Nineteenth Annual

# Biotechnology Training Retreat

Saturday,
March 27, 2010

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

# Nineteenth Annual Biotechnology Training Retreat

Co-sponsored by:

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

UC Davis Designated Emphasis in Biotechnology
Graduate Program (DEB)

UC Davis Biotechnology Program

# Table of Contents

# *2010 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 **2009-10 fellows and their preceptors**, as well as **our industry affiliates**. We also welcome the faculty and trainees associated with the NSF CREATE-IGERT Training Program (directed by Karen McDonald), as they are also members of the DEB program. It is hard to believe that we have been holding this retreat for the past 19 years!

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

I would like to introduce our Biotechnology Fellows. Our **6 NIH Fellows** include: **Sunny Shah**, Biomedical Engineering (preceptor is Alex Revzin), **Raquel Orozco-Alcaraz**, Chemical Engineering (preceptor is Tonya Kuhl); **David Dallas**, Nutritional Biology (preceptor is Bruce German), **Rena Goodman**, Chemistry (preceptor is Peter Beal), **Rashida Lathan**, Animal Biology (preceptor is Juan Medrano), and **Daniël Melters**, Cell and Developmental Biology (preceptors are Ian Korf and Simon Chan). Our **four Biotechnology Fellows** (industry and campus fellowships) include: **Dmitry Grapov,** Ag & Environmental Chemistry (preceptor is John Newman); **Thuc Nghi Nguyen,** Biomedical Engineering (preceptor is Soichiro Yamada); **Geetika Joshi**, Soils and Biogeochemistry (preceptor is Kate Scow), and **Huilan Han,** Mechanical & Aeronautical Engineering (preceptor is Cristina Davis, who graduated in Winter 2010 and therefore will not present her research) The **2010 CREATE-IGERT Trainees** are **Lucas Arzola, Geoffrey Benn, Marta Bjornson, Timothy Butterfield, Elenor Castillo, Dawn Chiniquy, Mitch Elmore, Tiffany Glavan, Rachel Kerwin, Ben Lindenmuth, Chris Simmons,** and **Mark Wolf.** Due to the limited time for oral presentations, we will showcase research performed by these students, as well as other students in the DEB program, in the poster session. Please congratulate all of these outstanding predoctoral candidates. We are very proud of all of them.

We will be selecting our **2010-11 NIH Fellows** in May. Nomination Forms are on the web at www.deb.ucdavis.edu and the application deadline is **Monday, April 19th.** 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 NSF CREATE-IGERT, the number of **DEB students is currently up to 170 and climbing.** Each of our students is showcased on the DEB website (www.deb.ucdavis.edu).

In regard to industrial internships for 2009, we placed many of our DEB students: Michael Howland interned with Accurion gmbH in Goettingen, Germany; David Sela completed his internship with The California Dairy Research Foundation (CDRF); Chun-Yi (Jimmy) Wu interned with Antibodies, Inc.; Jessica Houghton completed her internship with Amgen; Ksenyia Zakharyevich interned with LS9, Inc.; Kelly Williams and Karen Leung accepted internships with Genentech; Laura Gillies interned with Agilent; Cui Jing (Tracy) Zeng interned with Expression Systems; Meghan Rosen, Kristina Mahan, and Marina Meyerzon interned with Novozymes, and Alina Rabinovich Cao begins her internship with them this year. Prasad Gawande completed his internship with Novartis; Huilan Han interned in Prof. Kit Lam's lab and Daniel Garrido interned in Prof. Helen Raybould's lab. Currently, Connie Jen is interning with Amyris

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 2009 with their PhDs and a Designated Emphasis in Biotechnology: **Honglin Chen; Kevin Dietzel; Corey Dodge; Rita El-khouri; Laura Gillies; Michael Howland; Ting-Kuo (TK) Huang; Kou-San Ju; Karen Leung; Xianxian (Janice) Liu; Riccardo LoCascio; Artem Loukoianov; Marina Meyerzon; Gian Oddone; Andres Schwember; James Stice; and Andrew Wong.**

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

With warmest regards,

Judy Kjelstrom

Director,
UC Davis Biotechnology Program


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

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

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### Faculty:

Roland Faller (Chemical Engineering)
Ian Kennedy (Mechanical & Aeronautical Engineering)
Tonya Kuhl (Chemical Engineering)
J. Clark Lagarias (Molecular & Cellular Biology)
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Atul Parikh (Applied Science)
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# Designated Emphasis in Biotechnology (DEB) Graduate Program

www.deb.ucdavis.edu

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# UC Davis Biotechnology Program

www.biotech.ucdavis.edu

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# UC Davis Nineteenth Annual Biotechnology Training Retreat
# March 27, 2010
# 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**<br>8:45 am Sunny Shah ..... *Mentor: Alex Revzin*<br>9:10 am **Charlene Levering** **Monsanto, Calgene**<br>9:35 am Raquel Orozco-Alcaraz ..... *Mentor: Tonya Kuhl*<br>10:00 am David Dallas ..... *Mentor: J. Bruce German* |
| **10:25 – 10:45 am** | **Break / Poster Viewing** |
| **10:45 – 12:15 pm** | **Presentations**<br>10:45 am **Aaron Sato**..... **OncoMed Pharmaceuticals**<br>11:10 am Rena Goodman .....*Mentor: Peter Beal*<br>11:35 am Rashida Lathan .....*Mentor: Juan Medrano*<br>12:00 pm John Yoder- ..... Bioethics Question (Handout) |
| **12:10 – 1:10 pm** | **Lunch / Poster Viewing** |
| **1:10 – 1:25 pm** | **Photo Taking for NIH/Biotech Fellows & CREATE-IGERT Trainees** |
| | **Afternoon Session Chair**<br>David Segal<br>NIH Faculty Trainer |
| **1:25 – 3:05 pm** | **Presentations**<br>1:25 pm John Yoder ..... Bioethics Question (Discussion)<br>1:45 pm Daniël Melters ..... *Mentor: Ian Korf*<br>*Mentor: Simon Chan*<br>2:10 pm **Jim Kealey** ……. **Amyris Biotechnologies**<br>2:35 pm Dmitry Grapov ..... *Mentor: John Newman*<br>3:05 pm **Jos van Boxtel** ..... **Arcadia Biosciences** |
| **3:20 - 3:35 pm** | **Short Break (15 min)** |
| **3:35 – 4:45 pm** | **Presentations**<br>3:35 pm Thuc Nghi Nguyen ..... *Mentor: Soichiro Yamada*<br>4:05 pm Geetika Joshi ..... *Mentor: Kate Scow*<br>4:30 pm **Marina Roell**..... **XOMA** |
| **5:00 pm** | **Closing Remarks**<br>Karen McDonald;<br>Co-Director, NIH Training Grant in Biomolecular Technology |

**5:45 pm – Bus departs Napa**

# 2010 Poster Titles

A. **"Towards Gene Therapy for Angelman Syndrome"**
Barbara J. Bailus* and David Segal
Genome Center, University of California, Davis

B. **"Biological Synthesis of Higher Alcohols as Biofuels"**
Michael R. Connor, Edna Lamsen, Gabriel Rodriguez and Shota Atsumi
Department of Chemistry, University of California, Davis

C. **"Membrane Curvature Modeling and Lipid Organization on Supported Bilayers"**
Matthew I. Hoopes[1]*, Roland Faller[1,2], and Marjorie L. Longo[1,2]
[1]Biophysics Graduate Group, University of California, Davis
[2]Chemical Engineering and Materials Science Graduate Group, University of California, Davis

D. **"Altered Binding and Specificity of Polymorphic Zinc Finger Proteins"**
Sarah Lockwood*, Artem Zykovich, and David Segal
Genome Center, University of California, Davis

E. **"Solid Lipid Nanoparticles For Delivering Biomolecular Imaging Probes Across the Blood Brain Barrier (BBB) to Investigate Alzheimer's Disease**
Erica Andreozzi* and Angelique Louie
Department of Biomedical Engineering, University of California, Davis

F. **"Targeted Regulation of Phytochrome Signaling Using Constitutively Active Alleles and An Unnatural Chromophore"**
Timothy Butterfield*, Wei Hu, and J. Clark Lagarias
Department of Molecular and Cellular Biology, University of California, Davis

G. **"Using a TRBO-Based Plant Expression System to Accelerate Epithelial Regeneration"**
Tiffany Glavan[1]*, Sang-Kyu Jung[2], Larry Joh[2], Ben Lindenmuth[2], Satya Dandekar[1], Abhaya Dandekar[3], and Karen McDonald[2]
[1]Department of Medical Microbiology & Immunology, University of California, Davis
[2]Department of Chemical Engineering & Material Science, University of California, Davis
[3]Department of Plant Sciences, University of California, Davis

H. **"Allostery Unmasked in *E. Coli* Cytidine Triphosphate Sythetase"**
Roger Jesinghaus*, Kateryna Feoktistova, James Endrizzi, and Enoch Baldwin
Department of Molecular and Cellular Biology, University of California, Davis

I. **"Temperature-Induced Conformational Changes of Antifreeze Proteins Via Attenuated Total Reflectance Fourier Transform Infrared Spectroscopy (ATR-FTIR)"**
Terry Ng and Donald P. Land
Department of Chemistry, University of California, Davis

J. **"Chimeric Antimicrobial Protein Provides Resistance to Pierce's Disease In Grapevines"**
Hossein F. Gouran[1], Ana M. Ibáñez [1], Kevin Quzch[1], Sandie L. Uratsu[1], George E. Bruening[2], Cecilia Agüero[1], Gupta Goutam[3], and Abhaya M. Dandekar[1]
[1]Department of Plant Sciences, University of California, Davis
[2]Department of Plant Pathology, University of California, Davis
[3]Biosciences Division, Los Alamos National Laboratory

K. **"Synthesis of Modified Nucleotides As Probes and Inhibitors For DNA Repair Enzymes"**
JohnPatrick Rogers[1], Sheng Cao[2], and Sheila S. David[1]
1Department of Chemistry, University of California, Davis
[2]University of Utah, Department of Chemistry, Salt Lake City, UT

L. **"Xoma 052, A Monoclonal Antibody That Regulates Interleukin-1 Beta (IL-1BETA) Activity: An Example of a New Class of Regulatory Antibody Drugs That May Confer a Unique Advantage in the Treatment of Type 2 Diabetes Mellitus"**
M.K. Roell, M. White, H. Issafras, K. Michelson, S. Vanegas, L. Gross, S. Lee, A. Mirza, J. Hunter, J. Corbin, S. Kantak, S. Doberstein
XOMA, LLC, Berkeley, CA

M. **"A Genetically Encoded Probe For the Identification of Proteins that Form Cysteine Sulfenic Acid In Response To Oxidative Stress"**
Christina L. Takanishi and Matthew J. Wood
Department of Environmental Toxicology, University of California, Davis

N. **"Transient *In Planta* Expression of a Cellulose Degrading Enzyme"**
Ben Lindenmuth and Karen McDonald
Department of Chemical Engineering & Materials Science, University of California, Davis

O. **"*In Vivo* Breast Milk Glycopeptide Digestome for Human Infants"**
Dave Dallas
Department of Nutritional Biology, University of California, Davis

P. **"Quantitative Characterization of Kinetochores in Megabase Scale *Arabidopsis* Centromeres"**
Joseph Ramahi, Ravi Maruthachalam, Pak Kwong, and Simon Chan
Department of Plant Biology, University of California, Davis

Q. **"Transient In Planta Expression of a Cellulose Degrading Enzyme"**
Ben Lindenmuth and Karen McDonald
Department of Chemical Engineering & Materials Science, University of California, Davis

R. **"Development of Biotechnological Controls Tools For Crop Pathogen Vectors"**
Elenor Castillo, Abhaya Dandekar, and Florence Negre-Zakharov
Department of Plant Sciences, University of California, Davis

# 2010 Presentation Titles

1. **"On-Demand Release of Cells and Hydrogel Constructs From ITO Surfaces"**
Sunny Shah[1]*,Mihye Kim[2], Giyoong Tae[2], and Alexander Revzin[1]
[1]Department of Biomedical Engineering, University of California, Davis
[2]Department of Nanobio Materials and Electronics & Department of Material Science and Engineering, Gwangju Institute of Science and Technology, Oryong-dongBuk-gu, Gwangju 500-712, Korea

2. **"Reduced Lignin Alfalfa"**
Charlene Levering, Edward Kraft, Greg Peel, Erin Figoni, Bihua Huang, Alessandra Frizzi, Martin Ruebelt, Kathy Lardizabal, Bill Hiatt, and Stephen Temple
Monsanto, Calgene Campus, Davis, CA

3. **"Impact of Membrane Fluidity and Diffusion On Steric Stabilization of Liposomes"**
Raquel Orozco-Alcaraz* and Tonya Kuhl
Department of Chemical Engineering and Materials Science, University of California, Davis

4. **"*In Vivo* Breast Milk Glycopeptide Digestome For Human Infants"**
David Dallas*
Department of Nutritional Biology, University of California, Davis

5. **"Notch Pathway Antibodies for Targeting Cancer Stem Cells"**
Aaron K. Sato*
OncoMed Pharmaceuticals, Redwood City, CA

6. **"High Throughput Screening To Identify Inhibitors of RNA Editing"**
Rena Goodman*, Subhash Pokharel, and Peter Beal
Department of Chemistry, University of California, Davis

7. **"Genomic and Functional Analysis of Infertility In High Growth FVB/NJ Female Mice"**
Rashida Lathan, Thomas E. Adams, and Juan F. Medrano
Department of Animal Science, University of California, Davis

8. **"Centromere Repeat Sequences in Eukaryotes, Fast Diverging Genomic Nomads"**
Daniël Melters[1], Keith Bradnam[3], Simon Chan[1], and Ian Korf[2,3]
[1]Department of Plant Biology, University of California, Davis
[2]Department of Molecular & Cellular Biology, University of California, Davis
[3]Genome Center, University of California, Davis

9. **"Production of Renewable Fuels and Chemicals in Genetically Engineered *Saccharomyces cerevisiae*"**
Jim Kealey
Amyris Biotechnologies, Inc., Emeryville, CA

