EIGHTH ANNUAL BIOTECHNOLOGY RETREAT
CHRISTIAN BROTHERS RETREAT CENTER
NAPA VALLEY
April 10, 1999

PROGRAM OVERVIEW

8:15am Registration

8:40am Introduction

COMPANY PRESENTATIONS: Martina McGloughlin, Chair

8:50am	The future of Calgene research and product development	- Katayoun Dehesh Calgene Monsanto Inc.
9:10am	Chiron, a diversified biotechnology company	- Steven Rosenberg, Research Director, Chemical Therapeutics Group Chiron Technologies
9:30am	Dupont Research	- Claire Komives, Dupont
9:50am	**BREAK**	
10:00am	Research and development at Genentech	- Hanspeter Gerber Genentech
10:20am	Using DNA-Tagged Mutagenesis to Improve Heterologous Protein Production in Aspergillus oryzae	- Debbie Yaver, Department of Protein Chemistry, Novo Nordisk Biotech
10:40am	Research at Roche	- Jim Barnett, Roche Bioscience
11:00am	Scios Research	- John Lewicki, Vice President for Research
11:20 am	Biotechnology Training opportunities	- John Yoder, Biotech Major - Janice Morand, Internship and Career Center (ICC)
11: 40am	Presentation of Posters	
12:00pm	**LUNCH, DISCUSSION & POSTERS**	

COMPANY FELLOW PRESENTATIONS: George Bruening, Chair

1:30pm	Overview of Research	- Hanspeter Gerber, Genentech
	Characterization of LNCaP prostate cancer cell apoptosis induced by SERCA pump inhibition	- Ingrid Wertz MED: Biological Chemistry
2:00pm	Colloidal diffusion in polymer solutions and gels	- Ron Phillips Chemical Engineering - Rob Jennings, Scios
	Diffusion of nonionic surfactants in nonionic gels- delivery systems for drugs	- Kristan Buck Chemical Engineering
2:30pm	On-Going Research In The Hammock Lab; Or, Bugs And Drugs	- Bruce Hammock - Jean Kridl, Calgene
	Juvenile Hormone Epoxide Hydrolase Degradation Of JH In Insect Development	- Tonya Severson Entomology
3:00pm	Overview of Research	- John Yoder/ Dupont
	Cluster Analysis of Multi-dimensional Expression Data	- Manuel Torres Vegetable Crops

3:30pm BREAK

PRESENTATIONS CONTINUED: John Yoder, Chair

3:45pm	Plant – Plant Communication	- John Yoder, Vegetable Crops
	Host Plant Recognition By Root-Parasitic Plants	- Denneal Jamison, Vegetable Crops
4:15pm	Overview of research	- Dan Klionsky, Microbiology
	Characterization of autophagy and cytoplasm to vacuole protein targeting in yeast	- Michael George Microbiology
4:45pm	Overview of Research	- Marty Privalsky, Microbiology
	Mechanisms by which different thyroid hormone receptors repress, or not, in the absence of hormone	- Zhihong Yang Microbiology
5:15pm	Conclusion	
5:30 pm	Bus departs	

POSTER TITLES

A. ADSORPTION AND SYNERGISM OF ENDOGLUCANASE I AND CELLOBIOHYDROLASE I OF *TRICHODERMA REESEI* DURING HYDROLYSIS OF MICROCRYSTALLINE CELLULOSE

H. Ding, D. B. Johnston, E. Y. Vlasenko, C.F. Shoemaker and S.P. Shoemaker, Department of Food Science and Technology, California Institute of Food and Agricultural Research, University of California, Davis

B. Disease Resistance Conferred by Inducing H_20_2-Generation and Programmed Cell Death in Transgenic Rice Expressing Glucose Oxidase Gene Driven by PAL Promoter

Zuhua He[1,2,3], Qun Zhu[2], Aardraa Potms[4], Debao Li[3], Bharat B. Chattoo[4], Pamela Ronald[1], Chris Lamb[2]

[1]Department of Plant Pathology, UC Davis, Davis, CA 95616
[2]Plant Biology Laboratory, The Salk Institute for Biological Studies, La Jolla, CA 92037
[3]Biotechnology Institute, Zhejiang University, Hangzhou 310029, China
[4]Department of Microbiology and Biotechnology Centre, M.S. University of Baroda, Baroda 390002, India
*Current address: DuPont Company, Wilmington, DE19880-0402
**Current address: Institute of Cell and Molecular Biology, University of Edinburgh, Edinburgh EH9 3JR, Scotland, U.K.

C. AN ARABIDOPSIS ENZYME FOR REPAIR OF OXIDIZED DNA

Ming-Jun Gao and Terence M. Murphy
Plant Biology Section, University of California, Davis, CA 95616

D. Novel Ligand-Receptor Systems for Plant Disease Resistance Engineering

Zuhua He[1], Qun Zhu , Debao Li, Joanne Chory[2], Pamela Ronald, Chris Lamb[2]
'Department of Plant Pathology, UC Davis, Davis, CA95616
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Current address: Institute of Cell and Molecular Biology, University of Edinburgh, Edinburgh EH9 3JR, Scotland, U.K.

E. DEVELOPMENT OF CONTROLLED DELIVERY DOSAGE FORMS OF BASIC FIBROBLAST GROWTH FACTOR

Bing Yang[1], Robert Jennings*[1], Y. John Wang[1], Lisa Gregory[2] and Andrew Protter[2]
[1]Pharmaceutical Research and Development, and [2]Preclinical Development, Scios Inc.

F. XOMA CORPORATION POSTERS:

G-45 **PLASMA LEVELS OF LIPOLYSACCHARIDE BINDING PROTEIN (LBP) INDICATE THAT HEMORRHAGIC TRAUMA PATIENTS, PARTIAL HEPATECTOMY PATIENTS AND CYSTIC FIBROSIS PATIENTS HAVE BEEN SYSTEMATICALLY EXPOSED TO BACTERIA AND EDOTOXIN.**

By Stephen F. Carroll, Mark L. White, Kelly Lee and Russell L. Dedrick

L-67 **RECOMBINANT BACTERICIDAL/PERMEABILITY-INCREASING PROTEIN IN COMBINATION WITH SULFADIAZINE IS REMARKABLY ACTIVE AGAINST TOXOPLASMA GONDII**

By Anis A. Khan (1,3), Lewis H. Lambert, Jr. (2), Jack S. Remington (3) and Fausto G. Arujo (1).

(1) Research Institute, Pal Alto Medical Foundation, Palo Alto, CA.; (2) XOMA Corp., Berkeley, CA; (3) Stanford University Medical School, Palo Alto, CA.

F-172 **rBP (10-193) IS SECRETED BY CHO CELLS AND RETAINS THE ACTIVITY OF $rBPI_{21}$**

By Arnold H. Horowitz, W.S. Ammons, G. Baklayan, R. Dedrick, R. Nadell, and R.E. Williams and P.S. Liu.

