

# SoCalBio SYNERGIES

The Voice of the Life Sciences Community in the Greater Los Angeles Region

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Southern California  
Biomedical  
Council

Commemorating a Milestone in the Evolution of Modern Medicine

## Organ Transplantation: From Curiosity-Driven Research to Growth Industry

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December 23<sup>rd</sup>, 2004 marked the 50<sup>th</sup> anniversary of the first successful kidney transplantation. This surgery -- involving two identical twins and performed at what is now the Brigham and Women's Hospital in Boston (MA) -- was the first successful human organ transplantation performed against a background full of failed experiments. The success of this procedure was due in part to the progress made in the field of transplantation immunology during and after WW II, particularly Peter Medawar's research in Britain suggesting that grafts only succeed when performed between identical twins<sup>(1)</sup>.



### Turning Points:

Medawar's work — spurred by the wartime efforts to circumvent skin graft rejection by burn victims — implicated the immune system in transplantation rejection or tolerance. Not only did the research he published with colleagues such as Thomas Gibson open the door for modern cellular immunology, it also paved the way for identifying the role of human Major Histocompatibility Complex (MHC) in graft rejection or tolerance<sup>(2)</sup>.

We now know that MHC is made up of a collection of genes on Chromosome 6 responsible for orchestrating the immune system's response to foreign antigens. It is composed of four presently well-defined human leukocyte antigens (HLA), HLA-A, HLA-B, HLA-C (class-I), and HLA-D/DR (class-II). Following the earliest description of MHC components in humans by the French physician, Jean Dausset, in 1952, it took three decades of research to reveal the extreme complexity and polymorphism of these

antigens<sup>(3)</sup>. This led Dausset to argue in his 1980 Nobel lecture that, "If one considers all the genes of the human genome, it can be said that there is not and will never be on earth, apart from true twins, two identical people: every person is unique<sup>(4)</sup>." It is this uniqueness that explains why transplanted organs often fail.

### From the Lab to the Marketplace:

Medawar's and Dausset's "paradigm-shifting" research findings -- for which they won the Nobel Prize in 1960 and 1980 respectively -- contributed to transforming organ transplantation from an almost Frankenstein-like research curiosity during the first half of the 20<sup>th</sup> Century into an accepted tool (although not without controversy) for combating end-stage organ disease. Thus, in contrast to 50 years ago when organ failure meant death, there were at least 150,000 Americans living in 2002 with functioning transplants<sup>(5)</sup>. But the journey of transplantation from the research lab to the

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## Pursuing a New Research Paradigm with Stem Cells as the Catalyst



By Kenneth P. Trevett, J.D.  
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We are now beginning the implementation stage of Proposition 71, the California Stem Cell Bond Issue Initiative. Expectations are running high as we enter a new era of scientific research in California. While the initiative will have far reaching effects, perhaps its most significant impact will be to accelerate changes in the way we do research.

The system of biomedical research has been organized like a series of cottages, lumping researchers into broad areas and then

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February 18, 2005

## SoCalBio Education and Workforce Development Symposium

This is a by-invitation-only Symposium that addresses the growing human capital and employment needs of the Life Sciences industry cluster in the six counties of Greater Los Angeles.

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## Cracks in the Drug Development Regime? Three Views

### Big Pharma's Blues



By Faiz Kermani, Ph.D.  
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There has never been a more challenging time to be involved in drug development. In recent years, the market has become much more competitive, and the political, regulatory, social and economic pressures more intense. Merck's recent problems with Vioxx, concerns about Celebrex, and Bayer's withdrawal of Lipobay from the market in 2001 are reminders that there are no certainties in the field of drug development.

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### A Deeper Look at the VIOXX Scare



By Richard C. Hsu (photo right)  
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& Edwin P. Ching

Merck recently announced that it will discourage potential suitors by introducing a corporate poison pill that automatically grants bonuses to 140 of its managers if the company gets acquired. This announcement came on the heels of the Vioxx scare, which caused Merck's stock to drop an astounding 40 percent in one day.

The scandal over Vioxx was not just bad news for Merck's shareholders and board members. It also threatens to have a severe long term impact on the approval process for new drugs, as well as the entire health care system.

### Opportunities Abound for Biotech Companies



By Allan Wolfe, M.D.  
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Some well known "truths," along with a few of my personal convictions, tell me that this is a particularly good time to be a biotechnology entrepreneur or investor.

### Some "Truths:"

It's no secret that big pharma is interested only in blockbuster drugs. New drugs without multi-billion dollar market potential do not usually fit the business model, which requires enormous revenue to justify and pay for the research and marketing now part and parcel of pharma's institutional structure.

