Biotechnology: Focus on Medical & Health Applications

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University of California, Davis
December 17, 2004
To the students and faculty from Tokyo College of Biotechnology ....

Welcome to UC Davis ...

Let’s explore:

• The UC Davis Biotechnology Program
• The Future of Biotechnology
• Biotechnology Research related to medicine & health
• Educational opportunities
• Information sites
The UC Davis Biotechnology Program is active in Biotechnology Education & Training

- Administrative home for PhD graduate programs: DEB (Designated Emphasis in Biotechnology), ADP (Advanced Degree Program for Corporate Employees) and the NIH Biotech Training Grant.
- Co-PI on NSF “Train the Trainer” grant for bioinformatics for CC & HS teachers.
- University council member for AgrowKnowledge (a National Science Foundation center for K-14 agriscience education).
- Offers seminars, conferences & summer short courses in cutting-edge technology. Partners with industry for guest speakers and support.
- Serves on numerous advisory committees for biotech programs at high schools and community colleges. Helps in workforce training and economic development (such as SARTA).
- Information source on biotech issues for community, media and government officials.

www.biotech.ucdavis.edu
The New Millennium will be the Century for **Life Sciences**

- **Health Sciences**
  - Rapid diagnostics using microarrays, nanotechnology, etc.
  - New medical technology: laser surgery, non-invasive imaging, etc.
  - Personalized medicine and personalized diets based on genotype
  - Regenerative medicine using stem cells (adult and embryonic)

- **Pharmaceutical Biotechnology**
  - New vaccines and biologics for cancer treatments, autoimmune diseases such as rheumatoid arthritis, infectious diseases, etc.

- **Agricultural Biotechnology**
  - Genetically enhanced crops & livestock including “**Pharming**”- pharmaceuticals made by plants and livestock

- **Neurobiology** – understanding the brain and neurotransmitters; developing treatments for brain disorders such as Alzheimers Disease, Parkinson’s Disease, etc.

- **Microbiology/Immunology**
  - Control of infectious diseases such as SARS, TB, AIDS, malaria, etc. is a top priority in diagnosis, vaccine development & new therapies.
  - The application of microbial genomics will speed the process.

**Engineers are also key players in these efforts to Discover the Secrets of Life**
We need Factual Information about Biotechnology
Biotechnology or Bioengineering is generally defined as:

The use of living organisms, or parts thereof (DNA, RNA, proteins), to provide useful products, processes and services.

PRODUCT: Golden Rice - insertion of genes for beta-carotene (pro-vitamin A) production into white rice. (Agricultural Biotech)

PROCESS: Microbes manufacturing human insulin (a protein) for diabetes therapy. (Medical Biotech)

SERVICE: Genetically engineered poplar trees for cleaning up heavy metal contamination of land and water. (Bioremediation)
But.....Biotechnology is more than just gene splicing!

- In a broad sense, it includes:
  - Tissue Engineering with stem cells
  - Immunotherapy - monoclonal antibodies with radioisotopes for cancer treatments
  - Genomics, Proteomics, Metabolomics, & Bioinformatics
  - Microarray (“Chip”) technologies
  - RNAi for gene silencing
  - Biosensors for anthrax and other bioweapons
  - Quantum dots as “in vivo” biological probes (nanotechnology)
  - Biophotonics – using light (lasers, fluorescence, etc.) as a tool in life science.
  - BioMEMS (microelectronic systems) …… And much more!
Where we have been and … Where we are going?

Gene Knowledge

Time

1940 1970 1990 2001

Functional Genetics

DNA Genetics

Genomics

Functional Genomics

Systems-Biology
Human Genome Project

Impacting many disciplines

Global Carbon Cycles
Industrial Resources • Bioremediation
Evolutionary Biology • Biofuels • Agriculture • Forensics
Molecular and Nuclear Medicine • Health Risks

This work in the 1990’s is just the Start!

Courtesy
U.S. Department of Energy
Human Genome Program
LEVEL OF COMPLETE SET OF GENE ANALYSIS

GENOME

TRANSCRIPTION

TRANSCRIPTOME

mRNA

PROTEIN

TRANSLATION

PROTEOME
“14 Letters that Spell the Future”

- Washington Post (Aug 2, 2001)
- **Bioinformatics** is the new buzzword!
- It is difficult to define but a good one is:

  “The art and science of using computational tools to find answers to biological questions”
This website is a valuable resource in the classroom!!!!
National Institute for Biotechnological Information
TIGR is a good public database for looking at gene sequences from a number of species. This allows scientists to do comparative genomics (look for similarities in the DNA of other species)

www.tigr.org
The Challenge of Proteomics

Complex Proteome(s)

- Multiple Proteins for each Gene due to splicing
- Varied and fragile nature of proteins
- Quantitative and Qualitative changes of the proteome
- Structural and Functional Proteomics Studies

Per Tina Settineri, Ph.D., Applied Biosystems

10/1/2010
Review of the Immune System:

- **Antigen** – usually a protein, that is seen as foreign to the body...virus, bacteria, cancer cell, etc.

- **WBCs (Leukocytes)** – key blood cells that fight foreign invaders.
  - PMNs (neutrophils), macrophages (activated monocytes) and lymphocytes (T & B cells), and others.

- **Antibody** – glycoproteins, shaped like a “Y”, very specific in binding to **antigens** at the variable regions.
  - **Vaccines** – stimulate the production of antibodies (and T cells) to protect against a specific disease.
Cells of the Immune System……..

http://www.biology.arizona.edu/immunology/tutorials/immunology/02t.html

Stem Cells in Bone Marrow

Secretes Antibodies “Y”
Antibody = Immunoglobulin

This Y-shaped glyco-protein is critical for the immune system
Systems Biology is a Foundation Discipline to Bridge the Gap

- Ruedi Aebersold and Leroy Hood are key researchers at Institute of Systems Biology (http://www.systemsbiology.org)
- Goals:
  - To turn molecular biology into an exact science, with systematic and quantitative measurements.
  - To model a living cell “in silico” with predictive computer simulations.
- Move to Discovery Science from hypothesis-driven science as the initial step.