10. **"Type 2 Diabetes – Associated Changes in the Plasma Lipidome In Obese Women"**
Dmitry Grapov*[1], Sean Adams[1,2], W. Timothy Garvey[3], Kerry H. Lok[3], Theresa Pedersen[2], John W. Newman[1,2]
[1]Nutrition Department, University of California, Davis
[2]USDA/ARS Western Human Nutrition Research Center, Davis, CA
[3]Nutrition Sciences, University of Alabama, Birmingham, AL

11. **"High GLA Safflower Oil For Improved Nutritional Value"**
Isabel Dicely, Ken Mai, John Goodstal, Wynnie Ng, Kendra Williams, Ken Graham, Meir Gadisman, Daniel Facciotti, and Frank Flider
Arcadia Biosciences, Davis, CA

12. **"Zyxin-Mediated Actin Assembly At Cell-Cell Adhesion of Epithelial Cells"**
Thuc Nguyen and Soichiro Yamada
Department of Biomedical Engineering, University of California, Davis

13. **"Regulation of Methyl-Tert-Butyl Ether (MTBE) Degradation Pathway in *Methylibium Petroleiphilum* Strain PMI**
Geetika Joshi, Radomir Schmidt, Krassimira Hristova, and Kate Scow
Department of Land, Air and Water Resources, University of California, Davis, CA

14. **"Antibody Drugs: Molecular Mechanism of Action"**
Marina Roell
Xoma LLC, Berkeley, CA

# Oral Presentation Abstracts

## NIH FELLOW: Sunny Shah

# ON DEMAND RELEASE OF CELLS AND HYDROGEL CONSTRUCTS FROM ITO SURFACES

Presenter: Sunny Shah*
Authors: **Sunny Shah**[1]*, Mihye Kim[2], Giyoong Tae[2], and Alexander Revzin[1]
Affiliations: [1]Department of Biomedical Engineering, University of California, Davis
[2]Department of Nanobio Materials and Electronics & Department of Material Science and Engineering, Gwangju Institute of Science and Technology, Oryong-dongBuk-gu, Gwangju 500-712, Korea
Preceptor: Alexander Revzin

Deriving new sources of hepatocytes is critical for further advancement of liver-directed cell therapies and tissue engineering applications. In this study, we micropatterned heparin-based hydrogels on glass substrates using UV photopolymerization. We showed patterning of stem cells, primary hepatocytes and fibroblasts inside and around micropatterned heparin-based hydrogels. To test the bioactivity of heparin hydrogel, we incorporated hepatocyte growth factor (HGF) in heparin hydrogel and PEG hydrogel and studied its release kinetics. Results showed long-term sustained release of HGF from heparin-based hydrogel. In addition, immunostaining showed increased albumin production by primary hepatocytes patterned adjacent to heparin hydrogel compared to PEG hydrogel. Finally, we incorporated fibroblasts into heparin-based hydrogels and patterned the cell-containing hydrogels on a conductive indium tin oxide (ITO) substrate. Heparin hydrogel structures were registered with individually addressable ITO electrodes and anchored to the surface via an acrylated silane layer. Importantly, applying reductive potential (-1.8V for 60 sec) to the desired electrode resulted in desorption of the silane coupling layer and detachment of the cell-containing hydrogels. The use of an array of individually addressable ITO electrodes permitted temporal control in detachment and collection of cell-containing constructs. Viability assays revealed that greater than 80% of cells were viable after the electrochemical desorption process. We also demonstrated release of micropatterned heparin-based hydrogels from ITO substrates. The novel electroactive biointerface described here will enable sampling and harvesting of cells residing on micropatterned surfaces.

*Member of the DEB graduate program

## COMPANY AFFILIATE: Monsanto, Calgene Campus

# REDUCED LIGNIN ALFALFA


| | |
|---|---|
| Presenter: | Charlene Levering*, PhD |
| Authors: | **Charlene Levering**, Edward Kraft, Greg Peel, Erin Figoni, Bihua Huang, Alessandra Frizzi, Martin Ruebelt, Kathy Lardizabal, Bill Hiatt, and Stephen Temple |
| Affiliations: | Monsanto, Calgene Campus<br>Forage Genetics International<br>1920 Fifth Street<br>Davis, CA 95616 |
| Email: | charlene.levering@monsanto.com |



Lignin is an indigestible phenolic compound and a major component of alfalfa secondary cell walls. The majority of lignin in alfalfa is present in the lower stem, providing mechanical strength for the plant. Lignin content increases during maturation and flowering and reduces hay quality by limiting fiber digestibility. Monsanto and Forage Genetics International (FGI) have collaborated to produce transgenic alfalfa lines with reduced levels of lignin. Stabilized antisense technology was employed to down-regulate caffeoyl-CoA 3-O-methyltransferase (CCOMT), a key enzyme in the lignin biosynthetic pathway. This led to a reduction in lignin content and a corresponding increase in forage digestibility.

## NIH FELLOW: Raquel Orozco-Alcaraz

# IMPACT OF MEMBRANE FLUIDITY AND DIFFUSION ON STERIC STABILIZATION OF LIPOSOMES


Presenter: Raquel Orozco-Alcaraz*
Authors: **Raquel Orozco-Alcaraz*** and Tonya Kuhl
Affiliations: Department of Chemical Engineering & Materials Science, University of California, Davis
Preceptor: Tonya Kuhl



Polyethylene glycol (PEG) chains are used to sterically stabilize liposomes and increase their in-vivo circulation times for drug delivery applications. Here we investigate the impact of lipid diffusion and liposome phase state on the interaction of stealth liposomes with a surface. Using the Surface Force Apparatus (force spectroscopy) the interaction force profile of two interacting sterically stabilized liposomes can be determined with extremely high precision. The force-distance profiles show the presence of electrostatic and steric repulsion due to the PEG chains and negatively charged PEG-lipid. Similar behavior has been observed with solid phase bilayers containing PEG-lipid. The much greater lateral diffusivity in the fluid phase relative to gel phase allows exclusion of the PEG-lipid upon compression and may be used to achieve better liposome targeting. However a quantitative comparison between fluid and gel phases demonstrates a reduced rate of diffusion for PEG functionalized lipids. These findings suggest that the reduced diffusion of PEG-lipids results from lateral friction and entanglements between the polymer chains in restricted geometries and provides new information to better tailor drug delivery vehicles.


***Member of the DEB graduate program**

## NIH FELLOW: David Dallas

# *IN VIVO* BREAST MILK GLYCOPEPTIDE DIGESTOME FOR HUMAN INFANTS

Presenter: David Dallas*
Authors: **David Dallas**
Affiliations: Department of Nutritional Biology, University of California, Davis
Preceptor: J. Bruce German

Human milk is considered the ideal food for infants; however, in some respects, it may not be the ideal food for premature infants. As provocative and counter-intuitive as this may sound, the premature infant may not be developmentally ready to digest milk. Relative to full term infants, premature infants have reduced gastric acid-producing capabilities, and a greatly reduced level of enzymes in the stomach and intestines [1]. Therefore, I propose that the form in which milk molecules interact with the gut and the body may be different between premature and term infants.

Milk proteins are not just the sum of their amino acids. The ensemble of intact proteins are digested to intact peptides that are the fragments absorbed within gut. Scientists are now beginning to realize that fragments of peptides, rather than intact proteins, are responsible for specific bioactivities in the gut. For example, most of the proteins in breast milk have yet to be annotated for their functions, yet when they are partially digested, the peptide fragments exhibit an array of bioactivities [2, 3]. Breast milk has evolved for the term infant with its full complement of digestive capabilities. The underdeveloped, premature infant that cannot produce the specific digestive products may not have access to these bioactivities. There is a disparity in health between term and premature infants, which develop more slowly and have higher mortality rates.

Milk peptides produced in the gut of term- and preterm infants have been incompletely described. However, breakthroughs in analytical chemistry of complex biomolecules have provided the means to characterize them. As a result of a unique set of ongoing collaborations with a neonatologist and an analytical chemistry laboratory, digesta samples from full-term and pre-term infants will be obtained sequentially over time post-ingestion and subsequently analyzed for the peptides and glycopeptides released.

Among the peptides produced from digestion of milk proteins, I hypothesize that glycopeptides—those peptides with single or branched chains of sugars attached—will be the most important in terms of bioactivity. Glycosylations provide steric hindrance, which allows peptides to stay intact longer via increased resistance to proteolysis. This indigestible and

highly energetically expensive glycosylation must serve a specific purpose, as Darwinian selective pressure drives breast milk to be as efficient as possible to provide essential nutrients without overly taxing the mother. Currently, the "purpose" of glycosylation of peptides in breast milk remains unclear. I propose that glycosylations function to provide structural resistance to digestion for bioactive peptide sequences and are an integral part of their interactions with the gut and, hence, of their health effects.

This work will be done with highly reproducible nano-liquid chromatography (LC), attached to new chip technology (Agilent Technologies, Santa Clara, CA) with parts per million accuracy-mass spectrometry combined with a detailed mass spectral library uniquely identifies glycopeptides.

*Member of the DEB graduate program

## COMPANY AFFILIATE: OncoMed Pharmaceuticals, Inc.

# NOTCH PATHWAY ANTIBODIES FOR TARGETING CANCER STEM CELLS


| | |
|---|---|
| Presenter: | Aaron K. Sato, PhD |
| Authors: | **Aaron K. Sato, PhD** |
| Affiliations: | OncoMed Pharmaceuticals, Inc.<br>800 Cheasapeake Drivet<br>Redwood City, CA 94063 |
| Email: | aaron.sato@monsanto.com |



The Notch pathway is recognized to play a central role in the control of cell fate decisions, and has long been suspected to have a role in cancer. Cancer stem cells are thought to mediate tumor initiation, metastasis, and recurrence. These cells are also preferentially resistant to many "standard of care" therapies. Anti-DLL4 and Notch receptor antibodies were discovered and found to inhibit tumor growth through multiple mechanisms, including reduction in cancer stem cell frequency.

## NIH FELLOW: Rena Goodman

# HIGH THROUGHPUT SCREENING TO IDENTIFY INHIBITORS OF RNA EDITING

Presenter: Rena Goodman*
Authors: **Rena Goodman***, Subhash Pokharel, and Peter Beal
Affiliations: Department of Chemistry, University of California, Davis
Preceptor: Peter Beal

Deamination of adenosine to produce inosine in mRNA is one example of RNA editing. Inosine is translated as guanosine, so editing can result in codon changes including extension of a protein if a stop codon is involved. These differences in protein structural diversity caused by editing are necessary for a properly functioning nervous system in metazoa. In humans this reaction is catalyzed by ADAR1 or ADAR2, adenosine deaminases acting on RNA. Both lack of editing and over-editing can lead to problems in areas such as locomotion and behavior, yet there is no known method of pharmacological control for either ADAR protein, and rational design of small molecule inhibitors has proven extremely difficult. Therefore, the Beal lab developed a high throughput screen in yeast to screen for ADAR2 activity. We provided our screen to the UC Santa Cruz Chemical Screening Facility, and they screened 21,000 compounds. We have screened the top 15 of these compounds in a secondary, *in vitro*, screen to confirm editing inhibition. A low molecular weight inhibitor will allow our lab and labs around the world studying RNA editing to learn more about the regulation and control of this process.

*Member of the DEB graduate program

## NIH FELLOW: Rashida Lathan

# GENOMIC AND FUNCTIONAL ANALYSIS OF INFERTILITY IN HIGH GROWTH FVB/NJ FEMALE MICE

Presenter: Rashida Lathan*
Authors: **Rashida Lathan***, Thomas E. Adams, and Juan F. Medrano*
Affiliations: Department of Animal Science, University of California, Davis
Preceptor: Juan Medrano*

The inability to reproduce is an extreme pathology that challenges survival, and is a biological process that can be investigated to discover targets for restoration of fertility and for contraception. We are studying a phenotype of fertility regulation in a mouse model using tools of genetics, physiology, and pathway analysis. Females are fertile when the homozygous high growth (*hg*) locus, a natural deletion involving Socs-2, RAIDD/CRAD, and Plexin C1, is in a C57BL/6J background (C57BL/6J-*hghg*), however, complete absence of the ability to reproduce occurs when the homozygous *hg* locus is introgressed onto female FVB/NJ mice (FVB/NJ-*hghg*). This has lead us to conclude that infertility is the result of interaction between the *hg* locus and the strain background, and has provided us with a platform for testing functional pathways involved with genes in the *hg* locus and with reproduction.

We utilize a novel biotechnique called recombinant backcross with selection to simultaneously uncover putative QTL regions and to fine-map the causative region(s) behind FVB/NJ-*hghg* female infertility. This method requires the mating of fertile female C57BL/6J-*hghg* mice and fertile FVB/NJ-*hghg* males. Their resulting female offspring are recurrently backcrossed to FVB/NJ-*hghg* males to introgress the FVB/NJ background onto the C57BL/6J background. Preservation of the loci that render females fertile are maintained by selecting female progenitors based on their ability to contribute offspring in the next generation. Backcrossing will be continued for five generations to reduce the amount of C57BL/6J donor genome to <2%. Parental and offspring populations will be phenotyped for litter size and genotyped using a high density SNP panel capable of differentiating C57BL/6J and FVB/NJ SNP markers. Currently we have produced backcross-4 generation females.

This genomic analysis is complemented with phenotyping data derived from FVB/NJ-*hghg* mice and FVB/NJ controls. Data from experiments that evaluate physiological, hormonal, and candidate gene differences support an ovulatory defect downstream of the FSH and LH

pituitary pathway that affects the ability of the ovary to release competent ooctyes into the oviduct.

