Twentieth Annual

Biotechnology Training Retreat

Saturday,
April 2, 2011

Christian Brothers Retreat & Conference Center
Napa, CA

Twentieth Annual Biotechnology Training Retreat

Co-sponsored by:

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

UC Davis Designated Emphasis in Biotechnology
Graduate Program (DEB)

UC Davis Biotechnology Program

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2011 Welcome

Happy 20th Anniversary to biotechnology training at UC Davis! It is hard to believe that we have been holding this Biotechnology Training Retreat for 20 years. 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 **2010-11 NIH and Biotech 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** as they are also members of the DEB graduate program. We are honored to have our new Provost and Executive Vice Chancellor, Ralph Hexter, and new Vice Chancellor of Research, Harris Lewin, joins us on this very special day. We appreciate everyone's support for our competitive renewal of the NIH Training Grant in Biomolecular Technology to be submitted in May.

I would like to introduce our Biotechnology Fellows for 2010-11. Our **six NIH Fellows** include: **Dmitry Grapov,** Ag & Environmental Chemistry (preceptor is John Newman); **Mateo Hernandez** Chemistry, (preceptor is Donald Land); **Geetika Joshi**, Soils and Biogeochemistry (preceptor is Kate Scow); **Regina MacBarb**, Biomedical Engineering, (preceptor is Kyriacos Athanasiou); **Daniël Melters**, Cell and Developmental Biology (preceptor is Ian Korf and Simon Chan); and **Nancy Zeng**, Chemical Engineering (preceptor is Bill Ristenpart). Our **four Biotechnology Fellows** (funded by industry and campus fellowships) include: **Xiaoyan 'Helen' Chen,** Biomedical Engineering (preceptor is Tingrui Pan); **Sean Gilmore**, Applied Science (preceptor is Atul Parikh); **Silvia Hilt**, Biochemical & Molecular Biology (preceptor is John Voss); and **Jared Moore**, Chemistry (preceptor is Jared Shaw).

The **2010-11 CREATE-IGERT Trainees** are **Hyrum Gillespie, Mark Lemos, Patrick O'Dell, Tracy Zeng, and Steve Zicari.** They join the previous cohort trainees: **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.**

Our congratulations go out to all of these outstanding predoctoral candidates, we are very proud of them. We will be selecting our **2011-12 NIH Fellows** this spring. Nomination forms are on the web at www.deb.ucdavis.edu. Application deadline is **Monday, April 25th.** Remember, a student must be a member of the DEB and a U.S. citizen or permanent resident to be eligible to apply.

The DEB graduate program is the formal training program for the NIH biotechnology training grant as well as the NSF CREATE-IGERT. We stress team science across disciplines, seeing the "big picture" and entrepreneurship. Students are exposed to the business of science through an industrial internships and seminars. The number of **DEB PhD students is currently at 190 and climbing.** Each of our students is showcased on the DEB website, so check out our amazing scholars.

We placed eleven DEB students in their mandatory internship over the past year: Dominik Green, Alina Rabinovich Cao, and Xiguang (Ray) Chen, Kristina Mahan interned at **Novozymes** (Davis); Victor Haroldsen spent his time at **Nunhems** (Davis); Jared Townsend interned at **Sierra Sciences** in Reno, Nevada; ChengYuk Lee completed an internship with **Celgene, San Francisco,** working with Dr. Aaron Nguyen (a DEB grad); Chao Yu (Joy) Chen traveled to **OncoMed Pharmaceuticals**; and Chris Simmons completed his internship at the **Monsanto Calgene Campus.** We had two student complete international internships: Sunny Shah traveled to South Korea to intern at the **Gwangju Institute of Science and Technology** and visited numerous industries, and Mary Moore interned at **Helicos** in Sweden**.** 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 few students completed cross college internships or novel experiences to enhance their future careers. **Shannon Ceballos** is completing her internship in college teaching at American River College, where she is teaching, "Introduction to Biotechnology". **Mr. Yu-Shen Cheng,** a biosystems engineering student completed a cross college rotation in Prof. Labavitch's lab. He analyzed the glycosidic linkages of polysaccharides in the microalgal cell wall to learn more about the structure of cell walls. **Huilan Han**, a mechanical and aeronautical engineering recent graduate did her internship in Prof. Kit Lam's lab at the UC Davis Medical Center. **Thuc Nghi Nguyen** worked at the Allen Institute for Brain Science, a non-profit research institute in Seattle, WA. After her internship, she was offered a researcher position.

Nineteen doctoral students graduated this past year with a Designated Emphasis in Biotechnology: Zachary Bent; Yu-Shen "Joy" Cheng; Wen-Ying Feng; Prasad Gawande; Huilan Han; Kevin Holden; Matthew Hoopes; Jessica Houghton; Connie Jen; Vannarith Leang; Young (Lauren) Lee; Alina Rabinovich Cao; Meghan Rosen; David Sela; Christina Takanishi; Erin Tapley; Jared Townsend; Don-Hong Wang; Chun-Yi (Jimmy) Wu; and Kseniya Zakharyevich.

The logistics of this retreat has been overseen by our stellar team: Demian Sainz, Marianne Hunter, and Associate Director Denneal Jamison-McClung. Without their dedicated service, this annual event would not happen. Their hard work is much appreciated.

Thank you so much for coming to our annual celebration today. Please enjoy the great scientific presentations and posters, the delicious food and wine as well as the gorgeous scenery. Let us celebrate our accomplishments over the last 20 years and look forward to the next 20!

With warmest regards,

Judy Kjelstrom
Director,
UC Davis Biotechnology Program

NIH Training Program in Biomolecular Technology

(NIH-1-T32-GM08799)

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

Executive Committee

Faculty:

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

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Debbie Yaver, Novozymes, Inc.
Vishva Dixit, Genentech
Lyle Crossland, Monsanto, Calgene Campus

Judith A. Kjelstrom, Program Coordinator

Designated Emphasis in Biotechnology (DEB) Graduate Program

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Executive Committee

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Abhaya Dandekar
Karen McDonald
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Tiffany Glavan, Student Member

Judith A. Kjelstrom
Program Coordinator

UC Davis Biotechnology Program

www.biotech.ucdavis.edu

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UC Davis Twentieth Annual Biotechnology Training Retreat
April 2, 2011
Christian Brothers Retreat & Conference Center

Morning Schedule

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

Time	Event
8:00 – 8:30 am	**Registration/Continental Breakfast**
8:30 – 8:50 am	**Welcome** Bruce Hammock & Martina Newell-McGloughlin Director & Co-Director, NIH Training Grant in Biomolecular Technology
8:50 – 9:05 am	**Vision Statement for Campus** Provost and Executive Vice Chancellor Ralph Hexter
9:05 – 9:20 am	**Vision Statement for Research** Vice Chancellor of Research Harris Lewin
9:20 – 9:30 am	**Morning Session** Martina Newell-McGloughlin Co-Director, NIH Training Grant in Biomolecular Technology
9:30 – 10:40 am	**Presentations** 9:30 am Dmitry Grapov............................ *Mentor: John Newman* 9:55 am **Régine Behr**............................... **Novozymes** 10:15 am Mateo Hernandez......................... *Mentor: Donald Land* 10:40 am Geetika Joshi............................... *Mentor: Kate Scow*
10:40 – 10:50 am	**Break / Poster Viewing**
10:50 – 11:55 pm	**Presentations** 10:50 am **Greg Landes**........................ ...... **Takeda** 11:05 am Regina MacBarb.......................... *Mentor: Kyriacos Athanasiou* 11:30 am Daniël Melters............................ *Mentor: Ian Korf & Simon Chan* 11:55 pm Martina Newell-McGloughlin .... Bioethics Question (Handout)

Afternoon Schedule

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 Karen McDonald Co-Director, NIH Training Grant in Biomolecular Technology
1:25 – 3:05 pm	**Presentations** 1:25 pm Martina Newell-McGloughlin .... Bioethics Question (Discussion) 1:45 pm Nancy Zeng .... *Mentor: Bill Ristenpart* 2:10 pm **Lyle Crossland** .... **Monsanto, Calgene** 2:30 pm Xiaoyan 'Helen' Chen .... *Mentor: Tingrui Pan* 2:55 pm **Joan Greve** .... **Genentech**
3:15 - 3:35 pm	**Short Break (20 min)**
3:35 – 4:50 pm	**Presentations** 3:35 pm Sean Gilmore .... *Mentor: Atul Parikh* 4:00 pm Silvia Hilt .... *Mentor: John Voss* 4:25 pm Jared Moore .... *Mentor: Jared Shaw*
4:50 pm	**Closing Remarks** Bruce Hammock Director, NIH Training Grant in Biomolecular Technology

5:20 pm – Bus departs Napa

2011 Poster Titles

A. **"NMR Spectroscopy to Monitor and Characterize Lipids From Microalgae for Biofuel Applications"**
Lisa A. Anderson* and Annaliese K. Franz
Department of Chemistry, University of California, Davis

B. **"Transient Co-expression of Post-Transcriptional Gene Silencing Suppressors Increased *in planta* Expression of a Recombinant Anthrax Receptor Fusion Protein"**
Lucas Arzola*[1], Junxing Chen[1], Kittipong Rattanaporn*[1], James Maclean[2], and Karen McDonald[1]
[1]Department of Chemical Engineering & Materials Science, University of California, Davis
[2]Planet Biotechnology, Clawiter Rd, Hayward, CA

C. **"Investigating General Stress-Response Networks in Arabidopsis"**
Marta Bjornson*[1,2] and Katayoon Dehesh[2]
[1]Department of Plant Sciences, University of California, Davis
[2]Department of Plant Biology, University of California, Davis

D. **"Impact of Allergen and Ozone on the Peripheral Blood Immune Phenotype During Infancy"**
Candace M. Burke*, Justin Fontaine, Joan E. Gerriets, Dallas M. Hyde, and Lisa A. Miller
California National Primate Research Center, University of California, Davis

E. **"Expression and Regulation of rDEFA3: An Unusual Defensin"**
Patricia Castillo*, Hiutung Chu and Charles l. Bevins
Department of Medical Microbiology and Immunology, University of California, Davis

F. **"Positron Emission Tomographic (PET) Imaging of Activated Matriptase as a Mark for Cancer Progression"**
Julia Choi, et al.
Department of Biomedical Engineering, University of California, Davis

G. **"Shear Forces and High Affinity LFA-1 Drive PMN Recruitment"**
Neha Dixit*[1,2], Itsukyo Yamayoshi[2], Ari Nazarian[2], Scott Simon [1,2]*
[1]Graduate Group in Immunology, University of California, Davis
[2]Department of Biomedical Engineering, University of California, Davis

H. **"Quantitative Proteomics Reveals Dynamic Changes At the Plasma Membrane During Plant Immune Responses"**
J. Mitch Elmore*[1], Jun Liu[1], Brett Phinney[2], and Gitta Coaker[1]
[1]Department of Plant Pathology, University of California, Davis
[2]Genome Center Proteomics Core Facility, University of California, Davis

***DEB Graduate Student**

I. **“Docosahexanenoic Acid (DHA) Prevents Trans-10, Cis-12 Conjugated Linoleic Acid (CLA)-Induced Insulin Resistance (IR) and Non-Alcoholic Fatty Liver Disease (NAFLD) But Not Adipose Tissue Inflammatory Markers In Mice”**
Dawn M. Fedor*[1], Yuriko Adkins[1], Darshan S. Kelley[1,2]
[1]Department of Nutrition, University of California, Davis
[2]Western Human Nutrition Research Center, ARS, USDA, and

J. **“Mediation of Huanglongbing and Citrus Variegated Chlorosis Using Chimeric Antimicrobial Proteins”**
Hyrum Gillespie*, Hossein F. Gouran*[1], Ana M. Ibáñez [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. **“Identifying Eukaryotic Microbial Diversity: Linking Sequence With Morphology”**
Marissa B. Hirst*, Kari D. Hagen, and Scott C. Dawson
Department of Microbiology, University of California, Davis

L. **“Localization and Recovery of *In Planta* Produced Cellulase Enzyme”**
Nathaniel J. Kingsbury* and Karen McDonald
Department of Chemical Engineering and Materials Science, University of California, Davis

M. **“Expanding the Awesome Power of Phytochrome Signaling to Applications in Biotechnology and Agriculture”**
Wei Hu* and J. Clark Lagarias
Department of Molecular and Cellular Biology, University of California, Davis

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

O. **“Transient *In Planta* Production of a Cellulose-Degrading Enzyme”**
Ben Lindenmuth*and Karen McDonald
Department of Chemical Engineering & Materials Science, University of California, Davis

P. **“High Transient and Stable Production of Human Therapeutic Antibodies in Plants”**
James M. Maclean, Anita Jamin, Y Tran, Archana Belle, Leah Schaefer, and Keith Wycoff
Planet Biotechnology, 25571 Clawiter Road, Hayward, CA 94545

Q. **“Structure-Function Studies of Nitrobenzene 1,2-Dioxygenase”**
Kristina M. Mahan*, Juan V. Parales, and Rebecca E. Parales
Department of Microbiology, University of California, Davis

***DEB Graduate Student**

R. **“Oxygen Removal of Lignign-Derived Compound: Conversion of Guaiacol With Hydrogen Catalyzed By Platinum Supported on Alumina”**

Tarit Nimmanwuipong*[1], Ron C. Runnebaum*[2], David E. Block[1,2], and Bruce C. Gates[1]
[1]Department of Chemical Engineering and Materials Science, University of California, Davis
[2]Department of Viticulture and Enology, University of California, Davis

S. **“Investigation of Cellulose Microfibrils Using Atomic Force Microscopy”**

Patrick O’Dell*, Tina Jeoh, Monica Santa-Maria
Department of Biological and Agricultural Engineering, University of California, Davis

T. **“Catalytic Conversion of Anisole and 4-Methylanisole: Evidence of Reaction Networks, Classes of Chemistry, and Kinetics”**

Ron C. Runnebaum*[1], Tarit Nimmanwuipong*[1], David E. Block[1,2], and Bruce C. Gates[1]
[1]Department of Chemical Engineering and Materials Science, University of California, Davis
[2]Department of Viticulture and Enology, University of California, Davis

U. **“Flourescence Measurements and Visualization of Intracellular Lipids in Microalgae for Biofuel Applications”**

Diana M. Wong* and Annaliese K. Franz
Department of Chemistry, University of California, Davis

V. **“Effect of Protein Solubility on Antigen Removal From Xenogeneic Tissue Scaffolds”**

Maelene L. Wong[1] and Leigh G. Griffiths[2]
[1]Department of Biomedical Engineering
[2]Veterinary Medicine and Epidemiology, University of California, Davis