Use the Tools of Genomics and Bioinformatics to study the complex interactions of genes, proteins and nutrients at the cellular level.
Advances in sequencing and genome analysis and in the associated information technology will accelerate the discovery and characterization of genes having potential utility for human medicines as well as for crop or livestock improvement or enhancement.

Microarrays (DNA chips) representing thousands of individual genes allow very high throughput analysis of genes and gene expression patterns. Application to diagnostic medicine will revolutionize medicine. Ex: Virochip & SARS virus Identification (De Risi Lab, UCSF)
Learn about selected Biotechnology Research at UC Davis (& other places)

- **Genome Center**
  - Bioinformatics, Biomedical Engineering, Infectious Disease

- **CGF – plant genomics**
  - “Pharming” in plants and livestock
  - Metabolic engineering

- **Foods for Health Initiative**
  - Milk with enhanced antimicrobial properties
  - Center of Excellence for Nutritional Genomics
  - Center for Metabolomics

- **Immunotherapy**
  - Antibodies to target cancer & infectious diseases

- **Center for Biophotonics Science & Technology**

- **Tissue Engineering**
UC Davis Genome Center is housed in the 6-story Genome and Biomedical Sciences Facility (opened in Fall 2004)

- Goal: to establish the campus as an international leader in functional and comparative genomics.

- The center will include scientists from a multitude of disciplines: medicine; toxicology, pharmacology, biomedical engineering, agriculture, mathematics and the biological & physical sciences. It will also include a group of bioinformatics faculty members.

- Richard Michelmore (plant genomics) is the new director.
- Ken Burtis (animal genomics) is an associate director
- Craig Benham (assoc. director) is will direct the bioinformatics initiative.
UC Davis – Health Sciences District

Genome & Biomedical Sciences Facility

Future Vet Med

USDA

Future School of Medicine

Existing School of Medicine Laboratories

Veterinary Medicine Instructional Facility

Veterinary Medicine Laboratory

Existing VMTH

Center for Companion Animal Health

Stadium and Pool
GENOME AND MEDICAL BIOSCIENCES BUILDING

Molecular Medicine
Genomics & Bioinformatics
Pharmacology
Biomedical Engineering
Enabling Genomics Facility
Imaging & Vivarium

~70 Faculty
~25+ new
~700 people

Six floors
225,000 sq ft
$98M
On budget
September 2004
Garimendi funded
THE PHENOTYPIC CONSEQUENCES OF NATURAL GENETIC VARIATION

COMPUTATIONAL
- Ian Korf
- Craig Benham
- Yong Duan
- Patrice Koehl
- Open
- Bertram Ludaescher
- Bruce Rannala

SEQUENCE

STRUCTURE

ACTIVITY

PATHWAY

PHENOTYPE

POPULATION

WET LAB
- Peggy Farnham
- Julie Leary
- Mike Wright
- Oliver Fiehn
- Open
- Richard Michelmore
- Open

ENABLE COMPARATIVE FUNCTIONAL GENOMICS ACROSS CAMPUS
Dr. Doug Cook and Dr. Richard Michelmore are lead researchers for CGF on plant diseases.
Ralph M. Parsons Foundation Plant Transformation Facility (RMPFPTF)

College of Agriculture and Environmental Science

Manager: David Tricoli
Staff: Kim Carney

Director: Abhaya Dandekar
Scientific Advisory Board:
John Bowman
Kent Bradford
George Bruening
Dave Burger
Doug Cook
Chuck Gasser
Dave Gilchrist
Carole Meredith
Richard Michelmore

Transformation Service:
Tomato, Tobacco, Rice, Cannola, Lettuce, Alfalfa, Melon, Carrizo, Lemon

Protocol Development:
Alfalfa, Wheat, Walnut, Almond

Provide service to the research community
“Golden Rice”

High Provitamin A (β-carotene) rice is a major advance for plant biotechnology and focuses international attention on the metabolic engineering of output traits.

Picture of Ingo Potrykus
Over 120 million children worldwide are deficient in vitamin A. Rice has been engineered to accumulate β-carotene, which is converted to vitamin A in the body. Incorporation of this trait into rice cultivars and widespread distribution could prevent 1 to 2 million deaths each year.

Introduce antigenic proteins from disease-causing organisms into plants. Eating the fruit or vegetable can then induce antibodies just like a vaccination, rendering the person immune to the disease.

The feasibility of this approach has already been demonstrated. Dr. Charles Arntzen of Arizona State University. He is actively pursuing research to allow children to be immunized against debilitating diseases such as hepatitis B by simply eating a modified banana, potato or tomato. Bill Langridge, Loma Linda Univ. in California is also working in this area. (Sci. Am., Sept. 2000)
Are GMO’s Safe to Eat?

- **Read** - *Agricultural Biotechnology: What are the Issues?*
- Created by the CA&ES at UC Davis and other US Land Grant Universities, in cooperation with the UCD Biotechnology Program.
- [http://agribiotech.info/Brochure.htm](http://agribiotech.info/Brochure.htm) (brochure & power point talk)
  - Or contact Dr. Kjelstrom
Food Biotechnology: Benefits and Concerns

- 2002 American Society for Nutritional Sciences
- Article (0022-3166/02) - reprints $3.00
- Authors: Michael Falk (falkm@isro.faseb.org); Bruce Chassy; Susan Harlander, Thomas Hoban, Martina Newell-McGloughlin (director of UCBREP & adjunct faculty in Plant Pathology at UCD) and Amin Aklaghi.
- Good review of the issues. Many references are cited.
“Pharming” represents the Third Wave of Agricultural Biotechnology

- Use of Genetically Modified Plants or Livestock as factories, rather than food. Plant derived medicines is not new! Examples: Taxol, digitalis, quinine, etc.

- A plant/seed can be a high protein expression system (ex: Ventria Biosciences in Sacto will soon field test barley with a gene for lactoferrin to treat infants with severe diarrhea). They also use rice as an expression system for lysozyme and lactoferrin.