*Member of the DEB graduate program

## NIH FELLOW: Daniël Melters

# CENTROMETER REPEAT SEQUENCES IN EUKARYOTES, FAST DIVERGING GENOMIC NOMADS


Presenter: Daniël P. Melters*

Authors: **Daniël P. Melters[1]***, Keith Bradnam[3], Simon Chan[1], and Ian Korf[2,3]

Affiliations: [1]Department of Plant Biology, University of California, Davis
[2]Department of Molecular & Cellular Biology, University of California, Davis
[3]Genome Center, University of California, Davis

Preceptors: Simon Chan and Ian Korf



The centromere is a chromosomal locus that is essential for proper segregation of the chromosomes during cell division. Despite their conserved, essential function, centromeres are characterized by the rapid evolution of both centromeric DNA sequence and centromeric structure. Most animal and plant species studied thus far have high copy tandem repeats in their centromeric regions. This suggests that these tandem repeat sequences are a conserved feature of chromosomes in these species. One model to explain this observation is the 'library' hypothesis. This model predicts the presence of various tandem repeat arrays, which, through stochastic amplification, compete to become the functional centromere. If this model were to be correct, homology between centromeric sequences in species A and non-centromeric sequences in species B would be predicted. To test this hypothesis we analyzed whole genome shotgun sequences from 29 vertebrates. Using a specialized program to find tandem repeat sequences, called Tandem Repeat Finder we identified 251 tandem repeat sequences. Sequence homology was found using BLASTn. Surprisingly, we did find 90% sequence homology between a non-centromeric rat tandem repeat sequence and the consensus primate centromere sequence. These results tentatively confirm the 'library' hypothesis. Furthermore, we found contradictory results to the centromere nucleosome theory, as the centromere sequences ranged from 54 to 385 nucleotides.

The centromere is a chromosomal locus that is essential for proper segregation of the chromosomes during cell division. Despite their conserved, essential function, centromeres are characterized by the rapid evolution of both centromeric DNA sequence and centromeric structure. Most animal and plant species studied thus far have high copy tandem repeats in their centromeric regions, but the function of these repeats is not understood. One model to explain rapid centromere evolution is the 'library' hypothesis. This model predicts the presence of various tandem repeat arrays, which, through stochastic amplification, compete to become the functional centromere. This model predicts that there should be homology between centromeric sequences in species A and non-centromeric sequences in species B. To test the library hypothesis, we have developed a bioinformatic method to identify candidate centromere DNAs from whole genome shotgun sequences. We used our method to identify

251 tandem repeat sequences from 29 vertebrates. Surprisingly, we found 90% sequence similarity between a non-centromeric rat tandem repeat sequence and the consensus primate centromere sequence. These results tentatively confirm the 'library' hypothesis. A further model states that the repeat unit is the size of one nucleosome, because centromeres contain a specific version of histone H3. Our results are inconsistent with this model, as the centromere sequences ranged from 54 to 385 nucleotides.

*Member of the DEB graduate program

## COMPANY AFFILIATE: Amyris Biotechnologies

# PRODUCTION OF RENEWABLE FUELS AND CHEMICALS IN GENETICALLY ENGINEERED *SACCHAROMYCES CEREVISIAE*


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|---|---|
| Presenter: | Jim Kealey*, PhD |
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Amyris Biotechnologies uses proprietary technology to engineer microbial host systems for the production of renewable fuels and chemicals. As a primary area of focus, Amyris has identified the isoprenoids as an attractive natural product class from which to derive hydrocarbon-based fuels and chemicals. The scientific approach was initially validated through the development of a yeast microbial factory for the production of artemisinic acid, a precursor to a much needed anti-malarial treatment, artemisinin. The success of the artemisnin program was leveraged to launch the renewable fuels and chemicals campaign to provide an alternative to petroleum-derived fuels and chemicals. A company overview will be presented and progress towards the production of renewable fuels and chemicals will be discussed.

## BIOTECH FELLOW: Dmitry Grapov

# TYPE 2 DIABETES-ASSOCIATED CHANGES IN THE PLASMA LIPIDOME IN OBESE WOMEN


Presenter: Dmitry Grapov*

Authors: Dmitry Grapov*[1], Sean Adams[1,2], W. Timothy Garvey[3], Kerry H. Lok[3], Theresa Pedersen[2], John W. Newman[1,2]

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Preceptor: John Newman*



Type 2 diabetes mellitus (T2DM) is known to elevate plasma fasting glucose, glycosylated hemoglobin (HbA1c), non-esterified fatty acids (NEFA), and endocannabinoids (EC). An expanded assessment of lipidomic changes in diabetes is hypothesized to provide novel insights into metabolic changes associated with this malady. Targeted profiling of plasma lipids was performed in 43 diabetic and 12 non-diabetic obese women. Plasma ECs (n=35), oxylipids (OxL; n=80), and NEFA (n=54) concentrations were measured. Multivariate statistics and regression analyses were used to mine the data matrix. Multivariate models show a diverse array of NEFA, ECs, EC-like compounds, and OxLs to be significantly altered in the diabetic state. As opposed to single clinical variables, plasma fasting glucose or (HbA1c), an algorithm using subject age, body mass index (BMI), HbA1c, and fasting glucose was normally distributed and also segregated diabetic and non-diabetic subjects. A multiple linear regression model (adj$R^2$=0.89) for this metric given lipidomic measurements was developed. Modeling and bioinformatic evaluation of the data suggests that shifts in plasma levels of epoxides are associated with T2DM. These changes are hypothesized to parallel increase of vascular risk associated with this disease.



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* Member of the DEB graduate program

COMPANY AFFILIATE: Arcadia Biosciences

# HIGH GLA SAFFLOWER OIL FOR IMPROVED NUTRITIONAL VALUE


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|---|---|
| Presenter: | Jos van Boxtel*, PhD |
| Authors: | **Isabel Dicely,** Ken Mai, John Goodstal, Wynnie Ng, Kendra Williams, Ken Graham, Meir Gadisman, Daniel Facciotti, and Frank Flider |
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Clinical evidence indicates that certain omega-6 fatty acids, such as gamma linolenic acid (GLA), can deliver measurable therapeutic benefits to people who consume them regularly. GLA is an omega-6 fatty acid with health benefits that are similar and complementary to the benefits of omega-3 fatty acids. Among its many benefits, GLA and its metabolic derivatives have been shown to have significant anti-inflammatory effects. Areas where GLA may be beneficial include infant nutrition, atopic eczema, dermatitis, diabetic neuropathy, breast pain, premenstrual syndrome symptoms, rheumatoid arthritis, high blood pressure, skin health and general inflammation.

The two main sources of dietary GLA are evening primrose oil and borage oil, containing 10 percent and 20 percent GLA respectively. Because evening primrose and borage plants are difficult to cultivate commercially, these oils are difficult and expensive to produce. As a result, widespread and economical use of GLA and GLA-enriched products is hampered by cost and availability. Both evening primrose and borage are grown as identity-preserved specialty crops. Although yields and qualities of both have been improved through limited breeding programs, production costs could still be multiple times higher than other oilseed crops, such as safflower.

Since many consumers take a number of different vitamins and supplements in addition to GLA, daily consumption and the expense of such a large number of capsules is a significant commitment. High cost and low concentration also make it difficult to incorporate efficacious levels of GLA in nutritional and functional food products.
Through combinations of plant breeding and modern biotechnology, Arcadia's objective is to produce safflower seeds containing oil with as much as 40 percent GLA. This upper concentration represents a potential fourfold increase over evening primrose oil and a

twofold increase over borage oil GLA levels. Due to higher concentration levels, Arcadia's GLA oil will be considerably more efficient and cost competitive than current sources, driving increased usage in supplements, nutraceuticals and functional foods.

## BIOTECH FELLOW: Thuc Nghi Nguyen

# ZYXIN MEDIATED ACTIN ASSEMBLY AT CELL-CELL ADHESION OF EPITHELIAL CELLS

Presenter: Thuc Nghi Nguyen*
Authors: **Thuc Nghi Nguyen***, and Soichiro Yamada*
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Preceptor: Soichiro Yamada

Cytoskeletal regulation of cell adhesion is vital to the organization of multi-cellular structures. The focal adhesion protein zyxin emerged as a key regulator of actin assembly since zyxin recruits Ena/VASP proteins to promote actin assembly. Zyxin also localizes to cell-cell adhesion, and is thought to promote actin assembly with Ena/VASP. Using siRNA targeted to zyxin, we analyzed the roles of zyxin at adhesive contacts. Zyxin deficient cells failed to recruit VASP to focal adhesion, which were also sites of poor actin assembly. In contrast, VASP accumulated at cell-cell contacts despite the absence of zyxin. Surprisingly, actin assembly was reduced at VASP positive cell-cell contacts. Cell spreading on E-cadherin coated surface and the formation of cell clusters were slower for zyxin deficient cells than wildtype cells. While actin assembly at both focal adhesion and cell-cell adhesion was limited in zyxin deficient cells, only actin assembly at focal adhesion was VASP dependent. Our results suggest that zyxin regulates actin assembly by different mechanisms at the sites of focal adhesion and cell-cell adhesion.

*** Member of the DEB graduate program**

## BIOTECH FELLOW: Geetika Joshi

# REGULATION OF METHYL-TERT-BUTYL ETHER (MTBE) DEGRADATION PATHWAYS IN *METHYLIBIUM PETROLEIPHILUM* STRAIN PMI


Presenter: Geetika Joshi*
Authors: **Geetika Joshi***, Radomir Schmidt, Krassimira Hristova and Kate Scow*
Affiliations: Department of Land, Air & Water Resources, University of California, Davis
Preceptor: Kate Scow



MTBE is a primary groundwater contaminant in California with low biodegradation rate under oxygen-limited conditions. Its downstream metabolite, tert-butyl alcohol (TBA), is a potential carcinogen being increasingly encountered at sites historically known to be contaminated with MTBE. Human exposure and health risks to these compounds have necessitated the development of environmental monitoring and bioremediation at contaminated sites. There is a need to develop low-cost, high throughput detection platforms for these compounds. *Methylibium petroleiphilum* PM1 is a methylotrophic bacterium capable of completely degrading MTBE and TBA under aerobic conditions. With limited information available about the genetic mechanisms controlling this degradation pathway in PM1, it is imperative to understand the regulation of the metabolic pathway to develop efficient approaches to improvise and fine-tune current bioremediation and monitoring strategies. My project proposes to study the regulation of this metabolic pathway of PM1 by identification, analysis and characterization of promoter(s) of *mdpA* and *mpdJ* genes of PM1 using a custom-made transposon-based *gfp*-reporter vector. These genes are involved in enzymatic breakdown of MTBE and TBA by PM1, respectively. Additionally, the DNA-protein interaction of the putative activator protein (MdpC) in the pathway, as predicted by whole-genome analysis will be studied by employing *mdpC*- mutants. This information will provide the basis for construction, standardization and validation of a biosensor; proposed as a bacterial cell containing a plasmid housing promoterless gfp under the control of PM1 *mdpA* promoter, and *mdpC*. Interaction of MdpC with MTBE is expected to drive the expression of *gfp* via promoter which will be detected in environmental samples by fluorimetric spectrophotometry. This study will provide valuable insights into understanding the regulation of a novel metabolic pathway in an environmental bacterium, and a rapid way for environmental monitoring for MTBE.


*** Member of the DEB graduate program**

## COMPANY AFFILIATE: XOMA, LLC

# ANTIBODY DRUGS: MOLECULAR MECHANISM OF ACTION


| | |
|---|---|
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Interleukin-1β (IL-1β) has been described as a master cytokine involved in initiating the innate immune response in vertebrates[1]. The dual nature of its role in both protecting against and causing tissue damage or disease makes IL-1β a complex target for optimal therapeutic intervention. We have developed XOMA 052, a high affinity recombinant therapeutic antibody that potently neutralizes IL-1β activity. The molecular mechanism of action of XOMA 052 has been investigated at the molecular level using a variety of platforms, including surface plasmon resonance and kinetic exclusion assays. Predictions based on biophysical characteristics were tested in cell-based functional assays, demonstrating that the molecular mechanism translates into effects on biological function.



1.) Dinarello, C.A. The interleukin-1 family: 10 years of discovery. *FASEB J*, **1994** 8:1314-1325.

# Bioethics

# ETHICS QUESTION

## Walking On Eggshells and Sacred Cows

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

Presented by:
Denneal Jamison-McClung
Associate Director, Biotechnology Program

# Walking On Eggshells And Sacred Cows

1) Your thesis project is focusing on a field that has gender and ethnicity-specific polymorphism implications. A reporter calls you up and couches her questions in the context of the utterances of an eminent scientist with respect to the potential for genetics in informing various attributions of the human species – while she does not get into genetic determinism per se you are unclear as to her agenda. Your work potentially could lead to the development of intervention protocols, diet regimens and even therapeutics targeted to alleviate suffering for various haplotypes. But you are conscious of how this may appear in print lacking the context that you as a scientist can bring to bear on the issue. (Read Appendix I in your spare time!)

- How do you go about addressing the issue?
- If you are misquoted in your opinion what should be your course of action?
- She has quoted a competitor in the field who you know has unorthodox views (in your opinion!) and you are concerned with what she has attributed to them – what if anything should you do about this?

2) In 1995, a New York University physicist named Alan Sokal, frustrated by what he considered the misuse of science by academic philosophers and literary critics, decided to play a meaningful prank. After studying the arcane jargon of postmodernism, he cooked up a superficially au courant but patently ill-founded paper called "Transgressing the Boundaries: Toward a Transformative Hermeneutics of Quantum Gravity" and submitted it to the journal Social Text, edited by a collective of academic celebrities. Wooed by the article's apparent endorsement of their approach (and evidently unschooled in basic science!), the editors accepted and published the paper (see attached article by Sokal Appendix II.)

- Was this an ethical action by Sokal?
- Read his explanation in appendix II – Did he make an adequate case for his actions in your opinion?