Blockbuster drugs result from the usually symptomatic treatment of very common conditions such as arthritis, gastric reflux and type II diabetes, or amelioration of life-style altering conditions such as erectile dysfunction. These conditions usually require prolonged, if not lifelong, daily dosing. Alternatively, blockbusters may result from extraordinary prices charged for anti-cancer drugs that have a modest life lengthening effect, sometimes without much regard for the quality of the life that is being briefly extended.

Therefore, the prevalent approach to big pharma drug development is market driven, and focused on alternatives to compounds already available. The demand for these products has been demonstrated, and relies

on the aggressive marketing of small improvements to acquire market share and build revenue. The populations these drugs ultimately serve are so large that

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Southern California  
Biomedical Council

## Workshop

### Accessing & SBIR & STTR BIODEFENSE Funding

This is a unique opportunity to get information in one setting from the National Institutes of Health and the US Department of Defense about accessing billions of dollars in funding set aside for life-science SBIR & STTR grants, bio-defense projects, and R&D contracts.

January 27, 2005  
Los Angeles Biomedical Research Institute  
(at Harbor UCLA Medical Center in Torrance, CA)  
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## NIH GRANTS

### Grant Winner Spotlight



**David Rozzell, Ph.D.**  
Founder, President & CEO  
BioCatalytics

#### BioCatalytics At a Glance

- Founded:** 1996
- Founder:** David Rozzell, Ph.D.
- Location:** Pasadena (CA)
- Employees:** 22
- Revenues from Sale:** Yes
- Products:**
  - ◆ More than 100 enzymes
  - ◆ Pharmaceutical intermediaries
  - ◆ Animal-free enzyme products
  - ◆ Human cytochrome biocatalysts
  - ◆ Cofactors & recycling systems
- New NIH Grants in 2004:**
  - ◆ Five Phase-I grants: \$500,000
  - ◆ One Phase-II grant: \$375,000

Over the past few years, BioCatalytics has received numerous SBIR grants to support various research programs on enzymes and related products. According to David Rozzell, Ph.D. (photo left), the company's founder, president & CEO, "Grant funding through the SBIR program has had a very favorable impact on our business, providing support for the development of more than 50 current enzyme products."

The latest grant (see table below) is a phase-II award from the National Institute of General Medical Sciences. The funds will be used to develop a new form of formate dehydrogenase (FDH) to maximize the efficiency of recycling cofactors known as nicotinamide adenine dinucleotide (NAD) and its relative, nicotinamide adenine dinucleotide phosphate (NADP), in the course of producing pharmaceuticals.

Cofactors are nonprotein molecules needed to activate 25% of the enzymes currently known to exist. Derived from Vitamin B3, NAD and NADP are two of the most important cofactors. Inside the human body, NAD assists with sugar metabolism, while NADP contributes to the development of neurotransmitters.

Armed with knowledge of how NAD and NADP operate inside the cell, industrial biotechnologists learned how to put these cofactors to use manufacturing enzyme-based pharmaceuticals and foodstuffs<sup>(1)</sup>. But large quantities of these cofactors are required given their instability. As a result, NAD and NADP represent a significant cost in enzyme-based industrial processing. To reduce this cost, particularly in manufacturing pharmaceutical intermediaries, BioCatalytics' Phase-II project focuses on a new form of FDH designed to help stabilize NAD and NADP while recycling them back into the manufacturing processes. ❖

(1) For a useful overview of these efforts, see: Andreas Bommarius and Bettina Riebel, **Biocatalysis: Fundamentals and Applications**. WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, 2004.