- Proteins can also be expressed in milk, semen or urine of cows, pigs, rabbits, etc. Example: human blood proteins produced in cow’s milk is in clinical trials (GTC Biotherapeutics).

- Significantly less costly than stainless steel tanks due to low initial captital investment and scalability
Few drugs are as expensive as **Enbrel**, a therapeutic Mab (anti-TNF) for Lupus, RA and other autoimmune diseases. It was costly to make in tissue culture (CHO cells), that Immunex (the developer) was bought by Amgen, who spent billions to expand production capacity.

As more Mabs enter the marketplace, production in steel tanks is a bottleneck.

Transgenic goats and cows can produce Mabs in milk, under the control of the promoter for the milk protein Beta-casein. Tissue specific gene expression.
“As biomanufacturing capacity becomes strained, several new methods for producing biologics are being investigated by biotechnology companies”

Spokesperson from GTC Biotherapeutics (formerly Genzyme Transgenics) in Framingham, MA estimates a 200% increase in manufacturing capacity for Mabs alone over the next 10 years. Their solution is milking transgenic animals (“mammary bioreactors”). PPL Therapeutics (UK) and BioProtein (France) have similar projects. Goats, sheep and cows are the most common mammals.

Transgenic chicken eggs may also be feasible, but the research is still in early stages. Companies: Origen Therapeutics (Burlingame, CA); Avigenics (Athens, Ga); TranXenGen (Shrewsbury, MA); GeneWorks (Ann Arbor, MI) and Vivalis (France).
Therapeutic Protein Production in Plants

Important Considerations

See video
Why Make Pharmaceuticals in Plants?

- Supply the increasing demand for new biotech drugs (esp. antibodies)
  - Predict 50 Monoclonal antibodies will be FDA approved by 2008
- Significantly decrease unit costs
- Improve patients’ access to biotech medicines
- Plants are an efficient producer of proteins
  - Plants are scalable bioreactors
  - Plants provide cost advantages to mammalian cell culture systems
  - 3-5 times faster than mammalian systems
- Plant cells are similar to human cells
  - Similar protein synthesis machinery
  - Read the same genetic code
  - Assemble, fold and secrete complex proteins
Transgenic Maize Provides High-Capacity, Low Cost Option for Large Scale Mab Manufacturing

Significant cost associated with Mammalian Cell systems

7 x 15,000L Tanks

~$250-450M Construction

Transgenics provide a cost effective method at large scales

Example: Maize

~200-2000 Acres

~$80-120M Construction
UCD’s Foods for Health Initiative

- Increasing the Quality of Cow’s Milk - Jim Murray, Dept. of Animal Science
- One Project: Insert the gene for **human lysozyme** (found in human breast milk) into goats and ultimately cows to increase antimicrobial properties of milk.
- This modification could also decrease the incidence of mastitis in the animals.
Jim Murray’s Transgenic Goats
### Approximate composition of milk

<table>
<thead>
<tr>
<th></th>
<th>Bovine</th>
<th>Human</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein (mg/ml)</td>
<td>3.5</td>
<td>1.0</td>
</tr>
<tr>
<td>casein (%)</td>
<td>2.9</td>
<td>0.4</td>
</tr>
<tr>
<td>whey (%)</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Lysozyme (μg/ml)</td>
<td>0.1</td>
<td>3400</td>
</tr>
<tr>
<td>Lipid (wt%)</td>
<td>3.9</td>
<td>3.9</td>
</tr>
<tr>
<td>SFA</td>
<td>3.0</td>
<td>1.4</td>
</tr>
<tr>
<td>CLA</td>
<td>0.56</td>
<td>1.0</td>
</tr>
</tbody>
</table>
Nutritional Genomics: Linking nutrition, genomics and human health

Raymond L. Rodriguez, Director
Center of Excellence in Nutritional Genomics
Section of Molecular and Cellular Biology
University of California, Davis
Davis, California

http://nutrigenomics.ucdavis.edu
Nutritional genomics or "Nutrigenomics"

- January 21, 2002 – UC, Davis and the Children's Hospital Oakland Research Institute (CHORI) become a National Center of Excellence in Nutritional Genomics. A five-year, $6.5 million grant from the National Center on Minority Health and Health Disparities, a division of the National Institutes of Health.
- The Goal of the Center: Explore the links between diet, genes and diseases in minority populations, such as Type 2 diabetes, obesity, heart disease and some cancers.
- "The research we'll be doing in the Nutrigenomics Center is one of the first examples of taking the benefits of human genome research from the lab to the home," said Ray Rodriguez, professor of molecular and cellular biology at UC Davis and director of the new center.
- Good reference: “We are what we eat”, The Economist, Sept 4, 2003

For more information: [http://nutrigenomics.ucdavis.edu/](http://nutrigenomics.ucdavis.edu/)
Media contact: Raymond Rodriguez- (530) 752-3263, rlrodriguez@ucdavis.edu
Nutritional genomics examines the molecular interactions between genes and nutritional stimuli, and how these interactions promote health or cause disease.
Convergence in the Life Sciences

Medicine  Agriculture  Nutrition  Informatics

Cross platform technologies driving convergence:
High Throughput Analyses, Metabolomics, Genomics, Proteomics, Systems Biology, Nanotechnology

New Approaches and Technologies for Promoting Global Health and Food Security
“Single Nucleotide Polymorphisms (SNPs) provide a powerful tool for investigating the role of nutrition in human health and disease and ... can contribute to the definition of optimal diets.”
5 Tenets of Nutritional Genomics

1. Improper diets are risk factors for diseases
2. Dietary chemicals alter gene expression and/or genome structure
3. Influence of diet on health depends upon an individual’s genetic makeup
4. Genes regulated by diet play a role in chronic diseases
5. Diets based upon genotype, nutritional requirements and status can prevent or mitigate chronic disease
By Walter C. Willett and Meir J. Stampfer

REBUILDING
the Food Pyramid

The dietary guide introduced a decade ago has led people astray. Some fats are healthy for the heart, and many carbohydrates clearly are not.