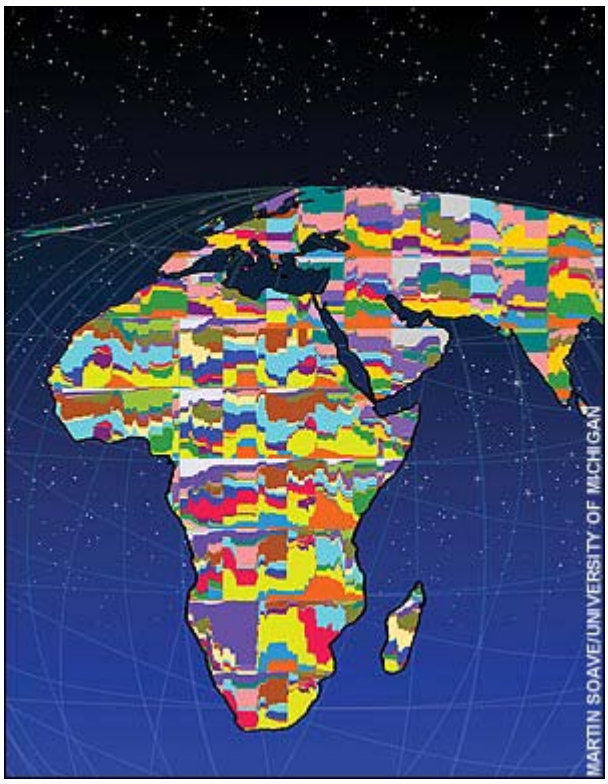
## Appendix I

### African DNA has more genetic diversity

The Telegraph UK
By Roger Highfield, Science Editor

Human migration from Africa to Europe more than 30,000 years ago appears to have left its mark on the genes of Europeans today.

The DNA of European-Americans appears to carry proportionately more harmful genetic changes than that of African-Americans, because they emerged from a smaller and less diverse population.



Schematic of worldwide human genetic variation, with colours representing different genetic types

The study of 35 people, published in Nature by a team led by Prof Carlos Bustamante of Cornell University, New York State, shows that the proportion of single letter spelling variations in the human genetic code that are probably harmful and unique to that particular population are significantly higher in the European-Americans (16 per cent) than in the African-American sample (12 percent) his team analysed.

"What is happening at an individual level will vary tremendously within and among populations," stressses Prof Bustamante, explaining that the effect can only be seen in the population level and it is not known how these deleterious mutations affects disease risk.

His team speculates that this is a consequence of a "bottleneck" - a huge decline in numbers - that Europeans experienced at about the time of the migration out of Africa, around 45,000 years ago.

"What we may be seeing is a 'population genetic echo' of the founding of Europe," says Prof Bustamante, and senior co-author with Prof Andrew Clark.

Because the founder population of Europeans was much smaller, they today have a higher proportion of harmful genetic mutations, which would have been diluted without the bottleneck, an effect that was only thought to affect small populations before this

Like astronomers who build ever-larger telescopes to peer deeper into space, population geneticists are probing the human genetic code in unprecedented detail, confirming our origns in Africa, where today the most genetically diverse range of people reside.

The work underlines why the scientific establishment recoiled at the claim by DNA pioneer James Watson that he was "inherently gloomy about the prospect of Africa" because "all our social policies are based on the fact that their intelligence is the same as ours - whereas all the testing says not really".

The furore led the Nobel laureate to abandon a recent book tour of Britain and the studies published in the journal Nature show why it was meaningless to talk about "Africa" in a discussion of the genetics of intelligence, since the continent has the biggest variation of DNA on the planet, reflecting how it was the cradle of humankind and that the DNA of its inhabitants has evolved and changed there the longest.

In a second study in Nature, this time of 485 people, University of Michigan's Prof Noah Rosenberg and colleagues, led by Andrew Singleton at the National Institute on Aging, Bethesda, outline how human genetic diversity decreases as distance from Africa increases.

People of African descent are more genetically diverse than Middle Easterners, who are more diverse than Asians and Europeans. Native Americans possess the least-diverse genomes. As a result, searching for disease-causing genes should require the fewest number of genetic markers among Native Americans and the greatest number of markers among Africans.

The patterns revealed by the new study support the idea that humans originated in Africa, then spread into the Middle East, followed by Europe and Asia, the Pacific Islands, and finally to the Americas.

They report more examples of a recently discovered type of human genetic variation, known as a copy-number variant or CNV. They found 507 previously unknown CNVs, which are large chunks of DNA - up to 1,000,000 consecutive "letters" of the genetic alphabet - that are either repeated or deleted entirely from a person's genome. Various diseases can be triggered by an abnormal gain or loss in the number of gene copies.

While previous studies have found that broad-scale geographic ancestry could be successfully traced, the new results indicate "it's becoming increasingly possible to use genomics to refine the geographic position of an individual's ancestors with more and more precision," Prof Rosenberg adds.

## Appendix II

### A Physicist Experiments With Cultural Studies

Alan Sokal is a Professor of Physics at New York University. He is co-author with Roberto Fernández and Jürg Fröhlich of *Random Walks, Critical Phenomena, and Triviality in Quantum Field Theory* (Springer, 1992),

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The displacement of the idea that facts and evidence matter by the idea that everything boils down to subjective interests and perspectives is -- second only to American political campaigns -- the most prominent and pernicious manifestation of anti-intellectualism in our time.

-- Larry Laudan, *Science and Relativism* (1990)

For some years I've been troubled by an apparent decline in the standards of intellectual rigor in certain precincts of the American academic humanities. But I'm a mere physicist: if I find myself unable to make head or tail of *jouissance* and *différance*, perhaps that just reflects my own inadequacy.

So, to test the prevailing intellectual standards, I decided to try a modest (though admittedly uncontrolled) experiment: Would a leading North American journal of cultural studies -- whose editorial collective includes such luminaries as Fredric Jameson and Andrew Ross -- publish an article liberally salted with nonsense if (a) it sounded good and (b) it flattered the editors' ideological preconceptions?

The answer, unfortunately, is yes. Interested readers can find my article, ``Transgressing the Boundaries: Toward a Transformative Hermeneutics of Quantum Gravity,'' in the Spring/Summer 1996 issue of *Social Text*. It appears in a special number of the magazine devoted to the ``Science Wars.'' What's going on here? Could the editors *really* not have realized that my article was written as a parody? In the first paragraph I deride ``the dogma imposed by the long post-Enlightenment hegemony over the Western intellectual outlook'':

that there exists an external world, whose properties are independent of any individual human being and indeed of humanity as a whole; that these properties are encoded in ``eternal'' physical laws; and that human beings can obtain reliable, albeit imperfect and tentative, knowledge of these laws by hewing to the ``objective'' procedures and epistemological strictures prescribed by the (so-called) scientific method. Is it now dogma in Cultural Studies that there exists no external world? Or that there exists an external world but science obtains no knowledge of it?

In the second paragraph I declare, without the slightest evidence or argument, that ``physical `reality' [note the scare quotes] ... is at bottom a social and linguistic construct.'' Not our *theories* of physical reality, mind you, but the reality itself. Fair enough: anyone who believes that the laws of physics are mere social conventions is invited to try transgressing those conventions from the windows of my apartment. (I live on the twenty-first floor.)

Throughout the article, I employ scientific and mathematical concepts in ways that few scientists or mathematicians could possibly take seriously. For example, I suggest that the ``morphogenetic field'' -- a bizarre New Age idea due to Rupert Sheldrake -- constitutes a cutting-edge theory of quantum gravity. This connection is pure invention; even Sheldrake makes no such claim. I assert that Lacan's psychoanalytic speculations have been confirmed by recent work in quantum field theory. Even nonscientist readers might well wonder what in heavens' name quantum field theory has to do with psychoanalysis; certainly my article gives no reasoned argument to support such a link.

Later in the article I propose that the axiom of equality in mathematical set theory is somehow analogous to the homonymous concept in feminist politics. In reality, all the axiom of equality states is that two sets are identical if and only if they have the same elements. Even readers without mathematical training might well be suspicious of the claim that the axiom of equality reflects set theory's ``nineteenth-century liberal origins.''

In sum, I intentionally wrote the article so that any competent physicist or mathematician (or undergraduate physics or math major) would realize that it is a spoof. Evidently the editors of *Social Text* felt comfortable publishing an article on quantum physics without bothering to consult anyone knowledgeable in the subject.

The fundamental silliness of my article lies, however, not in its numerous solecisms but in the dubiousness of its central thesis and of the ``reasoning'' adduced to support it. Basically, I claim that quantum gravity -- the still-speculative theory of space and time on scales of a millionth of a billionth of a billionth of a billionth of a centimeter -- has profound *political* implications (which, of course, are ``progressive''). In support of this improbable proposition, I proceed as follows: First, I quote some controversial philosophical pronouncements of Heisenberg and Bohr, and assert (without argument) that quantum physics is profoundly consonant with ``postmodernist epistemology.'' Next, I assemble a pastiche -- Derrida and general relativity, Lacan and topology, Irigaray and quantum gravity -- held together by vague rhetoric about ``nonlinearity'', ``flux'' and ``interconnectedness.'' Finally, I jump (again without argument) to the assertion that ``postmodern science'' has abolished the concept of objective reality. Nowhere in all of this is there anything resembling a logical sequence of thought; one finds only citations of authority, plays on words, strained analogies, and bald assertions.

In its concluding passages, my article becomes especially egregious. Having abolished reality as a constraint on science, I go on to suggest (once again without argument) that science, in order to be ``liberatory,'' must be subordinated to political strategies. I finish the article by observing that ``a liberatory science cannot be complete without a profound revision of the canon of mathematics.'' We can see hints of an ``emancipatory mathematics,'' I suggest, ``in the multidimensional and nonlinear logic of fuzzy systems theory; but this approach is still heavily marked by its origins in the crisis of late-capitalist production relations.'' I add that ``catastrophe theory, with its dialectical emphases on smoothness/discontinuity and metamorphosis/unfolding, will indubitably play a major role in the future mathematics; but much theoretical work remains to be done before this approach can become a concrete tool of progressive political praxis.'' It's understandable that the editors of *Social Text* were unable to evaluate critically the technical aspects of my article (which is exactly why they should have consulted a scientist). What's more surprising is how readily they accepted my implication that the search for truth in science must be subordinated to a political agenda, and how oblivious they were to the article's overall illogic.

**Why did I do it?** While my method was satirical, my motivation is utterly serious. What concerns me is the proliferation, not just of nonsense and sloppy thinking *per se*, but of a particular kind of nonsense and sloppy thinking: one that denies the existence of objective realities, or (when challenged) admits their existence but downplays their practical relevance. At its best, a journal like *Social Text* raises important questions that no scientist should ignore -- questions, for example, about how corporate and government funding influence scientific work. Unfortunately, epistemic relativism does little to further the discussion of these matters.

In short, my concern over the spread of subjectivist thinking is both intellectual and political. Intellectually, the problem with such doctrines is that they are false (when not simply meaningless). There *is* a real world; its properties are *not* merely social constructions; facts and evidence *do* matter. What sane person would contend otherwise? And yet, much contemporary academic theorizing consists precisely of attempts to blur these obvious truths -- the utter absurdity of it all being concealed through obscure and pretentious language.

*Social Text*'s acceptance of my article exemplifies the intellectual arrogance of Theory -- meaning postmodernist *literary* theory -- carried to its logical extreme. No wonder they didn't bother to consult a physicist. If all is discourse and ``text,'' then knowledge of the real world is superfluous; even physics becomes just another branch of Cultural Studies. If, moreover, all is rhetoric and ``language games,'' then internal logical consistency is superfluous too: a patina of theoretical sophistication serves equally well. Incomprehensibility becomes a virtue; allusions, metaphors and puns substitute for evidence and logic. My own article is, if anything, an extremely *modest* example of this well-established genre.

Politically, I'm angered because most (though not all) of this silliness is emanating from the self-proclaimed Left. We're witnessing here a profound historical *volte-face*. For most of the past two centuries, the Left has been identified with science and against obscurantism; we have believed that rational thought and the fearless analysis of objective reality (both natural and social) are incisive tools for combating the mystifications promoted by the powerful -- not to mention being desirable human ends in their own right. The recent turn of many ``progressive'' or ``leftist'' academic humanists and social scientists toward one or another form of epistemic relativism betrays this worthy heritage and undermines the already fragile prospects for progressive social critique. Theorizing about ``the social construction of reality'' won't help us find an effective treatment for AIDS or devise strategies for preventing global warming. Nor can we combat false ideas in history, sociology, economics and politics if we reject the notions of truth and falsity.

The results of my little experiment demonstrate, at the very least, that some fashionable sectors of the American academic Left have been getting intellectually lazy. The editors of *Social Text* liked my article because they liked its *conclusion*: that ``the content and methodology of postmodern science provide powerful intellectual support for the progressive political project.'' They apparently felt no need to analyze the quality of the evidence, the cogency of the arguments, or even the relevance of the arguments to the purported conclusion.

Of course, I'm not oblivious to the ethical issues involved in my rather unorthodox experiment. Professional communities operate largely on trust; deception undercuts that trust. But it is important to understand exactly what I did. My article is a theoretical essay based entirely on publicly available sources, all of which I have meticulously footnoted. All works cited are real, and all quotations are rigorously accurate; none are invented. Now, it's true that the author doesn't believe his own argument. But why should that matter? The editors' duty as scholars is to judge the validity and interest of ideas, without regard for their provenance. (That is why many scholarly journals practice blind refereeing.) If the *Social Text* editors find my arguments convincing, then why should they be disconcerted simply because I don't? Or are they more deferent to the so-called ``cultural authority of technoscience'' than they would care to admit?

In the end, I resorted to parody for a simple pragmatic reason. The targets of my critique have by now become a self-perpetuating academic subculture that typically ignores (or disdains) reasoned criticism from the outside. In such a situation, a more direct demonstration of the subculture's intellectual standards was required. But how can one show that the emperor has no clothes? Satire is by far the best weapon; and the blow that can't be brushed off is the one that's self-inflicted. I offered the *Social Text* editors an opportunity to demonstrate their intellectual rigor. Did they meet the test? I don't think so.

I say this not in glee but in sadness. After all, I'm a leftist too (under the Sandinista government I taught mathematics at the National University of Nicaragua). On nearly all practical political issues -- including many concerning science and technology -- I'm on the same side as the *Social Text* editors. But I'm a leftist (and feminist) *because* of evidence and logic, not in spite of it. Why should the right wing be allowed to monopolize the intellectual high ground? And why should self-indulgent nonsense -- whatever its professed political orientation -- be lauded as the height of scholarly achievement?