W. **“The Small GTPase SPGA Plays a Critical Role in Septation in the Filamentous Fungus *Aspergillus Nidulans*”**

Tracy Cui Zeng*, Hye-Ryun Kim, and Bo Liu
Department of Plant Biology, University of California, Davis

X. **“Optimizing Energy Beet Utilization for Production of Biofuels and Coproducts”**

Steven Zicari*, Jean VanderGhyenst, and Ruihong Zhang
Department of Biological and Agricultural Engineering, University of California, Davis

Y. **“Effect of Co-Expression of Cucumber Mosaic Virus (CMV) Coat Protein on Transient Expression of a Human Therapeutic Protein in Plant Tissue Using a CMV Viral Amplicon Based Expression System”**

Kittipong Rattanaporn*[1], Karen A. McDonald[1], and Bryce W. Falk[2]
[1]Department of Biological and Agricultural Engineering, University of California, Davis
[2]Department of Biological and Agricultural Engineering, University of California, Davis

***DEB Graduate Student**

Z. "Identifying the Biochemical and Molecular Components of Plant Stress Perception"

Geoffrey Benn*[1], Marta Bjornson*[1,2], Katayoon Dehesh[1]
[1]Department of Plant Biology, University of California, Davis
[2]Department of Plant Sciences, University of California, Davis

***DEB Graduate Student**

2011 Presentation Titles

1. **"Lipid Markers of Type 2 Diabetes and Uncoupling Protein 3"**
   Dmitry Grapov*[1], Sean Adams*[2,3], John W. Newman[2,3], *et al.*
   [1]Ag & Environmental Chemistry, University of California, Davis
   [2]USDA/ARS Western Human Nutrition Research Center, Davis, CA
   [3]Nutrition Department, University of California, Davis

2. **"*Bacillus* Tools For Industrial Applications"**
   Régine Behr[a], M. Thomas[a], A. Breünerb, S. Jørgensen[b], and M. Rasmussen[b]
   [a] Prokaryotic Expression Department, Novozymes, Davis, CA - USA
   [b] Bacterial Gene Technology Department, Novozymes, Bagsvaerd – Denmark

3. **"Infrared Spectroscopy of Biomolecule Reactions in Aqueous Solutions: Stability of Lipid Membrane Structures and Their Reactions with Solution Species"**
   Mateo Hernandez* and Donald P. Land
   Department of Chemistry, University of California, Davis

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

5. **"Takeda San Francisco: A New Drug Modality For a 230 Year Old Company"**
   Greg Landes
   Discovery, Antibody Research and Preclinical Development
   Takeda San Francisco, South San Francisco, CA

6. **"Optimizing Fibrocartilage Scaffold-Free Culture"**
   Regina MacBarb* and Kyriacos Athanasiou
   Department of Biomedical Engineering, University of California, Davis

7. **"DNA Sequences of a Paradox: General Properties of Centromeric Tandem Repeats in 170+ Plants and Animals"**
   Daniël Melters*[1], Keith Bradnam[2], Hugh Young[3], Christian Tobias[3], Simon Chan[1], and Ian Korf[2]
   [1]Department of Plant Biology, University of California, Davis
   [2]Genome Center, University of California, Davis
   [3]USDA, Agricultural Research Service, Genomics and Gene Discovery, Albany, California

8. **"Ethics Discussion"**
   Martina Newell-McGloughlin
   Director, International Biotechnology Program

***DEB Graduate Student**

9. **Microfluidic Investigation of the Effects of Oxidative Stress on Mechanotransduction in Human Erythrocytes"**
   Nancy Zeng* and William Ristenpart
   Department of Chemical Engineering and Materials Science, University of California, Davis

10. **"Crop Innovation and Monsanto Davis Site"**
    Lyle Crossland
    Monsanto, Calgene Campus, CA

11. **"Automatic Capillary Molding for 2D and 3D Scaffolds**
    Xiaoyan Chen* and Tingrui Pan
    Department of Biomedical Engineering, University of California, Davis

12. **"The Role of Imaging in Drug Development"**
    Joan Greve
    Department of Biomedical Imaging, Genentech, Inc., South San Francisco, CA

13. **"Folding On Command: Programmed Bending Activates Dynamic Mechanochemical Coupling in Supported Lipid Bilayers"**
    Sean Gilmore*[1], Harika Nanduri[2], and Atul N. Parikh[1]
    Department of Applied Science, University of California, Davis,
    Department of Biomedical Engineering, University of California, Davis

14. **"At the Cross Roads of Nanobiotechnology and Protein Engineering: A Nanoparticle Platform for Incorporating GPCRs Generated by a Cell Free System"**
    Silvia Hilt* and John Voss
    Department of Biochemistry and Molecular Biology, University of California, Davis

15. **"Synthetic Efforts Toward Inhibitors of Bacterial Cell Division Proteins"**
    Jared Moore* and Jared Shaw
    Department of Chemistry, University of California, Davis

***DEB Graduate Student**

Oral Presentation Abstracts

NIH FELLOW: Dmitry Grapov

LIPID MARKERS OF TYPE 2 DIABETES AND UNCOUPLING PROTEIN 3

Presenter: Dmitry Grapov*
Authors: **Dmitry Grapov*[1]**, Sean Adams*[2,3], John W. Newman[2,3], *et al.*
Affiliations: [1]Ag & Environmental Chemistry, University of California, Davis
[2]USDA/ARS Western Human Nutrition Research Center, Davis, CA
[3]Nutrition, University of California, Davis
Preceptor: John Newman

The quantitative measurement of the small-molecule end products of physiological processes through metabolomic profiling may improve our understanding of complex diseases such as type 2 diabetes (T2D). Chronic insulin resistance (IR) is a hallmark of T2D and can develop from obesogenic lifestyles including high fat, high carbohydrate diets, and lack of physical activity. The transition from short-term, “normal”, to chronic IR may involve changes in mitochondrial β-oxidation capacity. We hypothesize that non-esterified free fatty acid (NEFA), endocannabinoid (eCBs) and oxylipin (OxL) cellular signaling mediators will reflect organismal IR and cellular lipid/carbohydrate fuel selection. We further hypothesize that the quantitative metabolomic investigation of these species coupled with megavariate modeling will provide novel insight into their roles in the development of T2D. To test these hypotheses we conducted a study to evaluate the ability of these metabolites to report clinical diabetes and changes in mitochondrial function in a cohort of BMI- and age-matched obese African-American women. Study participants were comprised of diabetic (n=43) and non-diabetic (n=12) subjects who were also equally distributed between the wildtype (g/g) and missense (g/a) uncoupling protein 3 (UCP3) genotypes. UCP3 g/a carriers are thought to have a non-functional UCP3 which alters their carbohydrate/lipids utilization, and compared to g/a carriers, exhibit a ~50% reduction in whole body fat oxidation. Using megavariate and network modeling approaches we identified previously unknown relationships between NEFA, eCBs and 18-carbon epoxides. These species are shown to increase with decreasing glucose control. Among T2D, increases in c18-epoxides are strongly linked to changes in NEFA, which may suggest a common source for their release into circulation. Interestingly, we observed an inverse relationship between circulating eCB and OxL markers for T2D. Relative to g/g, g/a UCP3 carriers displayed increased eCB and decreased OxL markers. These findings suggest that increases in eCBs, which are potentiators of adipose differentiation and glucose uptake, may constitute a novel mechanism to offset reduced β-oxidation by facilitating increased glucose and fat storage, thereby reducing lipo- and glucotoxicity derived oxidative stress.

***DEB Graduate Student**

COMPANY AFFILIATE: Novozymes

BACILLUS TOOLS FOR INDUSTRIAL APPLICATIONS

Presenter: Régine Behr**, PhD

Authors: **R. Behr**[**a]**, M. Thomas[a], A. Breünerb, S. Jørgensen[b], and M. Rasmussen[b]

Affiliations: [a] Prokaryotic Expression Department, Novozymes, Davis, CA - USA
[b] Bacterial Gene Technology Department, Novozymes, Bagsvaerd – Denmark

Email: rbe@novozymes.com

Bacillus is one of the most important organisms in the bioindustrial revolution providing new sustainable biological solutions to society. Fortunately this genera, and in particular the model organism *Bacillus subtilis*, have been the subject of intense studies for more than 50 years. *Bacillus subtilis* was of interest primarily due to its ability to differentiate into resistant spores, but later it was discovered that this organism, as well as other related bacilli, are capable of secreting enzymes in very high yields. Since then, the bioindustry has gained interest and has exploited this ability to produce enzymes for a broad range of applications in a wide number of industries. Novozymes is today the largest supplier of enzymes in the world. *Bacillus subtilis* has become a Gram-positive giant when it comes to new studies, as exemplified by being one of the first genomes to be sequenced. Later it was subjected to an innovative functional analysis program to map the function of unknown genes and more recently numerous omics data has been generated. Bacillus is now the preferred bacterium when it comes to large scale expression of proteins. Many of the tools developed by universities and by Novozymes enable us to streamline the process from primary screening of new enzyme molecules, to mutagenesis of enzymes for optimized activity in applications, and finally to the construction of advanced production organisms. This talk will focus on a number of different genetic tools for bacillus which have been developed over the past 20 years by universities and the industry.

Presenter

NIH FELLOW: Mateo Hernandez

INFRARED SPECTROSCOPY OF BIOMOLECULE REACTIONS IN AQUEOUS SOLUTIONS: STABILITY OF LIPID MEMBRANE STRUCTURES AND THEIR REACTIONS WITH SOLUTION SPECIES

Presenter: Mateo Hernandez*
Authors: **Mateo Hernandez*** and Donald P. Land
Affiliations: Chemistry Department, University of California, Davis
Preceptor: Donald Land

Our group specializes in novel methods for using infrared spectroscopy to probe reactions in aqueous solutions. Of particular interest are the interactions between biomolecules and membrane bilayers at physiological pH, ionic strength, and temperature. Biomolecules interacting with lipid bilayers comprise the single most important class of functional biochemistry, encompassing cell-signaling, trans-membrane transport, cell recognition, selective drug delivery, and numerous other important aspects. In this talk, I will highlight several approaches to probing the reactivity and stability of various engineered nanoscale architectures of lipid bilayers in aqueous solution. Using a variety of approaches, we are able to produce stabile structures of 2-D extended lipid monolayer films, 2-D extended lipid bilayer films, 2-D lipid bilayer nano-particles (~10 nm diam. stabilized with apolipoprotein "belts"), or 3-D lipid bilayers in 100 nm spherical liposomes. IR spectroscopy can distinguish these different structures and probe changes in the structures. For each type of bilayer structure, we demonstrate how *in situ* IR spectroscopy can be used to monitor reactions of the bilayers in solution.

***DEB Graduate Student**

NIH FELLOW: Geetika Joshi

REGULATION OF METHYL-TERT-BUTYL ETHER DEGRADATION PATHWAYS IN *METHYLIBIUM PETROLEIPHILUM* 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 the primary groundwater contaminant 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. *Methylibium petroleiphilum* PM1 is a methylotrophic bacterium capable of completely degrading MTBE and TBA under aerobic conditions. It is imperative to understand the regulation of the pathway to develop efficient approaches to improvise current bioremediation and monitoring strategies. This study aims to (1) determine if the MTBE-degradation pathway in PM1 is inducible and (2) construct a green fluorescent protein (GFP) based reporter vector to identify promoters of *mdpA* and *mdpJ* genes that code for the enzymes involved in the degradation of MTBE and TBA, respectively. To accomplish this, (1) PM1 cells were grown on four substrates: MTBE, TBA, 2-hydroxy Butyric Acid (HIBA) and pyruvic acid. First three are metabolites in MTBE degradation pathway; pyruvate served as control. mRNA was extracted from cells and analyzed for expression of *mdpA* and *mdpJ* by RT-qPCR using gene-specific primers. Gene expression was also studied as a time-course study with MTBE and TBA as substrates for resting-cell experiments. (2) Reporter vector to identify promoters of *mdpA* and *mdpJ* was constructed to incorporate a multiple cloning site, *gfp* and streptomycin resistance gene as the selectable marker. It was observed that (1) Cells grown on MTBE and TBA had higher expression of *mdpA* and *mdpJ* than those grown on other substrates, indicating that MTBE and TBA degradation by PM1 is induced in the presence of these two substrates. Highest levels of expression were seen for both genes on exposure to both MTBE and TBA after 6 hours, peaking between 6h and 12h. (2) Constructs with promoterless *gfp* and that under the control of a native PM1 promoter as positive control have been cloned into a transposon vector to be used as the carrier vector. This study will further drive our future work on biosensor development for MTBE detection in environmental samples.

***DEB Graduate Student**

COMPANY AFFILIATE: Takeda San Francisco

TAKEDA SAN FRANCISCO: A NEW DRUG MODALITY FOR A 230 YEAR OLD COMPANY

Presenter: Greg Landes**

Authors: **Greg Landes****

Affiliations: Discovery, Antibody Research and Preclinical Development
Takeda San Francisco, South San Francisco, CA

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Takeda San Francisco is the newest member of the global Takeda family of companies. TSF is the Center of Excellence for biologics for Takeda and follows in the footsteps of other Takeda COEs including the research organization of Millennium Pharmaceuticals, which identifies drugs that selectively alter protein homeostasis in tumor cells, Takeda Cambridge, which utilizes knockout mice to uncover therapeutic phenotypes for targeted drug discovery, and Takeda San Diego, which leverages high throughput crystallography to enable structure-based drug design. Takeda Pharmaceutical Company is the oldest, largest and most respected pharmaceutical company in Japan with a history of success in the discovery and development of small molecule drugs. Its globalization efforts were recognized by *BioWorld* in 2008, when it named Takeda "Pharmaceutical Company of the Year."

TSF, as the COE for biologics, is responsible for the discovery and advancement of biologics drug candidates up to IND-enabling activities for clinical development. Greater than 85% of the TSF employees and contractors are members of the scientific team and involved in the drug discovery process with the remaining staff members playing critical general and administration roles that support discovery activities. Antibodies are the predominant drug modality at TSF and are exploited to identify the next generation treatments in the therapeutic areas of oncology, inflammation and autoimmunity, and metabolic disease. It follows that the skill sets at TSF include scientists with expertise in antibody discovery technologies including hybridoma and antibody phage display, antibody engineering methodologies such as humanization and affinity maturation, biochemical and cell-based assay development and screening, applied biophysical chemistry for the determination of K_D, k_a, k_d and epitope bins using Biacore, KinExa and FACS, established efficacy models in cancer, inflammation and metabolic disease, experimental pathology, translational medicine, toxicology, recombinant antigen and antibody expression and purification, recombinant protein analytical biochemistry, generation of manufacturing cell lines, initial optimization of upstream and downstream process sciences activities, and creation of bioanalytical assays in support of clinical development.