F-183 XMP ANTIFUNGAL PEPTIDES DEMONSTRATE ENHANCED SELECTIVITY AND OVERALL AVAILABILITY

By Roger Little, E. Lim, P. Wong, A. Malladi, J. Wilson, J. Lin, K. Gikomyo, M. Bakalinsky, P. Motchnik and S. Abrahamson

G. SCREENING *ARABIDOPSIS THALIANA* T-DNA INSERTIONAL LINES FOR UV-SENSITIVE MUTANTS

Amy K. Estrada*, Shirley Lei, Ana L. Fidantsef, and Anne B. Britt
Department of Plant Biology, University of California, Davis, CA, 95616

H. A SEARCH FOR T-DNA INSERTIONS IN THE EXCISION REPAIR GENES OF *ARABIDOPSIS THALIANA*

Jennifer R. Eads*, Ana L. Fidantsef, and Anne B. Britt
Section of Plant Biology, University of California, Davis, CA, 95616

I. REPAIR OF UV-INDUCED DNA DAMAGE IN ARABIDOPSIS

Fidantsef, A. L.*, Eads J. R., Estrada, A. K., Lei S., and Britt, A. B.
Section of Plant Biology, University of California, Davis, CA, 95616

J. *ARABIDOPSIS* ROOTS SIGNAL ORGAN DEVELOPMENT IN THE PARASITIC PLANT *TRIPHYSARIA*

John Yoder, Madeline Le, Hoa Phan, Russell Wrobel, Denneal Jamison, and Huguette Albrecht

Oral Presentation Abstracts

CALGENE – The Future of Calgene Research and Product Development

Katayoon Dehesh
Senior Scientist
Calgene

MOLECULAR, BIOCHEMICAL AND STRUCTURAL ANALYSIS OF ENZYMES RESPONSIBLE FOR PRODUCTION OF MEDIUM CHAIN FATTY ACIDS

Katayoon Dehesh♦, Jim Byrne, Dale Val, Patticia Edwards and Byron Froman.
Calgene, 1920 Fifth Street, Davis CA 95616

The end products of fatty acid synthase activities are usually 16 and 18-carbon fatty acids. There are however several plant species that store 8- to 14-carbon (medium-chain) fatty acids in their oil seeds. Among the medium chain fatty acids (MCFA), caprylic (8:0) and capric (10:0) are minor components of coconut oil, which are used in many industrial, nutritional and pharmaceutical products. Engineering crop plants such as Brassica could provide an economical source of these oils. To identify the key enzymes involved in biosynthesis of MCFA, we have cloned several thioesterases (TE) and β-ketoacyl-ACP synthases (KAS) from plant species containing high levels of these oils in their seeds. Expression of the thioesterase (TE) gene in Brassica resulted in the production of significant levels of MCFA in seed that otherwise do not accumulate any medium chain fatty acid. Substantial increases in MCFA levels were obtained when the TE gene was combined with a β-ketoacyl-ACP synthases (KAS) gene.

We are also interested in engineering oil with varying chain lengths. Towards this goal, we have obtained the crystal structure of recombinant *E. coli* Fab F (KASII) enzyme. This structure has been used for molecular modeling of plant KAS enzymes with the goal of identification and hence modification of functional residues involved in chain length determination.

CHIRON: A DIVERSIFIED BIOPHARMACEUTICAL COMPANY

Steve Rosenberg
Senior Director, Research
Chiron Technologies

A PROTEIN FRAGMENT WHICH FUNCTIONS AS AN ANGIOGENESIS INHIBITOR

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.

Development of Industrial Biotechnology at DuPont

Claire Komives, Bioprocess Engineering, DuPont Central Research & Development.

At DuPont, excellence in research and development has been a long-standing tradition. The successful coordination of several scientific and engineering disciplines can enable safe and cost-effective production of commodity chemicals and other products by biological agents, which is the focus of current research efforts in the Biochemical Sciences and Engineering Division.
A general overview of development efforts in biotechnology will be given, followed by a brief summary of a research project carried out by a summer intern from the University of Delaware Department of Chemical Engineering. His work focussed on the use of non-linear model predictive control for a continuous bioreactor.

THE SCIENCE OF BIOTECHNOLOGY

Hanspeter Gerber, Ph.D,
Scientist, Department of Molecular Oncology, Genentech, Inc.

Molecular biology, the basic science underlying biotechnology, is based on the premise that, since we have the tools to understand the body in molecular terms, we can understand diseases in molecular terms.

A primary tool for discovery at Genentech remains the technology at the foundation of the biotechnology industry: recombinant DNA technology -- recombining DNA from different organisms to produce new organisms that can make proteins that may provide medical benefit.

Our approach to discovery is based on the understanding of the body's own proteins, or molecules that block or mimic them, to treat or cure disease. Discovery is often a matter of systematically identifying which protein is causing problems in the body (either because it is absent, defective or present in excess) and then identifying or building a protein or related molecule to correct or counteract the problem. In this sense, biotechnology research relies on a singularly rational approach to discovery.

Discovery research at Genentech focuses on three major defined therapeutic areas of medicine: Cardiovascular Medicines, Endocrinology and Oncology.

In these areas Genentech has significant expertise and much room remains for medical advancement because few effective therapies exist. A fourth area of focus enables us to pursue promising research outside of these three defined areas. training.

OVERVIEW OF ENZYMES IN COMMERCIAL PROCESSES AND IMPROVEMENT OF FUNGAL EXPRESSION SYSTEMS

Debbie S. Yaver
Department of Molecular Biology
Novo Nordisk Biotech

Enzymes are used today in a wide variety of industries including paper, baking, brewing, textiles, animal feed, detergents and starch. The worldwide market for industrial enzymes is about one billion dollars annually and growing. Filamentous fungi are the source of about 40% of the enzymes used today. Many of these enzymes are produced using molecular biology techniques in the filamentous fungi *Aspergillus* and *Trichoderma*. The filamentous fungus *Fusarium venenatum* also has the potential to be used for the production of industrial enzymes. Because enzymes are often used to replace chemical processes that are relatively inexpensive, yields of enzyme from these systems must be very high (in multiple grams per liter). Often the primary transformant with the highest yield is put through several rounds of classical mutagenesis to identify improved mutants. Recently we have used insertion mutagenesis via restriction enzyme-mediated integration (REMI) to tag genes that play a role in heterologous protein production. Using this approach we have identified an *Aspergillus oryzae* gene *palB* that when deleted leads to an increase in production of a model heterologous protein.

RESEARCH AT ROCHE BIOSCIENCE

Jim Barnett
Research Section Leader
Roche Bioscience

Roche Bioscience is a research-based, business-oriented enterprise dedicated to the discovery of innovative pharmaceutical products that significantly improve the quality of human life. Our mission is to lead the industry in this effort through research excellence and the cost-effective, timely delivery of novel drugs.

Roche Bioscience was formed in 1995 following the acquisition of Syntex Corporation by Roche Holding Ltd. Established in 1944, Syntex was best known for innovation in the synthesis of steroidal and nonsteroidal compounds. Syntex scientists were world leaders in the research and development of corticosteroids to treat dermatological conditions and for the synthesis of compounds leading to the development of oral contraceptives.

Scios Research

John Lewicki,
Vice President for Research

The word Scios (pronounced as in science) originates from the word 'scio' meaning 'to know, understand or have knowledge of '. We believe this name showcases our strengths in science and
our continuing desire to develop new treatments for debilitating illnesses.

