Eleventh Annual

Biotechnology Training Retreat

Christian Brothers Retreat Center
Napa Valley

Saturday, May 11, 2002

We would like to thank the UC BioStar Program for its generous support.

Welcome to the Eleventh Annual Biotechnology Training Retreat

This special day in the beautiful hills of the Napa Valley is an opportunity to showcase our 2001-2002 Fellows and their Faculty Preceptors. It is an honor to receive one of these highly competitive fellowships. We want the biotechnology community to meet these scholars and share in their exciting research projects. Blythe Durbin (preceptor is David Rocke) and Jeff Murrell (preceptor is Ben Shen) are previous fellowship recipients and are anticipating graduation this year. Melody Trexler (preceptor is Karen McDonald) and Amanda Ellsmore (preceptor is J. Clark Lagarias) are new fellows. Please congratulate these outstanding predoctoral fellows and their mentors.

This also a time to officially thank our Biotechnology Company Affiliates for their support in the form of: fellowships; internships; participation on advisory boards; Picnic Day donors; and guest lecturers for seminars and summer short courses. The education of our interdisciplinary doctoral students is dependent on the support of our industrial partners. We hope they will continue to support our programs. We also welcome our invited companies to consider becoming affiliates.

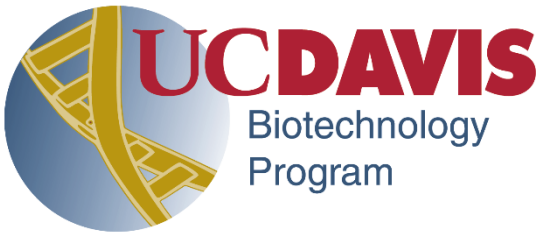
The UC Davis Biotechnology Program (established in 1986) is the administrative home for the Biotechnology Fellowships as well as the Designated Emphasis in Biotechnology (DEB) Graduate Program. Although not required, all of our current fellows are also members of the DEB. The retreat will also showcase research performed by other graduate students in the DEB program as well as UC Davis researchers.

This day-long gathering gives us an opportunity to network with fellow scientists through various vehicles. We have formal scientific presentations and posters, a leisurely luncheon and scenic gardens. Good science and delicious food are great ways to get communications flowing. Bon Appetit!

We would like to thank Professor Karen McDonald (BioSTAR grant) for co-sponsoring this academic-industrial outreach event. We want to also thank Professor John Yoder for serving as the first chair of the DEB Executive Committee (established in 1997) as he ends his term next month. We welcome Professor Abhaya Dandekar as the new chair.

A special thanks goes out to Martina Newell-McGloughlin (past director of the UC Davis Biotechnology Program and current director of UC BREP), whose vision and leadership has helped UC Davis become the home of biotechnology research and education for the University of California. Your love for academic excellence and passion for innovation serve as benchmarks for those who follow.

We hope you have a wonderful day!
The Faculty & Staff of the UC Davis Biotechnology Program



Designated Emphasis in Biotechnology (DEB) Executive Committee

John Yoder, Chair
Abhaya Dandekar, Chair-elect
Karen McDonald
Dewey Ryu
Bob Rice (member-elect)
David Rocke (member-elect)

UC Davis Biotechnology Program

Associate Director
Judith A. Kjelstrom
(DEB Program Coordinator)

Eleventh ANNUAL

BIOTECHNOLOGY TRAINING RETREAT

Christian Brothers Retreat Center
Napa Valley

Saturday, May 11, 2002

8:15 am	Registration & continental breakfast
8:45 am	Welcome by Martina Newell-McGloughlin
	Morning Session Chair: John Yoder DEB, Chair
9:00 - 9:20 am	Chiron - Eddie Moler
9:30 - 9:50 am	David Rocke/Blythe Durbin (Fellow)
9:55 - 10:15 am	Novozymes - Janine Lin
10:20 - 10:40 am	Jeffrey Murrell (Fellow)
10:45 - 11:15 am	Break/Poster session
11:15 - 11:35 am	Karen McDonald/Melody Trexler (Fellow)
11:40 – 12:00 pm	Monsanto, Calgene campus - Virginia Ursin
12:00 pm	John Yoder, discussion on scientific ethics
12:10 - 2:00 pm	Lunch & Poster session
	Afternoon Session Chair: George Bruening Biotechnology Advisory Committee, Chair
2:00 pm	Continued discussion on scientific ethics
2:20 - 2:40 pm	Clark Lagarias/Amanda Ellsmore (Fellow)
2:40 - 3:00 pm	Afternoon Break
3:00 - 3:20 pm	Genentech - Patrick McKay
3:20 - 4:00 pm	Presentation by visiting company: Agilent Technologies - David Hirschberg
3:40 pm	BioSTAR Program
4:00 pm	**Close**