### Greater LA Winners of New SBIR/STTR Grants from the NIH October - December 2004

Company	City Location	PI	Grant Focus	Type	Phase	Amount
CPM Systems	Los Angeles	Andrew Soll	Comprehensive Management Strategy for GI Disorders	SBIR	Phase II	\$1,595,777
Epicenter Software	Pasadena	Alex Ryutov	Integrated SNP, Gene Expression and Proteomic Analysis	SBIR	Phase II	\$586,927
Photon Imaging	Northridge	Carolyn Tull	High Efficiency Silicon Detectors for Synchrotron XRF	SBIR	Phase II	\$379,500
BioCatalytics	Pasadena	David Rozzell	Improved Formate Dehydrogenases	SBIR	Phase II	\$375,000
Twenty First Century Medicine	Rancho Cucamonga	Gregory Fahy	Cornea Preservation by Vitrification	SBIR	Phase I	\$195,024
Neurocomp Systems	Irvine	James O'Halloran	Clinical Interview Data Acquisition System	SBIR	Phase I	\$180,347
Chimeric Technologies	Los Angeles	Kote Chintalacharuvu	A Novel Antibody Therapeutic for Multiple Myeloma	SBIR	Phase I	\$128,100
Shape Change Technologies	Thousand Oaks	Daniel Levi	Pediatric Thin-Film TiNi Catheter-Based Heart Valve	STTR	Phase I	\$119,076
Sierra Scientific Instruments	Los Angeles	Thomas Parks	High-Definition Manometry: A Novel Diagnostic Tool	SBIR	Phase I FT	\$118,192
Medennium	Irvine	Stephen Zhou	Accommodative Intraocular Lens	SBIR	Phase I	\$102,657
ArmaGen Technologies	Santa Monica	Ruben Boado	Neuroprotection in Stroke w/ Recombinant Fusion Protein	SBIR	Phase I	\$100,000
Auritec Pharmaceuticals	Pasadena	Thomas Smith	Sustained Release Olanzapine	SBIR	Phase I	\$100,000
Chemat Technology	Northridge	Yuhong Huang	Nano-Composite Matching Layer	SBIR	Phase I	\$100,000
Scarless Laboratories	Beverly Hills	Chia Soo	Scarless Wound Repair	SBIR	Phase I	\$100,000
Innosense	Torrance	Kisholoy Goswami	Sensitive to Low PPM and Reversible Sensor for Carbon Monoxide	SBIR	Phase I	\$99,999
Shanbrom Technologies	Ojai	Edward Shanbrom	Cascade Iodination Pathogen Inactivated Plasma	SBIR	Phase I	\$99,750
Physical Optics Corp.	Torrance	Paul Shnitser	Tomographic Microscope for Assessing Microcirculation	SBIR	Phase I	\$76,758

### START UP

#### SIDMAP (Los Angeles):

Last September, SIDMAP — a Los Angeles Biomedical Research Institute (LABioMed) spin-off focusing on drug development and drug testing — announced the launch of its metabolic profiling services. The company utilizes smartly-labeled metabolic substrate molecules (tracers) to track disease-characteristic metabolic pathways. In a recent presentation to the Southern California Biomedical Council, SIDMAP's co-founder and chief scientific advisor, Dr. Laszlo Boros, said: "SIDMAP's technology opens the door to the era of 'Metabolomics,' which is the analysis of small metabolites in living organisms. It enables us to generate unique information on the cellular metabolic network critically important to the decision-making processes in drug research and development. Our goal is to help pharmaceutical companies and biomedical researchers shorten the time from discovery to FDA approval by using the knowledge gained from our SIDMAP test." ❖

### DARPA CONTRACTS

#### Pranalytica (Santa Monica):

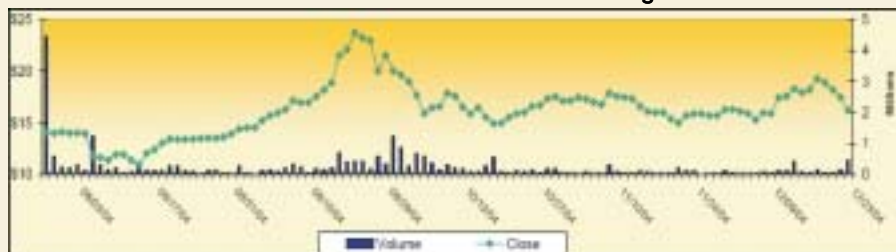
Pranalytica -- a developer of ultra-low level trace gas detection devices for use in the medical diagnostics, environmental, and semiconductor industries -- announced last September that it was awarded a major contract from DARPA. Under the terms of the contract, the company will develop new technology and instrumentation for detecting chemical warfare agents, toxic industrial chemicals, and explosives. Pranalytica's current gas detection sensors incorporate a technology for tuning and controlling the wavelength of high-power carbon dioxide lasers. Under the DARPA contract, Pranalytica will develop widely tunable high power quantum cascade semiconductor lasers to replace the carbon dioxide lasers. Its current technology has enabled the company to successfully commercialize sensors for detecting ammonia and several other gases at the parts-per-trillion levels. ❖

### CLINICAL TRIALS

#### MannKind Corp. (Valencia):

On December 23<sup>rd</sup>, MannKind (NASDAQ: MNKD) released the positive results of its Phase-2 US clinical study of Technosphere® insulin. When inhaled, Technosphere produces a rapid increase in blood insulin that approximates the normal early release of insulin observed in healthy individuals in response to a meal. According to a MannKind press release, the phase-II study reported, among other things, that (1) Technosphere helped diabetics achieve a reduction in HbA1c levels by the goal of more than 0.6 percentage points (HbA1c is a test to measure the number of glucose molecules attached to hemoglobin over a period of three to four months); (2) approximately four times as many patients in the Technosphere Insulin-treated group achieved a final HbA1c level of 6.5% or less as compared to the placebo-treated group; and (3) no serious adverse side-effects resulted from the use of Technosphere. MannKind is preparing to submit its Phase II results to the FDA. The company said it has already initiated its Phase-III clinical trials in Europe. ❖