Scios was incorporated in 1981 under the name California Biotechnology. The Company was founded to discover, develop and commercialize novel human therapeutics. Since its inception, the Company has made a number of discoveries which have advanced into major clinical programs.

In April 1998, a significant milestone was reached when Scios submitted its first new drug application (NDA) to the U.S. Food and Drug Administration (FDA). The NDA seeks marketing
approval for Natrecor® (nesiritide) in the short-term treatment of congestive heart failure. If approved, Natrecor would be the first new therapy for the short-term treatment of congestive
heart failure in more than a decade. In January 1999, the Cardiovascular and Renal Drug Advisory Committee to the U.S. Food and Drug Administration (FDA) recommended the approval of Natrecor in the short-term management of congestive heart failure.

Scios scientists were the first to clone Fiblast ® (trafermin), a potent angiogenic and neuroprotective factor. Scios is currently developing Fiblast in partnership with Wyeth-Ayerst Laboratories, a division of American Home Products. Fiblast is being studied in a Phase II/III
clinical trial for stroke in Europe and plans for development of Fiblast as a treatment for peripheral vascular disease and coronary artery disease include additional Phase II trials.

Once a small research boutique, Scios has grown to more than 330 employees and maintains collaborations with some of the most respected names in pharmaceutical development, including Bayer AG, Wyeth-Ayerst, Eli Lilly and Company, DuPont Pharmaceuticals Company, Novo Nordisk A/S and Kaken Pharmaceutical Co., Ltd. The Company's main headquarters is located in Mountain View, California. Scios' research facility is located in Sunnyvale, California. The Company is proud of its state-of-the-art drug discovery methods that complement its research efforts. In addition, Scios has a profitable commercial operations division that markets and co-promotes third-party products.

Company/Fellow

Abstracts

UNRAVELING THE MECHANISM OF PROGRAMMED CELL DEATH

Hanspeter Gerber, Ph.D,
Scientist, Department of Molecular Oncology, Genentech, Inc.

Programmed cell death or apoptosis plays a central role in development and in homeostasis of metazoans. Cells die by apoptosis in the developing embryo during morphogenesis or synaptogenesis and in the adult animal during tissue turnover or at the end of an immuneresponse. Survival signals from the cell's environment and internal sensors for cellular integrity (tumor suppressor genes) normally keep a cell's apoptotic machinery in check. In the event, that a cell loses contact with its surroundings or sustains irreparable internal damage, the cell initiates apoptosis. A third mechanisms that enables the organism actively to direct individual cells to self destruct is mediated by death receptors and is called instructive apoptosis. Understanding the mechanism underlying programmed cell death may identify targets for drug development for the treatment of diseases based on uncontrolled cell proliferation such as cancer.

CHARACTERIZATION OF LNCAP PROSTATE CANCER CELL APOPTOSIS INDUCED BY SERCA PUMP INHIBITION

Ingrid E. Wertz
MED: Biological Chemistry, Genentech Intern

Programmed cell death, also known as apoptosis, balances mitosis and is therefore a fundamental mechanism in tissue homeostasis. Accordingly, disruption of apoptosis leads to pathological conditions. With excess apoptosis AIDS, Multiple Sclerosis, and other degenerative diseases result whereas hyperplastic diseases, including cancer, occur with too little apoptosis. Specifically, inhibition of apoptosis results in benign prostatic hyperplasia (BPH) and prostatic adenocarcinoma (CaP) in the prostate gland. Over 25% of American men require treatment for BPH resulting in an annual loss of 5 billion dollars, and it was estimated that 41,800 men died from CaP in 1997 alone.

Several studies suggest that successful CaP and BPH therapies induce prostate regression via apoptosis. However, therapy-resistant cells fail to die in response to treatment. It is therefore important to characterize the apoptotic pathways induced by effective stimuli in therapy-resistant prostatic cells. Such knowledge could expedite the development of drugs that bypass blocks in apoptosis cascades in order to induce regression of BPH and CaP cells. Furthermore, calcium perturbation is a common finding in cells induced to undergo apoptosis by various stimuli, including chemotherapeutics. Thus, it is also of interest to investigate the role of calcium in apoptotsis of CaP cells.

The LNCaP prostate cell line is an ideal experimental system to study prostatic apoptosis because the cells retain some differentiated characteristics, such as secretion of prostatic specific antigen and the requirement of androgens for proliferation, yet also exhibit characteristics of aggressive carcinoma cells, including the failure to undergo apoptosis in the absence of androgens, resistance to radiation, and high expression levels of bcl-2, an oncoprotein thought to inhibit apoptosis.

Data presented will discuss the mechanism of apoptosis in LNCaP cells induced by the calcium perturbant thapsigargin (TG), an inhibitor of endoplasmic reticulum (ER)-localized Ca^{2+} ATPase (SERCA) pumps. Specifically, techniques to elucidate the subcellular localization of TG-induced calcium perturbation will be presented, as well as the role of aspartate-specific cysteine proteases, known as caspases, in TG-induced LNCaP apoptosis.

COLLOIDAL DIFFUSION IN POLYMER SOLUTIONS AND GELS

Ronald J. Phillips*
Department of Chemical Engineering and Materials Science, University of California, Davis

The diffusion of globular proteins, colloidal particles and colloidal aggregates (i.e., micelles) in polymer solutions and gels is of central importance in many bioseparation and controlled release strategies. The diffusion process itself can be separated into two components: a thermodynamic driving force (i.e., the gradient in the chemical potential) that causes solute to move from regions of high concentration to low concentration; and a hydrodynamic drag force or resistance that results from the solute moving through a viscous fluid. In a pure solvent at very low solute concentrations, this representation of diffusion leads to the well-known Stokes-Einstein equation. However, for diffusion in media that consists of a solvent plus crosslinked polymer (i.e., a polymer gel) or uncrosslinked polymer (i.e., a polymer solution), and for non-dilute solute concentrations, both the thermodynamic driving force and hydrodynamic resistance are altered. In our research group, we are performing experiments and doing theoretical calculations to develop a fundamental understanding of how diffusion is affected by such complex environments. Our experiments consist of directly measuring rates of diffusion in polymer solutions and gels. We are also observing the effect of dissolved polymer on the motion of large, macroscopic particles in order to isolate and examine the hydrodynamic problem alone. For our theoretical work, we are using the principles of fluid mechanics to study the effect of crosslinked and uncrosslinked polymer on solute motion.

THE EFFECT OF CONCENTRATION ON HINDERED GRADIENT DIFFUSION IN POLYMERIC HYDROGELS

Kristan K. S. Buck*, Stephanie R. Dungan, Ronald J. Phillips
Department of Chemical Engineering and Materials Science, University of California, Davis

Our lab is studying the properties of micelles in polymeric hydrogels. Gel/micelle materials have the potential to be very useful in the extraction and controlled release of hydrophobic solutes, such as toxic hydrocarbons, water-insoluble food compounds and pharmaceuticals. To enable the design of such systems, a fundamental understanding of the effects of micelle-gel fiber interactions on micelle thermodynamic and transport properties is required. Using holographic interferometry, we have measured micelle and protein diffusion coefficients in solution and in agarose hydrogels as a function of solute concentration. Our experimental results indicate solute concentration has an enhanced effect on diffusion in gel over its effect in solution. We compare our experimental data with a new theory we have developed for the diffusion of sphere-like, colloidal solutes in fibrous media. In this theoretical development, it is shown that the gel fibers serve to augment the thermodynamic influences that enhance diffusion at higher concentrations, while reducing hydrodynamic interactions which retard that diffusion. If the solutes are modeled as spheres with short-range repulsive interactions, then the experimentally measured concentration dependence of the diffusivities of both the protein and micelles is in good agreement with the theoretical predictions.