BIOTECHNOLOGY TRAINING RETREAT

Saturday, May 11, 2002

Program Overview

8:15am Registration

8:30 Welcome by Martina Newell-McGloughlin
Updates: Biotechnology Program
NIH Training Grant
New DEB Chair & Members

8:45 John Yoder, DEB Chair

Company & Fellow presentations:

9:00 Chiron - Eddie Moler

9:30 David Rocke (preceptor)/Blythe Durbin (fellow)

9:55 Novozymes - Janine Lin

10:20 Jeffrey Murrell (fellow) [Ben Shen (preceptor) unable to attend]

10:45 Break & poster session

11:15 Karen McDonald (preceptor)/Melody Trexler (fellow)

11:40 Monsanto Calgene Campus- Virginia Ursin

12:00 pm John Yoder, discussion on scientific ethics

12:10 pm Lunch, poster session & discussion

2:00 Continued discussion on scientific ethics

2:20 Clark Lagarias (preceptor)/Amanda Ellsmore (fellow)

2:40 Afternoon Break

3:00 Genentech - Patrick McKay

3:20 Presentation by visiting company
Agilent Technologies - David Hirschberg

3:40 BioSTAR Program

4:00 Close - Bus departs

POSTER TITLES

A. "Regulation of the PYP1 Tyrosine Phosphatase in Response to Heat Shock"
Aaron N. Nguyen* and Kazuhiro Shiozaki

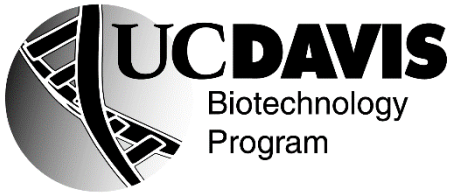
B. "Simultaneous conversion of hexose and pentose sugars to lactic acid by *Lactobacillus brevis*"
Jae-Han Kim, David A. Mills, David E. Block, Sharon P. Shoemaker

C. "The major envelope variants of an infecting simian immunodeficiency virus (SIV) predominate during the early stages of viral replication and dissemination in rhesus macaques"
Melinda Zaragoza*, Peter Dailey and Satya Dandekar

D. "Plant-plant interactions in the rhizosphere"
John I. Yoder, Denneal Jamison*, Manuel Torres*, Quy Ngo, Jean-Michel Petit, Natalya Tomilov, and Alexey Tomilov

E. "Resistance to Aflatoxin Contamination: Synthesis of Hydrolysable Tannins in Plants"
Ryann M. Muir* and Abhaya Dandekar

*Member of DEB graduate group



Oral Presentation Abstracts

CHIRON

Edward Moler
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Overview:

Chiron is a diversified biopharmaceutical company with businesses in vaccines, diagnostics and therapeutics, with a focus on infectious diseases, oncology, critical care and cardiovascular disease. Chiron's central research effort, Chiron Technologies, uses three methodologies: recombinant protein production; gene therapy and combinatorial chemistry to discover and develop new products for unmet medical needs. The targets for these efforts are discovered using high throughput functional gene discovery. In addition, this group has the mandate to develop new technologies, which can be used in the diagnosis, prevention and treatment of human disease. Examples of both present products and future directions will be presented.

Cancer Genomics:

In the area of cancer genomics, the main focus is to develop and apply methods using high-throughput expression screening to identify genes that are potentially useful as therapeutic intervention targets and diagnostic tests.

Overview of lab research: David Rocke/Blythe Durbin

Beyond Gene Expression Arrays: Statistical and Bioinformatics Issues in High Throughput Assays

David Rocke
Professor of Applied Science, University of California, Davis

Gene expression arrays have in a short time taken an important place in biological and medical research. To these will be added many new technologies that have similar problems in analysis and interpretation, including several varieties each of proteomics and metabolomics, as well as alternative methods for gene expression. We intend to address these technologies within a common bioinformatics framework.

FELLOW: Blythe Durbin

Outlier Detection in and Clustering of Microarray Data Using Minimum Spanning Trees

Blythe Durbin
Statistics

cDNA microarrays often include several clones intended to measure expression of the same gene. Given data over a number of experiments using the same array design, it is useful to be able to identify those cDNA clones within a group of clones corresponding to a particular gene whose expression patterns differ from those of the group as a whole. These outlying clones might be candidates for removal from the array, or they might provide useful biological information about the gene. We have designed and implemented an outlier-detection procedure based on Rohlf's minimum-spanning-tree test (Rohlf, 1975). The minimum spanning tree, or shortest connected graph, through the data provides a way of summarizing relationships between the data points which allows aberrant values to be easily identified. This procedure can identify outliers in groups of as few as 4 observations, even when the dimensionality of the data is quite high. We also introduce a method for clustering microarray data based in minimum spanning trees.

References: Rohlf, F.J. (1975). Generalization of the gap test for detection of multivariate outliers. _Biometrics_, 31, 93-101.

[Blythe completed her industrial internship at Chiron in 2001. She worked with Dr. Eddie Moler. Blythe is also a DEB member]

NOVOZYMES BIOTECHNOLOGY, INC.