#### MannKind's Stock Performance Since Going Public



## NEW VC FUND

### Accuitive Medical Ventures (Newport Beach):

Accuitive Medical Ventures -- a venture capital firm focused on early-stage medical device companies -- announced last November the closing of its inaugural \$55 million fund. According to Michael Partsch, Accuitive's Southern California-based general manager (photo right), the list of Accuitive's backers includes CalPERS, NIB, the Duke Family Endowment, General Motors, Brooke Private Equity Associates, and Whitehall Associates. Accuitive has partnered with the Duluth, GA-based medical device incubator, The Innovation Factory, to provide deal flow as well as benefit from The Innovation Factory's company-building experience. ❖



## FINANCING

### ProLacta Biosciences (Los Angeles & Temecula):

ProLacta -- an alumnus of the SoCalBio Investor Conference -- closed its first round of funding last November. This round was provided by DFJ Frontier (Santa Barbara & Sacramento). DFJ Frontier is a Draper Fisher Jurvetson-affiliated venture fund focused on seed and early-stage technology companies. ProLacta seeks to develop therapeutics derived from human milk. ❖

## IPOs

### IntraLase Corp. (Irvine):

IntraLase -- a developer of ultra-fast lasers, related software, and disposable devices used in LASIK vision correction surgery -- went public on October 6. The company sold 6.6 million shares priced at \$13 each, raising \$85.8 million. The pricing was at the high end of the expected \$11 to \$13 range. IntraLase -- an alumnus of the SoCalBio Investor Conference -- started trading on the NASDAQ on October 7 under the ticker symbol of "ILSE." Since its IPO debut, the company's stock has gained 53% in value (see chart below). ❖

### IntraLase's Stock Performance

Oct. 7 - Dec. 24, 2004



## EXPANSION

### Peptisyntha (Torrance):

Peptisyntha -- a wholly-owned subsidiary of Solvay America (Houston, TX) created in 2001 to manufacture therapeutic peptides -- unveiled last September plans to expand its cGMP-compliant manufacturing facilities located in Torrance. Construction of the new space will be completed by March 2005, and result in the addition of suites to accommodate the manufacture of large-scale cGMP peptides. ❖

## PARTNERSHIPS

### Nanostream (Pasadena):

Nanostream, a provider of high-throughput micro-fluidic analytical systems to companies involved in drug discovery and development, unveiled last November its marketing partnership with CTC Laboratory Systems Corporation in Japan. CTC provides technology solutions for life sciences companies, and is a subsidiary of Itochu Techno-Science Corporation (Tokyo). CTC will distribute Nanostream's Veloce™ micro parallel liquid chromatography (μPLC) system (pictured right) to scientists at Japanese pharmaceutical and biotechnology companies. Nanostream's flagship product, the Veloce system, is used in conjunction with 24-column Brio™ cartridges to increase the throughput of established high-performance liquid chromatography techniques. ❖

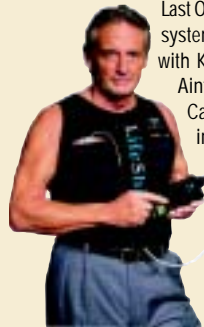


### Second Sight Medical Products (Sylmar):

Second Sight announced last October its partnership with the Department of Energy (DOE) Artificial Retina Project under a Cooperative Research and Development Agreement. In addition to Second Sight, this partnership involves scientists and clinicians from Argonne, Lawrence Livermore, Los Alamos, Oak Ridge, Sandia National Labs, University of Southern California, North Carolina State University, and University of California Santa Cruz. This broad collaborative effort will test advanced technologies to accelerate the commercialization of artificial retinas under development by Second Sight. The artificial retina is intended to restore useful vision to people with advanced outer retinal degenerative diseases. The DOE has already invested more than \$8M in this project, and is expected to spend an additional \$20M over the next three years. Second Sight will integrate the DOE technology into product designs ready for clinical testing. The company has commercialization rights to the technology resulting from the partnership. ❖