ON-GOING RESEARCH IN THE HAMMOCK LAB; OR, BUGS AND DRUGS

Bruce D. Hammock*
Department of Entomology, University of California-Davis

Research in the lab comprises three areas: 1) detection of toxic substances and metabolites through immunoassay, 2) investigation into mechanisms of toxicity and biological function of compounds produced or degraded through activity of epoxide hydrolases and carboxylesterases, and 3) investigation of mechanisms of insect enzymes involved in developmental regulation, and of the utility of these enzymes and insect-selective toxins for control of pest insect populations with the baculovirus expression system. These areas dovetail within the realm of agriculture by taking research through detection of substances in the environment, understanding thresholds at which these substances are harmful and how they exert their toxicity, and finally, in developing biological alternatives for chemical insecticides that may reduce exposure and work effectively with a variety of agricultural pest control measures.

JUVENILE HORMONE EPOXIDE HYDROLASE DEGRADATION OF JH IN INSECT DEVELOPMENT

Tonya F. Severson*, Christophe Morisseau, Marvin H. Goodrow, Deanna L. Dowdy, and Bruce D. Hammock
Department of Entomology, University of California-Davis

Juvenile Hormone is involved in regulating insect development, and its titer is controlled through synthesis and degradation. Previous work by scientists in the lab made available recombinant juvenile hormone epoxide hydrolase (JHEH) and juvenile hormone esterase (JHE), two enzymes which selectively degrade Juvenile Hormone. While the importance of juvenile hormone esterase in degradation of JH has been well characterized in the past, that of juvenile hormone epoxide hydrolase has been less well explored. We are currently screening several classes of chemicals for inhibitors of JHEH, and have found that JHEH activity on 3H-trans-diphenyl propene oxide is greatly reduced (IC50 ~3 μM) chemicals with a long alkyl chain and a short alkyl chain on either side of the pharmacophore. Interestingly, although the JHEH is a microsomal enzyme and has greater homology to rat microsomal EH, the JHEH inhibition profile is most similar to that of the soluble mouse and human EHs. In assays with 3H-JH III as the substrate, none of the compounds have proven effective inhibitors. Because adequate selective inhibition of JH degradation is essential to assess JHEH necessity, candidate inhibitors of greater similarity to JH with respect to branching are being synthesized.

PLANT – PLANT COMMUNICATION

John Yoder
Department of Vegetable Crops, University of California, Davis

The recognition of host plants by parasitic plants offers a unique opportunity to investigate plant-plant signaling. Phenolic molecules released by host roots trigger the development of haustoria in parasitic plants. Haustoria are globular outgrowths on parasite roots whose functions are to attach the parasite to the host, invade the host root cortex, and establish a vascular continuum through which the parasite robs host resources. The impact to the host plant can be debilitating, and agriculturally parasitic plants are devastating. In Africa, over two thirds of the 73 million hectares cultivated in cereals and legumes are infested with Striga. The FAO estimates that the lives of over 100 million Africans in 25 countries are threatened by crop losses by Striga. In the United States, dwarf mistletoe (Arcethobium) is estimated to destroy up to 3.2 billion board feet of lumber per year in western forests. Understanding the genetic mechanisms governing host recognition and haustorium development should enable us to develop rational strategies for engineering host resistance against parasitic weeds. We are using the parasitic plant Triphysaria to define the genetics of host recognition and haustorium development. Triphysaria is useful for these studies because it is a facultative parasite whose host range includes Arabidopsis, it is a simple diploid amenable to genetic analyses, and, haustorium development can be monitored in vitro. Using geographically defined ecotypes of Triphysaria, we have identified heritable variation in three parasite specific phenotypes; spontaneous haustorium formation, sibling recognition, and, responsiveness to exogenous phenolic signals. These may represent recognition races for different signal molecules. We are also using suppressive subtraction to identify cDNAs differentially abundant in Triphysaria roots after treatment with haustorial inducing factors. Sequence comparisons are being used to assign tentative functions. Gene expression is being characterized in Triphysaria and the closely related, non-parasite Antirrhinum by in vitro and in situ hybridizations. Multi-array technology is being used to examine the global expression pattern of HIF induced genes in both parasites and non-parasites. A long-term objective is to assign biological functions to cloned genes by combining our genetics and molecular approaches.

CLUSTER ANALYSIS OF MULTI-DIMENSIONAL EXPRESSION DATA

Manuel Torres*, Marta Matvienko, and John I. Yoder
Department of Vegetable Crops, University of California, Davis CA, 95616

We are interested in characterizing the signal, regulatory and developmental pathways of haustorium formation in parasitic plants. The defining feature of parasitic plants is their ability to form haustoria in response to host-plant recognition signals secreted in the rhizosphere. This parasite-specific organ attaches and invades host-plant tissue and transports fluid nutrients via a vascular connection. We have developed an in-vitro system that allows the identification of plant transcriptional responses during early haustorium development in parasitic and non-parasitic *Scrophulariaceae.* A phenolic derivative DMBQ (2,6 dimethoxybenzoquinone) present in plant-root exudates and a maize root exudate known to activate haustoria formation were used as haustorial inducers. We have isolated cDNAs of differentially abundant transcripts using PCR based subtraction hybridization. We assigned putative functions to 141 of these Early DMBQ Induced (EDI) transcripts using BLAST homology searches. These EDI transcripts were arrayed on nylon membranes and interrogated with normalized labeled gene–specific probes. Ninety-five percent of EDI transcripts induced by DMBQ were also induced by maize-root exudates. Only 6% of the EDI transcripts are induced in the non-parasite Lindenbergia after DMBQ exposure. Fifty percent of EDI transcripts are reduced in abundance in DMBQ exposed Lindenbergia. We are interested in differences in transcript abundance between these two closely related species and in identifying clusters of genes with similar expression patterns. These clusters of expressed transcripts are likely involved in recognition and transduction of host-root signals or in early morphological changes associated with haustorium formation in parasitic plants. One of our goals is to develop an image-analysis software application or to modify an existing one for analyzing gene expression profiles based on hybridization characteristics of multiple cDNA arrays.

HOST PLANT RECOGNITION BY ROOT-PARASITIC PLANTS

Denneal Jamison*, Coby Goldwasser, Kendra Kongkadee, Marta Matvienko, Julie Pelletier, Paul Richnavsky, Manuel Torres, Angela Wojtowicz, Russell Wrobel and John Yoder*
Department of Vegetable Crops, University of California, Davis

Root-parasitic plants in the Scrophulariaceae recognize molecular signals in the rhizosphere in order to direct developmental events critical to the parasitic lifestyle. Exuded by the roots of host plants, these molecular signals trigger the formation of the haustorium. The haustorium is a specialized parasitic root organ that attaches and penetrates the host root, forming a vascular continuum and facilitating the transfer of minerals, nutrients and water from the host to the parasite.