Exercise & Genotype must be included
Metabolomics =
The study of metabolites arising from the breakdown of chemicals in the body

- Lipomics Technologies in West Sacramento is creating lipid profiles in humans and lab animals (compare profiles of health vs. disease or drug therapy).
  - Dr. Steve Watkins, President and founder (graduate of the German lab)
- UC Davis has created a Center for Metabolomics.
  - Directed by Dr. Bruce German, Food Science and Technology.
  - **Goal**: build the basis knowledge framework to support personalized metabolic health.
A Message from Dean Neal Van Alfen:

Research indicates that it is increasingly likely that all humans do not respond identically to diet, but require different nutrients according to differences in their genetic make-up and metabolic needs. It is also clear that plants and animals differ in their metabolic profiles depending on their genetics and the conditions under which they grow.

The emerging field of comprehensive metabolic analyses -- metabolomics -- promises to create important new tools for nutritionists, food technologists, plant scientists, animal scientists, medical researchers and others studying the many aspects of health related to diet and overall metabolism. UC Davis and the College of Agricultural and Environmental Sciences have often been in the forefront of new areas of scientific endeavor, and metabolomics is no exception. To promote the study of this emerging field, the college has established a Center for Metabolomics, the hub of which will be a shared instrument facility in Everson Hall, expected to be fully operational by the end of March 2004.
Bruce German, Department of Food Science and Technology, has agreed to serve as director of the Center for Metabolomics faculty advisory committee, which is comprised of a multi-school, multi-disciplinary team, including Lindsay Allen of the Department of Nutrition; Jason Eiserich of the Department of Nephrology in School of Medicine; Bruce Hammock of the Department of Entomology & Cancer Research Center; Dan Kliebenstein of the Department of Vegetable Crops; David Rocke of the Department of Applied Science; and Gary Smith of the Department of Food Science and Technology.

Prof. German is a leader in the field of lipid metabolism and nutrition. He is on the advisory board on Lipomics Technologies in West Sacramento. Dr. Steve Watkins is the President and ex-graduate student of German.

Foods are, ideally, a source of nourishment as well as delight, comfort, fuel and protection.

However, inappropriate choices in diet lead to metabolic imbalances propelling diseases such as atherosclerosis, obesity and type II diabetes.

The problem is that the same diet is not ideal for everyone.

The basic knowledge framework to support personalized metabolic health will need several elements:

- Technology to measure metabolites
- Metabolite databases from various subsets of the population to describe different phenotypes
- Predictive methods how to change diet to guide metabolism
“Functional foods” are those that have health benefits beyond basic nutrition. [example: lactic acid bacteria in yogurt & milk (probiotics) and phytochemicals in soy products].

“Zoochemicals” are food components with health benefits that come from animal sources. [Bioengineering can enhance these chemicals in our food]

- **Iron and vitamin B12** from meats – “energy” boosting (RBC function and coenzymes components for ATP synthesis, respectively)
- **CLA (conjugated linoleic acid)** – a fatty acid found in ruminants (cows) – milk and meat. If CLA is added to feed, the cows are leaner and produce more milk. In animal studies, CLA appears to: suppress cancer cell growth; reduce risk of heart disease, boost the immune system and diminish body fat.
- **Lutein and Zeaxanthin** – found in both plants and animals (especially in egg yolks). These yellow carotenoids appear to shield the eyes from harmful blue light and may protect against age-related macular degeneration.
- **Omega-3-Fatty acids: DHA and EPA** – found in cold water fish [fish do not make the polyunsaturated fatty acids, but obtain them from plankton that are eaten]. Humans can obtain ALA (alpha-linoleic acid) from flax and walnuts, then convert ALA to EPA and DHA. Cardiovascular benefits have been shown to be derived from eating one-three servings of cold water fish* per week.

* Monsanto is working on a soybean oil with increased Omega –3-FA to address the mercury contamination issue in many fish.
Immunotherapy in medicine

- Radiolabeled antibodies for cancer therapy
- Monoclonal antibodies
- Vaccines to stimulate immune system
Cancer cells have unique proteins on their cell surface which can be recognized by the immune system.

Cancer cells are immortal and they lose contact inhibition.
Immunoconjugates shows promise in Cancer Treatment…. A Magic Bullet?

See Preclinica, Jan/Feb 2004, pg 27-30

Currently approved therapeutic antibodies:

- **Panorex** colorectal cancer
- **Rituxin** non-Hodgkin’s lymphoma
- **Herceptin** metastatic breast cancer
- **Mylotarg*** acute myeloid leukemia
- **Campath** B-cell chronic lymphocytic leukemia
- **Zevalin*** non-Hodgkin’s lymphoma

*conjugated with radioisotope or cytotoxin
Genentech is a World Leader in making Biotech Vaccines

- **Genentech facility to double size** by Matthew Bunk/McNaughton Newspapers Thursday, April 1, 2004. Genentech will expand its facility in Vacaville, a move that will create 575 new jobs and garner a visit by the governor.

- Genentech, with headquarters in San Francisco, plans to build three new buildings on company-owned land surrounding its existing building. The additions will almost double Genentech's operating space of 427,000 square feet, resulting in the world's largest biotechnology manufacturing facility, according to a press release issued by Genentech.

- Genentech, which develops and manufactures drugs to treat cancer and other immunological diseases and disorders, hopes its investment in Vacaville will allow it to meet "potential future demand" for its products, according to the press release. [**this plant currently produces Herceptin for breast cancer, Zolair for asthma & other products.**]

- In the past nine months, three new Genentech drugs received approval from the U.S. Food and Drug Administration, and the company anticipates future product growth, Krajnak said. The company has 18 biotech products on the market. They use various expressions systems: yeast, bacteria or CHO (mammalian cell culture) to produce the drugs]. Example: **Herceptin - a monoclonal antibody to the Her-2 receptor on aggressive breast cancer cells is produces in CHO cells**)
Dr. Yilma elected to the National Academy of Science for his Vaccine work

Two UC Davis Researchers Elected to National Academy of Sciences .... April 20, 2004

A neuroscientist (Edward Jones) and a veterinary virologist at the University of California, Davis, were elected today to the National Academy of Sciences, one of the highest honors accorded to scientists and engineers in the United States.