## SIDEBAR: EXCERPT FROM ARTICLE

Thus, general relativity forces upon us radically new and counterintuitive notions of space, time and causality; so it is not surprising that it has had a profound impact not only on the natural sciences but also on philosophy, literary criticism, and the human sciences. For example, in a celebrated symposium three decades ago on *Les Langages Critiques et les Sciences de l'Homme*, Jean Hyppolite raised an incisive question about Jacques Derrida's theory of structure and sign in scientific discourse ... Derrida's perceptive reply went to the heart of classical general relativity:

The Einsteinian constant is not a constant, is not a center. It is the very concept of variability--it is, finally, the concept of the game. In other words, it is not the concept of some*thing*--of a center starting from which an observer could master the field--but the very concept of the game ...

In mathematical terms, Derrida's observation relates to the invariance of the Einstein field equation $G_{\mu\nu} = 8\pi T_{\mu\nu}$ $G_{\mu\nu} = 8\pi G T_{\mu\nu}$ under nonlinear space-time diffeomorphisms (self-mappings of the space-time manifold which are infinitely differentiable but not necessarily analytic). The key point is that this invariance group ``acts transitively'': this means that any space-time point, if it exists at all, can be transformed into any other. In this way the infinite-dimensional invariance group erodes the distinction between observer and observed; the $\pi$ of Euclid and the $G$ of Newton, formerly thought to be constant and universal, are now perceived in their ineluctable historicity; and the putative observer becomes fatally de-centered, disconnected from any epistemic link to a space-time point that can no longer be defined by geometry alone.

# Poster Abstracts

# A. TOWARDS GENE THERAPY FOR ANGELMAN SYNDROME

**Barbara J. Bailus* and David J. Segal***
Genome Center, University of California, Davis

The current project explores the use of Zinc Finger based Artificial Transcription Factors for gene therapy involving Angelman Syndrome. Angelman Syndrome affects approximately 1 in every 12,000-20,000 people or 0.01% in the US. It is a rare neurogenetic disorder caused by de-novo deletions or an imprinting discrepancy involving the maternal copy of the *UBE3A* gene. Affected individuals fail to inherit the normally active maternal gene and the paternal gene is silenced, resulting in abnormal or no expression of UBE3A in the development of critical brain tissue. The disorder is characterized by severe mental retardation, ataxia, seizures, EEG abnormalities and outbursts of inappropriate laughter. Currently, there is no cure for Angelman Syndrome; it is managed by different therapies. The Artificial Transcription Factors (ATFs) being designed in this study will consist of six Zinc Fingers and an "activation domain." Having six fingers for the ATF allows for recognition of a unique eighteen base pair site in the DNA. These ATFs target a specific region upstream of the *Ube3a* transcript with the intention of up-regulating the expression of the *Ube3a* gene in mouse neuronal cells. It is expected that targeting this site with an ATF will result in increased paternal expression of Ube3a, compensating for the lack of maternal expression of Ube3a. The first set of ATFs has been designed taking specificity and affinity parameters into account and is currently in the testing phase. Some promising data has already been obtained using these ATFs.

***Member of the DEB graduate program**

# B. BIOLOGICAL SYNTHESIS OF HIGHER ALCOHOLS AS BIOFUELS

**Michael R. Connor, Edna Lamsen*, Gabriel Rodriguez* and Shota Atsumi***
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Global energy and environmental problems have stimulated increased efforts in synthesizing biofuels from renewable resources. Compared to the traditional biofuel, ethanol, higher alcohols offer advantages as gasoline substitutes because of their higher energy density and lower hygroscopicity. In addition, branched-chain alcohols have higher octane numbers compared to their straight-chain counterparts. However, these alcohols cannot be synthesized economically using native organisms. Here I present a synthetic biology approach to produce higher-order alcohols including isobutanol, 1-butanol, 2-methyl-1-butanol, 3-methyl-1-butanol and 2-phenylethanol. Arbitrary manipulation of metabolic synthetic pathway has many applications. However, systematic design and *de novo* construction of an artificial pathways based on such manipulation has been a long-standing challenge in the field of metabolic biotechnology. We built up unnatural synthetic pathways to produce higher-order alcohols. Moreover, we improved the productivity by combining gene deletion and overexpression techniques. Our demonstration shows that the strategy enables the exploration of biofuels beyond those naturally accumulated to high quantities in microbial fermentation.

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# C. MEMBRANE CURVATURE MODELING AND LIPID ORGANIZATION ON SUPPORTED BILAYERS

**Matthew I. Hoopes[1]*, Roland Faller[1,2]*, and Marjorie L. Longo[1,2]***
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Membranes in the cell exist in a wide range of shapes and provide for compartmentalization and transport throughout the cell. Curvature plays an important role in this cellular organization and even the organization of lipids within the membrane itself. Supported lipid bilayers (SLB) continue to be an important means of measuring the thermodynamic and mechanical properties of phospholipid membranes, but on some supports, the proximity of the solid surface may modify the behavior of the adsorbed bilayer. To overcome this problem, we use a technique for spin coating lipids on the substrate that creates multilamellar stacks of membranes[1] where the influence of the substrate on upper layers is weakened. The substrates we have used are nanoscopically patterned and these features induce curvature in the membranes providing a platform for adhesion, mobility and organizational studies. We show that multilamellar SLB on patterned substrates exhibit curvature induced phase separated domain organization and increased lateral lipid mobility. Molecular dynamics of coarse-grained supported lipid bilayers[2,3] are used to simulate membranes supported on corrugated surfaces and we discuss and compare the behavior with experimental systems.

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# D. ALTERED BINDING AND SPECIFICITY OF POLYMORPHIC ZINC FINGER PROTEINS

**Sarah Lockwood*, Artem Zykovich, and David J. Segal***
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Transcription factor (TF)-DNA interactions are some of the most important processes in biology because they directly impact the regulatory machinery that controls gene expression. Nearly half of all annotated TFs in the human genome belong to the C2H2 zinc finger (ZNF) superfamily. Our preliminary studies have identified 65 largely unstudied ZNFs with single nucleotide polymorphisms (SNPs) that alter key DNA-contacting amino acids. These mutations therefore have a high potential to alter the binding specificity of these TFs to their spectrum of target sites, and as a result their regulatory functions. Despite the vast amounts of binding information generated by the zinc finger community, it is still not possible to predict the binding behavior of uncharacterized ZNFs with reasonable accuracy. We will analyze the specificity and affinity of these proteins *in vitro* using Bind-n-Seq, a new high-throughput assay developed in our lab using massively parallel sequencing. The *in vivo* binding behavior will be assayed in living cells using ChIP-Seq. Finally, functional assays will characterize the consequences of altered DNA specificity on gene expression and regulation. This work will investigate an additional mechanism for how common genetic variations can cause functional consequences, will add new members to the list of human transcription factors with known DNA-binding sites (currently only 10% are known), and will develop new tools and information for the study of protein-DNA interactions and regulatory networks.

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# E. SOLID LIPID NANOPARTICLES FOR DELIVERING BIOMOLECULAR IMAGING PROBES ACROSS THE BLOOD BRAIN BARRIER (BBB) TO INVESTIGATE ALZHEIMER'S DISEASE

**Erica Andreozzi*, Angelique Louie***
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Activated microglia, macrophage-lineage cells located in the central nervous system (CNS), are known to play an important role in the neuroinflammatory response associated with Alzheimer's disease (AD). They are activated in the presence of senile plaques, current pathological hallmarks of AD, and this activation appears to be mediated by macrophage scavenger receptors. Microglia are attractive as therapeutic agents for AD since regions with high microglia content tend to be correlated with greater neurotoxicity. We plan to target biomolecular imaging probes to a type of scavenger receptor (SR-A) that is highly expressed by microglia in AD but not in normal microglia, allowing *in vivo* visualization of activated microglia associated with plaques. Since these probes cannot cross the blood brain barrier (BBB) by passive diffusion, we have investigated vehicles such as solid lipid nanoparticles (SLNs). SLNs constitute an attractive drug carrier system that has shown effective transport across the BBB in previous studies. SLNs consist of a solid hydrophobic core and a phospholipid shell that protects its cargo from clearance mechanisms and facilitates transport into the brain, where the SLNs then breakdown and their cargo is released. Researchers have hypothesized that the deposition of blood plasma apolipoproteins onto the surface of SLNs causes them to mimic low density lipoprotein (LDL) molecules, which brain endothelial cells naturally take across the BBB through receptor-mediated endocytosis/ followed by transcytosis. In current work, we have demonstrated both the uptake of probe-encapsulated SLNs by human primary brain endothelial cells (HPBECs), as well as the transport of probe-encapsulated SLNs in an *in vitro* blood brain barrier (BBB) model. Our preliminary data lends strong support that a fluorescent derivative our imaging probe can be encapsulated into SLNs and transported across an *in vitro* BBB model, therefore offering promise in our goal of using these encapsulated probes to facilitate imaging of activated microglia in the brain of AD mice models.

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# F. TARGETED REGULATION OF PHYTOCHROME SIGNALING USING CONSTITUTIVELY ACTIVE ALLELES AND AN UNNATURAL CHROMOPHORE

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Plants must be adept at capturing and utilizing available resources, the most critical being light in the photosynthetically active red and blue wavelength regions. Not surprisingly, photoreceptors such as the red/far-red (R/FR) light-sensing phytochromes (Phys) and blue light-sensing proteins have evolved which perceive distinct light wavelength/intensity/direction/duration cues and regulate signaling cascades that ensure appropriate adaptive responses to the changing light environment. Phytochrome activated signaling networks encompass altered protein-protein interactions, release of second messengers and changes in gene expression impacting nearly every stage of plant growth and development. In *Arabidopsis* there are five phytochromes: phyB is dominant, and it activities are overlapped and modulated by physA, C, D and E. This feature of the phytochrome family has made it difficult to identify genes and gene products specific to a single phytochrome signaling pathway. Our laboratory has recently identified a class of dominant, constitutively active mutant alleles of phyB that faithfully recapitulate phyB-regulated gene expression networks in a light-independent manner. By exploiting the chromophore-dependent activity of the Y276H allele (YHB) of *Arabidopsis* phyB, we are developing a bilin-inducible system to manipulate phyB signaling. This system permits investigation of phyB signaling in darkness without activation of other phytochromes, and offers the potential to study phyB-specific signaling pathways in light-grown plants under conditions where other phytochromes are inactive. Through expression of the cyanophage bilin biosynthetic enzymes HO and PebS to produce the unnatural bilin precursor phycoerythrobilin in transgenic plants, YHA and YHB alleles are activated while wild-type alleles are photoinactive. By driving the expression of these enzymes with an exogenously inducible promoter, we can selectively activate phyB activity at a given developmental time-point. In this way, signaling activity by phyB can be exogenously regulated in light-grown plants without activation of other phytochromes

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# G. USING A TRBO-BASED PLANT EXPRESSION SYSTEM TO ACCELERATE EPITHELIAL REGENERATION

**Tiffany Glavan[1]*, Sang-Kyu Jung[2], Larry Joh[2]*, Ben Lindenmuth[2]*, Satya Dandekar[1]*, Abhaya Dandekar[3]*, and Karen McDonald[2]***

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Cells that comprise the intestinal epithelium are continually differentiating and migrating upward into the villi. Regeneration and renewal of this single cell layer is an ongoing process that is integral to gastrointestinal health and immune function. We are interested in developing a plant-based therapeutic aimed at accelerating mucosal regeneration and repair mechanisms, thus increasing barrier function in the gastrointestinal tract. The mitogenic protein of interest is R-spondin1, a growth factor known to positively regulate cell signaling in the Wnt pathway through an interaction with DKK1. As a therapeutic, this protein has the potential to provide a restoration of function in the context of multiple disease states that disrupt the intestinal epithelium, including radiation and chemotherapy-induced mucositis and inflammatory bowel disease.

A multidisciplinary collaborative project has been initiated to develop an *Agrobacterium*-based plant expression system to produce this protein in tobacco plants. The human gene for R-spondin1 has been re-designed for expression in *N.benthamiana* through codon optimization and the addition of Kozak's context sequence, a six-histidine tag, and mRNA secondary structure aimed at decreasing degradation. This synthetic gene construct was inserted into a tobacco mosaic virus RNA-based overexpression (TRBO) vector, which was then electroporated into *Agrobacteria*. *N.benthamiana* leaves were co-infected with this construct along with a vector coding for the p19 gene silencing suppressor. Initial dotblot, SDS-PAGE, and western blot analyses of the crude protein extract reveal positive expression of R-spondin1 with a molecular weight of approximately 32.8kDa. We plan to purify the protein using nickel-based affinity chromatography and analyze its bioactivity using a BrdU assay on treated Caco-2 cells. Transcriptional kinetics will be investigated using pRT-PCR and post transcriptional modifications will be determined through mass spectrometry.

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# H. ALLOSTERY UNMASKED IN *E. COLI* CYTIDINE TRIPHOSPHATE SYTHETASE

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Cytidine triphosphate synthetases (CTPSs) catalyze formation of CTP using UTP, ATP and glutamine. CTPSs are regulated by four ribonucleotide triphosphates. ATP and UTP promote formation of active tetramers from inactive dimers, and CTP is a feedback inhibitor competing with UTP limiting intracellular [CTP]. Elevated CTP levels resulting from CTP-resistance mutations confer cytidine drug resistance to certain cancers. We investigated kinetic behaviors of E. coli CTPS with resistance mutation E155K; it has decreased CTP binding, but is also defective in oligomerization. E155K participates in an intersubunit salt-network, but does not contact bound CTP. Unexpectedly, E155K also has altered cooperativity of UTP, ATP and CTP binding and ATP Km. Three additional mutations that either contact bound CTP or participate in the intersubunit contact also different patterns of CTP inhibition, cooperativity, and oligomerization defects. The effects of these mutations unmask a previously unrecognized allosteric communication network between ATP, UTP and CTP binding sites.

