engineering

**Paul Luciw**
Pathology

**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

**Marion Miller-Sears**
Environmental Toxicology

**David Mills**
Viticulture & Enology

**Terence Murphy**
Plant Biology

**James Murray**
Animal Science

**Krishnan Nambiar**
Chemistry

**Thomas North**
Center for Comparative Medicine

**Martha O'Donnell**
Physiology & Membrane Biology

**David Ogrydziak**
Food Science & Technology

**Rebecca Parales**
Microbiology

**Atul Parikh**
Biomedical Engineering

**Anthony Passerini**
Biomedical Engineering

**Timothy Patten**
Chemistry

**Niels Pedersen**
Medicine & Epidemiology

**Ronald Phillips**
Chemical Engin. & Material Sciences

**Martin Privalsky**
Microbiology

**David Reid**
Food Science & Technology

**Michael Reid**
Environmental Horticulture

**Alexander Revzin**
Biomedical Engineering

**Robert Rice**
Environmental Toxicology

**Subhash Risbud**
Chemical Engin. & Material Science

**David Rocke**
Inst. for Data Analysis & Visualization

**Raymond Rodriguez**
Molecular & Cellular Biology

**Pamela Ronald**
Plant Pathology

**Robert Rucker**
Nutritional Biology

**John Rutledge**
Endocrinology

**Dewey Ryu**
Chemical Engin. & Material Science

**Earl Sawai**
Chemical Engin. & Material Science

**Kate Scow**
Land, Air & Water Resources

**David Segal**
Pharmacology

**Kazuhiro Shiozaki**
Microbiology

**Scott Simon**
Biomedical Engineering

**David Slaughter**
Biomedical & Agricultural Engineering

**Jay Solnick**
Infectious & Immunological Diseases

**Henning Stallberg**
Molecular & Cellular Biology

**Daniel Starr**
Center for Genetics & Development

**Francene Steinberg**
Nutrition

**Pieter Stroeve**
Chemical Engin. & Material Science

**Gang Sun**
Textiles & Clothing

**Alice Tarantal**
Pediatrics, School of Medicine

**Steven Theg**
Plant Biology

**Michael Toney**
Chemistry

**Jose Torres**
Microbiology & Immunology

**Renee Tsolis**
Microbiology & Immunology

**Richard Tucker**
Cell Biology & Human Anatomy

**Alison Van Eenennaam**
Animal Science

**Jean VanderGheynst**
Biological & Agricultural Engineering

**Patricia Wakenell**
VM: Population Health & Reproduction

**Robert Weiss**
Internal Medicine

**Valerie Williamson**
Nematology

**Barry Wilson**
Animal Science & Environ. Toxicology

**David Wilson**
Molecular & Cellular Biology

**Matthew Wood**
Environmental Toxicology

**Reen Wu**
Pulmonary & Critical Care Medicine

**Stefan Wuertz**
Civil & Environmental Engineering

**Yin Yeh**
Applied Science

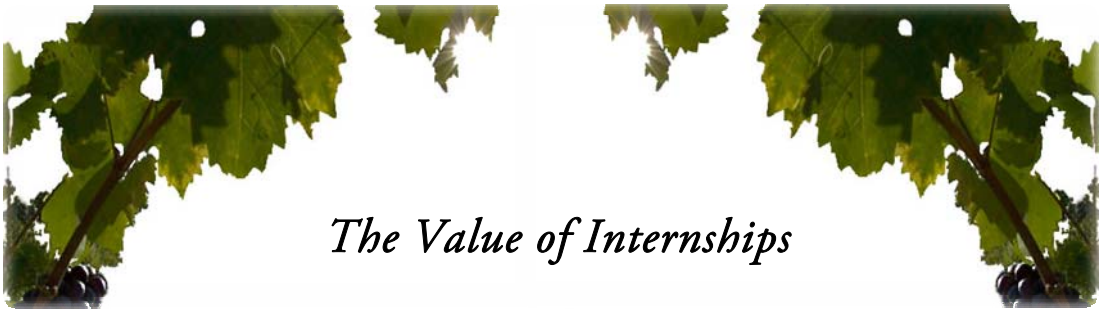
**Tilahun Yilma**
VM: Pathology, Micro. & Immunology

**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 15 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 150 students enrolled, so we need more Academic-Industry Partnerships.