Triphysaria is an annual, root-parasitic angiosperm belonging to the Scrophulariaceae. This springtime wildflower is commonly found in California grasslands and has a broad host range, including maize and *Arabidopsis*. Using an *in vitro* assay, haustorium development can be readily induced and monitored in *Triphysaria* root tips. Induction occurs both in response to the presence of a host root and in response to host root exudate.

In analyses of host root exudates, specific signal molecules have been identified that are thought to mediate host recognition by root-parasites. DMBQ, dimethoxy-benzoquinone, is one such signal molecule and is commonly used to induce haustorium development in root-parasitic species. Phenolic acids (i.e. syringic acid), quinones (i.e. p-benzoquinone) and anthocyanidins (i.e. peonidin) are included in this group of signal molecules. Characterization of the induction kinetics of these different signal molecules will be important in determining the host recognition mechanism employed by root-parasitic plants.

Differential recognition of DMBQ has been observed among three species of *Triphysaria.* Genetic analyses of the DMBQ recognition trait in defined *T. pusilla* families and in F1 progeny generated between inducing and non-inducing species have shown that DMBQ recognition is a heritable phenotype. Using a subtractive PCR method, the molecular basis of DMBQ recognition has also been investigated in the lab and our ultimate goal will be to correlate DMBQ-induced transcripts with observed phenotypes.

CYTOPLASM TO VACUOLE PROTEIN TRANSPORT IN YEAST

Daniel J. Klionsky*, Valerie M. Dalton, Kip P.-T. Eggerton, Michael D. George, Ann Hefner-Gravink, Maria U. Hutchins, John N. Kim and Sidney V. Scott
Section of Microbiology, University of California, Davis

Eukaryotic cells contain a variety of discrete membrane-enclosed organelles. This highly compartmentalized organization is essential to the normal functioning of the cell. The vacuole/lysome is the major organelle responsible for intracellular degradation in eukaryotic cells. Our goal is to develop a precise understanding of the molecular events involved in the recognition, targeting and transport of proteins to this organelle using yeast as a model system. While most characterized vacuolar proteins transit through the secretory pathway, aminopeptidase I (API) reaches this organelle through an alternative mechanism; API enters the vacuole directly from the cytoplasm. This suggests that API utilizes components of the subcellular sorting machinery that are distinct from those used by secretory pathway-mediated vacuolar proteins. Recently we have demonstrated that the mechanism of API import partially overlaps with that of autophagy. Both processes involve the formation of double membrane vesicles in that sequester proteins from the surrounding cytosol. Upon completion of formation, the vesicles target to the vacuole, fuse with the membrane and deliver a single membrane vesicle that is subsequently degraded, allowing access to the lumenal contents. However, there are distinct differences between autophagy and API import, again suggesting a unique set of targeting components is needed for API delivery. We are using a combined genetic and biochemical approach to characterize the import of API. First, we have identified a vacuolar targeting signal in the propeptide of API that is required for membrane binding and import. One of these mutants confers a temperature sensitive targeting phenotype. We used this propeptide mutant to demonstrate that precursor API transits to the vacuole as a dodecamer. The large size of the precursor complex would necessitate transport via a vesicular intermediate. Second, we have isolated a set of mutants that are specifically defective in vacuolar localization of API. Most of these mutants accumulate precursor API that is incorrectly localized to the cytoplasm. In one case, the precursor protein accumulates with subvacuolar vesicles. These mutants will allow us to define components of the sorting and transport apparatus that recognize and target this protein to the vacuole. Third, we have initiated the reconstitution of API targeting *in vitro* to allow the assignment of a biochemical function to cytosolic or membrane components that are required for its localization. A characterization of the proteins involved in API recognition and delivery will further our understanding of vacuolar/lysosomal protein targeting and biogenesis.

CHARACTERIZATION OF AUTOPHAGY AND CYTOPLASM TO VACUOLE TARGETING IN YEAST

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The cytoplasm to vacuole targeting (Cvt) pathway and macroautophagy are dynamic events, involving the rearrangement of membrane to form a sequestering vesicle in the cytosol. This process requires the concerted action of various proteins, including the E1-like *APG7* gene product. Recently it was shown that Apg7p carries out a novel non-ubiquitin conjugation reaction that covalently links two proteins, Apg12p and Apg5p, which are required for import of aminopeptidase I (API) and autophagy (Mizushima, et al., *Nature*, 1998. 395:395). We have undertaken an analysis of Apg5p function to gain a better understanding of the role of the conjugation reaction in these pathways. For this purpose, we generated the first temperature-sensitive mutant in the Cvt pathway, designated *apg5*^{ts}. Biochemical analysis of API import in the *apg5*^{ts} strain indicated that Apg5p is involved in the sequestration step, and confirmed that it is directly required for import of aminopeptidase I via the Cvt pathway. Characterization of the Apg5 protein revealed that it is part of a larger, membrane associated protein complex. Localization by fluorescence microscopy and subcellular fractionation indicated that Apg5p is associated with a structure adjacent to the vacuole prior to the conjugation event. Covalent linkage to Apg12p drives redistribution of Apg5p as part of the sequestration reaction.

OVERVIEW OF RESEARCH

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Our general interest is in the mechanisms by which proliferation and differentiation is regulated in normal cells, and in the abnormal processes that occur in neoplasia. Our specific goal is a better understanding of the actions of the nuclear hormone receptors in normal cells and in oncogenesis. Nuclear hormone receptors are a family of ligand-regulated transcription factors, and include the steroid, retinoid, and thyroid hormone receptors. These receptors directly modulate gene expression in response to hormones of extracellular origin, and play critical roles in metazoan homeostasis, differentiation, and reproduction. In addition, aberrant nuclear hormone receptors have been implicated as causal or contributory factors in a variety of human and non-human cancers. My research seeks to exploit these aberrant oncogenic receptors, both to better elucidate the actions of their normal counterparts, and to determine the molecular pathways that operate in neoplasia.

ANTI-REPRESSION BY THYROID HORMONE RECEPTORS: UNIQUE N-TERMINUS OF THE β-2 ISOFORM BINDS TO AND INHIBITS THE FUNCTION OF COREPRESSORS

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Thyroid hormone receptors (T3Rs) belong to the nuclear hormone receptor superfamily and function as hormone-regulated transcription factors. The T3Rα-1, β-0, and β-1 isoforms exhibit bimodal transcriptional regulation, typically repressing target gene expression in the absence of hormone and activating transcription in the presence of hormone. It has been demonstrated that the physical interaction between the receptor and corepressors is crucial for transcriptional repression mediated by most T3R isoforms. However, the T3Rβ-2 isoform fails to repress, and instead activates transcription even in the absence of hormone. We wished to understand the molecular mechanism behind this absence of transcriptional repression by T3Rβ-2. *In vitro* GST-pull-down assays were employed to detect interactions between T3Rβ-2 and corepressors. Transient transfections of mammalian cells were used to investigate the transcriptional properties of T3R isoforms. We report here that in the absence of hormone, T3Rβ-2 interacts with corepressors in a unique manner distinct from that of other isoforms that do repress in the absence of hormone. Further *in vitro* and *in vivo* genetic studies indicated that the unique N-terminus of T3Rβ-2 mediates inhibitory contacts with corepressors, and thus appears to prevent the subsequent formation of a functional corepressor complex. Future studies will be carried out to address the possible physiological consequence resulted from this absence of repression by T3Rβ-2.