### VivoMetrics (Ventura):

Last October, VivoMetrics -- developer of the first-of-its-kind non-invasive ambulatory monitoring system called the LifeShirt (pictured left) -- announced a series of collaboration agreements with Kaiser Permanente Colorado (Denver, CO), Aintree Chest Center at University Hospital Aintree (Liverpool, UK), and the Tom Baker Cancer Center, University of Calgary (Calgary, Canada). Researchers at these institutions will use the LifeShirt to diagnose sleep problems in children, observe breathing patterns in patients with dyspnea, and study stress-reducing activities in breast cancer patients respectively. The LifeShirt is a lightweight, machine-washable garment fitted with sensors that collect pulmonary, cardiac, posture and activity signals. Data collected by integrated peripheral devices measure blood pressure, blood oxygen saturation, EEG/EOG, periodic leg movement, temperature, end tidal CO2 and cough. An electronic diary captures user input, with all physiologic and subject data correlated over time. The LifeShirt System has received FDA clearance and the CE Mark. ❖



### Xencor (Monrovia):

On December 1st, Xencor -- a privately-held biopharmaceutical company focused on discovery and development of protein therapeutics for treating cancer, inflammation and autoimmune disorders -- announced a collaboration agreement with Genentech, Inc. (NYSE: DNA). Under the terms of the agreement, Xencor will grant Genentech an exclusive worldwide license to use its XmAb technology for developing products directed against antibody targets, CD20, Her2, and a third undisclosed antigen. In return, Xencor will receive an upfront payment of \$5 million and annual licensing fees. In addition, Xencor is eligible to receive pre-clinical, clinical, and regulatory milestone payments for each collaboration target, as well as royalties on the sale of licensed products. Xencor's XmAb technology consists of a suite of proprietary engineered antibody Fc domains designed to be incorporated into therapeutic candidates to stimulate the immune system's ability to fight diseases. In early 2004, Xencor unveiled two collaborations: one focused on protein optimization with Eli Lilly (NYSE: LLY), and another with Protein Design Labs (Nasdaq: PDLI), whereby the latter uses Xencor's XmAb technology to enhance antibody activity. ❖

## PMA's

### Endologix, Inc. (Irvine):



On October 29<sup>th</sup>, Endologix (NASDAQ: ELGX) earned FDA conditional approval for its Powerlink® stent (see adjacent graph) for minimally invasive treatment of abdominal aortic aneurysms. An aneurysm results from the weakening of the aorta's wall. When an aneurysm develops, it continues to enlarge and, if left untreated, becomes increasingly susceptible to rupture. The Endologix Powerlink® system is a catheter-introduced, one-piece, endoluminal stent graft designed to improve ongoing, long-term exclusion of the aneurysm. While the FDA's conditional approval permits the commercial distribution of the Powerlink® system, Endologix is required to engage in post-marketing surveillance, and provide updates to the FDA and physician users. ❖

### Biosense Webster (Irwindale and Diamond Bar):

In November, the FDA approved Biosense Webster's PMA for its NaviStar and Celsius ThermoCool® cardiac ablation catheters. These devices are indicated for cardiac electrophysiological mapping, and can also be used with the Stockerd 70 generator for treating Type-I atrial flutter in patients age 18 and older. ❖

## 510(k)s

### 510(k) Decisions

Aug. - Dec., 2004

	All 510(K)s	CA 510(K)s	Greater LA 510(K)s
August	262	49	20
September	293	52	25
October	277	56	27
November	285	57	32
December	284	52	28

### Featured 510(k)s

### Areeda Associates (Los Angeles):

In August, the FDA cleared Areeda's SeeMorTM 5.0 PACS package which is used for transferring and viewing diagnostic medical images. The company added an optional feature to enable the reorientation and reconstruction of SPECT & PET gated and un-gated myocardial perfusion image data sets. Areeda was founded by Joseph Areeda, an ex-Cedars Sinai nuclear medicine researcher. ❖

### Chad Therapeutics (Chatsworth):



In August, Chad received clearance for its Lotus Model OM-700 (without Alarm) & Chad Therapeutics Lotus Model OM-700S (with Alarm) portable oxygen delivery devices (photo left). These devices are intended for prescription use only by patients who require supplemental oxygen in their home. ❖

### Industrial & Medical Design, Inc. (Monterey Park):



The FDA cleared Industrial & Medical Design's aspiration pump (photo left) in September. The device is composed of a microprocessor-controlled diaphragm pump, pressure release valve, disposable collection chamber with bacterial filter and overflow protection, and suction tubing from a patient connected to the collection chamber by means of a lure connector. This device is designed for the extraction and removal of surgical fluids, bodily fluids, and infection materials during surgical procedures. ❖

### Medtronic Neurosurgery (Goleta):

This Medtronic subsidiary, formerly known as PS Medical, received clearance last October from the FDA for its Strata II valve and shunt assemblies. This shunt is designed to reduce pressure on the brain resulting from the excessive accumulation of cerebrospinal fluid (CSF). This implantable device drains CSF from the ventricles of the brain into another absorption site (e.g., the right atrium of the heart or the peritoneal cavity). The cleared shunt allows the physician to non-invasively adjust valve pressure level pre and post-implantation by using a special magnetic adjustment tool, without the need for radiographic confirmation. ❖