Tilahun Yilma, a professor of virology and director of the International Laboratory of Molecular Biology for Tropical Disease Agents, are among 72 new U.S. members and 18 foreign associates chosen this year by the academy. Overall, 15 new members were elected from the University of California.

Tilahun Yilma, 60, was born in Ethiopia. He earned his bachelor's degree in veterinary science in 1968 and a doctor of veterinary medicine degree in 1970, both from UC Davis. He then returned to Ethiopia and spent two years as a veterinarian vaccinating nomadic cattle herds against rinderpest, a deadly viral disease affecting cattle and wildlife.

In 1977, he earned a doctoral degree in microbiology and joined the UC Davis faculty as an assistant professor in the School of Veterinary Medicine. In that position and as a research associate for New York State College of Veterinary Medicine at Cornell University, he worked for three years at the U.S. Department of Agriculture's Plum Island Animal Disease Center in New York. He then served five years as a faculty member at Washington State University, returning to UC Davis in 1986.

One of Yilma's landmark achievements has been development in 1986 of a genetically engineered vaccine for rinderpest. The vaccine was approved in 1997 for widespread use throughout Africa. It was the first genetically engineered vaccine to be released by a U.S.-funded researcher in a foreign country. Yilma went on to develop rinderpest diagnostic kits and organize training programs in order to make the kits available to African scientists. His current research is aimed at developing an AIDS vaccine and an improved smallpox vaccine.

Contact: Tilahun Yilma, tel: (530) 752-8306, tdyilma@ucdavis.edu
Large Scale Biology (Aka Biosource) in Vacaville, Ca. is using the tobacco plant as a production system for human vaccines, cancer therapies (ex: lymphoma) and other pharmaceuticals. “Pharming in Plants” but no gene flow!

(Transient expression of mRNA of vaccine gene)
Engineers are involved in Biotech too!

- Bioprocessing
- Nanotechnology
- Biophotonics
- Biosensors & Microfluidics
- Biomedical Engineering
  - Tissue engineering
  - Micro-PET scans
NSF Center for Biophotonics Science and Technology (CBST)

Use of lasers in medicine and basic research

Will be located across from the UCD Med Center in Sacramento

~100 participants
$52M over 10 yrs
Dennis Matthews, Director
Emphasis on integrative research, education, and knowledge transfer in biophotonics
~20 research projects
Portable Pathogen Detector

To detect anthrax spores, MDRTB, smallpox virus, toxins, etc.

Immunoassay using optically encoded beads for multiplex capability

Image bead and reporter fluorescence, perform image analysis, and score results
UCDMC’s Center for Tissue Regeneration & Repair is using a Systems Approach. Led by Dr. Hari Reddy

Tissue engineering is an example of using biotechnology in medicine.

It takes multidisciplinary teams to approach Big Problems in Medicine
Stem-Cell Lab in California Is Planned
Advanced Cell is encouraged by a ballot initiative (Prop 71) that would guarantee $3 billion in state funding to support the research. From Bloomberg News September 30, 2004

Advanced Cell Technology Inc., which conducts embryonic stem-cell research, plans to open a laboratory in California because the state supports the work, the company's chief medical officer said Wednesday. California residents will vote in November on an initiative that would guarantee $3 billion in state funding over 10 years for stem-cell research including experiments using material from human embryos. The federal government is spending $24.8 million on embryonic stem-cell research this year.

"I think you are going to see a massive movement west" if the California measure passes, said Robert Lanza, vice president of medical and scientific development at Worcester, Mass.-based Advanced Cell. (it passed)

The California initiative would create the largest source of funding for embryonic stem-cell studies, Lanza said.

Scientists say embryonic stem cells have the capacity to develop into any of the body's hundreds of tissue types. Proponents of the research say that one day, scientists may learn how to use the cells to treat spinal injuries or cure diseases such as diabetes and Parkinson's.

Advanced Cell reported success last week in coaxing embryonic stem cells to specialize into retinal cells, which it said might one day lead to treatments for forms of blindness.
Stem Cell Research in Asia

- Stem cells in Asia by Stephen Pincock (The Scientist, Nov 22, 2004)
- Stephen Minger, an American expatriot, who is now one of the UK’s highest profile stem cell researchers was impressed with the facilities in Beijing, Shanghai, Seoul and Singapore.
- The UK science delegation found “a staggering level of technology and commitment being put into stem cell research.”
- “The U.S. has the technological prowess equal to the Asians” but the U.S. is talking….The Asians are doing.”

An umbilical cord blood plant outside Beijing

Part of a $7.5M/yr stem cell lab in Korea
Stem cells: 'spark of life' may end ethical controversy by Vik Iyer in New Scientist (Dec 1, 2004)

- A University of Wales College of Medicine team in Cardiff, led by Karl Swann, tricked the eggs into dividing by injecting an enzyme produced by sperm [which he discovered two years ago with Cardiff colleague Tony Lai].
- Swann said: "It's the spark of life. It tricks the egg into thinking it has been fertilised. "Ethical" stem cells have been created by using an enzyme dubbed the "spark of life" which tricks human eggs into enacting a fertilisation-type process. Embryos created by the procedure do not contain any paternal chromosomes and so cannot develop into babies.
- Stem cells are "mother" cells with the ability to turn into different kinds of tissue. Those found in early-stage embryos are "pluripotent", which means they can potentially become any kind of tissue in the human body.
- Scientists believe with the right chemical cues they could produce replacement tissues for patients suffering degenerative brain illnesses, heart damage and a host of other conditions.
- Researchers believe the "spark of life" technique should remove the ethical objections some people have to harvesting from donated human embryos. The tricked eggs divide for four or five days until they reach 50 to 100 cells - the blastocyst stage. These blastocysts should in theory yield stem cells, but because they are parthenogenetic [produced from the egg only], they cannot be viewed as a potential human life.
- Human eggs contain two sets of chromosomes, one of which is normally jettisoned within two hours of fertilisation. Swann and his team used a standard chemical treatment to prevent this, so both sets in the parthenogenetic embryos come from the mother.
- According to researchers. Bob Lanza, head of research at the cloning company Advanced Cell Technology in Worcester, Massachusetts, in the United States, "This could eliminate one of the main sources of ethical controversy in this research.”
Now that you are hooked ...... Where can you get educated in these biotech fields?