Poster Abstracts

A. ADSORPTION AND SYNERGISM OF ENDOGLUCANASE I AND CELLOBIOHYDROLASE I OF *TRICHODERMA REESEI* DURING HYDROLYSIS OF MICROCRYSTALLINE CELLULOSE

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Endoglucanase I and cellobiohydrolase I (EG I and CBH I) were purified *from Trichoderma reesei* cellulases. Capillary zone electrophoresis was used as a method to detect the adsorption of EG I and CBH I onto a microcrystalline cellulose (Avicel). Two sets of experiments were designed for the adsorption studies. In the adsorption kinetics experiments, the incubation time was varied while enzyme/substrate ratio was fixed. In the adsorption isotherm studies, the adsorption time was fixed, and enzyme/substrate ratio was varied. Experiments were performed with EG I and CBH I alone and in reconstituted mixtures. Adsorption of enzymes was found to follow the Langmuir Adsorption Equation. The maximum amount of adsorbed enzymes and the adsorption partition coefficient were compared for EG I and CBH I.

B. DISEASE RESISTANCE CONFERRED BY INDUCING H_2O_2-GENERATION AND PROGRAMMED CELL DEATH IN TRANSGENIC RICE EXPRESSING GLUCOSE OXIDASE GENE DRIVEN BY PAL PROMOTER

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Hydrogen peroxide (H_2O_2) during oxidative burst in incompatible interactions between plants and pathogens has been recognized as a key component of plant defense responses. Manipulating H_2O_2-generation could function in the similar way as oxidative burst by transgening H_2O_2-generating enzymes. We isolated glucose oxidase gene (GOX) from *Aspergillus nigar*, which generates H_2O_2 as glucose is oxidized. Transgenic rice carrying the rice phenylalanine ammonia-lyase (PAL) gene promoter driving GOX gene was generated. In these transgenic lines, H_2O_2 level is elevated when GOX expression is induced by wounding. Significant programmed-like cell death was observed in wounded leaves. GOX gene expression was induced 2 hours with a peak level appearing 8-12 hours after wound treatment. Rice defense pathway genes such as RCH10 (chitinase) and PIR2 (thaumatin-like) were activated earlier and RCH10 expression was stronger in the PAL::GOX plants, whereas PIR3 (peroxidase) gene expression was completely inhibited in GOX-expressing plants, suggesting that GOX protein or GOX-generated H_2O_2 has a negative effect on peroxidase gene expression. PAL::GOX plants exhibits enhanced disease resistance to *Xanthomonas oryzae* pv. oryzae and *Magnaporthe grisea*, two main diseases of the crop, accompanied with large areas of cell death. Bacterial growth and disease development of blast were significantly inhibited in the PAL::GOX plants. These results suggest that pathogen inducing H_2O_2-generation then leading to cell death in transgenic rice can provide a new approach for engineering durable and broad spectrum disease resistance in plants.

References:

1) Alvarez, M.E., Pennell., R.I., Meijer, P.J., Ishikawa. A., Dixon, R.A., and Lamb, C. Reactive oxygen intermediates mediate a systemic signal network in the establishment of plant immunity. Cell **1998,** 92: 773-784.
2) Chen, Z., Silva, H., and Klessig, D.F. Active oxygen species in the induction of plant systemic acquired resistance by salicylic acid. Science **1993,** 262: 1883-1886.
3) Wu, G., Shortt, B.J., Lawrence, E.B., Levine, E.B., Fitzsimmons, K.C., and Shah. D.M.. Disease resistance conferred by expression of a gene encoding H2O2-generating glucose oxidase in transgenic potato plants. Plant Cell, **1995,** 7: 1357-1368.

C. AN ARABIDOPSIS ENZYME FOR REPAIR OF OXIDIZED DNA

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In plants, oxidation stress is a factor in normal senescence, air pollution stress, and stress caused by chilling, freezing and high light intensity. Reactive oxygen species (including superoxide, hydrogen peroxide, hydroxyl radical, and/or singlet oxygen) are produced under these contitions, and these compounds are expected to oxidize DNA bases. In bacteria, the enzyme formamidopyrimidine-DNA glycosylase (FPG) catalyzes the initial steps in the repair of DNA containing oxidized purines by removing the purines from the sugar-phosphate backbone and cleaving the polynucleotide chain at the resulting apurinic sites. Two cDNA clones encoding homologs of bacterial FPG were isolated from *Arabidopsis thaliana* and named *Atfpg*-1 and *Atfpg*-2. The two clones are identical at their 5′ ends, but differ at their 3′ ends. Southern analysis with a probe representing a common nucleotide sequence of the two clones indicated that there are 2-3 genes sharing that sequence. DNA blots hybridized with *Atfpg*-1-specific and *Atfpg*-2-specific probes indicated that both mRNAs come from only one of those genes. The two clones are thought to represent the products of alternative splicing of the one gene's transcript: in RNA blots specific probes hybridized with substantial amounts of very large RNA, suggesting that processing of transcripts is a limiting step in the production of the two kinds of mRNA. Northern analysis demonstrated that the expressions of the two clones are different and organ-specific. Protein coded by the *Atfpg*-2 clone was expressed in *Escherichia coli* and purified, and its activity was assayed and compared with T4 endonuclease V, an enzyme with DNA glycosylase and apurinic lyase activities. The protein preferentially cleaved DNA that contained apurinic sites, indicating that this protein has an apurinic endonuclease activity like T4 endonuclease V. The protein also demonstrated a limited endonuclease activity on UV-C-irradiated DNA. We suggest that this protein, like the homologous proteins of bacterial and the related protein coded by *Atfpg*-1, is involved in the excision reprir of oxidatively damaged DNA.

D. NOVEL LIGAND-RECEPTOR SYSTEMS FOR PLANT DISEASE RESISTANCE ENGINEERING

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Plants and their pathogens have evolved a "gene-for-gene" recognition mechanism. In this system, a plant resistance (R) gene confers resistance to a pathogen carrying a specific avriulence (avr) gene. There exists direct evidence for physical interaction between R gene products (receptors) and avr gene products (ligands), this interaction initiates a defense response, including an oxidative burst, hypersensitive cell death and defense gene activation. Because R gene/avr gene interactions are highly specific, the development of a non-specific resistance strategy would be agronomically useful. To this end, chimeric receptors were constructed which combined the domains of the rice bacterial blight resistance gene Xa21 encoding a receptor-like kinase and other ligand binding domains. We first tested if Xa2l alone could induce cell death in cell lines. Race-specific cell death was observed in the cell line expressing Xa21 gene when this cell line was inoculated with the avr strain P099A of *Xathomonas oryzae* pv. oryzac, and no cell death was observed in the cell line inoculated with virulent strain J 18 and in the wildtype cell line inoculated with the both strains. One of the chimeric receptors which consists of the Brassinosteroid (BR) binding/interaction domain of the Arabidopsis BR receptor (BRI.1) and the Xa21 kinase domain, was constitutively expressed in rice cell lines. These cell lines showed specific cell death and defense gene activation when the cell lines were treated with the presumed ligand BR. Another construct which combines the chitin binding Hevein domain of rice chitinase with the Xa21 transmembrane and kinase domains also showed significant cell death when the constitutively expressed cell lines were treated with chitin. These results suggest a novel approach for engineering plant resistance to pathogens.