OVERVIEW OF ENZYMES IN COMMERCIAL PROCESSES AND APPROACHES TO DISCOVER AND IMPROVE ENZYME PRODUCTION

Janine Lin
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Enzymes are environmentally friendly technologies that can be applied to a wide variety of industries including paper, baking, brewing, textiles, animal feed, detergents and starch. As the world's largest supplier of enzymes for industrial use, Novozymes uses different approaches to discover and produce enzymes in high yields. Novozymes has a large culture collection containing bacteria and fungi as well as a large collection of soil samples that are a source of diversity for the discovery of wild type microorganisms that produce high yield of enzymes. Classical mutagenesis, recombinant DNA, and high throughput screening technologies facilitate discovery of modified enzymes that can be highly expressed as well as the isolation of production strains with improved characteristics. The enzyme-producing microorganisms we use include *Bacillus*, *Aspergillus*, *Trichoderma*, or *Fusarium*. We also have a subcontract from the Department of Energy to work on improving enzymes used in the conversion of plant biomass to fermentable sugars or ethanol more efficiently. During the past year Novozymes has also begun using our core technology platform to discover and produce non-industrial enzyme products including small molecules, metabolites and antimicrobial compounds

PRECEPTOR: Ben Shen, Chemistry (currently at University of Wisconsin, Madison)

FELLOW: Jeffrey Murrell

Industrial applications of lignin degradation*

Jeff Murrell[1], Barbara Weber[2], and Debbie Yaver[2]
[1]Department of Chemistry, University of California, Davis
[2]Novozymes Biotech, Davis, CA

We are interested in elucidating and generating enzymes responsible for lignin degradation in order to further their use in pulp and paper processing. Our efforts were focused on the white-rot fungus *Ceriporiopsis subvermispora* due to its rapid degradation of lignin *in vivo* and its apparent lack of any ligninase enzyme. DNA microarray analysis was used to identify genes whose expression was induced due to growth on pulp. Genes identified by microarray analysis were subsequently cloned for expression in *Aspergillus oryzae* and the resultant proteins were assayed for function. This presentation will focus on a putative manganese peroxidase identified as being induced when the fungus was grown on pulp.

*Jeff completed his industrial internship this winter quarter (2002) at Novozymes Biotech, Inc. His presentation will focus on the work performed at the company. Jeff is also a DEB member.

Overview of lab research: Karen McDonald

PLANT CELL CULTURES: CURRENT STATUS AND FUTURE PROSPECTS

Karen McDonald
Department of Chemical Engineering and Materials Science, University of California, Davis

Using the tools of genetic engineering, foreign proteins can now be produced using a variety of expression systems and host cells, including microbial, mammalian or insect cells, as well as transgenic animals and plants. Although the first commercial applications have utilized microbial and mammalian expression systems, plant cells offer a number of advantages for large-scale production of heterologous proteins, particularly for human therapeutics [1,2]. These include low medium cost, low risk of contamination by mammalian viruses, blood-borne pathogens, prions and bacterial toxins, ease of culturing and ability to perform complex glycosylation.

Research in our lab focuses on the development, scale-up and optimization of plant cell culture based methods for the production of proteins. Projects include: 1) scale-up of alpha-· 1-antitrypsin (a human blood protein) production using a metabolically regulated rice cell culture expression system[3], 2) extracellular targeting and recovery of recombinant trichosanthin, a cucumber-derived antiviral protein, from transgenic tobacco[4]; and 3) development of a plant cell culture/recombinant plant virus system for heterologous protein production.

References:

1. Fischer, R., Emans, N., Schuster, F., Hellwig, S. and Drossard, J. 1999 Towards Molecular Farming in the Future: Using Plant-Cell-Suspension Cultures as Bioreactors, Biotechnol. Appl. Biochem., 30: 109-112.
2. Doran, P. 2000 Foreign Protein Production in Plant Tissue Cultures, Current Opinion in Biotechnology, 11: 199-204.
3. Trexler, M.M., McDonald, K.A. and Jackman, A.P. 2002 Bioreactor Production of Human alpha-1-Antitrypsin Using Metabolically Regulated Plant Cell Cultures, Biotechnology Progress (In Press)
   Krishnan, R., McDonald, K.A., Dandekar, A.M., Jackman, A.P., and Falk, B. 2002 Expression of Recombinant Trichosanthin, a Ribosome-Inactivating Protein, in Transgenic Tobacco, J. of Biotechnology (In Press).