- Funny you should ask?
- UC Davis has programs in all of these areas!!!!
The Genome Center is a centerpiece of a cross-disciplinary initiative in functional genomics and bioinformatics that will see the opening of a new Genome and Biomedical Sciences Building and hiring of 25 new faculty members.

Interim Director and Associate Director for Bioinformatics: Craig J. Benham, Ph.D.
http://genomics.ucdavis.edu

The Jackson Laboratory (JAX West) at UC Davis provides selected mouse models and custom breeding services to support research that will accelerate today's major human diseases.

Vice President and General Manager: Susie Altemeier
E-mail: sda@jax.org
http://www.jax.org/

The Mouse Biology Program provides comprehensive services and new technology development for genetically altered mice, and teaching and training programs for mouse biologists.

Associate Director: K.C. Keat Lloyd, D.V.M., Ph.D.
E-mail: kclloyd@ucdavis.edu (330) 725-2874
http://sec.ucdavis.edu/mousebiology/

More than 200 investigators at the UC Davis Cancer Center pursue research in basic cancer biology, animal models of cancer, and translational studies in drug development and clinical trials.

Director: Shiang-Jien Kung, Ph.D.
http://cancer.ucdavis.edu/

The Center for Comparative Medicine investigates host-agent interactions and develops intervention strategies for persistent infectious diseases common to humans and animals.

Director: Stephen W. Benhold, D.V.M., Ph.D.
E-mail: sbenhold@ucdavis.edu (530) 752-1265
http://ccm.ucdavis.edu/

The California Regional Primate Research Center assists more than 1,200 scientists who use nonhuman primates as the most appropriate animal models for studies of AIDS, cancer and many other human health problems.

Interim Director: Dolores Hyde, Ph.D.
http://www.crpr.ucdavis.edu/crpr/homepage.html

Research at the Center for Neuroscience ranges from molecular neurobiology to studies of isolated neuronal cells to human perception, attention, memory, language, and the nature of consciousness.

Director: Edward Jones, M.D., Ph.D.
http://neuroscience.ucdavis.edu/

The M.I.N.D. Institute is committed to the understanding, prevention, care and cure of neurodevelopmental disorders including autism, fragile X syndrome, dyslexia and attention deficit disorder.

Director: Randi Hagerman, M.D.
http://mind.institute.ucdavis.edu/

Some examples of what you can discover at UC Davis.

“New NCI center”
Member of the prestigious Association of American Universities
(only invited 62 members)
Ranked 6th for graduate programs in biology among US public universities
Has nationally ranked programs in:
Agriculture & Plant Biology
Bioengineering
Veterinary Medicine & Animal Science
Medicine
Food Science & Nutrition
Toxicology & Environmental Sciences
Biochemistry
Microbiology
Molecular & Cell Biology . . & more
Division of Biological Sciences offers biotech-related degrees:

- Biochemistry
- Microbiology
- Molecular & Cell Biology
- Plant Biology
- Neurobiology, Physiology & Behavior
- Biological Sciences

For Undergraduate Research opportunities:  
http://www.dbs.ucdavis.edu/undergrad/uro/
As one of the largest producers of life-sciences graduates in the country, UC Davis is well positioned to change the culture of biology in the United States. And with a $436,000 NIH Roadmap grant, Professor Martin Wilson plans to do just that.

The Roadmap proposal is the first from UC Davis to receive funding and is one of only two awards nationwide that focus exclusively on undergraduate education. Biological Sciences is the largest major on campus.

Creating a new kind of scientist

For example, Wilson said, "a CAT-scan, now a routine medical procedure, is based on a piece of math that allows a computer to reconstruct a two-dimensional image of internal organs. How many biologists could tell you how this works?"

To address the dramatic changes not just in medical science but the whole of biology over the past 10 years and to help undergraduates develop "interdigitated" skills,

Two goals for his Roadmap proposal: 1) to cultivate a substantial cadre of students with advanced skills in both biology on the one hand and mathematics, engineering, chemistry, computer science or physics on the other; and 2) to make all biology students more facile with quantitative material.
Wilson's Roadmap proposal will address these goals by:

- **Developing a new lower-division class called "Modeling in Biology".**
  - This course will teach students how to use Mathcad, a software program designed to do the "heavy lifting" of numerical simulations. The course will be offered as a pilot in the fall of 2004, with the goal of teaching 2,500 students per year by full scale-up.

- **Introducing quantitative material into existing intermediate-level courses.**
  - Students in these classes will have already taken a year of calculus and physics and should be able to apply Mathcad to more complex quantitative problems. Carole Hom, an award-winning instructor who has extensive experience teaching mathematics to biology undergraduates, will be developing the curriculum to include models involving predator/prey interactions and conduction of nerve impulses, for example, as well as material from evolution, physiology and molecular biology.

- **Launching a minor degree in Quantitative Biology and Bioinformatics by the spring of 2005.**
  - This minor will serve students majoring in either biology or a mathematical or physical science and complement their coursework with interdisciplinary studies. "A minor like this will make students highly employable," Wilson said.