References:

1) Lamb, C. A ligand-receptor mechanism in plant-pathogen recognition. Science **1996,** 274: 2038-2039.
2) Li J.-M and Chory, J. A putative leucine-rice repeat receptor kinase involoved in Brassinosteroid signal transduction. Cell **1998**, 90: 929-938.
3) Song, W.-Y, Wang, G.-L, Chen., L.-L, Kim, H.S., Pi, L.-Y., Holsten, T., Gardner, J., Wang. B., Zhai,W.-X., Zhu, L.-H., and Ronald, P.C. A receptor kinase-like protein encoded by the rice disease resistance gene, Xa2l. Science **1995**, 270: 1804-1806.
4) Staskawicz, B.J., Ausubel, F.M., Baker. B.J., Ellis. J.G., and Jones, J.D.G. Molecular genetics of plant disease resistance. Science **1995**, 268: 661-667.

E. DEVELOPMENT OF CONTROLLED DELIVERY DOSAGE FORMS OF BASIC FIBROBLAST GROWTH FACTOR

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Purpose. To develop controlled delivery dosage forms of basic fibroblast growth factor (bFGF) and to investigate the glass transition temperature (Tg) effect on protein stability during preparation of the dosage form. **Methods.** Basic FGF was lyophilized with a series of excipients to obtain bFGF lyophiles with a range of glass transition temperatures. The lyophiles were then incorporated into a biodegradable polymer, polycaprolactone (PCL), at the polymer's melting point. The mixture was stretched or pressed to form either rods or thin films. The effect of lyophile Tg on protein stability during preparation of the dosage forms was studied using ion-exchange HPLC. The in vitro release of bFGF from several rod formulations was characterized over a five day period. The angiogenic response was determined at five days after subcutaneous injection of rods into rats. **Results.** The rods were about 10 mm in length and 1 mm in diameter. Recovery of bFGF after incorporation into PCL was related to lyophile Tg. Lyophiles with glass transition temperatures higher than the polymer melting point (65°C), such as bFGF-trehalose lyophile (Tg = 84°C), stabilize bFGF during preparation of the dosage forms. However, lyophiles with Tg lower than 65°C could not fully protect the protein from degradation during the incorporation process. The in vitro release test from the rods showed the amount of bFGF released after 5 days ranged from 5% to 15% depending on the formulation. As expected, the release rate can be controlled by varying the ratio of protein to excipient. Additionally, the lyophile content affects the release rate. A strong angiogenic effect was observed in the rats five days after injection of rods with each of the formulations tested. Placebo rods and bFGF solution showed no angiogenesis at the same time point. **Conclusions.** This work describes a method to stabilize a protein so that it can be incorporated into a polymer at its melting point. The resulting dosage forms provide a controlled release rate which is necessary to obtain biological activity of bFGF.

F. XOMA CORPORATION (2910 7th Street, Berkeley, CA, 94710) POSTERS:

G-45 **PLASMA LEVELS OF LIPOLYSACCHARIDE BINDING PROTEIN (LBP) INDICATE THAT HEMORRHAGIC TRAUMA PATIENTS, PARTIAL HEPATECTOMY PATIENTS AND CYSTIC FIBROSIS PATIENTS HAVE BEEN SYSTEMATICALLY EXPOSED TO BACTERIA AND EDOTOXIN.**

By Stephen F. Carroll, Mark L. White, Kelly Lee and Russell L. Dedrick

L-67 **RECOMBINANT BACTERICIDAL/PERMEABILITY-INCREASING PROTEIN IN COMBINATION WITH SULFADIAZINE IS REMARKABLY ACTIVE AGAINST TOXOPLASMA GONDII**

By Anis A. Khan (1,3), Lewis H. Lambert, Jr. (2), Jack S. Remington (3) and Fausto G. Arujo (1).Research Institute, Pal Alto Medical Foundation, Palo Alto, CA.; (2) XOMA Corp.; (3) Stanford University Medical School, Palo Alto, CA.

F-172 **rBP (10-193) IS SECRETED BY CHO CELLS AND RETAINS THE ACTIVITY OF $rBPI_{21}$**

By Arnold H. Horowitz, W.S. Ammons, G. Baklayan, R. Dedrick, R. Nadell, and R.E. Williams and P.S. Liu.

F-183 XMP ANTIFUNGAL PEPTIDES DEMONSTRATE ENHANCED SELECTIVITY AND OVERALL AVAILABILITY

By Roger Little, E. Lim, P. Wong, A. Malladi, J. Wilson, J. Lin, K. Gikomyo, M. Bakalinsky, P. Motchnik and S. Abrahamson

G. SCREENING *ARABIDOPSIS THALIANA* T-DNA INSERTIONAL LINES FOR UV-SENSITIVE MUTANTS

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UV-induced DNA damage has been thoroughly studied in mammalian and microbial cells. In plants there are two repair pathways for UV-induced DNA damage, a light-dependent and a light-independent pathway. The genes responsible for DNA repair via the light-dependent pathway have been cloned and characterized. However, the genes involved in DNA repair via the light-independent pathway have not yet been identified. The purpose of this project is to identify *A. thaliana* UV-sensitive mutants produced by random T-DNA insertions. This will help us to determine which genes are responsible for DNA repair via the light-independent pathway and to identify the biochemical pathways involved in this repair.

H. A SEARCH FOR T-DNA INSERTIONS IN THE EXCISION REPAIR GENES OF *ARABIDOPSIS THALIANA*

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A T-DNA is a sequence of DNA that can be inserted into the plant genome by *Agrobacterium tumefaciens*. Since insertion of the T-DNA is random, it may integrate anywhere throughout the genome. If DNA from enough lines of plants is examined, each with an independent insertion event, these insertion lines can be used in a reverse genetics screen for detection of a knockout within a particular gene of interest. This screen can be performed by designing specific primers for the gene of interest, as well as T-DNA primers, and running polymerase chain reactions (PCR). The short term goal of this project is to use such a screen to detect mutations (knockouts) within the homologs of DNA excision repair genes in *Arabidopsis thaliana*. The long term goal is to use these knockout mutations to determine whether these repair gene homologs are required for DNA damage resistance and repair in Arabidopsis.