FELLOW: Melody Trexler

A CYCLICAL SEMI-CONTINUOUS PROCESS FOR HETEROLOGOUS PROTEIN PRODUCTION USING METABOLICALLY REGULATED PLANT CELL SUSPENSION CULTURES

M.M. Trexler, K.A. McDonald, and A.P. Jackman
Department of Chemical Engineering and Materials Science, University of California, Davis, CA 95616

A metabolically regulated transgenic rice cell (Oryza sativa L.) suspension culture utilizes an α-amylase regulatory system for production of a recombinant human therapeutic protein, $_1$-α-antitrypsin (rAAT). In wild type rice cell cultures, under conditions of low sugar concentrations, the RAmy3D promoter directs high level expression of α-amylase proteins, and a rice α-amylase signal peptide directs secretion of the α-amylase proteins (up to 40% of the total secreted protein) into the culture medium. A codon optimized gene (for expression in rice) encoding AAT was inserted into a vector containing the RAmy3D promoter, signal peptide, and terminator sequences. The rice α-amylase promoter functions to express rAAT under conditions of sugar depletion and to shut down expression in the presence of sugar. The rice α-amylase signal peptide directs efficient secretion of rAAT into the culture medium.

The transgenic rice cell cultures were scaled-up from shake flasks into a 5-L bioreactor, and the cells were retained inside the bioreactor while medium exchanges were performed for consecutive growth or protein expression phases since the rAAT was secreted into the medium. Cyclical, semi-continuous bioreactor operations were performed, consisting of three cycles over a 28 day period, where expression of rAAT was induced under conditions of sugar depletion and inhibited in the presence of sugar. Kinetic data for growth, nutrient consumption, rAAT production, and bioprocess variables will be presented. A cyclical, semi-continuous process results in higher volumetric productivities and improved process economics due to the high cell densities attained and the reduced "turn-around" time and inoculum costs normally associated with batch cultures.

*Melody is also a DEB member. She completed her industrial internship in 2001 at Excelixis Corporation.

Monsanto, Calgene Campus

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GENETIC MODIFICATION OF OILS FOR IMPROVED HEALTH BENEFITS: PRODUCTION OF OMEGA-3 FATTY ACIDS IN PLANTS

Genetic modification of oil seed crops can provide an abundant, relatively inexpensive source of dietary fatty acids with wide ranging health benefits. Production of such lipids in vegetable oil provides a convenient mechanism to deliver healthier products to consumers without the requirement for significant dietary changes. Examples of such modified oils include: low- and zero-saturated fat soybean and canola oils, canola oil containing meduim chain fatty acids, (MCFAs), high sterate canola oil (for trans-fatty acid-free products), high oleic acid (monounsaturated) soybean oil, and canola oil containing the polyunsaturated fatty acids PUFAs), gamma-linolenic (GLA; 18:3 n-6) and stearidonic acids (SDA; 18:4 n-3).
Production of a readily available source of LC-PUFA, specifically omega-3 fatty acids, delivered in widely consumed, prepared foods could deliver much needed omega-3-fatty acids to large sectors of the population with skewed n6/n3 ratios, including those unwilling to take supplements or commit to dietary changes. We propose that delivering to consumers, omega-3 fatty acids in the form of SDA, the 18:4 n-3 precursor to EPA and DHA, would provide a more effective omega-3 fatty acid than · -linolenic acid (ALA), and that vegetable oil-derived SDA, as an environmentally-friendly alternative to fish oil, could provide LC-omega-3 fatty acids with enhanced stability and taste, which can be incorporated into a wide variety of food. In clinical study designed to determine the relative efficacy of SDA, metabolism of ALA, SDA and EPA to LC PUFAs (EPA + DPA n-3 + DHA) in humans, we observed that SDA was superior to ALA by a factor of 3.6. These data support our contention that dietary SDA can be an effective pro-EPA/DHA omega-3 fatty acid source, conferring the cardiovascular and other benefits of EPA and DHA. To develop an SDA-containing vegetable oil, we have cloned plant and fungal PUFA desaturase genes, and expressed them in canola. Transgenic canola oil was obtained that contain over 23% SDA, with an overall n6/n3 (ALA + SDA/ LA + GLA) ratio of 0.5.

PRECEPTOR: Clark Lagarias, Molecular and Cellular Biology, UC Davis

FELLOW: Amanda Ellsmore

DIRECTED EVOLUTION OF PHYTOCHROME

Amanda J. Ellsmore* and J. Clark Lagarias
Plant Biology Graduate Group, Section of Molecular and Cellular Biology, University of California