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# I. TEMPERATURE-INDUCED CONFORMATIONAL CHANGES OF ANTIFREEZE PROTEINS VIA ATTENUATED TOTAL REFLECTANCE FOURIER TRANSFORM INFRARED SPECTROSCOPY (ATR-FTIR)

**Terry Ng, and Donald P. Land***
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Protein structural studies are commonly performed using techniques such as X-ray diffraction and Nuclear Magnetic Resonance (NMR). Unfortunately, these techniques make it difficult to study proteins in their native environment. Studies on protein structures via FTIR are often done with high protein concentration or in deuterated solvent. Tethering a protein near the interface of a gold-coated germanium internal reflection element (IRE) concentrates the protein near the interface and allows one to detect the protein with an increased signal-to-noise. By analyzing the amide I spectral region of the protein, the secondary structure of the protein can be determined and any conformational changes in these structures can be monitored. The secondary structure of an antifreeze protein extracted from *Dendroides canadensis* is determined in the aqueous and frozen states and show a decrease in the amount of beta sheet structures and an increase in the amount of turn structures upon freezing.

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# J. CHIMERIC ANTIMICROBIAL PROTEIN PROVIDES RESISTANCE TO PIERCE'S DISEASE IN GRAPEVINES

**Hossein F. Gouran[1], Ana M. Ibáñez[1], Kevin Quzch[1], Sandie L. Uratsu[1], George E. Bruening[2*], Cecilia Agüero[1], Gupta Goutam[3], and Abhaya M. Dandekar[1*]**

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Pierce's disease (PD) in grapevines is a vector transmitted disease where the causative agent a Gram-negative bacterium *Xylella fastidiosa* is deposited into the xylem tissue by the feeding action of the Glassy Winged Sharpshooter (GWSS), an insect vector that efficiently transmits the disease and is of greatest concern to growers in California. The virulence of the bacterium is associated with its ability to colonize xylem and its ability to move through pit pore membranes into adjacent water conducting elements. Because *X. fastidiosa* is xylem-limited, xylem-targeted expression of potential antimicrobial therapeutic proteins needs to occur to prevent and control PD infestations. We have designed a chimeric anti-microbial protein with 2 functional domains, one a surface recognition domain, SRD that specifically targets the bacterium's outer membrane accomplished using human neutrophil elastase (HNE) that recognizes MopB, the major outer membrane protein of *X. fastidiosa*. The second domain connected to the first by a flexible linker contains Cecropin B (CecB) a lytic protein domain to lyse the outer/inner membrane and to clear *X. fastidiosa* from xylem elements. Transgenic grapevines expressing this HNE-CecB chimeric anti-microbial gene have been generated. Individual lines have been propagated in the greenhouse and mechanically inoculated with *X. fastidiosa*. Four out of eleven mechanically inoculated transgenic lines expressing HNE-CecB showed significant resistance to *Xylella fastidiosa*. Furthermore, magnetic resonance imaging (MRI) of stem sections from these resistant transgenic grape lines above the point of inoculation revealed noticeably less number of clogged xylem vessels than controls.

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# K. SYNTHESIS OF MODIFIED NUCLEOTIDES AS PROBES AND INHIBITORS FOR DNA REPAIR ENZYMES

**JohnPatrick Rogers*[1], Sheng Cao[2], and Sheila S. David*[1]**
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When a cell is under conditions of oxidative stress, Guanine, the most susceptible base to oxidative damage, can be oxidized to produce oxidation products such as 8-oxo-7,8-dihydroguanine (OG), guanidinohydantoin (Gh) and spiroiminodihydantoin (Sp). If these oxidized products are not removed from DNA by enzymes belonging to the Base Excision Repair Pathway (BER), further replication events can result in permanent mutations within the genome. To understand how the enzymes in the BER pathway process these oxidized guanine products within a DNA duplex, we have synthesized substrate mimics of OG containing fluorine at the 2'alpha or 2'beta position of the nucleotide. The modified phosphoramidite monomers were incorporated into oligonucleotide strands which were then oxidized to make the corresponding 2'fluoroderivatives of FGh and FSp. They were used for biochemical studies of DNA repair enzymes. Our preliminary data indicates that the processing of the 2'-fluoro-containing oligonucleotides by BER glycosylases is highly influenced by the sugar conformation, the damaged base, as well as the specific DNA glycosylase examined.

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# L. XOMA 052, A MONOCLONAL ANTIBODY THAT REGULATES INTERLEUKIN-1BETA (IL-1 BETA) ACTIVITY: AN EXAMPLE OF A NEW CLASS OF REGULATORY ANTIBODY DRUGS THAT MAY CONFER A UNIQUE ADVANTAGE IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS

**M.K. Roell*, M. White, H. Issafras, K. Michelson, S. Vanegas, L. Gross, S. Lee, A. Mirza, J. Hunter, J. Corbin, S. Kantak, S. Doberstein**
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**Background and aims:** IL-1 beta exerts biphasic effects on pancreatic beta cell function; it is beneficial at low concentrations and pathological at high concentrations. At low concentrations IL- 1 beta acts as a stimulatory, growth, and survival factor for beta cells, leading to increased insulin secretion, increased proliferation, and reduced apoptosis. In type-II diabetes, increased secretion of IL-1 beta by beta cells results in macrophage infiltration which is hypothesized to contribute to loss of beta cell function and mass. Here we describe XOMA 052, an ultra-high affinity (0.3 pM) antibody that regulates, rather than blocks, IL-1 beta activity.

**Materials and methods:** XOMA 052 activity was characterized in vitro by analysis of binding kinetics for IL-1 beta and its receptors using surface plasmon resonance and kinetic exclusion assays. Neutralization of IL-1 beta mediated cytokine induction and proliferation by XOMA 052 was evaluated in multiple cell-based functional assays, including cell lines and whole blood assays.

**Results:** We demonstrate that XOMA 052 reduces the affinity of IL-1 beta for the soluble form of its signaling receptor, IL-1 Receptor I (RI) approximately ten-fold, and further reduces binding by IL-1 Receptor Accessory Protein (RAcP) extracellular domain another two-fold. Such a reduction in affinity would predict that binding of IL-1 beta by XOMA 052 will result in less efficient formation of the complex responsible for initiation of IL-1 beta-stimulated signal transduction, and thus a less sensitive dose-response to IL-1 beta stimulation. We have shown in multiple cellbased functional assays that XOMA 052 causes such a shift in the dose-response curve for IL-1 beta-stimulated responses. We have shown that XOMA 052 does not reduce the binding affinity of IL-1 beta to soluble IL-1 Receptor II (RII), which neutralizes IL-1 beta, and in its membrane bound form may facilitate clearance of IL-1 beta. We hypothesize that XOMA 052 may allow for low levels of beneficial IL-1 beta signaling while attenuating pathologically high levels and permitting the normal physiological mechanisms to clear IL-1 beta.

**Conclusion:** XOMA 052 regulates, rather than blocks IL-1 beta activity through its differential effects on the cytokine's binding to receptors responsible for signaling, neutralization, and clearance of IL-1 beta. This may be the first example of a new class of therapeutic antibodies that uses a novel strategy to regulate rather than shut down a targeted pathway to mitigate disease pathology while facilitating homeostatic regulation.

# M. A GENETICALLY ENCODED PROBE FOR THE IDENTIFICATION OF PROTEINS THAT FORM CYSTEINE SULFENIC ACID IN RESPONSE TO OXIDATIVE STRESS

**Christina L. Takanishi*, and Matthew J. Wood***
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Reactive oxygen species (ROS), such as superoxide ($O_2^-$) and hydrogen peroxide ($H_2O_2$), cause a wide variety of intracellular effects, such as DNA damage or the initiation of signal transduction pathways. Many cellular proteins can detect oxidation, leading to detoxification of the oxidant or the initiation of a downstream response. One such detection method is the formation of cysteine sulfenic acid (Cys-SOH), which is the initial product of the reaction between $H_2O_2$ and a reactive cysteine thiolate. Sulfenic acid is an intermediate to subsequent disulfide bond formation and signal initiation. Though Cys-SOH plays a large role in many oxidative pathways, its transient nature and the lack of biochemical tools means that many proteins that form Cys-SOH remain unknown. In *Saccharomyces cerevisiae*, the Orp1-Yap1 redox-relay system senses and responds to oxidants via the initial formation of Cys-SOH on Cys36 of the peroxidase Orp1[1]. This results in the intermolecular disulfide-bond formation between Orp1 Cys36 and Yap1 Cys598 and subsequent intramolecular disulfide bond formation on the Yap1 transcription factor leading to the upregulation of a variety of antioxidant genes. We were able to re-engineer the Cys-SOH sensitive c-terminal cysteine rich domain of the Yap1 protein to create a genetically encoded probe (Yap1-cCRD) which traps sulfenic acid-forming proteins *in vivo*, allowing for protein identification by *de novo* peptide sequencing with mass spectrometry. The Yap1-cCRD probe interacts with proteins in a peroxide-dependent, time-dependent manner, and is also inhibited by the sulfenic acid specific molecule dimedone. Our probe was previously used to identify proteins that form sulfenic acid in *Escherichia coli*[2]. Here we present a eukaryotic version of the Yap1-cCRD probe for the identification of proteins in *Saccharomyces cerevisiae*.

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# N. TRANSIENT *IN PLANTA* PRODUCTION OF A CELLULOSE-DEGRADING ENZYME

**Ben Lindenmuth* and Karen McDonald***
Department of Chemical Engineering & Materials Science, University of California, Davis

Biofuels such as ethanol are fermented from glucose, and the cellulose in biomass is a potential source of this sugar. Large quantities of low-cost enzymes are needed to degrade the cellulose into glucose. In this project, leaves harvested from *Nicotiana benthamiana* plants are infiltrated with recombinant *Agrobacterium tumefaciens* to produce these enzymes. These bacteria carry the gene encoding endoglucanase from *Acidothermus cellulolyticus*, which is transferred to the host plant and expressed transiently.

Various buffers for extracting the endoglucanase from the plant tissue have been explored. Enzyme activity is measured by cleavage of a fluorescent substrate. A recombinant endoglucanase standard has also been produced in *Pichia pastoris*. These techniques can be applied to production of other enzymes in the synergistic set required for cellulose hydrolysis.

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# O. IN VIVO BREAST MILK GLYCOPEPTIDE DIGESTOME FOR HUMAN INFANTS

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Human milk is considered the ideal food for infants; however, in some respects, it may not be the ideal food for premature infants. As provocative and counter-intuitive as this may sound, the premature infant may not be developmentally ready to digest milk. Relative to full term infants, premature infants have reduced gastric acid-producing capabilities, and a greatly reduced level of enzymes in the stomach and intestines [1]. Therefore, I propose that the form in which milk molecules interact with the gut and the body may be different between premature and term infants.

Milk proteins are not just the sum of their amino acids. The ensemble of intact proteins are digested to intact peptides that are the fragments absorbed within gut. Scientists are now beginning to realize that fragments of peptides, rather than intact proteins, are responsible for specific bioactivities in the gut. For example, most of the proteins in breast milk have yet to be annotated for their functions, yet when they are partially digested, the peptide fragments exhibit an array of bioactivities [2, 3]. Breast milk has evolved for the term infant with its full complement of digestive capabilities. The underdeveloped, premature infant that cannot produce the specific digestive products may not have access to these bioactivities. There is a disparity in health between term and premature infants, which develop more slowly and have higher mortality rates.

Milk peptides produced in the gut of term- and preterm infants have been incompletely described. However, breakthroughs in analytical chemistry of complex biomolecules have provided the means to characterize them. As a result of a unique set of ongoing collaborations with a neonatologist and an analytical chemistry laboratory, digesta samples from full-term and pre-term infants will be obtained sequentially over time post-ingestion and subsequently analyzed for the peptides and glycopeptides released.

Among the peptides produced from digestion of milk proteins, I hypothesize that glycopeptides—those peptides with single or branched chains of sugars attached—will be the most important in terms of bioactivity. Glycosylations provide steric hindrance, which allows peptides to stay intact longer via increased resistance to proteolysis. This indigestible and highly energetically expensive glycosylation must serve a specific purpose, as Darwinian selective pressure drives breast milk to be as efficient as possible to provide essential nutrients without overly taxing the mother. Currently, the "purpose" of glycosylation of peptides in

breast milk remains unclear. I propose that glycosylations function to provide structural resistance to digestion for bioactive peptide sequences and are an integral part of their interactions with the gut and, hence, of their health effects.

This work will be done with highly reproducible nano-liquid chromatography (LC), attached to new chip technology (Agilent Technologies, Santa Clara, CA) with parts per million accuracy-mass spectrometry combined with a detailed mass spectral library uniquely identifies glycopeptides.

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# P. QUANTITATIVE CHARACTERIZATION OF KINETOCHORES IN MEGABASE-SCALE *ARABIDOPSIS* CENTROMERES

**Joseph Ramahi*, Ravi Maruthachalam, Pak Kwong, and Simon Chan***
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The centromere is the chromosomal location of kinetochore assembly and is essential for proper cell division in mitosis and meiosis. While most animals and plants have "regional" centromeric DNAs spanning megabases of tandem repeats, centromeres are believed to be epigenetically determined by the localization of the centromere specific H3 variant CENH3. The kinetochore itself is assembled on centromere DNA and is the site of microtubule attachment to chromosomes by the NDC80 complex. While CENH3 is known to be required for kinetochore nucleation, the amount of CENH3 and other kinetochore proteins assembled into regional kinetochores has been difficult to determine due to the fact that only a subset of centromere repeat DNA is loaded with CENH3.

We are using a fluorescence microscopy method to count kinetochore proteins in megabase-scale *Arabidopsis thaliana* centromeres in living cells. *Saccharomyces cerevisiae* kinetochores contain a single CENH3 nucleosome, and there are thus a known number of GFP-CENH3 molecules in a yeast kinetochore cluster. GFP fluorescence can be used to count the number of molecules in cellular structures. We are using GFP-tagged kinetochore proteins of known amount in *S. cerevisiae* as fluorescence standards for calculating the amount of GFP-tagged *Arabidopsis* kinetochore components. In *Arabidopsis*, the recent isolation of a *cenh3* null allele allows complete replacement of endogenous CENH3 with a GFP-CENH3 transgene. We have also used *Arabidopsis* genetics to replace NUF2, a member of the NDC80 complex, with transgenic NUF2-GFP. This allows the quantification of GFP signal from *Arabidopsis* kinetochores to calculate the total amount of GFP-CENH3 and NUF2-GFP in individual *Arabidopsis* kinetochores.