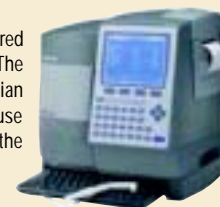
### Beckman Coulter (Fullerton):



Beckman (NYSE: BEC) received clearance in November to market its Unicel DxC 600 and Unicel DxC 800 Synchron analyzers. These systems are designed for the in vitro determination of a variety of general chemistries, therapeutic drugs, and other chemistries of clinical interest in biological fluids such as serum, plasma, urine, or cerebrospinal fluid. The analyzers utilize reagents, calibrators, and controls designed for Beckman's SYNCHRON systems. The DxC instruments (pictured left) feature bar code identification of samples and reagents, closed tube sampling, obstruction detection and correction, and a dual carousel reagent storage compartment with onboard capacity of 59 cartridges. ❖

### LifePoint (Ontario):

In November, the FDA cleared LifePoint's (AMEX: LFP) IMPACT® Test System (pictured right) for prescription use in detecting opiate (morphine and heroin) in human saliva. The clearance permits use of the IMPACT Test System in hospitals, laboratories, physician office laboratories, home health care, etc. The device was also cleared for workplace use to rapidly detect opiate in human saliva. These clearances come in the wake of the company's successful \$4 million private placement completed in November. ❖



### Edwards Lifesciences (Irvine):

In December, Edwards (NYSE: EW) received clearance for its LifeStent NT35 Biliary Stent System. This stent is a permanently implanted device indicated for maintaining the openness of a major bile duct obstructed by the tissue of an impinging tumor. ❖

## FDA 483

### General Medical Company (West Los Angeles):

The FDA issued a warning letter last September to General Medical Company, a manufacturer of devices to control excessive sweating, for violation of the Quality System regulation, Title 21, Code of Federal Regulations (CFR), Part 820; and the Medical Device Reporting (MDR) regulation, Title 21 CFR Part 803. ❖

### AMF Support Surfaces, Inc. (Corona):

In November, the company received a warning letter from the FDA for marketing the Cool Heat Versatility Heating Mattress System (for the prevention and treatment hypothermia) and the TempurPlus 3 Advanced Therapy Mattress System (for apical turning, low air loss, and alternating pressure therapy) without first obtaining either premarket approval or a determination of substantial equivalence. ❖