I. REPAIR OF UV-INDUCED DNA DAMAGE IN ARABIDOPSIS

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Our laboratory is interested in studying repair and tolerance mechanisms of UV-induced DNA damage using *Arabidopsis thaliana*. In plants, DNA damage is repaired by two pathways, a light-dependent and a light-independent pathway. We have already isolated and characterized the genes required for photoreactivation. However, the molecular mechanism for the "dark repair" pathway remains to be determined. To accomplish this objective, we are currently screening T-DNA tagged lines for mutants defective in the genes involved in the dark repair of UV-induced DNA damage products using two different approaches. The first approach consists of a classical mutant screening, where T-DNA tagged line seedlings are irradiated with UV-B and putative mutants are selected based on a characteristic UV-sensitive phenotype. The second approach consists of a reverse "molecular" genetic approach. This approach uses the sequence information available for dark repair genes that have been cloned from yeast and humans. Homologous sequences to those can be found in the Arabidopsis genome database. We can then use PCR to screen for insertions in these homologs and then check their function. Also, we are checking to see if these homologs, when expressed in Arabidopsis, complement our repair mutants.

J. *ARABIDOPSIS* ROOTS SIGNAL ORGAN DEVELOPMENT IN THE PARASITIC PLANT *TRIPHYSARIA*

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Parasitic plants recognize molecular signals in the rhizosphere in order to direct developmental events critical to the parasitic lifestyle. These signals, exuded by the roots of host plants, lead to the formation of the haustorium, the root organ, which attaches, penetrates, and forms a xylem bridge between the parasite and host roots. The xylem bridge facilitates transfer of host water and minerals to the parasite. In this system, we have tested over fifty Arabidopsis lines, including phenylpropanoid mutants. It was found that xylem bridge formation was reduced in response to lowered host auxin. We suspect that host auxin is co-opted in the formation of the xylem bridge during haustorium development.

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Designated Emphasis in Biotechnology Program

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 purpose is to provide graduate students an opportunity to explore biotechnology through seminars and courses and examine the relationship of academia to industry through internships. This program supplements a student's Ph.D. curriculum and those completing the DEB program will obtain an official designation on their transcript indicating a qualification in biotechnology.

Students interested in participating in DEB must be enrolled in the Ph.D. program of one of the participating graduate groups. Participating graduate programs currently include Genetics, Nutrition, Plant Biology, Biochemistry and Molecular Biology, Physiology, Microbiology, and Chemical Engineering and Material Sciences. In addition to the specific graduate group requirements, students wishing to obtain DEB must enroll in MCB 263 - Biotechnology Fundamentals and Application, and MCB 294/ECH 294 - Current Progress in Biotechnology Seminar. In addition, students must complete a minimum of three months internship at a participating biotechnology company. This last requirement should be particularly appealing to students interested in working for such a company after graduation.

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David Gilchrist
Tom Gradziel
John Hershey
Michele Igo
Clarence Kado
Daniel Klionsky
Bill Lucas
Paul Luciw
Harry Matthews
Bernie May
Richard Michelmore
James Murray
Marty Privalsky
Kathryn Radke
Pam Ronald
Michael Syvanen
Brett Tyler
Thea Wilkins
Valerie Williamson
Reen Wu
John Yoder

Horticulture
Don Durzan
Tom Gradziel
John Labavitch
Richard Michelmore
Michael Reid

Human Development
Ursula Abbott

Hydraulic Sciences
Alan Jackman

Immunology
Hilary Benton
Patricia Conrad
Eric Gershwin
Paul Luciw
Dick Robbins

International Agricultural Development
Paul Gepts
Michael Reid

Microbiology
Linda Bisson
George Bruening
Robert Cardiff
Ronald Chuang
Patricia Conrad
Michael Dahmus
Satya Dandekar
Roy Doi
Eric Gershwin
John Hershey
Michele Igo
Clarence Kado
Daniel Klionsky
Paul Luciw
Karen McDonald
John Meeks
David Ogrydziak
Bennie Osburn
Niels Pedersen
Chester Price
Marty Privalsky
Kathryn Radke
Dewey Ryu
Michael Syvanen
Frederic Troy
Tilahun Yilma

Neuroscience
Michael Hanley

Nutrition
Robert Rucker
Quinton Rogers
Chris Calvert

Pharmacology & Toxicology
Hilary Benton
Ronald Chuang

Michael Denison
Bruce Hammock
Michael Hanley
Fumio Matsumura
Charles Plopper
Robert Rice
Robert Rucker
Barry Wilson
Reen Wu

Physiology
Gary Anderson
Hilary Benton
Fitz-Roy Curry
James Jones
Barry Wilson
Reen Wu

Plant Biology
Alan Bennett
Richard Bostock
Don Durzan
Charles Gasser
Paul Gepts
Tom Gradziel
Daniel Klionsky
John Labavitch
Clark Lagarias
Bill Lucas
Terence Murphy
Vito Polito
Michael Reid
Pam Ronald
Brett Tyler
Thea Wilkins
Valerie Williamson
John Yoder

Plant Pathology
David Gilchrist
Pam Ronald
Brett Tyler
Valerie Williamson

COMPANY TRAINERS

NAME	COMPANY	POSITION
James Barnett	Roche Bioscience	Research Section Leader
Rae Lyn Burke	Chiron Technologies	Director, Virology Department
Steven Chamow	Genentech	Senior Scientist
RichardEglen	Roche Bioscience	Vice President and Director
Luis Perez-Grau	Calgene	Senior Scientist
Vic Knauf	Calgene	Vice President of Research
Anthony Kossiakoff	Genentech	Director
Jean Kridl	Calgene	Senior Scientist
Randall Mrsny	Genentech	Senior Scientist
Glenn Nedwin	Novo Nordisk Biotech	President
John Ransom	Roche Bioscience	Senior Staff Researcher
Steven Rosenberg	Chiron Technologies	Director Biological Chemistry
Christine Shewmaker	Calgene	Senior Scientist
James Swartz	Genentech	Senior Scientist
Patricia Tekamp-Olson	Chiron Technologies	Director, Molecular Biology
Wendy Fantl	Chiron Technologies	Senior Scientist
Klaus Giese	Chiron Technologies	
Mark Sliwkowski	Genentech	
David Swinney	Roche Bioscience	
Christophyer Walker	Chiron Technologies	
Phyllis Whiteley	Roche Bioscience	
Gregory Thompson	Calgene	Senior Scientist
Michael Urdea	Chiron Technologies	VP, Research and Development
Harold Van Wart	Roche Bioscience	Distinguished Scientist
Richard Vandlen	Genentech	Director
James Wells	Genentech	Staff Scientist
Alan Klotz	Novo Nordisk Biotech	Research Manager, Protein Chemistry

BIOTECHNOLOGY
EXECUTIVE COMMITTEE
1998-99

Name	Affiliation
Roy Doi	Molecular & Cellular Biology
Dewey Ryu	Chemical Engineering & Materials Science
Gary Anderson	Animal Science
George Bruening	Plant Pathology
Don Carlson	Molecular & Cellular Biology
Patricia Conrad	VM: Pathology, Microbiology & Immunology
Michael Hanley	MED: Biological Chemistry
Claude Meares	Chemistry
Kathryn Radke	Avian Sciences
Tilahun Yilma	VM: Pathology, Microbiology & Immunology
John Yoder	Vegetable Crops
Jim Barnett	Roche Bioscience
Vic Knauf	Calgene
Steve Rosenberg	Chiron Technologies
Dick Vandlen	Genentech
Glenn Nedwin	Novo Nordisk Biotech
Melissa Joerger	DuPont
Steve Chamow	Scios