Our capabilities will be illustrated using a program that has advanced rapidly from concept to preclinical proof-of-concept.

**Presenter

NIH FELLOW: Regina MacBarb

OPTIMIZING FIBROCARTILAGE SCAFFOLD-FREE CULTURE

Presenter: Regina MacBarb*
Authors: **Regina F. MacBarb*** and Kyriacos Athanasiou
Affiliations: Department of Biomedical Engineering, University of California, Davis
Preceptor: Kyriacos Athanasiou

The fibrocartilages of the temporomandibular joint (TMJ) lack an innate ability to self-repair once afflicted by temporomandibular joint disorders (TMD). Due to the high morbidity and prevalence of TMD, the global objective of this work is to optimize and employ a biomimetic approach toward the repair and replacement of TMJ tissues. To address this objective, we will create a spectrum of fibrocartilaginous tissues by employing co-cultures of meniscus cells (MCs) and articular chondrocytes (ACs) in the self-assembling process. To enhance the functional properties of the scaffold-free constructs, we will investigate the effects of temporally-coordinated application of bioactive and matrix-modifying agents. One such matrix-modifying agent is chondroitinase-ABC (C-ABC), an enzyme that cleaves glycosaminoglycan side chains and, previously, has been shown to enhance the tensile properties of tissue engineered cartilage. For the application of this enzyme in this culture system, we hypothesized that a one-time C-ABC treatment after both 1 & 3 weeks of culture would enhance the tensile properties of constructs when compared to those receiving a single treatment at either 1 or 3 weeks. Co-culture constructs were prepared at 50:50, 75:25, and 100:0 MC:AC ratios, and treated with C-ABC at either 1 week, 1 & 3 weeks, 3 weeks, or never during a 5 week culture period. The 50:50 co-culture groups were found to have an instantaneous modulus of 700 – 1000 kPa, falling within in the range of native tissue values (400 – 1500 kPa). The 75:25 group was found to have a relaxation modulus of 40 – 50 kPa, just slightly higher than the native tissue range (30 – 40 kPa). With regards to tensile properties, C-ABC treatment at 1 & 3 weeks enhanced the Young's modulus of the 50:50 group to 2400 kPa. This is a highly exciting result due to the difficulty in obtaining adequate tensile properties in tissue engineered cartilage. In addition to a biomechanical evaluation, these constructs will be assessed via biochemical, histological, immunohistochemical and scanning electron microscopy. Through this work, we will focus on enhancing the functional properties of scaffold-free, fibrocartilaginous neotissue in an effort to provide relief for those patients suffering from TMD.

***DEB Graduate Student**

NIH FELLOW: Daniël Melters

DNA SEQUENCES OF A PARADOX: GENERAL PROPERTIES OF CENTROMERIC TANDEM REPEATS IN 170+ PLANTS AND ANIMALS

Presenter: Daniël Melters*

Authors: **Daniël Melters***[1], Keith Bradnam[2], Hugh Young[3], Christian Tobias[3], Simon Chan[1], and Ian Korf[2]

Affiliations: [1]Department of Plant Biology, University of California, Davis
[2]Genome Center, University of California, Davis
[3]USDA, Agricultural Research Service, Genomics and Gene Discovery, Albany, California

Preceptors: Ian Korf and Simon Chan

One of the most important biological events is cell division. First the whole genome needs to be duplicated and subsequently equally divided. This is to guarantee that both the daughter cells get the same genome as the mother cell. The chromosomal locus that facilitates this process is the centromere. Despite being one of the first chromosomal loci to be discovered, little progress has been made in understanding the evolution of centromeres. This is largely due to the centromere paradox. Where the centromere as a functional unit is essential, proteins associated with the centromere and centromeric DNA appear to be fast evolving.

Centromeric DNA largely consist of large tandem repeat arrays. Therefore, we have developed a bioinformatics approach to identify centromeric tandem repeats. This high-throughput method allows us to study any species with a sequenced genome. By comparing the centromeric tandem repeats from over 250 plants and animal, we tried to reconstruct the evolution of centromeric DNA. Whereas homologous proteins are commonly found over a large phylogenetic group, centromeric tandem repeat appear to have a very limited phylogenetic spread. In addition, no general sequence characteristics were found to be conserved between species. Surprisingly, in several grass species we found evidence supporting the 'library' hypothesis. The 'library' hypothesis attempt to explain the rapid evolution of centromere DNA. In a given tandem repeat array, multiple variants exist and through stochastic amplification and shrinkage, each variant could become the dominant centromeric tandem repeat. This hypothesis can now be studied on a large phylogenetic scale.

***DEB Graduate Student**

UCDAVIS Biotechnology Program

Bioethics Discussion

Written and Presented by

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

ETHICS QUESTION

In Flagrante Delicto?

In Flagrante Delicto?

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

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

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

But in the next few weeks the interaction between busilis and chrysopoeia that is discussed in the paper remains in Dr. Purloin's mind. Busilis was not a line of inquiry that Dr. Purloin and Ms. Arcana were following in their research. They were focusing on other stimulatory proteins, but with little success. Dr. Purloin suggests to Ms. Arcana that she add a compound to the cell culture system that stimulates the cell to produce its own busilis, a method that is somewhat different from the one described in the paper by Dr. Abstentia which is under review. The enhancement method works. The cells live for a month.

Ms. Arcana and Dr. Purloin draft a paper based on the results, which includes appropriate controls. *Cell* a prestigious journal, accepts the paper. Several months later, *Protein Connections* publishes a revised paper from the laboratory of Dr. Abstentia. But after Dr. Abstentia sees the article in *Cell* he suspects that Dr. Purloin, who was an anonymous peer reviewer on the paper, might have taken some of the ideas for the *Cell* article from his paper under review. Dr. Abstentia knows that Dr. Purloin hadn't been working on busilis because

it was hard to purify, and deduces that he used material in the unpublished manuscript to stimulate busilis activity (he ground it up and added it to the media!!).

[1]

What is responsible peer review?

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

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

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

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

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

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

Other thoughts

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

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

[1] With thanks to various RCR sources for ideas

NIH FELLOW: Nancy Zeng

MICROFLUIDIC INVESTIGATION OF THE EFFECTS OF OXIDATIVE STRESS ON MECHANOTRANSDUCTION IN HUMAN ERYTHROCYTES

Presenter: Nancy Zeng*
Authors: **Nancy F. Zeng*** and William D. Ristenpart
Affiliations: Department of Chemical Engineering and Materials Science, University of California, Davis
Preceptor: William Ristenpart

Due to their lack of nucleus and inability to take part in gene transcription, red blood cells (RBCs) have traditionally been considered to serve primarily as passive transporters of oxygen. Recent work, however, has suggested that RBCs are able to sense and respond to small changes in their environment through post translational modifications (PTMs) in membrane proteins. Via modification through redox or phosphorylative pathways, RBCs are now hypothesized to actively participate in vasodilatory mechanotransduction to control local circulation and meet the metabolic needs of the body.

Oxidative stress is an important driving force to induce PTMs, and accordingly the effects of oxidative stress on membrane deformability, lipid peroxidation, and cytoskeletal/hemoglobin crosslinking have been studied extensively. However, experimental work to date on the effects of oxidative stress on mechanotransduction has been limited to applied forces dissimilar to those experienced by RBCs *in vivo*. Furthermore, very little is known about the dynamics of mechanotransduction in response to oxidative stress.

Here we investigate the dynamics of mechanotransduction in RBCs subjected to varying degrees of oxidative stress by using hydrogen peroxide as a generator of oxidizing radicals. We use a microfluidic platform to impose precisely defined fluid flows that mimic in vivo conditions. The RBCs are visualized using high speed video at 15,000 frames per second, and quantitative hematological information including cell deformability, elongation, and velocity are extracted via custom algorithms in Matlab. We present preliminary results regarding the effect of H_2O_2 on RBC deformability, and we discuss the implications for future work on the corresponding mechanotransductive pathways for vasodilatory signaling.

***DEB Graduate Student**

COMPANY AFFILIATE: Monsanto, Calgene Campus

CROP INNOVATION AND MONSANTO DAVIS SITE

Presenter: Lyle Crossland**, PhD

Authors: **Lyle Crossland**

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

Population growth and rising incomes are driving continued increase in the need for food. Most experts suggest a need to double agricultural production by 2050, but opportunities for bringing new land into production are limited. Availability and cost of inputs, especially water, also will constrain production growth. Advances in breeding, biotechnology and agronomic practices will be required to meet future food production needs. Monsanto is developing biotech traits to improve yield and resource use and the Davis site has an emphasis on improving water use efficiency in key crops. Progress in this effort and the Davis site's role will be discussed.

****Presenter**

BIOTECH FELLOW: Xiaoyan "Helen" Chen

AUTOMATIC CAPILLARY MOLDING FOR 2D AND 3D SCAFFOLDS

Presenter: Xiaoyan Chen*
Authors: **Xiaoyan Chen***and Tingrui Pan
Affiliations: Department of Biomedical Engineering, University of California, Davis
Preceptor: Tingrui Pan

Conventional methods of fabricating tissue scaffolds such as 3D-printing, fused deposition modeling, and selective laser sintering all either require the use of toxic organic solvents, high processing temperatures, or limited pore size ranges.[1] We have developed a simple and repeatable way to fabricate tissue scaffold of any shape using surface microfluidic platform. Device fabrication only requires a mask, dry film, UV lamp, and glass. We utilize photolithography technique to pattern dry film on glass. Sodium alginate can be driven into the patterned channels automatically by capillary force. The chip is then immersed in calcium chloride solution to form gelled patterns. After the sol to gel transition is complete, the scaffold can then be peeled off in water using tweezers. We have generated alginate fiber mesh of 10 to 100 microns using this method. To allow cells to grow on the scaffold, we have modified the scaffold with RGDC peptide. By tagging a fluorescent molecule, fluorescein-5-maleimide, to RGDC, we have confirmed the RGD modification of alginate hydrogel. This simple method can be applied to a wide range of polymers and fabricate scaffolds to suit different biological needs.

References:

1) Ma, X. P.; Elisseeff J. Scaffolding in Tissue Engineering. Boca Raton, FL: CRC Press, **2006**

***DEB Graduate Student**

COMPANY AFFILIATE: Genentech, Inc.

THE ROLE OF IMAGING IN DRUG DEVELOPMENT

Presenter: Joan M. Greve**, PhD

Author: **Joan M. Greve****

Affiliations: Department of Biomedical Imaging, Genentech, Inc.
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Considered the founder of the biotechnology industry, Genentech has been delivering on the promise of biotechnology for more than 30 years, using human genetic information to discover, develop, manufacture and commercialize medicines to treat patients with serious or life-threatening medical conditions. Today, Genentech is among the world's leading biotech companies, with multiple products on the market and a promising development pipeline.

Just one contributing factor to the success of Genentech's development pipeline is the foresight Genentech had to invest in translational technology such as biomedical imaging (magnetic resonance imaging, computational tomography, ultrasound, positron emission tomography, and optical methods). The Biomedical Imaging group, composed primarily of bioengineers and physical scientists, uses these technologies to answer biological questions pertinent to successful drug development. Their pursuits include phenotyping (anatomical, physiological, pathophysiological), applying different modalities at different stages in the development process, and intertwining preclinical and clinical imaging data to more rapidly understand the pathophysiology and therapeutics under investigation. This presentation seeks to elucidate Genentech's vision and structure, the Biomedical Imaging group's resources and philosophy, and how the two combine to provide the opportunity to do impactful science.

****Presenter**

BIOTECH FELLOW: Sean Gilmore

FOLDING ON COMMAND: PROGRAMMED BENDING ACTIVITIES DYNAMIC MECHANOCHEMICAL COUPLING IN SUPPORTED LIPID BILAYERS

Presenter: Sean Gilmore*

Authors: **Sean Gilmore*[1]**, Harika Nanduri[2], and Atul N. Parikh[1]

Affiliations: [1]Department of Applied Science, University of California, Davis
[2]Department of Biomedical Engineering, University of California, Davis

Preceptor: Atul Parikh

In living cells, mechanochemical coupling represents a dynamic means by which membrane components are spatially organized. An extra-ordinary example of such coupling involves curvature-dependent polar localization of chemically-distinct lipid domains at bacterial poles, which also undergo dramatic reequilibration upon subtle changes in their interfacial environment such as during sporulation. Here, we demonstrate that such interfacially-triggered mechanochemical coupling can be recapitulated in vitro by real-time introduction of mechanically-generated periodic curvatures and attendant strain-induced lateral forces in lipid bilayers supported on elastomeric substrates. In particular, we show that real-time wrinkling of the elastomeric substrate prompts a dynamic domain re-organization within the adhering bilayer, producing large, oriented liquid-ordered domains in regions of low curvature. The results suggest a mechanism in which interfacial forces generated during surface wrinkling and the topographical deformation of the bilayer facilitate dynamic re-equilibration prompting the observed domian reorganization. This model system will hopefully prove to be a simple and versatile tool for a broad range of studies of curvature-dependent dynamic reorganizations in membranes that are constrained by the interfacial elastic and dynamic frameworks including the cell wall, glycocalyx, and cytoskeleton. We also expect it to prove to be a useful platform in studies of force sensitive membrane proteins.

***DEB Graduate Student**

BIOTECH FELLOW: Silvia Hilt

AT THE CROSS ROADS OF NANOBIOTECHNOLOGY AND PROTEIN ENGINEERING: A NANOPARTICLE PLATFORM FOR INCORPORATING GPCRs GENERATED BY A CELL FREE SYSTEM

Presenter: Silvia Hilt*
Authors: **Silvia Hilt*** and John Voss
Affiliations: Department of Biochemistry and Molecular Biology, University of California, Davis
Preceptor: John Voss

A cross-disciplinary biomolecular research project, it uses a novel cell-free method to generate, optimize and characterize G-protein coupled receptors (GPCRs) using nanobiotechnology combined with advanced protein engineering and analysis tools. GPCRs represent the single largest protein target of pharmaceuticals, however their membrane embedment complicates the development of screens and diagnostic reporters due to the uncertainty in the homogeneity of reconstituting the proteins in liposomes. Furthermore, liposome reconstitution methods require detergents during the purification step, often resulting in protein unfolding or aggregation. The recent application of nanolipoprotein particles (NLPs; aka nanodiscs) to solubilize membrane proteins in small (~10 nm) discoidal particles composed of bilayer lipid and surrounding scaffold protein represents a reliable and reproducible platform for generating and characterizing GPCRs. As such, an NLP-associated GPCR can be evaluated at the molecular level for structure and activity, and therefore used in drug screens, as well as a diagnostic reporter for more complex events related to cell signaling.