We have found there to be ~300 GFP-CENH3 loaded into *Arabidopsis* kinetochores, the first quantification of CENH3 in large tandem repeat centromeres. These results are interesting in that a very small subset of the megabases of centromere DNA is used to assemble a kinetochore, and substantially fewer NDC80 complexes for each CENH3 molecule in *Arabidopsis* versus budding yeast. This indicates that kinetochore structure of megabase scale centromeres is different than that in point centromeres of yeast.

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# Q. TRANSIENT *IN PLANTA* EXPRESSION OF A CELLULOSE DEGRADING ENZYME

**Ben Lindenmuth & Karen McDonald**
Department of Chemical Engineering & Materials Science, University of California, Davis

Biofuels such as ethanol are fermented from glucose, and the cellulose in biomass is a potential source of this sugar. Large quantities of low-cost enzymes are needed to degrade the cellulose into glucose. In this project, leaves harvested from *Nicotiana benthamiana* plants are infiltrated with recombinant *Agrobacterium tumefaciens* to produce these enzymes. These bacteria carry the gene encoding endoglucanase from *Acidothermus cellulolyticus*, which is transferred to the host plant and expressed transiently.

Various buffers for extracting the endoglucanase from the plant tissue have been explored. Enzyme activity is measured by cleavage of a fluorescent substrate. A recombinant endoglucanase standard has also been produced in *Pichia pastoris*. These techniques can be applied to production of other enzymes in the synergistic set required for cellulose hydrolysis.

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# R. DEVELOPMENT OF BIOTECHNOLOGICAL CONTROLS TOOLS FOR CROP PATHOGEN VECTORS

**Elenor Castillo*, Abhaya Dandekar*, and Florence Negre-Zakharov***
Department of Plant Sciences, University of California, Davis

The goal of this project is to develop alternative methods to pesticide applications by using volatile compounds naturally produced by plants. Volatiles make up the natural bouquet of aroma in plants fruit and vegetables. They are more commonly associated with attracting insects to flowers for pollination, but are also involved in the plants innate immune system and can repel herbivores that feed on plants. The defense-related function of volatile compounds will be harnessed to design control strategies against the psyllid, *Diaphorina citri* (or Asian Citrus Psyllid) that carries the bacterial disease Huanglongbing (HLB), also known as citrus greening disease. This disease, caused by *Candidatus Liberibacter*, is extremely virulent and has spread to many areas in the United States. Currently there is no cure and infection of a citrus tree leads to death within two years. In Vietnam, small growers plant guava trees next to citrus trees to repel the psyllid and a recent characterization of the guava tree volatile profile indentified sulfur-containing compounds as the likely repellent (Rouseff et al., 2006). The sulfur volatiles dimethyl sulfide (DMS) and dimethyl disulfide (DMDS) were hypothesized to provide protection from the psyllid carrying the disease.

As of now, a bacterial gene responsible for DMS and DMDS biosynthesis has been introduced, (after codon optimization) into MicroTom tomato plants using *Agrobacterium*-mediated transformation. Fifteen transgenic lines are being characterized for their volatile profiles using solid-phase microextraction followed by gas chromatography and detection by chemiluminescence (Scarlata and Ebeler, 1999). Six transgenic lines were found to produce sulfur volatiles at higher levels than control plants; analysis of the remaining lines is currently in progress. Furthermore, the repellent properties of sulfur volatile-producing transgenic plants will be assessed by using bio-insect assays, which will determine if the psyllid is repelled by the transgenic plant.

The ultimate goal is to create transgenic citrus rootstocks that will produce sulfur volatiles to repel the psyllid carrying HLB. Once developed and deployed, this system will be compatible with biocontrol and other integrated pest management (IPM) practices, and will allow small growers to successfully grow citrus in areas where the disease is endemic.

*Member of the DEB graduate program

# Company Affiliates

## *Company Affiliates ** Support Biotech Training at UC Davis*

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

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

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

## Agilent Technologies

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

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

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

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

## AgraQuest, Inc.

Contact:
**Magalie Guilhabert, Ph.D.,** Scientist

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

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

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

## Amgen, Inc

Contacts:
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**Dave Lacey, M.D.**, Vice President; Basic Research, Metabolic Disorders
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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.

## Amyris Biotechnologies, Inc.

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

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

## Bayer HealthCare Pharmaceuticals, Inc.

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

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

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

## BioMarin Pharmaceutical, Inc.

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

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

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

## Genencor (A Danisco Division)

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**Colin Mitchinson, Ph.D.**, Director; Biomass Applications

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

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

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

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

## Genentech, Inc.

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

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**Caryle Vann**, Senior Project Manager & Engineer
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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

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

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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.

*** DEB Graduate**

## Novartis AG (formerly Chiron Corporation)

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### Mission

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

### Leadership Strategy

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

### Ethical Standards

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

### Values

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

## Quality

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

## Novozymes, Inc

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

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

## OncoMed Pharmaceuticals, Inc.

Contact:
**Aaron Sato, Ph.D.**, Senior Director; Antibody Engineering

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OncoMed Pharmaceuticals is a biotechnology company dedicated to improving cancer treatment, by developing monoclonal antibodies that target the biologic pathways critical to tumor initiating cells, also known as "cancer stem cells". We are leveraging our understanding of these tumor initiating cells to discover and develop novel therapeutics that could provide important alternatives for the treatment of cancer.

## Tethys Bioscience, Inc.

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

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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.

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

We approach the market with a unique combination of strengths:

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

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

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

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

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

## Ventria Biosciences

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

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

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

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

# Participants

# Retreat Participants

| NIH Fellows 2009 - 2010 | |
|---|---|
| Sunny Shah | Biomedical Engineering |
| Raquel Orozco-Alcaraz | Chemical Engineering |
| David Dallas | Nutritional Biology |
| Rena Goodman | Chemistry |
| Rashida Lathan | Animal Biology |
| Daniël Melters | Cell & Developmental Biology |
| **Biotech Fellows 2009 - 2010** | |
| Dmitry Grapov | Agricultural & Environmental Chemistry |
| Thuc Nghi Nguyen | Biomedical Engineering |
| Geetika Joshi | Soils and Biogeochemistry |
| **CREATE-IGERT Fellows, Cohort 1** | |
| Timothy Butterfield | Plant Biology |
| Dawn Chiniquy | Plant Biology |
| Tiffany Glavan | Microbiology |
| Ben Lindenmuth | Chemical Engineering |
| Christopher Simmons | Biological Systems Engineering |
| **CREATE-IGERT Fellows, Cohort 2** | |
| Lucas Arzola | Chemical Engineering |
| Elenor Castillo | Plant Biology |
| Mitch Elmore | Plant Pathology |
| Rachel Kerwin | Plant Biology |
| Mark Wolf | Biochemistry & Molecular Biology |
| **Tuskegee Participants** | |
| Ankumah Ramble | Tuskegee Faculty Trainer |
| Lakisha Odom | Tuskegee Trainee |
| Sharina Richard | Tuskegee Trainee |
| **Graduate Students/Post-docs** | |
| Zachary Bent | DEB, Microbiology |
| Abhinav Bhushan | Post-doc, Mechanical & Aeronautical Engineering |
| Heather Bolstad | Environmental Toxicology |
| Patricia Castillo | DEB, Immunology |
| Pauline (JoJo) Chang | DEB, Electrical & Computer Engineering |
| Michelle Lozada Contreras | Chemical Engineering |
| David Dallas | DEB, Nutritional Biology |
| Myra de la Pena | DEB, Immunology |
| Erik Fostvedt | DEB, Biochemistry & Molecular Biology |

| | |
|---|---|
| Daniel Garrido | DEB, Viticulture & Enology |
| Prasad Gawande | DEB, Chemistry |
| Yolanda Gogorcena | Plant Science |
| Rena Goodman | DEB, Chemistry |
| Dominik Green | DEB, Biochemistry & Molecular Biology |
| Michael Howland | DEB, Chemical Engineering |
| Ting-Kuo Huang | DEB, Chemical Engineering |
| Patty Yi-Hwa Hwang | DEB, Biochemistry & Molecular Biology |
| Kara Jensen | DEB, Comparative Pathology |
| Roger Jesinghaus | DEB, Chemistry |
| Geetika Joshi | DEB, Soils & Biogeochemistry |
| Sang-Kyu Jung | Chemical Engineering |
| Nate Kingsbury | DEB, Chemical Engineering |
| Katarzyna Koscielska | DEB, Biochemistry & Molecular Biology |
| Rashida Lathan | DEB, Animal Science |
| ChengYuk Lee | DEB, Chemical Engineering |
| Wei Li | Molecular & Cellular Biology |
| Kinjal Maniar | DEB, Immunology |
| Marina Meyerzon | DEB, Genetics |
| Alex Morris | Chemistry |
| Raquel Orozco-Alcaraz | DEB, Chemical Engineering |
| Kittipong Rattanaporn | DEB, Chemical Engineering |
| Ana Riveros | Environmental Toxicology |
| Ron Runnebaum | DEB, Chemical Engineering |
| Mindy Simon | DEB, Biomedical Engineering |
| Zane Starkewolf | DEB, Chemistry |
| Vu Trinh | DEB, Biochemistry & Molecular Biology |
| Chen Wang | Microbiology |
| Ambrose Williams | DEB, Biochemistry & Molecular Biology |
| Tracy Cui Zeng | Plant Biology |
| Kseniya Zakharyevich | DEB, Microbiology |
| Weixiang Zhao | Post-doc, Mechanical & Aeronautical Engineering |
| **UC Davis Faculty** | |
| Kristina Able | DEB, Med: Internal Medicine, Infectious Diseases |
| Peter Beal | DEB, Chemistry |
| Simon Chan | DEB, Plant Biology |
| Abhaya Dandekar | DEB, Pomology |
| Cristina Davis | DEB, Mechanical Engineering |
| Roland Faller | DEB, Chemical Engineering & Materials Science |
| J. Clark Lagarias | DEB, Molecular & Cellular Biology |
| Marjorie Longo | DEB, Chemical Engineering & Materials Science |

| | |
|---|---|
| Karen McDonald | DEB, Chemical Engineering & Materials Science |
| Rebecca Parales | DEB, Microbiology |
| Alexander Revzin | DEB, Biomedical Engineering |
| David Segal | DEB, Pharmacology |
| Sharon Shoemaker | Food Science & Technology, CIFAR |
| Dan Starr | DEB, Molecular and Cellular Biology |
| John Yoder | DEB, Plant Biology |
| **Industry** | |
| Gia Fazio | Arcadia Biosciences |
| Chandra Kilburn | E & J Gallo |
| Suchindra Maiyuran | Novozymes, Inc. |
| Kevin Holden | LS9, Inc. |
| Marie Cecile van de Lavoir | Crystal Bioscience |
| Alberto Iandolino | Monsanto, Calgene Campus |
| Martin Ruebelt | Monsanto, Calgene Campus |
| **Guests** | |
| Jason Brennan | Sheldon High School Instructor |
| Stephanie Faldwell | Sheldon High School Student |
| Rebecca Faulds | Dixon High School Instructor |
| Shaun Martins | Enochs High School Instructor |
| Carol Schutt | Enochs High School Instructor |
| My-Hai Ha | Chabot Community College |
| Hamza | Chabot Community College |
| Anna Rogatkin | Chabot Community College |
| Aaron Simmons | Sheldon High School Student |
| **UC Davis Staff** | |
| Cheryl Guadagna | Internal Medicine |
| Larry Joh | Chemical Engineering & Material Science (DEB Graduate) |
| **Biotechnology Program** | |
| Marianne Hunter | Biotechnology Program, Program Manager |
| Denneal Jamison-McClung | Biotechnology Program, Associate Director |
| Judy Kjelstrom | Biotechnology Program, Director |
| Demian Sainz | Biotechnology Program, Program Assistant |


www.biotech.ucdavis.edu

## The Mission of the Biotechnology Program:

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

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

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

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

## Biotechnology Program Office:

Dr. Judith Kjelstrom - Director
Dr. Denneal Jamison-McClung – Associate Director
Marianne Hunter – Program Manager
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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, and left campus in 2003.

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 these foci, the program provides predoctoral graduate students with well-coordinated multidisciplinary training in critical areas of biotechnology research and experiences in 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 successfully obtained the NIH training grant within the time period of this review. The NIH Training Grant in Biomolecular Technology (1-T32-GM08799) which was awarded on July 1, 2002 for 5 years, and was subsequently renewed for an additional 5 years. Currently, there are 14 NIH biotechnology training grants funded nationwide and only three in California (UC Berkeley, UC Davis, and Stanford).