The phytochrome family of photoreceptors enables photosynthetic organisms to adapt their growth and development in response to light intensity, light direction, spectral quality and day-length. Phytochromes are chromoproteins that exist in two photointerconvertible forms -

the red light absorbing Pr form and the far-red light absorbing Pfr form. This photoreversible reaction is due to a linear tetrapyrrole (bilin) chromophore which photoisomerizes upon absorption of red or far-red light. This isomerization leads to a conformational change in the phytochrome protein that initiates a biochemical-signaling cascade. The ability to reconstitute phytochromes with natural and unnatural bilin precursors both in vitro and in vivo provides a powerful approach to tailor the spectroscopic properties of these photoreceptors. In this regard, binding of an unnatural bilin precursor that is unable to photoisomerize upon light absorption affords a strongly fluorescent bilin-apophytochrome adduct, that we name a phytofluor. Phytofluors have been shown to be useful probes that can be produced in living cells. The primary objective of my research is to identify new phytochromes by directed evolution having the ability to bind natural precursors to yield fluorescent-adducts. Various mutagenesis techniques will be employed to generate missense, nonsense and insertion/deletion mutations using a bacterial phytochrome template. An in vitro approach was initially used to generate a library of mutations in the domain adjacent to the bilin-binding domain of phytochrome. This domain is critical for the Pr to Pfr photoconversion process. In this study random mutations were generated using an error-prone PCR technique. One hundred of these mutants were sequenced to reveal the profile of mutations generated by this method. Interesting mutants with amino acid changes in key regions of this domain were identified and will be selectively assayed for altered spectral properties. An in vivo approach using holophytochrome-expressing mutator cell-lines also will be used in attempts to identify florescent mutants using flow cytometry, and a colony based fluorimaging system.

*Amanda is a DEB member

GENENTECH

Patrick McKay
Department of Recovery Services
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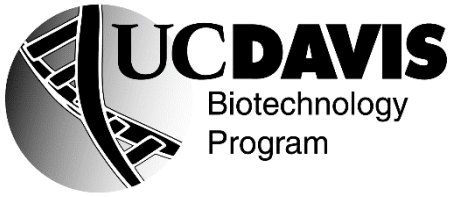
McKay.Patrick@gene.com

Lab focus: **Process development for the purification of recombinant proteins.**

Presentation: From bench top to manufacturing - the development of an ion-exchange chromatography step for the purification of a recombinant protein.



Poster Abstracts

A. Regulation of the Pyp1 tyrosine phosphatase in response to heat shock

Aaron N. Nguyen* and Kazuhiro Shiozaki
Section of Microbiology, University of California at Davis

In eukaryotic species from yeast to human, stress-activated protein kinases (SAPKs), members of the MAP kinase (MAPK) family, regulate the transcriptional response to various environmental stress. Like mammalian JNK and p38 SAPKs, the *S. pombe* Spc1 (also known as Sty1/Phh1) SAPK is activated by diverse forms of stress, including osmostress, oxidative stress and heat shock. We previously demonstrated that although osmostress and oxidative stress induce strong activation of the Wis1 SAPK kinase, which phosphorylates and activates Spc1, activation of Wis1 upon heat shock is weak and transient. On the other hand, in heat-shocked cells, Pyp1, the major tyrosine phosphatase that dephosphorylates and inactivates Spc1, is inhibited for its interaction with Spc1, which leads to strong activation of Spc1. However, the molecular mechanism of Pyp1 inhibition by heat shock remains unknown. To address this question, we used the yeast two-hybrid method to identify proteins that interact with Pyp1. We have isolated various clones that all encode for a single protein, named Tpb1 (tyrosine phosphatase binding protein). Biochemical experiments have confirmed that Tpb1 and Pyp1 proteins physically interact *in vivo*. Current investigations attempt to uncover the physiological link between Tpb1 and Pyp1.

*DEB member and gratuate student in Microbiology. Aaron is planning to do his internship at Scios, Inc. this summer.

B. Simultaneous conversion of hexose and pentose sugars to lactic acid by *Lactobacillus brevis*

Jae-Han Kim[1], David A. Mills[2], David E. Block[2], Sharon P. Shoemaker[1]

[1] Department of Food Science and Technology, University of California, Davis and California Institute of Food and Agricultural Research, University of California, Davis, California 95616
[2] *Department of Viticulture and Enology, University of California, Davis, California 95616*

A prominent goal of bio-based chemical production from agricultural waste materials is efficient co-utilization of both the hexose and pentose sugars derived from lignocellulose. A screen of several lactobacilli revealed that the heterofermentative strain, *Lactobacillus brevis,* can utilize glucose and other fermentable carbohydrates simultaneously without apparent catabolite repression. In this work, we examined the effects of substrates and their ratio on the fermentation kinetic parameters of cell growth and lactic acid production. Fermentations were carried out in MRS media at 30°C with varying concentration glucose and xylose and/or arabinose. *L. brevis* was shown metabolize glucose, xylose, and arabinose simultaneously. Moreover, pentose sugars were consumed at similar rates as glucose though there was some difference between strains. Surprisingly, lactic acid productivity was similar to those obtained with other homofermentative lactobacilli. Though lactic acid production was not significantly affected by sugar substrate, the ratio of two carbon end products (acetate and ethanol) was altered during growth on xylose. While the molecular basis for lack of catabolite repression remains to be determined, simultaneous utilization of both hexose and pentose sugars suggests *L. brevis* is a good candidate for lactic acid production schemes that employ substrates derived from lignocellulosic matter.