***DEB Graduate Student**

BIOTECH FELLOW: Jared Moore

SYNTHETIC EFFORTS TOWARDS INHIBITORS OF BACTERIAL CELL DIVISION PROTEINS

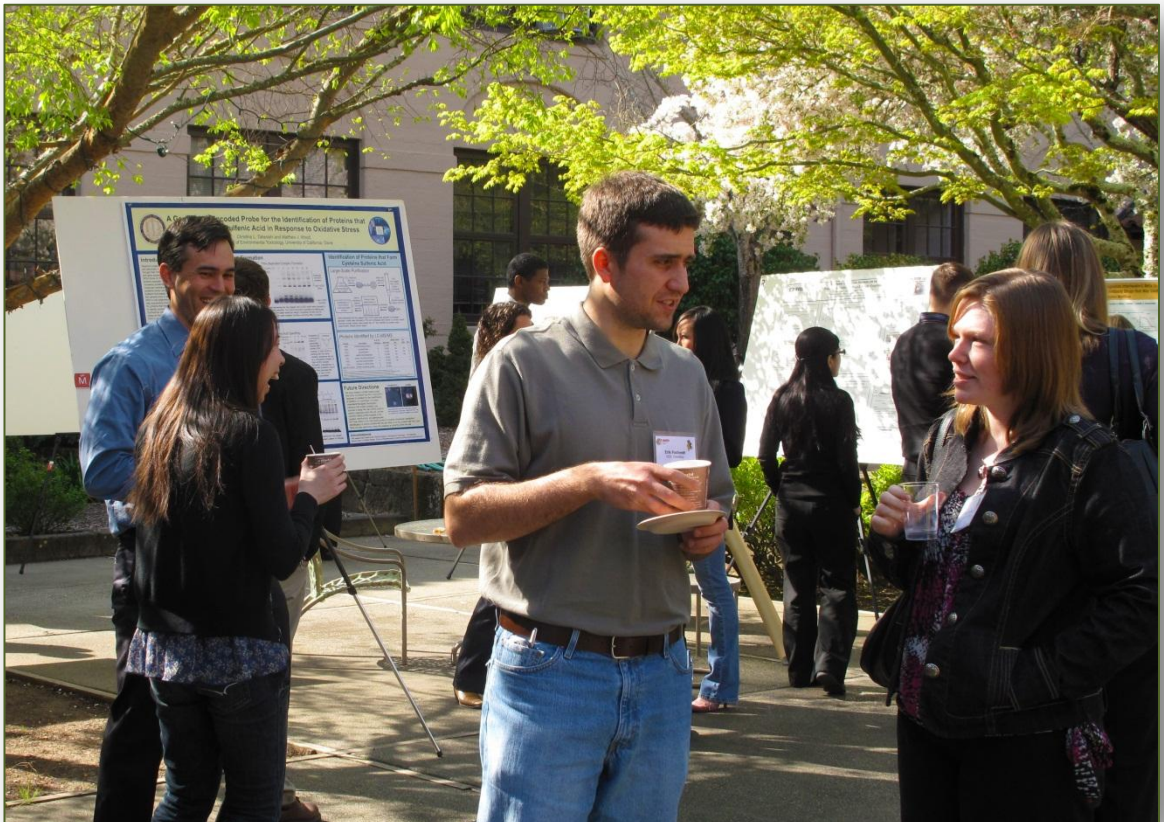
Presenter: Jared Moore*
Authors: **Jared Moore***and Jared Shaw
Affiliations: Department of Chemistry, University of California, Davis
Preceptor: Jared Shaw

Designing and synthesizing new compounds to investigate emerging targets of bacterial cell division is an essential step in development of antibiotics and target validation. The goal of my project is to develop highly selective inhibitors of the prokaryotic skeletal protein FtsZ. FtsZ (filamenting temperature sensitive protein Z) is the prokaryotic homolog of tubulin and is known to play an important, though not fully characterized, role in bacterial cell division. FtsZ is highly conserved among bacteria and is essential for cellular division making this protein a valuable target for the development of antibiotics. One naturally occurring compound that has activity against FtsZ is totarol. Totarol has been shown to inhibit the GTPase activity of FtsZ and cause filamentation of Gram-positive bacteria, including MRSA, indicating that totarol is a promising starting point for structure-activity relationship studies to increase its inhibition of FtsZ. Previously, our lab designed and synthesized multiple analogs of totarol that have shown an increase in potency compared to the original natural product. The totarol analogs I have accessed proceed via a novel catalytic hetero-polycyclization reaction. The structural basis for the inhibition of FtsZ will be evaluated using the new compounds in NMR chemical shift perturbation studies. Once binding sites are established, our goal is to identify pharmacophores and design better compounds in an iterative cycle to design more potent inhibitors of FtsZ.

***DEB Graduate Student**

UC DAVIS Biotechnology Program

Poster Abstracts



A. NMR SPECTROSCOPY TO MONITOR AND CHARACTERIZE LIPIDS FROM MICROALGAE FOR BIOFUEL APPLICATIONS

Lisa A. Anderson* and Annaliese K. Franz
Department of Chemistry, University of California, Davis

Microalgae as feedstocks for biofuels are a promising renewable energy source because of their efficient photosynthetic conversion of sunlight, CO_2, and water into carbohydrates, lipids, and biomass. This research aims to improve current algae biotechnology by characterizing microalgae lipid extracts directly using ^1H nuclear magnetic resonance (NMR) spectroscopy and developing a novel method for real-time whole cell NMR spectroscopic analysis of intracellular lipids. We have currently optimized NMR spectroscopy methods to quantify triacylglyceride (TAG) fatty acid composition and compare the TAGs of six lipid-producing algae species. Our results provide direct measurements of increased levels of C18:3 polyunsaturated fatty acids (PUFA) for certain algae strains compared to more mono-unsaturated fatty acid constituents of other microalgae strains. To avoid the tedious extraction process, preliminary results show that whole cell NMR water suppression techniques can be used to monitor increased cellular lipid production. We are also investigating growth conditions to increase lipid production in order to make microalgal biofuels a more economically viable alternative energy fuel source. Microalgae growth conditions are being optimized in microplates with varying concentrations of additives, such as sodium bicarbonate as a source of supplemental CO_2. Increased growth rates and lipid levels in some species have been observed and other preliminary results will be discussed.

***DEB Graduate Student**

B. TRANSIENT CO-EXPRESSION OF POST-TRANSCRIPTIONAL GENE SILENCING SUPPRESSORS INCREASED *IN PLANTA* EXPRESSION OF A RECOMBINANT ANTHRAX RECEPTOR FUSION PROTEIN

Lucas Arzola*[1], Junxing Chen[1], Kittipong Rattanaporn*[1], James Maclean[2], and Karen McDonald[1]

[1] Department of Chemical Engineering and Materials Science, University of California, Davis

[2] Planet Biotechnology, Clawiter Rd, Hayward, CA

Potential epidemics of infectious diseases and the constant threat of bioterrorism demand rapid, scalable, and cost-efficient production of therapeutic proteins. Molecular farming of tobacco plants provides a cost-effective alternative for production of pharmaceutical proteins. *Agrobacterium tumefaciens* mediated transformation, utilizing agroinfiltration, can be used to rapidly induce the transient expression of a protein of interest. We have developed a transient production platform for a novel anthrax receptor decoy protein (immunoadhesin), PBI-220, in *Nicotiana benthamiana* plants. This chimeric fusion protein is composed of the von Willebrand factor A (VWA) domain of human capillary morphogenesis 2 (CMG2), an effective anthrax toxin receptor, and the constant region of human immunoglobulin G (IgG). PBI-220 mitigates the effects of anthrax by preventing production of the deadly anthrax toxins.

We have evaluated, in intact plants and detached leaves, the co-expression of PBI-220 with nine different viral suppressors of post-transcriptional gene silencing (PTGS): p1, p10, p19, p21, p24, p25, p38, 2b, and HCPro. *Nicotiana benthamiana* plants and leaves were sampled at 3.5 days, 7 days, and 14 days post agroinfiltration. ELISA and Bradford assay were performed to quantitatively measure the PBI-220 protein concentration and total soluble protein concentration, while Western Blot was used to confirm the identity of the expressed PBI-220. Overall, transient expression of PBI-220 was higher on intact plants than detached leaves. It was observed to be highest with p1 co-expression at 3.5 days, resulting in a maximum production of 0.56 g PBI-220 per kg fresh weight of leaf. Co-expression with certain PTGS suppressors - particularly p1, p19, and p21 - significantly improved PBI-220 expression levels under 35S promoter control, while the other viral suppressors had no effect on the recombinant protein expression level.

***DEB Graduate Student**

C. INVESTIGATING GENERAL STRESS-RESPONSE NETWORKS IN ARABIDOPSIS

Marta Bjornson*[1,2] and Katayoon Dehesh[2]
[1]Department of Plant Sciences, University of California, Davis
[2]Department of Plant Biology, University of California, Davis

Plants are subjected to a myriad of environmental stresses both biotic and abiotic in nature. Although plant responses to these stresses have been studied, the mechanisms of stress perception and induction of stress response have remained elusive. In microarrays conducted after wounding and after *Phytophthora* infection, abiotic and biotic stresses respectively, the expression levels and patterns of many genes are altered. Among these are four genes that are up-regulated under both conditions. Based on additional bioinformatics analysis, these genes are co-expressed, suggesting they belong to the same or closely related plant stress- responsive signaling networks. Two of these stress-responsive genes encode CAF1a and CAF1b, enzymes belonging to a family of deadenylases previously studied in the Dehesh lab. Transgenic lines with altered expression of these two genes are available in the lab. The other two genes are an ethylene response factor and a gene of unknown function. I have generated transgenic plants that either enhance or reduce the expression of these two genes. In order to complete a genetic toolbox for studying this stress response network, I will generate higher order mutants, silenced in multiple genes, and transgenic plants, which overexpress multiple genes in this network. The response of these singly and combinatorially genetically modified plants to various stresses will clarify the role of these genes within the plant stress perception and signal transduction network.

***DEB Graduate Student**

D. IMPACT OF ALLERGEN AND OZONE ON THE PERIPHERAL BLOOD IMMUNE PHENOTYPE DURING PREGNANCY

Candace M. Burke*, Justin Fontaine, Joan E. Gerriets, Dallas M. Hyde, and Lisa A. Miller
California National Primate Research Center, University of California, Davis

In affected individuals, asthma pathogenesis follows a progressive path starting at infancy. We hypothesized that environmental exposure to allergens and air pollutants during infancy can differentially affect the immune profile of peripheral blood. To test this hypothesis, we determined the impact of *in vivo* allergen and ozone exposure on peripheral blood immune cells and cytokine expression in a monkey model of childhood asthma during the first six months of life. Rhesus monkeys were sensitized to house dust mite antigens via systemic and intranasal administration, followed by cyclic exposure to aeroallergen and/or ozone beginning at 1 month of age. Complete blood counts, along with qRT-PCR on whole blood samples, were used to measure the longitudinal effects of exposure on the peripheral blood immune profile. Total circulating leukocyte numbers fluctuated significantly with age, with a peak observed at 20 weeks of age. The total T cell population, defined by expression of CD3 mRNA, was significantly elevated in animals exposed to either ozone or combined ozone/allergen. Although CD3 mRNA significantly increased with age across all exposure groups, this did not correlate to higher lymphocyte numbers, suggesting preferential expansion of CD3+ T cells in the lymphocyte pool. There was a progressive increase in IFN , a key cytokine in regulating the Th1 immune response, with maturity, although exposure condition had no significant effect on expression. IL-4, an important mediator of Th2 cell differentiation, was significantly reduced in groups exposed to HDM alone or combined HDM+ozone. HDM exposure resulted in significantly reduced levels of IL-6 mRNA. Interestingly, this suppression was also observed upon *in-vitro* HDM restimulation of PBMCs collected at necropsy, indicating preferential expansion of an altered specific memory T cell population. Early life allergen and air pollutant exposure results in an altered peripheral blood immune profile, with significant fluctuations in cell numbers and cytokines occurring in a non-linear fashion. Further studies aimed at elucidating early life mechanisms mediating persistent immune profile changes and determining windows of susceptibility will help develop novel therapeutic strategies for asthma.

***DEB Graduate Student**

E. EXPRESSION AND REGULATION OF Rdefa3: AN UNUSUAL DEFENSIN

Patricia Castillo*, Hiutung Chu and Charles L. Bevins
Department of Medical Microbiology and Immunology, University of California, Davis

Alpha-Defensins are a major class of antibiotic peptides in mammals that are active against a broad spectrum of microorganisms. Most Alpha-defensins are expressed in either neutrophils or small intestinal epithelial cells termed Paneth cells. One unique alpha-defensin, *rDefa3* is expressed in both cellular locations. This unique feature of *rDefa3* indicates special regulatory mechanisms for this gene that has never been explored. To determine the innate immune function of defensins in vivo, our laboratory has studied transgenic mouse models. We hypothesize that these transgenic mice will have an enhanced immune function compared to their wild type littermates. To analyze the regulation and innate immune function of r*Defa3*, we created a transgenic model using a 5.5kb genomic DNA encompassing the rDefa3 gene. To determine the transcription start site, we generated full length cDNA from bone marrow and small intestine using RNA ligase mediated 5' RACE PCR. We converted RNA to cDNA and used qRT-PCR to quantify the expression levels of rDefa3. To localize *rDefa3* protein expression, we performed IHC. ISH will determine rDefa3 mRNA localization. To determine if *rDefa3* alters the microflora, bacterial DNA will be isolated and analyzed with 16s rDNA. To determine the innate immune function of *rDefa3*, transgenic and wild type mice will be orally infected with S. Typhimurium, E. coli and Y. enterica. Two independent transgenic mouse lines were generated and both showed germ-line transmission of the rDefa3 transgene. 5'RACE determined that the *rDefa3* transcripts of the bone marrow and small intestine of rats are identical. *rDefa3* mRNA is expressed in the small intestine of transgenic mice at levels similar to that observed in rats. IHC showed that the *rDefa3* protein is localized to the Paneth cell. Conclusion: We have created a new alpha-defensin transgenic mouse model that will further define the in vivo biological function of these peptides.