The relationship between the DEB and the Training Program in Biomolecular Technology may be described 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 interdisciplinary biotechnology training.
- Not all of 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 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 (http://www.deb.ucdavis.edu/NIHTG/nihinfo.cfm) website.

| NIH Training Grant Faculty | |
|---|---|
| Director: Bruce Hammock | |
| Co-Directors: Karen McDonald and Martina Newell-McGloughlin | |
| Enoch Baldwin | Molecular & Cellular Biology |
| Peter Beal | Chemistry |
| 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 |
| Christina Davis | Mechanical & Aeronautical Engineering |
| 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 |
| Noelle L'Etoile | Psychiatry |
| Ian Korf | Molecular & Cellular Biology, Genome Center & Bioinformatics Program |
| Richard Michelmore | Plant Sciences – Vegetable Crops |
| David Mills | Viticulture & Enology |
| John Newman | Nutrition |
| Rebecca Parales | Microbiology |
| Atul Parikh | Applied Science |
| Robert Powell | Chemical Engineering & Materials Science |
| Martin Privalsky | Microbiology |
| Robert Rice | Environmental Toxicology |
| David Rocke | Applied Science |
| David Segal | Pharmacology |
| Scott Simon | Biomedical Engineering |
| Henning Stahlberg | Molecular & Cellular Biology |
| Oliver Fiehn | Genome Center & Bioinformatics Program |
| Andrew Fisher | Chemistry |
| J. Bruce German | Food Science & Technology |
| Ian Kennedy | Mechanical & Aeronautical Engineering |
| Patrice Koehl | Computer Science |
| Ian Korf | Molecular & Cellular Biology |
| 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 |

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|---|---|
| Julie Leary | Molecular & Cellular Biology |
| Marjorie Longo | Chemical Engineering & Materials Sciences |
| Claude Meares | Chemistry |
| Juan Medrano | Animal Science |
| Alex Revzin | Biomedical Engineering |
| John Rutledge | Endocrinology |
| Kate Scow | Land, Air, and Water Resources |
| Daniel Starr | Molecular & Cellular Biology |
| Michael Toney | Chemistry |
| Jean VanderGheynst | Biological & Agricultural Engineering |
| David Wilson | Molecular & Cellular Biology |
| Matthew Wood | Environmental Toxicology |
| Michael Wright | Genome Center & Bioinformatics Program |
| Stefan Wuertz | Civil & Environmental Engineering |
| Soichiro Yamada | Biomedical Engineering |
| John Yoder | Plant Sciences – Vegetable Crops |
| Yohei Yokobayashi | Biomedical Engineering |

# *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 established graduate programs.

The DEB provides a **formal accreditation** (on diploma & transcript) to reflect interdisciplinary biotechnology training.

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

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

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


# Designated Emphasis in Biotechnology Program (DEB)

## Goals and Mission of the DEB

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

### DEB Mission:

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

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

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

Students come from a wide array of disciplines: Participating graduate programs currently include **28 programs**: Agricultural and Environmental Chemistry; Animal Biology; Applied Science; Biochemistry and Molecular Biology; Biological Systems Engineering; Biomedical Engineering; Biophysics; Cell & Developmental Biology; Chemical Engineering; Chemistry; Civil and Environmental Engineering; Comparative Pathology; Electrical and Computer Engineering; Entomology; Food Science; Genetics; Immunology; Materials Science and Engineering; Mechanical and Aeronautical Engineering; Microbiology; Molecular, Cellular and Integrative Physiology; Neurosciences; Nutritional Biology; Pharmacology & Toxicology; Plant Biology; Plant Pathology; Soils & Biogeochemistry; and Statistics. The DEB program supplements a student's Ph.D. curriculum and those completing the program will obtain an official designation on their diploma & transcript indicating a qualification in biotechnology. Example: **Doctoral Degree in Microbiology with a Designated Emphasis in Biotechnology.**

## Brief History:

The DEB was formally established in 1997 as an outgrowth of the first NIH Training Grant in Biotechnology (funded in the early 1990s). The DEB became the formal training program for the current NIH Training Grant in Biomolecular Technology (1-T32-GM08799: July 1, 2007 - June 30, 2012). The DEB provides a very effective multidisciplinary biotechnology concentration, which includes exposure to bioethics, business and legal aspects of biotechnology as well as a 3-6 month internship in a biotechnology company or research laboratory in another college or national laboratory. As of March 2010 the DEB has 28 affiliated graduate groups or departmentally based graduate programs. The number of students in the Designated Emphasis in Biotechnology has increased dramatically over the last two years and now boasts 170 members, with many being first year students. We have graduated over 70 students with a DEB notation on their diplomas as of December of 2009.

## 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 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 also listed on the site. We have linked the website to graduate home pages of most of the 28 DEB program affiliates in the College 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 2010 | |
|---|---|
| Danielle Aldredge | Chemistry |
| Erica Andreozzi | Biomedical Engineering |
| Lucas Arzola | Chemical Engineering |
| Roberto Barrozo | Immunology |
| Zachary Bent | Microbiology |
| Crystal Berger | Biochemistry & Molecular Biology |
| Jennifer Bratt | Biochemistry & Molecular Biology |
| Timothy Butterfield | Plant Biology |
| Milo Careaga | Immunology |
| Anna Cartier | Plant Biology |
| Jennifer Cash | Chemistry |
| Elenor Castillo | Plant Biology |
| Patricia Castillo | Immunology |
| Shannon Ceballos | Cellular & Developmental Biology |
| Jeffrey Chan | Immunology |
| Astra Chang | Comparative Pathology |
| Pauline (JoJo) Chang | Electrical & Computer Engineering |
| Chao-Yu Chen | Pharmacology & Toxicology |
| Honglin Chen | Genetics |
| Yu-Shen Cheng | Biological Systems Engineering |
| Dawn Chiniquy | Plant Biology |
| Stephanie Crockett | Comparative Pathology |
| David Dallas | Nutrition |
| Ryan Davis | Chemistry |
| Kevin Dietzel | Microbiology |
| Neha Dixit | Immunology |
| Matthew Doherty | Microbiology |
| Collin Ellis | Nutritional Biology |
| James Elmore | Plant Pathology |
| Brett Fite | Biophysics |
| Erik Fostvedt | Biochemistry and Molecular Biology |
| Paula Garay | Biochemistry & Molecular Biology |
| Daniel Garrido | Food Science |
| Prasad Gawande | Chemistry |
| Laura Gillies | Food Science Technology |
| Tiffany Glavan | Microbiology |
| Barbara Gluvers | Chemical Engineering |
| Felipe Godinez | Biomedical Engineering |
| Elianna Goldstein | Plant Biology |
| Rena Goodman | Chemistry |
| Myra Grace dela Pena | Immunology |
| Dmitry Grapov | Agricultural & Environmental Chemistry |
| Dominik Green | Biochemistry & Molecular Biology |

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

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

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

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

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

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|---|---|
| Tom Gradziel | Pomology |
| Jeffrey Gregg | MED: Pathology |
| Andrew Groover | Plant Biology |
| Paul Gumerlock | MED: Hematology/Oncology |
| Ting Guo | Chemistry |
| Bruce Hammock | Entomology & Cancer Center |
| Stacy Harmer | Plant Biology |
| Richart W. Harper | Division of Pulmonary/Critical Care Medicine |
| Volkmar Heinrich | Biomedical Engineering |
| Wolf-Dietrich Heyer | Microbiology |
| Krassi Hristova | Soils and Biogeochemistry |
| You-Lo Hsieh | Textiles & Clothing |
| Neil Hunter | Microbiology |
| Kentaro Inoue | Plant Sciences |
| M. Saif Islam | Electrical & Computer Engineering |
| Roslyn-Rivkah Isseroff | MED: Dermatology |
| Tina Jeoh | Biological & Agricultural Engineering |
| Thomas Jue | MED: Biochemistry |
| Clarence Kado | Plant Pathology |
| Carl Keen | Nutrition |
| Darshan Kelley | Western Human Nutrition Research Center, ARS, USDA Dept. of Nutrition |
| Ian Kennedy | Mechanical & Aeronautical Engineering |
| Richard Kiehl | Electrical & Computer Engineering |
| Dan Kliebenstein | Vegetable Crops & Weed Science |
| Anne Knowlton | Cardiovascular Division, Department of Medicine & Department of Medical Pharmacology and Toxicology |
| Patrice Koehl | Computer Science |
| Ian Korf | Section of Molecular & Cellular Biology |
| Stephen Kowalczykowski | Microbiology |
| Tonya Kuhl | Chemical Engineering & Material Science |
| Hsing-Jien Kung | MED: Biochemistry / UC Davis Cancer Center |
| J. Clark Lagarias | Molecular & Cellular Biology |
| Kit Lam | MED: Hematology & Oncology |
| Donald Land | Chemistry |
| Delmar Larsen | Chemistry |
| Janine LaSalle | MED: Microbiology & Immunology |
| Jerold Last | Pulmonary / Critical Care Medicine |
| Kent Leach | Biomedical Engineering |
| Julie Leary | Biochemistry & Mass Spectrometry, Dept. of Chemistry |
| Carlito Lebrilla | Chemistry |

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|---|---|
| Noelle L'Etoile | Center for Neuroscience & Dept. of Psychiatry & Behavioral Sciences |
| Ronald Li | Cell Biology and Human Anatomy - MED |
| Su-Ju Lin | Center for Genetics & Development & Section of Microbiology - UCD Cancer Center |
| Bo Liu | Plant Biology |
| Gang-yu Liu | Chemistry |
| Gang-yu Liu | Chemistry |
| Marjorie Longo | Chemical Engineering & Material Sciences |
| Angelique Louie | Biomedical Engineering |
| Paul Luciw | MED: Pathology |
| Neville Luhmann, Jr. | Electrical & Computer Engineering |
| Laura Marcu | Biomedical Engineering |
| Fumio Matsumura | Environmental Toxicology |
| Karen McDonald | Chemical Engineering & Material Sciences |
| Claude Meares | Chemistry |
| Juan Medrano | Animal Science |
| Richard Michelmore | Vegetable Crops |
| Lisa Miller | Department of Anatomy, Physiology and Cell Biology, CNPRC, School of Veterinary Medicine |
| Marion Miller-Sears | Environmental Toxicology |
| David Mills | Viticulture & Enology |
| Terence Murphy | Plant Biology |
| William J. Murphy | Department of Dermatology |
| James Murray | Animal Science / Genetic Engineering Large Animals |
| Krishnan Nambiar | Chemistry |
| Florence Negre-Zakharov | Department of Plant Sciences |
| John Newman | Nutrition - USDA, ARS, Western Human Nutrition Research Center |
| Stephen Noctor | Neuroscience |
| Jan Nolta | UCDHS: HEMATOLOGY & ONCOLOGY,DEPARTMENT OF : MED |
| Thomas North | Center for Comparative Medicine |
| Martha O'Donnell | Physiology & membrane Biology; School of Medicine |
| David Ogrydziak | Food Science & Technology |
| Tingrui Pan | Biomedical Engineering |
| Rebecca Parales | Microbiology |
| Atul Parikh | Biomedical Engineering |
| Anthony Passerini | Dept. of Biomedical Engineering |
| Timothy Patten | Chemistry |
| Niels Pedersen | Department of Medicine and Epidemiology |

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|---|---|
| Ronald Phillips | Chemical Engineering & Material Science |
| Jerry Powell | Hemat & Oncol: Med |
| Robert Powell | Chemical Engineering & Material Science |
| Martin Privalsky | Microbiology |
| Jinyi Qi | Biomedical Engineering |
| Subhadip Raychaudhuri | Biomedical Engineering |
| David Reid | Food Science & Technology |
| Michael Reid | Environmental Horticulture |
| Alexander Revzin | Biomedical Engineering |
| Robert Rice | Environmental Toxicology |
| Subhash Risbud | Chemical Engineering & Material Science |
| William Ristenpart | Chemical Engineering & Materials Science and Dept. of Food Science |
| David Rocke | Inst. For Data Analysis & Visualization |
| Ray Rodriguez | Molecular & Cellular Biology |
| Pamela Ronald | Plant Pathology |
| Robert Rucker | Nutritional Biology |
| John Rutledge | MED: Endocrinology |
| Dewey Ryu | Chemical Engineering & Material Sciences |
| Earl Sawai | Pathology & Laboratory Medicine |
| Kate Scow | Land, Air & Water Resources |
| David Segal | Pharmacology |
| Jared Shaw | Chemistry |
| Kazuhiro Shiozaki | Microbiology |
| Wendy Silk | Soils and Biogeochemistry |
| Scott Simon | Biomedical Engineering |
| David Slaughter | Biological & Agricultural Engineering |
| Jay Solnick | MED: Infectious & Immunological Diseases |
| Henning Stallberg | Molecular & Cellular Biology |
| Daniel Starr | Center for Genetics and Development |
| Francene Steinberg | Dept. of Nutrition |
| Pieter Stroeve | Chemical Engineering & Material Science |
| Gang Sun | Textiles & Clothing |
| Dean Tantillo | Chemistry |
| Alice Tarantal | Pediatrics, School of Medicine, CA National Primate Center |
| Steven Theg | Plant Biology |
| Li Tian | Plant Sciences |
| Michael Toney | Chemistry |
| Jose Torres | MED: Medical Microbiology & Immunology |
| Renee Tsolis | Med Microbiology & Immunology: MED |
| Richard Tucker | Cell Biology & Human Anatomy |
| Jamal Tuqan | Electrical & Computer Engineering |
| Judy Van de Water | Division of Rheumatology/Allergy and Clinical |

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|---|---|
| | Immunology |
| Alison Van Eenennaam | Animal Science |
| Jean VanderGheynst | Biological & Agricultural Engineering |
| John Voss | Biochemistry and Molecular Medicine |
| Patricia Wakenell | Population Health & Reproduction: Vet Med |
| Robert Weiss | Internal Medicine: Division of Nephrology, School of Medicine |
| Valerie Williamson | Nematology |
| Barry Wilson | Animal Science & Environmental Toxicology |
| David Wilson | Molecular & Cellular Biology |
| Matthew Wood | Environmental Toxicology |
| Reen Wu | MED: Pulmonary / Critical Care Medicine |
| Stefan Wuertz | Civil & Environmental Engineering |
| Soichiro Yamada | Biomedical Engineering |
| Yin Yeh | Applied Science |
| Tilahun Yilma | VM: Pathology, Microbiology & Immunology |
| John Yoder | Vegetable Crops |
| Yohei Yokobayashi | Biomedical Engineering |
| Glenn Young | Food Science & Technology |
| Ruihong Zhang | Biological & Agricultural Engineering |

# *The Value of Internships*

Over the last 16 years (even before the formal DEB program was established), we have placed pre-doctoral students in a variety of biotechnology companies for their industrial research experience. They include:

Advanced Micro Devices (AMD)
Agilent Technologies
AgraQuest
Alza
Amgen
Amyris
Aqua Bounty
Bayer
Berlex Biosciences
BioMarin Pharmaceuticals, Inc.
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 170 students enrolled, so we need more Academic-Industry Partnerships.