## REQUIEM

### Parcel (Pasadena):

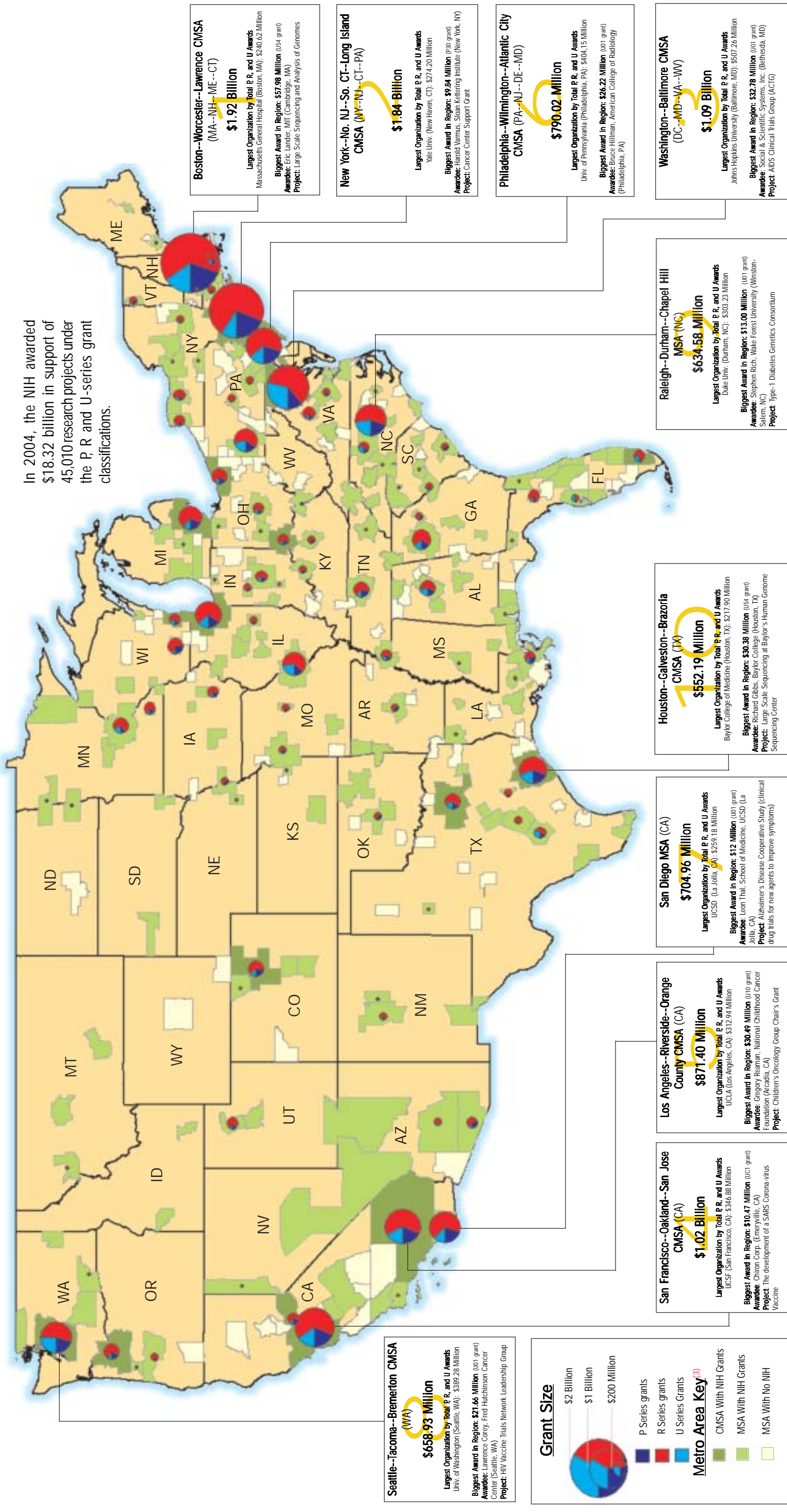
Celera Genomics (Rockville, MD) announced last September that it discontinued all operations of its Pasadena-based bioinformatics subsidiary Parcel, Inc. Celera acquired Parcel in 2000 in a stock-for-stock transaction with a then market value of \$283 million. Parcel was established in 1992 as a TRW spin-out. In addition to pioneering parallel computing, Parcel adapted TRW's Fast Data Finder (FDF) technology -- originally used by the military to handle large quantities of electronic text in multiple languages -- for use in genomic data analysis. Its products included the GeneMatcher, a massively parallel genetic data analysis engine for high-throughput search and annotation, and TextFinder, a text search supercomputer. Celera announced that its decision to cease operations at Parcel was driven by the shift in focus at Celera from genomics data and services to the development of targeted therapeutics. As a result of this shift, Parcel was no longer deemed strategic to the parent company's business plan. ❖

# NIH Funding of Biomedical Research<sup>(1)</sup>

## 2004

Aggregated by Metro Areas<sup>(2)</sup>

In 2004, the NIH awarded \$18.32 billion in support of 45,010 research projects under the P, R, and U-series grant classifications.



(1) Based on NIH extramural support of research projects and centers (P-series), cooperative research agreements (U-series).  
 (2) Awards were geocoded by the five-digit zip-code location of award recipients. Metro area shares were then aggregated by zip-code to metro-area correspondence.  
 (3) Metro areas are based on the 2000 US Census Bureau's definition of both Metropolitan Statistical Areas (MSAs) and Consolidated Metropolitan Statistical Areas (CMSAs).

Founded in 1984, One Lambda is one of the Los Angeles region's premiere life-science companies serving the transplantation market (see market overview on page 1). The Canoga Park-based company has grown to become the market-leading provider of human leukocyte antigen (HLA) typing tools for the transplantation community. HLA refers to proteins on white blood cells that make each person's tissue unique. The HLA A, B, C and DR proteins are important in matching patients and donors for tissue, marrow, or blood stem cell transplants<sup>(1)</sup>.

Although HLA typing represents a small and sometimes overlooked component of the transplantation field (accounting for just 2% of the \$11 billion-plus market in the US), it is a key enabling technology. Transplant surgeons rely on HLA tests to determine the best possible match between organ donors and recipients. Such matching is crucial in minimizing the chance of organ rejection due to the body's natural defense mechanisms.

The earliest "standard" test for HLA typing was developed and refined at the UCLA Tissue Typing Laboratory headed by Paul Terasaki, Ph.D., a pioneer among post WW II transplantation geneticists. Dr. Terasaki started his post-doctoral research in 1957 with Sir Peter Medawar, the father of modern transplantation immunology. Upon his return to UCLA in 1959, Dr. Terasaki focused on developing HLA testing tools. In 1964, he succeeded in developing the microlymphocytotoxicity test, which was adopted by the NIH and around the world as the standard serological method for HLA typing.