***DEB Graduate Student**

F. POSITRON EMISSION TOMOGRAPHIC (PET) IMAGING OF ACTIVATED MATRIPTASE AS A MARKER FOR CANCER PROGRESSION

Julia Choi, et al.**
Department of Biomedical Engineering, University of California, Davis

Background and objectives: The serine protease matriptase is a putative biomarker for survival independent of HER-2/*neu*. Overexpression of matriptase relative to its endogenous inhibitor HAI-1 is associated with poor outcome in breast and other cancers. Very low levels of active matriptase are present in normal0 tissues due to tightly regulated activation. This regulation is disrupted in cancer suggesting that active matriptase may be a marker of tumor progression. Therefore we developed radiotracers against activated matriptase for *in vivo* imaging using PET, with the aim to improve noninvasive imaging, detection, and specificity for breast cancer patients.

Brief description of methodologies: M69, an antibody against activated matriptase, was functionalized to coordinate [64Cu]copper or [89Zr]zirconium: 64Cu-BAT-2IT-M69 and 89Zrdesferrioxamine-M69 were evaluated in a mouse model for human breast cancer. Tetracyclineinducible matriptase expressing and control cell-lines were injected bilaterally into female nude mice to generate matriptase-positive and control tumors. Mice were fed dox chow *ad libitum*, administered radiotracer, imaged using small-animal PET at 1-4d p.i.; and through 14d for 89Zr; corresponding biodistribution studies were performed.

Results to date: PET images indicated specific tumor retention, with higher uptake of both 64Cu-BAT-2IT-M69 and 89Zr-desferrioxamine-M69 in positive tumor over control from 3d; a two-fold difference was also observed 3-14d for 89Zr-DFO-M69 and confirmed by biodistribution. Immunostaining of FFPE tissues confirmed tumor expression status.

Conclusions and potential impact on breast cancer treatment: We have developed novel radiotracers and demonstrated that the *in vivo* imaging of activated matriptase is feasible. Activated matriptase is therefore a potential imaging target that may prove to be a valuable diagnostic and prognostic marker.

****Presenter**

G. SHEAR FORCES AND HIGH AFFINITY LFA-1 DRIVE PMN RECRUITMENT

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Acute inflammation triggers the innate immune response of neutrophils that efficiently traffic from the blood stream to concentrate at high numbers at the site of tissue infection or wounding. A gatekeeper in this process is activation of β_2-integrins, which forms bond clusters with ICAM-1 on the endothelial surface. These bond clusters serve dual functions of providing adhesive strength to anchor neutrophils under the shear forces of blood flow and directional guidance for cell polarization and subsequent transmigration on inflamed endothelium. We hypothesized that shear forces transmitted through high affinity LFA-1 facilitates their cooperation with the calcium release activated channel (CRAC) Orai1 in directing localized cytoskeletal activation and directed migration. Employing vascular mimetic microfluidic channels we observed neutrophils arresting on a substrate of either ICAM-1 or allosteric antibodies that stabilize a high or low affinity conformation of LFA-1. Neutrophils captured via low affinity LFA-1 did not exhibit intracellular calcium flux, F-actin polymerization, cell polarization, or directional migration under shear flow. In contrast, high affinity LFA-1 provided orientation along a uropod-pseudopod axis that required calcium flux through Orai1. We demonstrate how the shear stress of blood flow can transduce distinct outside-in signals at focal sites of high affinity LFA-1 that provides contact mediated guidance for neutrophil emigration.

***DEB Graduate Student**

H. QUANTITATIVE PROTEOMICS REVEALS DYNAMIC CHANGES AT THE PLASMA MEMBRANE DURING PLANT IMMUNE RESPONSES

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Most classes of plant pathogens remain extracellular during their lifecycle. As a result, the plant plasma membrane mediates critical aspects of plant immunity including pathogen recognition, signal transduction, and downstream defense responses. Investigating how the plasma membrane proteome changes during these events will identify novel components of plant defense responses and lead to a better understanding of plant immune signaling. We have used quantitative proteomics to investigate plasma membrane dynamics during effector-triggered immunity (ETI).

Transgenic *Arabidopsis* plants expressing the bacterial effector AvrRpt2 under the control of a dexamethasone-inducible promoter were used to induce ETI. Expression of the AvrRpt2 protease results in RIN4 cleavage and activation of the Resistance (R) protein RPS2. Plasma membrane vesicles were isolated 6 hours post-Dex treatment and subjected to gel-enhanced liquid chromatography tandem mass spectrometry (GE LC-MS/MS) for protein identifications. The QSpec spectral counting program was used to quantify relative protein abundance between treatments. Approximately 2300 proteins were identified across 3 biological replicates and over 20% are significantly changing during ETI. Proteins that are up-regulated at the plasma membrane during ETI include proteins involved in membrane scaffolding and transport, signal transduction, primary and secondary metabolism, and known regulators of plant immune responses. These experiments highlight the dynamic nature of the plasma membrane proteome during plant defense responses.

***DEB Graduate Student**

I. DOCOSAHEXAENOIC ACID (DHA) PREVENTS TRANS-10, CIS-12 CONJUGATED LINOLEIC ACID (CLA)-INDUCED INSULIN RESISTANCE (IR) AND NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) BUT NOT ADIPOSE TISSUE INFLAMMATORY MARKERS IN MICE

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We previously reported that CLA induced IR and NAFLD in mice, both of which could be prevented by the concomitant supplementation with DHA. The objective of this study was to investigate if DHA prevented CLA-induced IR and NAFLD by attenuating adipose tissue inflammation. Eight-week-old C57BL/6J female mice (n=12) were fed either a control diet or diets containing 0.5% CLA (wt %), 1.5% DHA or 0.5% CLA + 1.5% DHA for 4 weeks prior to termination. CLA supplementation increased circulating insulin by 6.6-fold, homeostatic model assessment of IR by 7.2 fold, circulating monocyte chemotactic protein-1 (MCP-1) by 1.6 fold, and liver weight by 2 fold when compared to the corresponding values in the control group. It also increased inflammatory marker gene expression in adipose tissue for F4/80, tumor necrosis factor alpha (TNF) and MCP-1 by 4,-, 4.5- and 7.4-folds, respectively, when compared to the control group. DHA prevented the CLA-induced IR and fatty liver and decreased the circulating MCP-1; however, it did not decrease F4/80, TNF and MCP-1 gene expression in adipose tissue. Furthermore, DHA decreased liver MCP-1 gene expression by 65% compared to CLA alone. Our results suggest that the CLA-induced increase in expression of adipose tissue MCP-1, TNF , and F4/80 may not mediate the CLA-induced IR and NAFLD. Further studies are needed to determine the underlying mechanisms.

***DEB Graduate Student**

J. MEDIATION OF HUANGLONGBING AND CITRUS VARIEGATED CHLOROSIS USING CHIMERIC ANTIMICROBIAL PROTEINS

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Huanglongbing (HLB), an extremely destructive vector born disease caused by *Candidatus* Liberibacter *asiaticus,* has been found in citrus groves throughout Florida. Citrus Variegated Chlorosis (CVC), caused by *Xylella fastidiosa (Xf)* which inhabits the xylem of sweet oranges, has had a devastating economic impact on citrus groves throughout Brazil. While as of yet these pathogens have not entered California, both of these pathogens are posed to cause vast losses to California growers similar to those experienced worldwide. A chimeric antimicrobial protein (CAP) was designed in our lab to specifically target *Xylella fastidiosa,* and confers marked plant resistance to *Xf,* causative agent of Pierce's disease in grape. Transgenic citrus trees expressing this CAP will be tested to determine resistance to CVC. Further, a new CAP using a HLB specific outer membrane protein will be developed and tested for effectiveness in transgenic rootstock.

***DEB Graduate Student**

K. IDENTIFYING EUKARYOTIC MICROBIAL DIVERSITY: LINKING SEQUENCE WITH MORPHOLOGY

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Traditional methods for identifying microbes in the environment, particularly protists, has relied on cultivation and microscopic descriptions coupled with dichotomous keys. Unfortunately, cultivation is often unsuccessful and identification by microscopy is often biased towards the most ubiquitous organisms. Alternative culture-independent approaches, including sequencing of 18s small subunit ribosomal RNA provides a more sensitive method to identify and quantify microbial diversity. In order to fully characterize the eukaryotic diversity of a microbial community, however, classical morphological features identified using microscopy need to be linked to environmental sequence data. For this study, fluorescent oligonucleotide ssu 18s rDNA probes (eukaryote, parabasalid, or ciliate-specific) were used in whole cell, rRNA-targeted, fluorescent in situ hybridization (whole cell FISH) in combination with immunostaining (anti-cytoskeletal or anti-heat shock protein 70 [Hsp70]). This permitted us to link eukaryote morphology with ssu rRNA sequence in freshly fixed environmental samples (termite hindgut, Putah Creek, and hay infusion). This work revealed a cytoplasmic distribution of ssu 18s rDNA probes in parabasalids, ciliates, and a variety of previously uncharacterized eukaryotes. Cytoskeletal immunostaining illustrated intact cilia, flagella, and in some cases, internal microtubules. Hsp70 immunostaining was targeted to hydrogenosomes in eukaryotes allowing for an approximation of the number hydrogenosomes in each cell. This was the first time FISH and immunostaining were used in succession to characterize eukaryotes in any uncultivated sample. Future use of this powerful technique permits us to both identify and characterize uncultivated protists and couple classical microscopic morphological imaging with sequence-based identification in environmental samples.

***DEB Graduate Student**

L. LOCALIZATION AND RECOVERY OF *IN PLANTA* PRODUCED CELLULASE ENZYME

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In planta production of apoplast-targeted cellulose degrading enzymes may be a valuable approach either for in-situ decomposition of cellulose into sugars that can then be microbially fermented into advanced biofuels or for efficient recovery of concentrated enzyme preparations that are free from components that may inhibit biological conversion of other feedstocks. A vacuum infiltration-centrifugation method is being developed for obtaining apoplast wash fluid that removes the *Acidothermus cellulyticus* thermostable endoglucanase E1 that is transiently expressed in tobacco leaves. Using this method we are able to recover active E1 produced and found that the vast majority of the E1 removed was indeed localized to the apoplast. For optimal recovery of endoglucanase activity in the apoplast wash fluid, it may be necessary to add components to the infiltration buffer that will release E1 bound to the plant cell walls and increase cell wall porosity.

***DEB Graduate Student**

M. EXPANDING THE AWESOME POWER OF PHYTOCHROME SIGNALING TO APPLICATIONS IN BIOTECHNOLOGY AND AGRICULTURE

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Phytochromes are red/far-red photosensors in plants that promote expression of genes involved in light capture and photosynthetic carbon fixation when light conditions are optimal. In high-density field crop plantings however, the inactivation of phytochrome triggers shade avoidance responses, e.g., increased stem elongation, early flowering, premature leaf senescence, and increased susceptibility to insectivory. Important for reproductive success in the competitive natural environment, shade avoidance responses are deleterious to grain yield under high density, monoculture farming practices. Thus, manipulating shade avoidance has been a major target of conventional plant breeding programs for centuries. We previously identified a tyrosine-to-histidine (YH) mutation that confers dominant, constitutive signaling activity of phytochromes A and B in the model eudicot species, *Arabidopsis thaliana* [1]. Phenotypic measurements indicate that shade avoidance behavior is strongly suppressed in transgenic plants expressing constitutively active alleles of phytochrome B (CAAP-B), which also exhibit light-independent development in complete darkness [2]. The agronomic potential of CAAP expression was first evaluated in tobacco. Greenhouse experiments have validated the potential of CAAP-B to mitigate shade avoidance by delaying flowering and leaf senescence. Companion studies seek to exploit CAAP-Bs as antibiotic/herbicide-free selection markers for cruciferous crop plant species. CAAP–B expression also can be used to regulate photomorphogenesis of a cereal crop species and the monocot annual grass species *Brachypodium distachyon*. Using two cultivars of rice (*Oryza sativa)*, we will show that T_2 CAAP-B transgenic plants, but not T_2 plants expressing wild-type rice PHYB, exhibit phenotypes consistent with a constitutive signaling activity of the former. More comparative phenotypic analyses of homozygous T_2 lines are underway and we soon hope to test whether the CAAP expression will enhance photosynthetic carbon fixation, tillering and seed yield in the field. Our studies thus set the stage for commercially viable cereal high yield grain species expressing a plant-derived, non-allergenic gene product.

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***DEB Graduate Student**

N. BIOLOGICAL SYNTHESIS OF HIGHER ALCOHOLS AS BIOFUELS

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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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***DEB Graduate Student**

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

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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.

***DEB Graduate Student**

P. HIGH TRANSIENT AND STABLE PRODUCTION OF HUMAN THERAPEUTIC ANTIBODIES IN PLANTS

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Plant expression systems are gradually gaining widespread acceptance and could provide an alternative platform for the cost-effective, large-scale production of monoclonal antibodies (mAbs), which have been in increasing demand for therapeutic and diagnostic use. Here we demonstrate high transient and stable production in plants using three human mAbs that bind to non-overlapping epitopes on botulinum neurotoxin serotype A (BoNT/A).

The three antibodies (RAZ1, CR2, 2G11) were expressed either as human IgG1 molecules or as IgG1/IgG2 chimeras (IgG2/1) consisting of the IgG2 CH1, upper and middle hinge fused to the lower hinge, CH2 and CH3 regions of IgG1. When expressed transiently in *Nicotiana benthamiana* plants, using a scalable vacuum infiltration method, RAZ1-IgG1 accumulated to an average of 2 g IgG/kg fresh plant weight (FW) (approx. 8 % TSP), and the RAZ1-IgG2/1 chimera expressed at levels averaging 3 g IgG/kg FW (approx. 13 % TSP). The affinity of the plant-made chimeric antibodies for BoNT/A A1 was comparable to the affinity of the corresponding CHO-made IgG1 antibodies.

IgG2/1 also accumulated better than IgG1 in stable transgenic tobacco plants. For the three anti-BoNT/A IgG2/1 chimeric antibodies we attained expression values greater than 100 mg IgG/kg FW (in mature plants); with numerous RAZ1-IgG2/1 lines expressing between 200 and 400 mg IgG/kg FW.

At these expression levels, plants offer a very economical alternative for the large-scale production of antibodies. Our cost model suggests that a sterile filtered plant concentrate (equivalent to a clarified cell culture supernatant) is about 5 % of the cost of producing the same protein using CHO cells.