C. "The major envelope variants of an infecting simian immunodeficiency virus (SIV) predominate during the early stages of viral replication and dissemination in rhesus macaques."

Melinda Zaragoza*[1], Peter Daily[2], and Satya Dandekar[1]
University of California, Davis, CA 95616[1], Bayer Diagnostics, Emeryville, CA 94608[2]

Development of viral genetic diversity during the clinical course is an important feature of HIV and SIV infections. The majority of information about viral genomic diversity has been obtained to determine its role in evasion of virus-specific host immune responses or in development of resistance to anti-viral therapy. However, our understanding is limited on the role of viral diversity of the infecting virus on the early stages of viral replication in the lymphoid tissues and overall dissemination in the host. Using the SIV-infected rhesus macaque model for AIDS, we examined the role of viral variants present in the infecting viral inoculum on the early viral replication and dissemination in lymphoid and non-lymphoid tissues. Rhesus macaques were infected with the biologic SIVmac251 inoculum (utilized for its diversity of major and minor viral envelope variants) and various lymphoid and non-lymphoid tissues and blood samples were obtained from 3 days to 4 weeks post-infection (PI). The tissue and blood samples were analyzed for viral replication by measuring viral FNA copy numbers using the branched DNA signal amplification assay and for the evolution of viral genomic envelope variants by heteroduplex mobility assay (HMA) and nucleotide sequencing. The results demonstrated that (1) the viral infection was widely disseminated, as was evident by the presence of proviral DNA in various tissues and PBMC. (2) The level of viral replication varied from one tissue to another, but appeared to be highest in the lymph nodes and GALT. (3) The peak of early viral replication was seen at 2 weeks PI. (4) The major envelope variants present in the viral inoculum maintained dominance in vivo, at all sites examined in early infection. In summary, the major SIV envelope variants in the infecting inoculum predominate the early stages of viral replication and dissemination prior to the development of anti-viral specific host responses and are independent of tissue-specific selection. The major viral variants present in the infecting virus population at the time of initial exposure of the susceptible hosts may impact the subsequent virological and clinical course in HIV and SIV infections.

* Member of Microbiology Graduate Group & DEB

D. Plant-plant interactions in the rhizosphere

John I. Yoder, Denneal Jamison*, Manuel Torres*, Quy Ngo, Jean-Michel Petit, Natalya Tomilov, and Alexey Tomilov

Department of Vegetable Crops and Weed Science, University of California, Davis, CA.

Weed control is the single biggest challenge in agriculture worldwide. We are interested in understanding the genetic mechanisms governing plant - plant interactions with the goal of optimizing crop plants for subterranean performance. Parasitic plants in the Scrophulariaceae develop invasive organs called haustoria on their roots within hours after exposure to exudates released by neighboring plant roots. Because haustorium development in parasitic plants is rapid, synchronous, and highly dependent on the signals released by other plants, it offers an excellent system for investigating interactions between roots.

We are investigating haustoria development in the parasitic plant *Triphysaria*. *Triphysaria* is closely related to the parasitic weeds *Orobanche* and *Striga* but unlike these species, *Triphysaria* is non-weedy and can be grown without quarantine or environmental concerns. *Triphysaria* is useful as a model because it is a facultative parasite, it is a simple diploid amenable to genetic manipulations, it has a broad host range that includes *Arabidopsis* and maize, and, parasitism can be readily assayed in vitro. Haustoria develop on *Triphysaria* roots within hours after exposure to host root exudates. Using subtractive hybridization, we have isolated several hundred cDNAs that are induced within hours of exposure to host exudates. Several of these genes are specifically induced in parasitic species in response to host plant signals. We have also isolated genetic variants of *Triphysaria* that are altered in there responsiveness to haustorial-inducing factors. These variants will be useful for assigning functions to the cloned genes.

*Members of the Genetics Graduate Group & DEB. Both are previous fellows.

E. Resistance to Aflatoxin Contamination: Synthesis of Hydrolysable Tannins in Plants

Ryann M. Muir* and Abhaya Dandekar
Department of Pomology, University of California, Davis

Hydrolysable tannis (HTs) are polyphenolic compounds that have anti-herbivore, anti-microbial, and anti-fungal toxicities. They precipitate proteins, interfering with the digestion and nutrient absorption of pathogens on plants. We have determined that a precursor and/or breakdown product of HTs (i.e. gallic acid) also imparts a type of fungal resistance. Specifically, gallic acid prevents formation of th efungal contaminate, aflatoxin. Therefore, we have been investigating th esynthesis of gallic acid and th esynthesis and breakdown of HTs. Two walnut cultivars (i.e. *Juglans regia* ssp. Chandler and ssp. Tulare) exhibit variable levels of gallic acid within their seed coat tissues. Thus comparison between these two lines will serve as a novel means by which to identify HT specific genes. Current technology will be employed including two dimensional gel electrophoresis, electron spray ionization - mass spectrometry (ESI-MS-MS) and *Agrobacterium* mediated plant transformation. This research potentially furthers the understanding of the regulation of tannins and their complex role in plants.