- **Placing advanced undergraduates in faculty labs, where they will work with faculty mentors in interdisciplinary teams** (e.g., a student from computer science with a molecular biology student) on real science problems.
Undergraduate Degree Program in Biotechnology

- One of the Fastest Growing Majors at UC Davis
- Created in 1997
- Housed in College of Agriculture and Environmental Sciences
- 3 specialty areas: microbial, plant or animal biotechnology
- Laboratory Internship required (off-campus preferred)
Engineering Programs


Send for the Engineering bulletin:
UC Davis is Tops in Producing PhDs in Biosciences:


2002
1. University of Wisconsin-Madison (113) 2. UCLA (112) ... 6. UC Davis (96)

2001
1. Johns Hopkins 111
2. Harvard 103
3. UC Davis 102

2000
1. University of Wisconsin, Madison 143
2. UC Davis 113
3. UCLA 100
4. Johns Hopkins 92

1999
1. University of Wisconsin, Madison 119
2. UC Davis 118
3. Harvard 112
4. Johns Hopkins 94
5. Cornell 89

1998
1. UC Davis 129
2. University of Wisconsin, Madison 123
3. Harvard 107

Note: UC Davis was number one from 1986-1998. (first survey was in 1986)
**DEB Program (www.deb.ucdavis.edu)**

- The **Designated Emphasis in Biotechnology** (DEB) is an interdisciplinary program that allows Ph.D. students to receive and be credited for training in the area of biotechnology. They 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*.

- The purpose is to provide graduate students an opportunity to explore biotechnology through seminars, courses and examine the relationship of academia to industry through 3-6 month internships at biotech companies. Currently over **70 students** are enrolled and ~ **50% of our 20 graduates work in industry**.

- Participating graduate programs currently include **23 programs**: Agricultural and Environmental Chemistry; Biochemistry and Molecular Biology; Biological Systems Engineering (formerly Biological & Agricultural Engineering); Biomedical Engineering; Biophysics; Cell & Developmental Biology; Chemical Engineering; Chemistry; Civil and Environmental Engineering; Comparative Pathology; Entomology; Genetics; Immunology; Materials Science and Engineering; Mechanical and Aeronautical Engineering; Food Science; Microbiology; Molecular, Cellular and Integrative Physiology (formerly Physiology); Nutrition; Pharmacology & Toxicology; Plant Biology; Plant Pathology; and Statistics.
Advanced Degree Program (ADP) for Corporate Employees

- Directed by Dr. Kjelstrom

  This is a unique program to retain outstanding employees, by allowing a BS/MS level employee pursue a PhD in a life science major at UC Davis, while still being employed by their biotechnology company.

- It is jointly run by the Biotechnology Program and the Division of Biological Sciences, in cooperation with Graduate Studies.

- Majors currently offered: Biochemistry & Molecular Biology; Cell & Developmental Biology; Genetics; Physiology and Plant Biology.

  [Chemical Engineering, Biophysics and Pharmacology/Toxicology may be added]

For more information see the ADP link on the Biotechnology Program website: www.biotech.ucdavis.edu.
Websites for more information

- There are many good sites for biotechnology and health information
- Here are a few that I have used:
Science Information on the Web

2. The Biology Project:  [www.biology.arizona.edu](http://www.biology.arizona.edu)
   Dr. Ken Kubo at American River College helped to develop
3. Stratagene Educational Materials:  
   [http://www.stratagene.com](http://www.stratagene.com) (Banana DNA extraction experiment)
4. National Genome Research Institute Glossary:  
5. Institute of Forest Genetics:  (UCD/Lab in Placerville, CA)
6. Science’s Next Wave:  
   [http://nextwave.sciencemag.org](http://nextwave.sciencemag.org) (HOT JOBS site)

Request this multimedia kit which includes a CD-ROM, video, poster and a brochure. On the website, you can view some exciting instructional material with excellent graphics and flash 3D animation on many molecular biology topics including "How to Sequence a Genome". Very useful for teachers and students. The kit, called The Human Genome Project: Exploring our Molecular Selves, includes: a CD-ROM with seven varied segments * an award-winning video documentary, The Secret of Our Lives * a commemorative poster * an informational brochure, Genetics: The Future of Medicine, Basic Genetics- a glossary of genetic terms, The Human Genome Project Exploring Our Molecular Selves, Goals of the Human Genome Project, Unlocking the Mysteries of Health and Disease: Gene Discovery Understanding Biological Function, Genetic Testing and Gene-based Medicine, Development of Genetic Medicine"
Biotech Resources:

1. **The Council for Biotechnology** has interesting information and breaking news for students, teachers, parents, and scientists of all ages. [http://www.whybiotech.com/](http://www.whybiotech.com/)

2. **The Biotech Institute** develops the definition and concerns of biotechnology and relates this to our modern world. This website has an interactive "Question of the Month" and also sponsors the children's Biotechnology-focused magazine, *Your World*. [http://www.biotechinstitute.org/](http://www.biotechinstitute.org/) (excellent teaching resource for K-8...download free).

3. **Bio-IT World**, concerned with the technology of the Life Sciences, produces a magazine and newsletters about the changing world in which we live. This website has a variety of views and seriously explores the breaking news of our times. [http://www.bio-itworld.com/](http://www.bio-itworld.com/)

4. The DNA from the Beginning Web site from the **Dolan DNA Learning Center** in Cold Spring Harbor Laboratory has animated learning experiences of over 30 major discoveries in biotechnology and prepare to be amazed!" [http://www.dnaftb.org/dnaftb/](http://www.dnaftb.org/dnaftb/)
   - DNA Interactive Site - Subsite of Dolan DNA Learning Center, HHMI, Cold Spring Harbor Laboratory [www.DNAi.org](http://www.DNAi.org)

5. **Biotech Knowledge Center** (sponsored by Monsanto). Good source of information on the basics of plant biotech, Good Glossary of Biotech Terms. A Biotech Timeline shows the history of the achievements in plant breeding [www.biotechknowledge.com](http://www.biotechknowledge.com)

Bioinformatics Resources:

- 5-day summer (in residence) workshop for AP High School biology teachers and Community College Science Professors (joint NSF project with American River College and UC Davis Biotechnology program): http://www.arc.losrios.edu/~biotech/NSF/workshopsite.html

Information on the 2003 course: http://biosci.ucdavis.edu/SIB/ or http://www.arc.losrios.edu/~biotech/NSF/SummerInstitute.htm

- Good links (other resources):
  http://www.arc.losrios.edu/~biotech/NSF/CurriculaResources.htm

  Bioinformatics links:
  http://www.arc.losrios.edu/~biotech/NSF/BioinfoWebLinks2002.htm

- Dr. Sandra Porter is developing bioinformatics curriculum for college students through an NSF grant: http://www.geospiza.com/outreach
Highway to Accurate Health Information:

- Medical Library Association
  - http://mlanet.org
- Tufts University Nutrition Navigator
  - navigator.tufts.edu
- MEDLINE
  - medlineplus.gov
- Healthfinder
  - healthfinder.gov
- IFIC Foundation On-line
  - ific.org
- Mayo Clinic
  - www.mayoclinic.com
Access Excellence (www.accessexcellence.org)

Health Education Resources

- **Fighting Disease: Health At The End Of The Millennium**
  This health curriculum from The United Nations CyberSchoolBus addresses questions - basic and of global importance - in an engaging set of lessons helping students to understand both personal and global implications of health issues.