****Presenter**

Q. STRUCTURE-FUNCTION STUDIES OF NITROBENZENE 1,2-DIOXYGENASE

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Nitroaromatic compounds are toxic, synthetic chemicals commonly used in the production of pesticides, dyes, plastics, and explosives. These synthetic compounds are resistant to biological and chemical degradation, and therefore they persist in the environment for long periods of time. Only a few microorganisms have been able to adapt and evolve new metabolic pathways that utilize these man-made compounds as their sole carbon, nitrogen, and energy sources. One such microbe is *Comamonas* sp. JS765, a strain capable of completely mineralizing the toxic nitroaromatic compound nitrobenzene to carbon dioxide and nitrite. We are interested in characterizing nitrobenzene 1,2-dioxygenase (NBDO), the initial enzyme in the nitrobenzene degradation pathway. NBDO requires specific electron transfer proteins (reductase and ferredoxin) to transfer electrons from NADH to the catalytic oxygenase component. Using structural data we identified residues on the surface of the oxygenase and ferredoxin that may be involved in protein-protein interactions between the two components. Site-directed mutagenesis was used to make amino acid substitutions in the oxygenase and ferredoxin components at sites near the Rieske clusters predicted to interfere with electron transfer. Using whole cell biotransformation assays, we found that amino acid substitutions at position 98 (changing Val 98 to Asp, Glu, or Phe) of the oxygenase and amino acid substitutions on the acidic region of the ferredoxin (changing Asp 53, Glu 62, Leu 66, or Pro 81 to Ala or Pro 65 to Lys) resulted in severely reduced enzymatic activity. We also developed a strategy and have identified mutant ferredoxins with compensatory mutations that restore wild-type activity to the Val 98 oxygenase mutants. These studies identify residues on the surface of the oxygenase and ferredoxin that are involved in protein-protein interactions and electron transfer.

***DEB Graduate Student**

R. OXYGEN REMOVAL OF LIGNIN-DERIVED COMPOUND: CONVERSION OF GUAIACOL WITH HYDROGEN CATALYZED BY PLATINUM SUPPORTED ON ALUMINA

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Although lignin constitutes as much as about 30 wt% of lignocellulosic biomass and offers excellent potential as a feedstock for catalytic conversion processes, it has received less attention than cellulose with regard to catalytic upgrading to biofuels and value added chemicals. In contrast to the literature of cellulose-derived compounds (carbohydrates), the literature of lignin-derived compounds provides little fundamental understanding of the reaction networks characterizing the catalytic conversions. Detailed and quantitative information about the products, the important reaction pathways, and kinetics is limited. Our goal was to provide such information and to begin unraveling the chemistry of conversion of compounds characteristic of lignin-derived bio-oils—and specifically to understand crucial catalytic oxygen-removal reactions. Our approach was to investigate the conversion of prototypical compounds that represent key lignin monomers (*p*-coumaryl alcohol, coniferyl alcohol, and sinapyl alcohol) catalyzed by a solid acid (HY zeolite) and a supported metal ($Pt/\gamma\text{-}Al_2O_3$). The work summarized here is focused primarily on compounds that are characteristic of coniferyl alcohol, namely, guaiacol (2-methoxyphenol). The conversion of guaiacol catalyzed by $Pt/\gamma\text{-}Al_2O_3$ in the presence of H_2 was investigated with a flow reactor at 573 K and 140 kPa. Dozens of reaction products were identified, the most abundant being phenol, catechol, and 3-methylcatechol. The kinetically significant reaction classes were hydrogenolysis (including hydrodeoxygenation, HDO), hydrogenation, and transalkylation. Selectivity-conversion data were used to determine an approximate quantitative reaction network accounting for the primary products, and a qualitative network was also inferred. Catalytic HDO was evidenced by the production of anisole and phenol. The HDO selectivity increased with increasing H_2 partial pressure and decreasing temperature. Products formed by transalkylation reactions match those produced in the conversion catalyzed by HY zeolite, in which no deoxygenated products were observed. The network of these reactions combined with knowledge of the kinetics provides a valuable step towards prediction of the catalytic conversion of lignin-derived bio-oils.

***DEB Graduate Student**

S. INVESTIGATION OF CELLULOSE MICROFIBRILS USING ATOMIC FORCE MICROSCOPY

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Lignocellulosic materials compose the large source of plant biomass on earth, and cellulose has been proposed as a feedstock for renewable biofuels. However, fuels from lignocellulosic biomass has not been commercialized for a number of reasons. Currently, the use of naturally occurring enzymes from fungus have been used to decompose lignocellulose, however the mechanism of action of these enzymes is not well understood. Our laboratory uses atomic force microscopy (AFM) to study the interaction between cellulose-degrading enzymes (cellulases) and cellulose microfibrils. In a recent imaging of bacterial cellulose, we noticed spherical aggregates (nanoparticles) with diameters in the range of 40 – 120 nm. These nanoparticles were observed to be resistant to hydrolysis by purified the cellulose degrading enzyme, Trichoderma reesei Cel7A (TrCe7A). This study is focused on determining the chemical composition and mechanical characteristics of these nanoparticles, the factors leading to nanoparticle formation. This study will refine the procedure for preparing cellulose microfibrils for AFM imaging and use data collected from the AFM to classify the nanoparticles. Understanding the effects of pretreatments on the molecular structure of lignocellulosic biomass will increase the fraction of biomass that can successfully be converted into biofuel. In addition, a better understanding of the mechanisms behind enzymatic hydrolysis of lignocellulosic biomass will lead to improvements in the saccharification process.

***DEB Graduate Student**

T. CATALYTIC CONVERSION OF ANISOLE AND 4-METHYLANISOLE: EVIDENCE OF REACTION NETWORKS, CLASSES OF CHEMISTRY, AND KINETICS

Ron C. Runnebaum*[1], Tarit Nimmanwudipong*[1], David E. Block[1,2], and Bruce C. Gates[1]

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Anisole and 4-methylanisole are compounds that are representative of bio-oils made by pyrolysis of biomass, especially lignin. Catalytic upgrading of bio-oils offers the prospect of major processes for fuels to replace fossil fuels. We report the conversions of each of these compounds in the presence of catalysts (including platinum supported on Al2O3 and on SiO2-Al2O3), determining the catalytic activity, selectivity, and stability in operation in a once-through packed-bed flow reactor. On-line GC-TCD/FID and off-line GC-MS and GC-FID were used to analyze the major, minor, and even trace products. The data demonstrate the kinetically significant reaction classes, namely, transalkylation, hydrodeoxygentation, and hydrogenation. The data determine a reaction network for each of these conversions and the connections between them.

***DEB Graduate Student**

U. FLOURESCENCE MEASUREMENTS AND VISUALIZATION OF INTRACELLULAR LIPIDS IN MICROALGAE FOR BIOFUEL APPLICATIONS

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Microalgae produce triacylglycerides (TAGs) as a natural oil that can be converted into biodiesel fuel by chemical modifications. Previous literature reports have shown that as microalgae growth proceeds from exponential (logarithmic) to stationary (linear) growth phase, the overall production of triacylglycerides increases. Triacylglycerides serve as storage lipids where levels increase in stationary growth phase as nutrients are depleted. In this study, we use a high-throughput method with a lipophilic dye to measure intracellular neutral lipids and investigate the optimal day to harvest microalgae that will give the maximum TAGs for biodiesel production. Confocal scanning laser microscopy (CSLM) imaging with several lipophilic dyes is used in complement to visualize and verify TAG storage. Our preliminary results provide answers regarding the nature of the increased production of TAGs observed in stationary phase cultures.

***DEB Graduate Student**

V. EFFECT OF PROTEIN SOLUBILITY ON ANTIGEN REMOVAL FROM XENOGENEIC TISSUE SCAFFOLDS

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Biomaterial xenoantigenicity represents the critical barrier to use of unfixed bovine pericardium (BP) as a tissue engineering scaffold. Current decellularization techniques fail to recognize that (1) antigen removal (AR) from xenogeneic biomaterials is largely diffusion dependent and (2) proteins only diffuse into solutions in which they are soluble. We hypothesize that xenoantigen solubilization is critical for facilitating AR from intact BP. We investigated the effect of increasing reducing agent (DTT) and salt (KCl) concentrations on AR from BP in a pair of two-phase studies. Phase 1 determined the effect of increasing DTT or KCl concentration on residual antigenicity of BP post-AR (BP-AR). Optimal phase 1 concentration was then tested in phase 2 for its ability to influence AR for buffers containing no additional additive, 134 mM NDSB-256, or 0.1% SDS. Residual antigens extracted from BP-AR were subjected to electrophoresis and Western blot, probed with rabbit serum generated against native BP. Increasing concentrations of DTT up to 100 mM significantly enhanced AR ($p<0.0001$). Residual antigens in BP-AR were reduced by almost 70% in the presence of 100 mM DTT compared to the absence of DTT. Presence of 100 mM DTT significantly reduced residual antigenicity of BP-AR compared to 1 mM DTT for no additive, 134 mM NDSB-256, and 0.1% (w/v) SDS ($p<0.005$). Increasing KCl concentrations up to 100 mM resulted in an additional significant decrease in residual antigenicity ($p<0.0001$). Residual antigens on BP-AR were reduced by 52% in the presence of 100 mM KCl compared to the absence of KCl. Presence of 100 mM KCl significantly reduced residual antigenicity of BP-AR compared to 10 mM KCl for no additive and 134 mM NDSB ($p<0.05$), but not 0.1% SDS. Moreover, residual antigenicity of BP-AR following treatment with 100 mM DTT and 100 mM KCl was not significantly different between no additive, 134 mM NDSB-256, and 0.1% (w/v) SDS. These results suggest maintenance of protein solubility, through modulation of reducing agent and salt concentrations, significantly enhances AR from BP. Moreover, solubilizing factors are greater determinants of AR efficiency than additive used.

**Presenter

W. THE SMALL GTPase SPGA PLAYS A CRITICAL ROLE IN SEPTATION IN THE FILAMENTOUS FUNGUS *ASPERGILLUS NIDULANS*

Tracy Cui Zeng*, Hye-Ryun Kim, and Bo Liu
Department of Plant Biology, University of California, Davis

Filamentous ascomycetes form mycelia of multinucleate hyphal cells. It is unclear how cytokinesis/septation is temporally regulated in these fungi. In *Aspergillus nidulans*, the kinase cascade of the septation initiation network (SIN) triggers the assembly and contraction of the actomyosin ring contraction at the septation site during cytokinesis. The *spgA* gene encodes a homolog of the small GTPase Spg1p which turns on the SIN pathway in fission yeast. Surprisingly, the null *spgA*Δ mutation did not cause an obvious cytokinetic phenotype. In order to test whether SPGA acted as a trigger of cytokinesis, mutant forms of SPGA were expressed in the null *spgA*Δ background. Over-expression of two constitutively active forms of SPGA, SPGAQ135L and SPGAD191A, did not cause an obvious phenotype in colony growth or conidiation when compared to wild type. But over-expression of the dominant negative form of SPGA, SPGAT108A, almost completely abolished conidiation. All three mutant forms of SPGA localized to spindle pole body as the wild type form. The two constitutively active SPGA forms induced cytokinesis to take place more frequently than wild type. When the dominant negative SPGAT108A was over-expressed, the SIN components were no longer detected at the spindle pole body and the septation site. Our results suggest that SPGA forms part of the trigger regulating the SIN pathway, and at least another small GTPase acts in parallel as SPGA.

***DEB Graduate Student**

X. OPTIMIZING ENERGY BEET UTILIZATION FOR PRODUCTION OF BIO9FUELS AND COPRODUCTS

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Energy Beets, non-food sugar beets customized for energy production, are an attractive feedstock for renewable biofuel production in California, although thorough technical, economic, and environmental assessments have not yet been completed. Optimized Energy Beet production, processing, and fuel conversion methods may deviate significantly from existing sugar beet refining or fuel ethanol conversion schemes. Utilization of the whole beet (roots and leaves) employing multiple conversion pathways, including fermentation and anaerobic digestion, as well as consolidation and optimization of traditional processing, extraction, and fermentation operations are expected to increase project technical, financial, and environmental efficiencies. This research will serve to better characterize Energy Beet non-sucrose compositions, study their influence on conversion to fuels, and optimize downstream processing steps. Opportunities for upstream genetic plant modifications will also be identified. Immediate objectives include, firstly, identifying lower cost methods for extracting and storing beet juice and pulp and, secondly, maximizing fermentative bioethanol or biobutanol production and coproduct recoveries from both sucrose and non-sucrose components. Recombinant *Saccharomyces cerevisiae* and *Escherichia coli KO11* organisms and consolidated fermentation schemes will be investigated. Utilization of the whole beet, including both the roots and greens (leaves), will be investigated in the framework of an integrated biorefinery model.

***DEB Graduate Student**

Y. EFFECT OF CO-EXPRESSION OF CUCUMBER MOSAIC VIRUS (CMV) COAT PROTEIN ON TRANSIENT EXPRESSIONOF A HUMAN THERAPEUTIC PROTEIN IN PLANT TISSUE USING A CMV VIRAL AMPLICON BASED EXPRESSION SYSTEM

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Plant-made pharmaceuticals have significant benefits for large-scale production compared with conventional biological manufacturing processes that utilize mammalian or microbial cultures in terms of low risk of product contamination by mammalian viruses, prions and bacterial toxins, and eukaryotic posttranslational modification capabilities. However, large scale production of some plant made recombinant proteins has been hindered by low protein yield and also the long time required for generating transgenic plants. Plant-made recombinant proteins can be produced either with stable transgenic plants or with transient expression in wild-type plants. However, transient expression has advantages over the stable transgenic plants due to rapid production, scalability and fewer ecologic and environmental concerns. Our research team has developed a novel chemically-inducible plant viral amplicon expression system based on Cucumber Mosaic Virus genome referred to as **CMViva** (**CMV** **i**nducible **v**iral **a**mplicon) that allows controllable, high level expression of recombinant proteins in plant hosts. Using the CMViva expression system, we have replaced the open reading frame of the CMV coat protein with the plant codon optimized human alpha-1-antitrypsin (AAT) gene. We also have developed an efficient, scalable process for the production of AAT protein in harvested leaves of *Nicotiana benthamiana* based on the transient vacuum agroinfiltration method.

In this study, we evaluated the effect of transient co-expression of the CMV coat protein (CMV subgroup I and II) on the transient AAT expression level in harvested plant leaves using the vacuum agroinfiltration method. The functional AAT expression level slightly increased with the co-expression of the coat protein of CMV subgroup I and the gene silencing suppressor, P19 resulting in an expression level of 278±78 mg AAT/kg fresh weight after 6 days post-induction. However, the average value of AAT expression level was not statistically significant compared to transiently co-expressed with P19 without CMV coat protein (217±45 mg AAT/kg FW) which may be caused by the variation of the expression level in the leaves from different plants.