* Ryann is a DEB member

BIOTECHNOLOGY AT THE
UNIVERSITY OF CALIFORNIA

BioSTAR

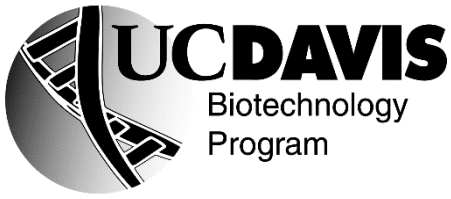
(Biotechnology Strategic Targets for Alliances in Research)

Biotechnology Strategic Targets for Alliances in Research (BioSTAR): launched Summer 1996, invests $12 million in Industry, State, and University funds in 40-45 new research partnerships every year focused on healthcare, agriculture, and natural resource

Technology transfer & conference awards:
Small seed grants of up to $15,000 to support activities that communicate developments in biotechnology research at UC and in California firms, or enhance faculty, student, and staff understanding of commercial biotechnology research, technology transfer, and opportunities for cooperative research with private sponsors, or assess and improve university approaches to technology transfer and administration of industry-sponsored research.

Research matching grants:
The UC BioSTAR solicits proposals for basic to proof-of-concept research in the field of biotechnology. Applications are encouraged for new projects and for competitive renewals. All proposals will include a binding letter from a Private Sponsor, who will provide required matching funds.

For additional information on the BioSTAR program, please see their web page at: http://www-biotech.berkeley.edu



Company Affiliates

Company Affiliates* Support Biotech at UC Davis

- Chiron
- DuPont
- Genentech
- Monsanto, Calgene Campus
- Novozymes Biotech, Inc
- Scios

*These Biotechnology companies have donated at least $15,000 per year for a biotechnology fellowship, have offered an internship site for our biotechnology graduate students and have presented at the annual Biotechnology Training Retreat. Company representatives also serve as advisors for training grants and other educational programs.

The success of our programs depend on the continued support of our affiliates and the Biotechnology Program would like to thank them for their continued support.

Chiron
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Chiron's success in bringing important products to market is based on its solid research and development capabilities.

The company has a strong commitment to research as an essential component of its product development effort. The company focuses its research and development activities primarily on areas in which it has particular strengths, including infectious diseases, cancer and cardiovascular diseases, with specialization in the areas of recombinant technology, gene therapy, vaccines, small molecule discovery, and genomics.

An important part of the company's research and development effort is undertaken through collaborations with third parties that are able to contribute significant enabling technologies and other resources to the development and commercialization of the product, including in some cases marketing and sales expertise.

DuPont
Bill Niebur
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Email: niebur@phibred.com

- Principal Technology Areas of DuPont Research and Development:
  - Chemical Science and Catalysis
  - Leveraged Technologies
  - Life Sciences
  - Material Science and Engineering
  - Petroleum Engineering
  - Petroleum Refining
  - Process Science and Engineering

See URL for more details:
http://www.dupont.com/corp/science/technology.html

Genentech
Contact: Pat McKay
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South San Francisco, CA 94080-4990
Email: McKay.Patrick@gene.com

Founded in 1976, Genentech was the pioneer in the field of biotechnology. Thirteen of the approved products in biotechnology stem from our science. Genentech, Inc. was founded by venture capitalist Robert A. Swanson and biochemist Dr. Herbert W. Boyer. In the early 1970s, Boyer and geneticist Stanley Cohen pioneered a new scientific field called recombinant DNA technology.

Fourteen of the approved products in biotechnology stem from Genentech science. Genentech manufactures and markets nine protein-based pharmaceuticals. Some are listed below:

I. BioOncology:

Herceptin®(Trastuzumab) Anti-HER2 antibody: For the treatment of metastatic breast cancer in HER2 overexpressed tumors.

Rituxan (Rituximab) Anti-CD20 antibody: For the treatment of relapsed or refractor low-grade or follicular, CD20 positive, B-cell non-Hodgkin's lymphoma.

II. Cardiovascular:

TNKase™ (Tenecteplase)
Single-bolus thrombolytic agent: For the treatment of acute myocardial infarction (AMI).

Activase®(Alteplase, recombinant) A tissue-plasminogen activator: For the treatmen of AMI, acute ischemic stroke and acute massive pulmonary embolism.

Mosanto-Calgene Campus
Contact: Nordine Cheikh
Site Manager
1920 Fifth Street
Davis, CA 95616
nordine.cheikh@stl.Monsanto.com

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

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

Novozymes Biotech, Inc
Contact: Glenn Nedwin, President
Debbie Yaver, Research Manager
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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.