- **Healthy B.A.S.I.C.S Program**
  These simple, accurate, and culturally relevant health education brochures, lesson plans, and parent’s guide suitable for children and families of all backgrounds are reviewed for cross-cultural appropriateness.

- **Health Lessons**
  Health lessons for grades K-5 written by pre-service education students at Georgia State University and practicing K-12 teachers include National Health Education Standards and Georgia Quality Core Health Curriculum objectives.

- **The National Institute of Environmental Health Sciences**
  NIEH, a branch of the National Institute of Health (NIH), has graded curriculum materials available for K-2, 3-5, 6-8, and 9-12 teachers and students in print and on the web. "Environmental Diseases from A to Z" and "You and Your Genes" are two examples of their popular publications.

- **Nutrition Navigator, Reviews for Educators**
  Nutrition Navigator is an annotated list of links reviewed by Tufts University nutritionists to be certain that information is accurate and current.

- **PBS TeacherSource: Health and Fitness**
  Activities and Lesson Plans, related to PBS programs are searchable by keyword and by grade level. These pages can help teachers, parents and other care-givers "establish a useful context for teaching a variety of social and academic skills."
Diseases and Conditions

• **CDC Health Topics A to Z**
  Health Topics A to Z provides a listing of disease and health topics found on the Centers for Disease Control ([CDC](#)) Web site. New topics are added on an ongoing basis.

• **ClinicalTrials.gov - Linking patients to Medical Research**
  The U.S. National Institutes of Health ([NIH](#)), through its National Library of Medicine ([NLM](#)), has developed ClinicalTrials.gov to provide patients, family members and members of the public current information about clinical research studies.

• **familydoctor.org**
  Health information for the whole family from the American Academy of Family Physicians.

• **NHLBI: Health Information**
  These resources on hypertension, cholesterol, obesity, and heart attack are organized into two categories: patients/general public and healthcare/other professionals. The National Heart, Lung and Blood Institute ([NHLBI](#)) is part of the U.S. National Institutes of Health ([NIH](#)).

• **National Health Information Center**
  The National Health Information Center (NHIC) puts health professionals and consumers who have health questions in touch with those organizations that are best able to provide answers. You can search the [Health Information Database](#) or select the disease or condition from the **Keyword List**.

• **Spanish Language Health Resources**
  Health information from the Centers for Disease Control ([CDC](#)) designed to address the specific needs of the Hispanic and Latino populations is now available in Spanish.
The web sites listed below contain some spectacular images which capture different organisms, chemicals, and everyday objects using a variety of microscopic techniques.

• **CELLS alive!**
  A fascinating collection of still and moving microscopic images, animations, and diagrams. Many have explanations and links to more information. An excellent teaching resource.

• **Microscopy and Imaging Resources on the WWW**
  This web page includes links to a suite of related pages including pages on confocal microscopy, digital imaging, electron microscopy, histology, a list of free publications of Interest to Microscopists and a reciprocal links page.

• **Molecular Expressions: Images from the Microscope**
  Check out the Photo Gallery for images ranging from amino acids to DNA to dyes and more. Their interactive Microscopy Primer: Virtual Microscopy section has a number of interactive tutorials on Scanning Electron Microscopy, Translational Microscopy, Magnifying Microscopy and more.

• **The Protist Image Data**
  A collection of microscopic images of algae and protozoa amassed by Charles J. O'Kelly and Tim Littlejohn. Links to additional sources of information about protists are also available on this site.

• **Selected Microscopy Resources for K-12 Education**
  A rich collection of web resources tailored to K-12 teachers and students interested in bringing the microworld into the classroom. Sponsored by MicroWorlds Resources and News.

• **The Visible Embryo**
  The Visible Embryo is an on-line tutorial teaching the first four weeks of human development.
Access Excellence  (www.accessexcellence.org)

(Selected) Teacher's Websites

• **zeroBio**
  This site is fun, easy to look at and invites students to test their knowledge at their current level of study or another level. Many resources of value to both students and teachers.

• **Cody's Science Education Zone**
  This site, the work of an Oakland, CA science teacher, features a variety of science lessons, and an active online collaborative teacher research project, focusing on Science instruction using an inquiry approach.

• **Ken's Bio-Web References**
  Contains 9 biological subject areas with over 750 web site references in biological topics taught in high schools and colleges. Ken checks each page monthly for accessibility.

• **Michael J. V. Lazaroff**
  A great resource for both teachers and students. The [Biology](#) link leads you to online practice quizzes, tutorials and much more. [Anatomy](#) takes you to interactive anatomy and physiology sites and a great tutorial on "[How to Use a Microscope](#)".

• **Mr.Biology's Bio Page**
  Charles Zaremba's web page offers explanations, worksheets and homework help to biology students.
Graphics Gallery

Graphics Gallery is a series of labeled diagrams with explanations representing the important processes of biotechnology. Each diagram is followed by a summary of information, providing a context for the process illustrated.

Table of Contents

From Gene to Function
Biological Engineering
Cell Processes

Building Blocks
Genetics

Chromosomes and Cell Division
Viruses

Also biological engineering, genetics, viruses, and cell processes.
Questions?

For More information on Biotechnology, please contact:

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