***DEB Graduate Student**

Z. IDENTIFYING THE BIOCHEMICAL AND MOLECULAR COMPONENTS OF PLANT STRESS PERCEPTION

Geoffrey Benn*[1], Marta Bjornson*[1,2], Katayoon Dehesh[1]
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As sessile organisms, plants are unable to flee abiotic and biotic stresses in their environment. Therefore, the perception of stress and the subsequent initiation of appropriate responses are critical for plants. The physiological responses of plants to a variety of stresses have been intensely studied. However, the molecular and biochemical basis of the perception event leading to the initiation of these stress responses is poorly understood. Previous work in our lab using *Arabidopsis* identified a cis-element, the rapid stress response element (RSRE), which is sufficient to confer a rapid and transient transcriptional response to biotic and abiotic stressors, including cold, wounding, and pathogen attack. The goal of my research is to identify the molecular and biochemical basis for stress-induced up-regulation of RSRE-containing genes. I have shown that RSRE-containing genes are upstream of plant hormones involved in defense responses and have established a possible role for superoxide signaling in stress perception. To identify transcription factors that bind the RSRE, we will use a yeast one-hybrid screen in parallel with an affinity purification approach. Putative RSRE-binding factors will be further characterized using T-DNA knockout lines and ChIP-Seq.

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Company Affiliates

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- **Novozymes, Inc.****
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- **Takeda Pharmaceuticals**
- **Tethys Bioscience, 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

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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.

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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

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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, Inc.

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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.

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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.

Celgene Corp.

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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 Celgene is a global biopharmaceutical company committed to improving the lives of patients worldwide.

At Celgene, we seek to deliver truly innovative and life-changing drugs for our patients. Our mission as a company is to build a major global biopharmaceutical corporation while focusing on the discovery, the development, and the commercialization of products for the treatment of cancer and other severe, immune, inflammatory conditions.

There are more than 300 clinical trials at major medical centers using compounds from Celgene. Investigational compounds are being studied for patients with incurable hematological and solid tumor cancers, including multiple myeloma, myelodysplastic syndromes, chronic lymphocyte leukemia (CLL), non-Hodgkin's lymphoma (NHL), myelofibrosis, small cell lung cancer and prostate cancer.

As committed as we are to clinical accomplishment, we are equally committed to patient support, which is a guiding principle at Celgene. We believe all who can benefit from our discoveries should have the opportunity to do so. Celgene puts patients first with industry-leading programs that provide information, support and access to our innovative therapies.

***DEB Graduate**

Genencor (A Danisco Division)

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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.

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

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

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

Development Pipeline:
As a biotechnology leader, Genentech has a long-standing tradition of reinvesting a significant percentage of revenues back into research and development — a practice that has proved successful in transforming promising candidates into important new products. With the projects below under way, Genentech's development pipeline has never been more robust and promising. More than half of Genentech's pipeline is composed of potential antibody therapies.

Monsanto Company – Calgene Campus

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

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

***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.

***DEB Graduate**

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.

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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.

Takeda San Francisco

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Takeda San Francisco, Inc.(TSF) is Takeda's global center for excellence for biologics. TSF was founded in November 2007 and supports Takeda's therapeutic antibody research through our antibody technology platform. This platform is based on discovery, optimization and development technologies used to efficiently generate Investigational New Drug (IND) candidates for the treatment of cancer, inflammatory and metabolic diseases.

Tethys Bioscience, Inc.

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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.

UCDAVIS
Biotechnology
Program

Participants

Retreat Participants

NIH Fellows 2010 - 2011	
Dmitry Grapov	Agriculture & Environmental Chemistry
Mateo Hernandez	Chemistry
Geetika Joshi	Soils & Biogeochemistry
Regina MacBarb	Biomedical Engineering
Daniël Melters	Cellular & Developmental Biology
Nancy Zeng	Chemical Engineering
Biotech Fellows 2010 - 2011	
Xiaoyan “Helen” Chen	Biomedical Engineering
Sean Gilmore	Applied Science
Silvia Hilt	Biochemistry & Molecular Biology
Jared Moore	Chemistry
CREATE-IGERT Fellows, Cohort 1	
Timothy Butterfield	Plant Biology
Tiffany Glavan	Microbiology
Ben Lindenmuth	Chemical Engineering
Christopher Simmons	Biological Systems Engineering
CREATE-IGERT Fellows, Cohort 2	
Lucas Arzola	Chemical Engineering
Mitch Elmore	Plant Biology
CREATE-IGERT Fellows, Cohort 3	
Geoffrey Benn	Plant Biology
Marta Bjornson	Horticulture & Agronomy
CREATE-IGERT Fellows, Cohort 4	
Hyrum Gillespie	Genetics
Mark Lemos	Plant Biology
Patrick O’Dell	Biological & Systems Engineering
Tracy Zeng	Plant Biology
Steve Zicari	Biological & Systems Engineering
Graduate Students/Post-docs	
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Erica Andreozzi	DEB, Biomedical Engineering
Barbara Bailus	DEB, Genome Center / Genetics
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Atul Parikh	DEB, Applied Science
William Ristenpart	DEB, Chemical Engineering & Materials Science
Jon Sack	DEB, Neurobiology, Physiology and Behavior
Jared Shaw	DEB, Chemistry
John Voss	DEB, Chemistry
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Lyle Crossland	Monsanto, Calgene Campus
Joan Greve	Genentech, Inc
Alberto Iandolino	Monsanto, Calgene Campus
Greg Landes	Takeda San Francisco
James Maclean	Planet Biotechnology
Eddie Moler	Tethys Bioscience, Inc.
Martin Ruebelt	Monsanto, Calgene Campus
Guests	
Liz Anthony	Rensselaer Polytechnic Institute
Parteek Bansal	UC Davis – Chemical Engineering & Materials Science
Jeff Camp	University of Maryland, College Park
Manfred Kollmeier	
Mandi Landes	
Rosane Oliveira	DVM, PhD, Plant Sciences
UC Davis Staff	
Madhu Budamagunta	Biochemistry & Molecular Medicine
David Speca	Pharmacology
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Marianne Hunter	Biotechnology Program, Program Manager
Denneal Jamison-McClung	Biotechnology Program, Associate Director
Judy Kjelstrom	Biotechnology Program, Director
Martina Newell-McGloughlin	International Biotechnology Program, Director
Demian Sainz	Biotechnology Program, Account Manager

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The Mission of the Biotechnology Program:

The Biotechnology Program was created in 1986, to assist in the organization of university activities related to biotechnology and to coordinate such activities with other efforts on the Davis campus. It is a 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

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NIH Training Grant in Biomolecular Technology
July 1, 2002- 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 NIH Training Grant in Biomolecular Technology (T32-GM08799) which was awarded on July 1, 2002 for five years was subsequently renewed for an additional five years. We are in the process of preparing a competitive renewal this spring. Currently, there are 20 NIH biotechnology training grants funded nationwide and only five are in California (UC Davis, UCLA, UC San Diego, Scripps and Stanford).

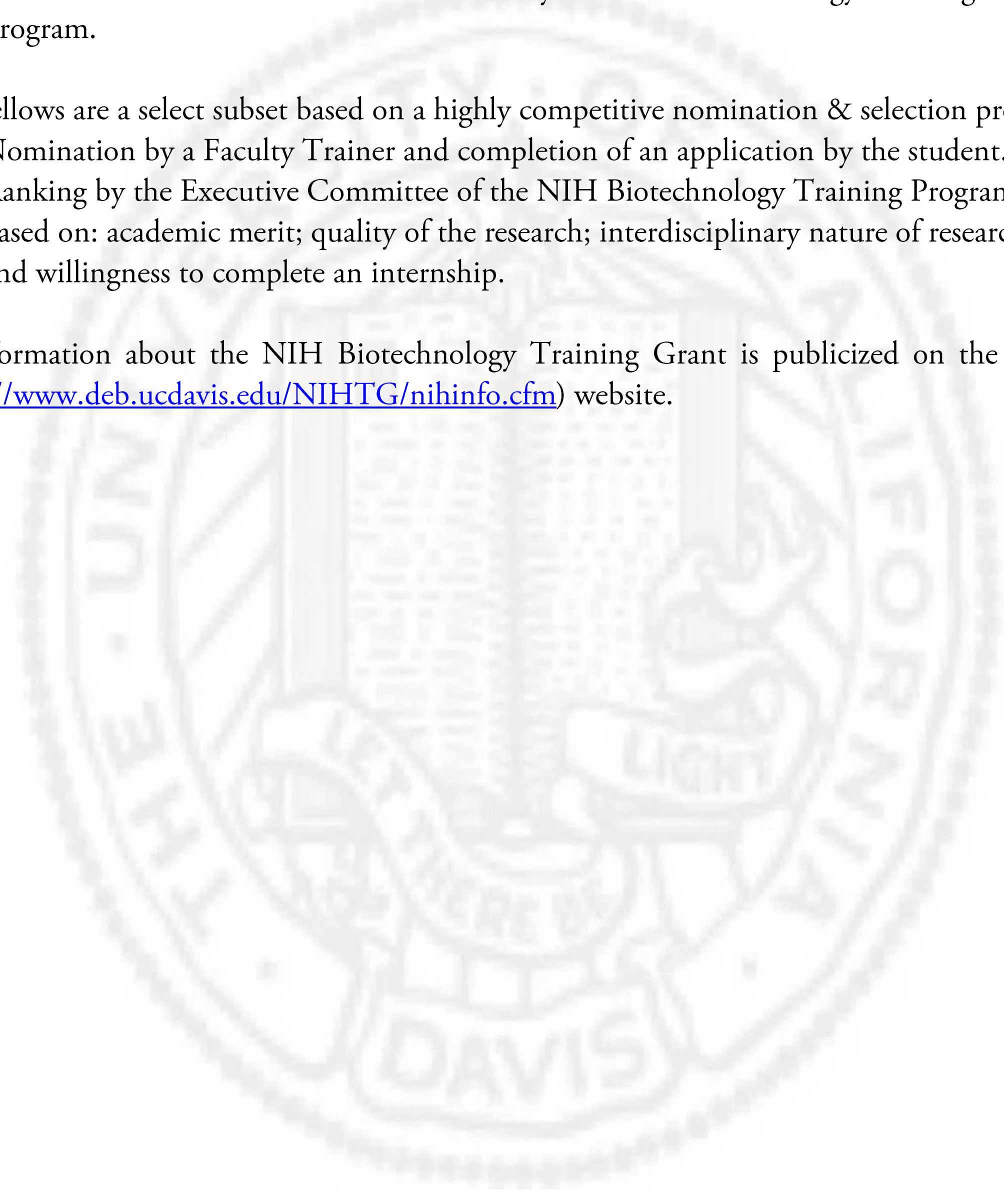
The relationship between the DEB and the Training Program in Biomolecular Technology may be described as follows:

- 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.

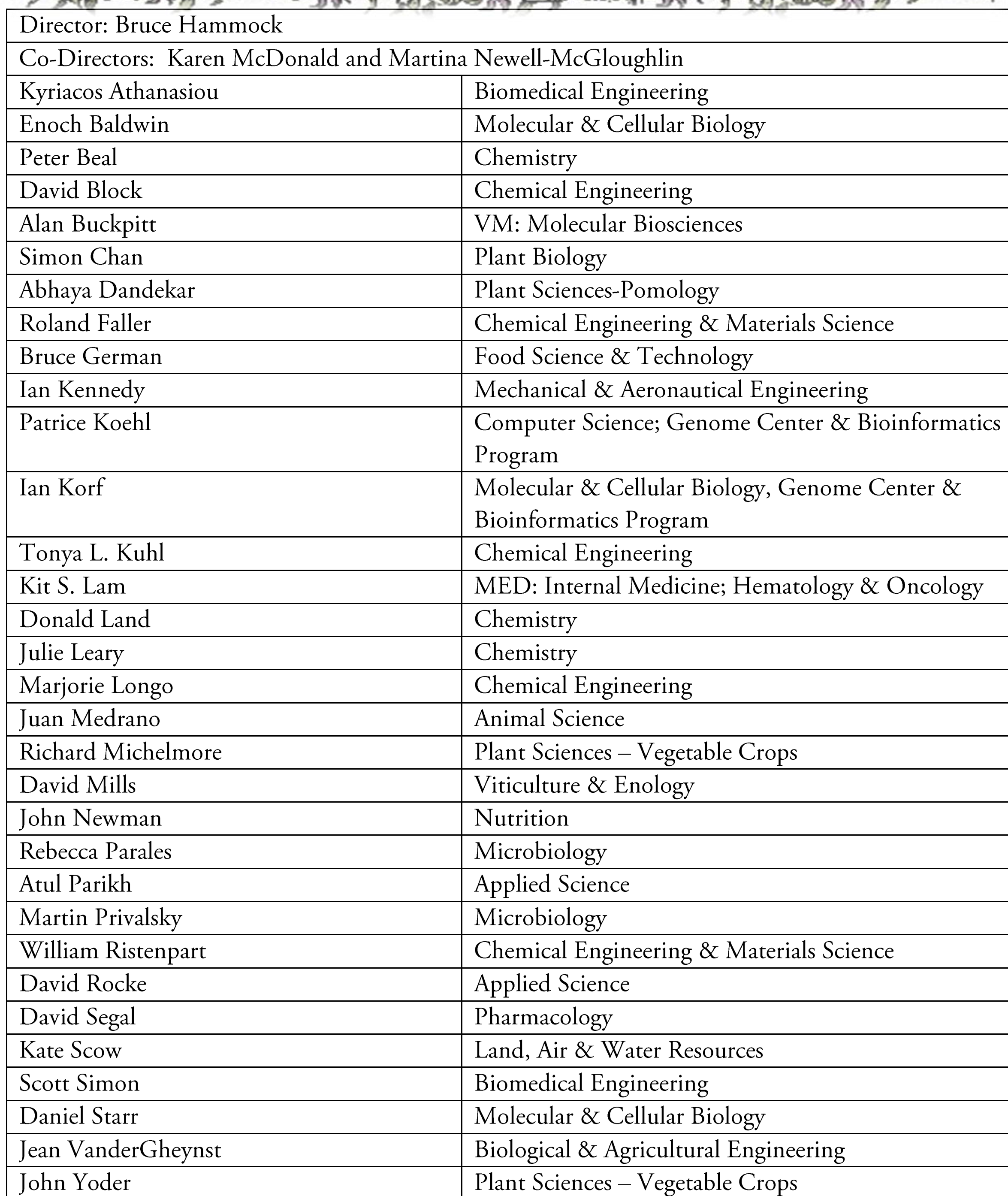
- The DEB provides a formal accreditation (on diploma & transcript) to reflect interdisciplinary biotechnology training.
- Not all of the DEB students will be funded by the NIH Biotechnology Training Program.