Scios, Inc.
Contact: David Liu, Research Scientist
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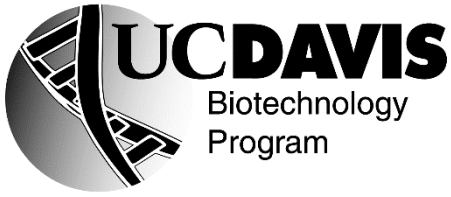
liud@sciosinc.com

The overall objective of Scios' research program is to discover innovative new treatments for specific cardiorenal and inflammatory diseases and Alzheimer's disease. These disease areas are associated with substantial unmet medical needs. Scios scientists have developed an in-depth understanding of the molecular basis of these diseases and have discovered numerous product candidates, including those currently in the Scios clinical development pipeline.

The application of advanced technologies in the traditional areas of cellular and molecular biology, protein chemistry, medicinal chemistry, and pharmacology supports the ongoing discovery process. Over recent years, the Company has taken steps to develop and apply state-of-the-art platform technologies to facilitate the discovery of naturally occurring proteins and novel small molecules that can serve as potential new therapeutic agents. These technologies include genomics, combinatorial chemistry, high throughput screening and advanced models of diseases of interest. The application of these technologies has factored centrally in our success with numerous projects, like our P38-Kinase inhibitor program. In less

than two years, our scientists have applied these advanced methods to identify highly potent and selective inhibitors of this key pro-inflammatory enzyme.



Invited Companies (prospective affiliates)

Agilent
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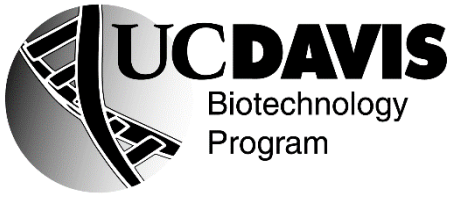
Agilent Technologies is on the leading edge of nearly every major trend in communications and life sciences. From optical and wireless communications to disease and discovery research, Agilent delivers product and technology innovations that benefit millions of people around the world. Leading companies - communications equipment manufacturers, Internet service providers, biopharmaceutical companies and more - depend on Agilent's more than 20,000 test, measurement and monitoring devices, semiconductor products and chemical analysis tools to help drive the communications and life sciences revolutions that transform the modern world.


UCDAVIS
Biotechnology
Program

Participants

Participants

Fellows (2001-2002)	**Department/Organization**
Blythe Durbin	Statistics
Amanda Ellsmore	Plant Biology
Jeffrey Murrell	Chemistry
Melody Trexler	Chemical Engineering & Materials Science

Graduate students/post docs

Ibrahim Abdallah	Vegetable Crops
Steve Christenson	Chemistry
Melissa Erickson	Entomology
Jun Fan	Cell Biology
Alberto Iandolino	Viticulture and Enology
Denneal Jamison-McClang	Vegetable Crops

Lawrence Joh	Biological and Agricultural Engineering
Mary Kalamaki	Food Science and Technology
Jae-Han Kim	California Institute of Food & Agriculture Research, CIFAR
Ryann Muir	Pomology
Aaron N. Nguyen	Microbiology
Jean-Michel Petit	Vegetable Crops
Wyatt Smith	Chemistry
Dafna Tamir	Food Science
Alexey Tomilov	Vegetable Crops
Natalya Tomilov	Vegetable Crops
Manuel Torres	Vegetable Crops
Bob Ward	Food Science & Technology
Melinda Zaragoza	Medical division of Internal Medicine

Faculty & Staff

George Bruening	Plant Pathology
Abhaya Dandekar	Pomology
Bruce Hammock	Entomology & Cancer Research Center
Clark Lagarias	Plant Biology
Karen McDonald	Chemical Engineering & Materials Science
Janice Morand	Internship & Career Center
Martina Newell-McGloughlin	UC Systemwide Biotechnology Research and Education Program/Plant Pathology
David Rocke	Applied Science
Kazuhiro Shiozaki	Microbiology
Sharon Shoemaker	California Institute of Food & Agricultural Research, CIFAR
John Yoder	Vegetable Crops

Affiliated Companies

Chiron	Edward Moler
Monsanto, Calgene Campus	Virginia Ursin
Genentech	Patrick McKay
Novozymes Biotech, Inc.	Janine Lin

Invited Companies (Sponsored by BioSTAR)

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Designated Emphasis in Biotechnology Program (DEB)

Description

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 UCD Biotechnology Program is the administrative home for this program.

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 cross-college or biotech company laboratories.

Students come from a wide array of disciplines: Biochemistry & Molecular Biology, Biological & Agricultural Engineering, Cell & Developmental Biology, Chemical Engineering, Comparative Pathology, Entomology,Genetics, Microbiology, Plant Biology, Plant Pathology, Statistics, etc. This program supplements a student's Ph.D. curriculum and those completing the DEB 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

For more information

DEB program: www.deb.ucdavis.edu
UC Davis Biotechnology Program: www.biotech.ucdavis.edu

DEB PARTICIPATING FACULTY

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