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	
Kyriacos Athanasiou	Biomedical Engineering
Enoch Baldwin	Molecular & Cellular Biology
Peter Beal	Chemistry
David Block	Chemical Engineering
Alan Buckpitt	VM: Molecular Biosciences
Simon Chan	Plant Biology
Abhaya Dandekar	Plant Sciences-Pomology
Roland Faller	Chemical Engineering & Materials Science
Bruce German	Food Science & Technology
Ian Kennedy	Mechanical & Aeronautical Engineering
Patrice Koehl	Computer Science; Genome Center & Bioinformatics Program
Ian Korf	Molecular & Cellular Biology, Genome Center & Bioinformatics Program
Tonya L. Kuhl	Chemical Engineering
Kit S. Lam	MED: Internal Medicine; Hematology & Oncology
Donald Land	Chemistry
Julie Leary	Chemistry
Marjorie Longo	Chemical Engineering
Juan Medrano	Animal Science
Richard Michelmore	Plant Sciences – Vegetable Crops
David Mills	Viticulture & Enology
John Newman	Nutrition
Rebecca Parales	Microbiology
Atul Parikh	Applied Science
Martin Privalsky	Microbiology
William Ristenpart	Chemical Engineering & Materials Science
David Rocke	Applied Science
David Segal	Pharmacology
Kate Scow	Land, Air & Water Resources
Scott Simon	Biomedical Engineering
Daniel Starr	Molecular & Cellular Biology
Jean VanderGheynst	Biological & Agricultural Engineering
John Yoder	Plant Sciences – Vegetable Crops

NIH Training Program in Biomolecular Technology

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

The DEB provides **training and a structure for interdisciplinary interactions**, in addition to 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, Molecular, Cellular & Developmental Biology; Biological Systems Engineering; Biomedical Engineering; Biophysics; Chemical Engineering; Chemistry; Civil and Environmental Engineering; Comparative Pathology; Electrical and Computer Engineering; Entomology; Food Science; Genetics; Horticulture & Agronomy (pending); 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 (T32-GM08799: 2002 - 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 2011 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 190 members, with many being first year students. We have graduated over 102 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. Judy 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. It is strongly recommended that DEB students become involved in public service and many opportunities are presented to them via email invitations (i.e. K-14 outreach and mentoring, etc.)

DEB Program Students as of March 2011

Danielle Aldredge	Chemistry
Lisa Anderson	Chemistry
Erica Andreozzi	Biomedical Engineering
Lucas Arzola	Chemical Engineering
Brian Avanzino	Biochemistry, Molecular, Cellular & Developmental Biology
Barbara Bailus	Genetics
Jesse Bakke	Nutritional Biology
Roberto Barrozo	Immunology
Geoffrey Benn	Plant Biology
Crystal Berger	Biochemistry & Molecular Biology
Marta Bjornson	Horticulture & Agronomy
Bárbara Blanco-Ulate	Plant Biology
Candace Burke	Immunology
Timothy Butterfield	Plant Biology
Milo Careaga	Immunology
Jennifer Cash	Chemistry
Elenor Castillo	Plant Biology
Patricia Castillo	Immunology
Shannon Ceballos	Cellular & Developmental Biology
Astra Chang	Comparative Pathology
Pauline (JoJo) Chang	Electrical & Computer Engineering
Chao-Yu “Joy” Chen	Pharmacology & Toxicology
Xiaoyan “Helen” Chen	Biomedical Engineering
Xiguang “Ray” Chen	Biological Systems Engineering
Dawn Chiniquy	Plant Biology
Sum Ying “Annie” Chiu	Biochemistry, Molecular, Cellular & Developmental Biology
Caitlin Cooper	Animal Biology
Stephanie Crockett	Comparative Pathology
David Dallas	Nutritional Biology
Ryan Davis	Chemistry
Derek Decker	Biophysics
Neha Dixit	Immunology
Matthew Doherty	Microbiology
Jean Du	Plant Biology
Collin Ellis	Nutritional Biology
James Elmore	Plant Pathology
Marjannie Eloi	Immunology
Anna Erickson	Biochemistry, Molecular, Cellular & Developmental Biology
Eugenel Espirtu	Biochemistry, Molecular, Cellular & Developmental Biology
Kenneth Eum	Molecular, Cellular & Integrated Physiology

Dawn Fedor	Nutritional Biology
Kateryna Feoktistova	Biochemistry, Molecular, Cellular & Developmental Biology
Brett Fite	Biophysics
Erin Fong	Electrical & Computer Engineering
Greg Foster	Biomedical Engineering
Erik Fostvedt	Biochemistry and Molecular Biology
Amanda Fox	Immunology
Daniel Garrido	Food Science
Prasad Gawande	Chemistry
Ehson Ghandehari	Biomedical Engineering
Hyrum Gillespie	Genetics
Sean Gilmore	Applied Science
Tiffany Glavan	Microbiology
Aiza Cathe Go	Biochemistry, Molecular, Cellular & Developmental Biology
Rena Goodman	Chemistry
Hossein Gouran	Plant Biology
Dmitry Grapov	Agricultural & Environmental Chemistry
Dominik Green	Biochemistry & Molecular Biology
Alex Gulevich	Biochemistry, Molecular, Cellular & Developmental Biology
Pasha Hadidi	Biomedical Engineering
Siobhan Halloran	Chemical Engineering
Brian Hamilton	Biochemistry & Molecular Biology
Oldham (Scott) Hamilton	Biochemistry & Molecular Biology
Mitchell Harkenrider	Plant Biology
Victor Haroldsen	Biochemistry & Molecular Biology
Jason Harrison	Chemistry
Christine Hastey	Microbiology
Mateo Hernandez	Chemistry
Kristin Hewett	Plant Biology
Thomas Hill III	Pharmacology & Toxicology
Silvia Hilt	Biochemistry, Molecular, Cellular & Developmental Biology
Marissa Hirst	Microbiology
Laura Ho	Pharmacology & Toxicology
Allison Hoch	Biomedical Engineering
Serenus Hua	Chemistry
Jonathan Hughes	Microbiology
Tu Anh Huynh	Food Science Technology
Vicki Hwang	Genetics
Yi-Hwa (Patty) Hwang	Biochemistry & Molecular Biology
Darren Hwee	Molecular, Cellular & Integrative Physiology
Shirin Jenkins	Biochemistry, Molecular, Cellular & Developmental Biology
Roger Jesinghaus	Chemistry
Rogelio Jimenez Espinoza	Chemical Engineering
Geetika Joshi	Soils and Biogeochemistry

Yun Joon Jung	Biomedical Engineering
Sercan Karav	Food Science & Technology
Robert Kauffman	Microbiology
Rachel Kerwin	Plant Biology
Zahra Khedri	Chemistry
Nathiel Kingsbury	Chemical Engineering
Brenna Kiniry	Microbiology
Lyndsey Kirk	Biochemistry, Molecular, Cellular & Developmental Biology
James Kurniawan	Chemical Engineering
Diana Lac	Pharmacology & Toxicology
Edna Lamsen	Chemistry
Rashida Lathan	Animal Biology
Katherine Lawrence	Cell & Developmental Biology
ChengYuk Lee	Chemical Engineering
Jennifer Lee	Biomedical Engineering
Karen LeGrand	Microbiology
Mark Lemos	Plant Biology
Ingrid Leth	Chemical Engineering
Zachery Lewis	Microbiology
Ben Lindenmuth	Chemical Engineering
Sarah Lockwood	Biochemistry & Molecular Biology
Alan Lombard	Biochemistry, Molecular, Cellular & Developmental Biology
Michelle Lozada-Contreras	Chemical Engineering
Thomas Luu	Biochemistry & Molecular Biology
Regina MacBarb	Biomedical Engineering
Kristina Mahan	Biochemistry & Molecular Biology
Hamed Malekan	Chemistry
Kinjal Maniar	Immunology
Amelia Manlove	Chemistry
Kevin Martin	Chemistry
Philip Matern	Molecular, Cellular & Integrative Physiology
Jordan McEwen	Chemistry
Samuel McMahon	Biochemistry, Molecular, Cellular & Developmental Biology
Daniël Melters	Cell & Developmental Biology
Emily Mills	Immunology
Angela Monterrubio	Biochemistry, Molecular, Cellular & Developmental Biology
Jason Mooney	Chemistry
Jared Moore	Chemistry
Mary Moore	Biochemistry & Molecular Biology
Diana Morales-Hernandez	Biomedical Engineering
Alexi Morris	Chemistry
Sucheta Mukherjee	Microbiology
Andrew Murley	Biochemistry, Molecular, Cellular & Developmental Biology
Meghan Murphy	Biomedical Engineering

Bernadette Nera	Biochemistry, Molecular, Cellular & Developmental Biology
Alice Ngo	Chemistry
Tarit Nimmanwudipong	Chemical Engineering
Charles Nwosu	Chemistry
Patrick O'Dell	Biological Systems Engineering
Maria Olubunmi Ogunyankin Marquez	Chemical Engineering
Alanna O'Leary	Immunology
David Olivos	Comparative Pathology
Nadia Ono	Biochemistry, Molecular, Cellular & Developmental Biology
Charity Onore	Immunology
Raquel Orozco-Alcaraz	Chemical Engineering
Richard Osibanjo	Chemistry
Gulustan Ozturk	Food Science & Technology
Angela Papalamprou	Molecular, Cellular & Integrated Physiology
Dipali Patel	Biomedical Engineering
Mira Patel	Biomedical Engineering
Maria Peralta	Chemistry
Khavong Pha	Biochemistry, Molecular, Cellular & Developmental Biology
Jonathan Pham	Microbiology
Stephanie Pulford	Mechanical & Aeronautical Engineering
Jingyao Qu	Chemistry
Joseph Ramahi	Cell and Developmental Biology
Kittipong Rattanaporn	Chemical Engineering
Gabriel Rodriguez	Chemistry
Patrick Rogers	Chemistry
Shailise Ross	Chemistry
Ron Runnebaum	Chemical Engineering
Juan Pedro Sanchez	Plant Biology
Mary Saunders	Comparative Pathology
Amy Schroeder	Biochemistry, Molecular, Cellular & Developmental Biology
Erin Schwartz	Biochemistry & Molecular Biology
Gail Sckisel	Immunology
Sunny Shah	Biomedical Engineering
Mojtaba Sharifzadeh	Electrical & Computer Engineering
Laura Shih	Biomedical Engineering
Jamie Silangcruz	Biomedical Engineering
Christopher Simmons	Biological Systems Engineering
Priyashiela Singh	Land, Air & Water Resources
Padmini Sirish	Molecular Cellular Integrative Physiology
Chelsea Snyder	Microbiology
Zane Starkewolfe	Chemistry
Michael Starr	Biomedical Engineering
John Strum	Chemistry
Wesley Sughrue	Biochemistry & Molecular Biology

Anandkumar Surendrarao	Plant Biology
Vu Trinh	Biochemistry & Molecular Biology
Michelle Tu	Cell & Developmental Biology
Gordon Walker	Biochemistry, Molecular, Cellular & Developmental Biology
Breanna Wallace	Molecular, Cellular & Integrative Physiology
Ambrose Williams	Biochemistry, Molecular, Cellular & Developmental Biology
Kelly Williams	Biological & Systems Engineering
David Woessner	Microbiology
Mark Wolf	Biochemistry & Molecular Biology
Diana Wong	Chemistry
Mon Shuan "Phoebe" Wu	Microbiology
Shuai Wu	Chemistry
Fei Yian Yoong	Plant Biology
Chao Wei Yu	Biological System Engineering
Cui Jing (Tracy) Zeng	Microbiology
Nancy Zeng	Chemical Engineering
Wade Zeno	Chemical Engineering
Steve Zicari	Biological Systems Engineering

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
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 Medicine
Joanna Chiu	Entomology
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
Katherine Ferrara	Biomedical Engineering
Oliver Fiehn	Genome Center
Andrew Fisher	Chemistry
Paul Fitzgerald	MED: Cell Biology & Human Anatomy
Ching Yao Fong	Physics
Annaliese Franz	Chemistry
David Furlow	Section of Neurobiology, Physiology, and Behavior
Charles Gasser	Molecular & Cellular Biology
Shu Geng	Agronomy & Range Science
J. Bruce German	Food Science & Technology
Jacquelyn Gervay-Hague	Chemistry
Soheil Ghiasi	Electrical & Computer Engineering

David Gilchrist	Plant Pathology
Tom Gradziel	Pomology
Jeffrey Gregg	MED: Pathology
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, Dept. of Medicine & Dept. of Medical Pharmacology & 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
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
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
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
Lorena Navarro	Microbiology
Florence Negre-Zakharov	Department of Plant Sciences
John Newman	Nutrition - USDA, ARS, Western Human Nutrition Research Center
Stephen Noctor	Neuroscience
Jan Nolta	UCDHS: Dept. of Hematology & Oncology
Thomas North	Center for Comparative Medicine
Martha O'Donnell	Physiology & membrane Biology; School of Medicine
David Ogrydziak	Food Science & Technology
Tingrui Pan	Biomedical Engineering
Rebecca Parales	Microbiology
Atul Parikh	Biomedical Engineering
Anthony Passerini	Dept. of Biomedical Engineering
Timothy Patten	Chemistry
Niels Pedersen	Department of Medicine and Epidemiology
Ronald Phillips	Chemical Engineering & Material Science
Jerry Powell	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
Jon Sack	Neurobiolgy, Physiology & Behavior
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
Ilias Tagkopoulos	Computer Science
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 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
Lifeng Xu	Microbiology
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 20 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
Antibodies, Inc.
Aqua Bounty
Bayer
Berlex Biosciences
BioMarin Pharmaceuticals, Inc.
Carollo
Celera AgGen
DuPont
Exelixis
Expression Systems
Genencor
Genentech
Hoffmann Eitle
ICOS
Institut Charles Sadron,
Maxygen
Monsanto, Calgene Campus;
Novartis (formerly Chiron)
Novozymes Biotech
OncoMed
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 190 students enrolled, so we need more Academic-Industry Partnerships.