As organ transplantation surgery became more frequent, demand for HLA typing gradually increased. Through the federally-funded UCLA Tissue Typing Lab, Dr. Terasaki supplied HLA typing trays (which carry his name) to the transplantation community from 1968 to 1984<sup>(2)</sup>. But, when UCLA ceased production of these trays, One Lambda was formed by Dr. Terasaki to continue serving the HLA community.

Last December, George Ayoub, One Lambda's president and CEO (see background at right), and Ricardo Ordonez, One Lambda's director of public relations, spoke with **SoCalBio Synergies** about the company's role in meeting the transplantation community's needs since its founding over 20 years ago.

# Interview

## A Matchmaker That Saves Lives

### Q. How was One Lambda formed?

A. One Lambda grew out of the UCLA Tissue Typing Lab that Dr. Terasaki directed for a number of years. In 1972, federal funding that supported the lab was cut off. Rather than discontinuing typing tray production, the UCLA Lab arranged to have healthcare providers purchase the trays directly from UCLA, which at the time was the only supplier in the world. But the market changed dramatically when the FDA deregulated HLA typing reagents in the early '80s, and allowed commercial organizations to produce similar typing trays. At that point, it was no longer suitable for UCLA to continue production and distribution of the Terasaki typing trays and reagents. When UCLA decided to discontinue serving as a provider, Dr. Terasaki sought permission to begin production outside of the academic setting. During the latter months of 1983, UCLA agreed to Terasaki's proposal, and One Lambda became a reality. The company was incorporated on January 27, 1984.

### Q. Where does the firm's name come from?

A. The typing reagents in Dr. Terasaki's lymphocyte microcytotoxicity assay require analysis of very scarce patient lymphocytes. The Company's name refers to the smallest unit of volume, one millionth of a liter, or *one lambda*, that could be analyzed.

### Q. Did the company raise any outside funding?

A. One Lambda was formed with money provided solely by the company's founders. From day one, we generated revenues from sales and, therefore, didn't feel the need to raise any outside funding from venture or any other sources of capital.

### Q. Was there any substantial intellectual property that got transferred to the company from UCLA at that time?

A. Actually, there was none because most of what we did at One Lambda was already in the public domain. Since the early '60s, members of the HLA community fostered a culture of openness and information sharing that continues to this day. It is comparable to that of the open source-movement in software development.



The UCLA Tissue Typing Lab was the only source of the Terasaki HLA typing trays during the '60s and '70s.

Photo courtesy of One Lambda

### Q. Were there reasons related to the HLA body of knowledge that necessitated fostering such a culture?

During the early days of transplantation immunology research, the full structure of HLA antigens had not yet been fully discovered. Furthermore, its polymorphism, that is how it differs from one individual to the other, not only confounded researchers, but also made the outcome of early HLA typing tests uncertain. Researchers struggled in the early '60s with how to standardize HLA tests and increase their reliability. This is what triggered the formation of the International Histocompatibility Workshop as a forum for information sharing and learning by interaction. The first such workshop was organized in 1964 by Bernard Amos<sup>(3)</sup> of Duke University. Dr. Terasaki organized two workshops in Los Angeles in 1970 and 1980. Through these gatherings, the HLA community shared reagents, instruments, and information about testing techniques. The workshops facilitated collaborations to remove technical hurdles in standardizing HLA typing.

### Q. Was One Lambda the first to market HLA typing products when the FDA deregulated the market?

A. By the time One Lambda was up and running, we were catching up with companies such as Pel-Freez<sup>(4)</sup> in Wisconsin, Biotest in Germany, and Cooper Diagnostics in Irvine, CA<sup>(5)</sup>.



In this photo taken over 20 years ago at UCLA, Dr. Paul Terasaki, founder of One Lambda, holds the famous "Terasaki Tray," an indispensable tool in HLA typing.

Photo courtesy of One Lambda

### One Lambda At a Glance

**Founded:** 1984  
**Headquarters:** Canoga Park, CA  
**Facility Size:** 85,000 sq. ft.  
**Employment:** 187  
**R&D Employment:** 50  
**Industry Segment:** In Vitro Diagnostics  
**Business Focus:** A pioneer and leader in human leukocyte antigen (HLA) typing products to ensure matching between organ donors and recipients  
**Products:** Serology, molecular, and antibody detection products. Instruments and software for automating HLA typing and data analysis.

to manufacture HLA Typing products. Second, and more importantly, the network of users that we fostered over the years through the UCLA Lab was our main asset. In short, we knew how to manufacture the HLA typing products, and we knew whom to sell them to. Last but not least was the name recognition of our founder, Dr. Terasaki. His status as a pioneer in organ transplantation opened a lot of doors for One Lambda.

### Q. Was there a moment in One Lambda's history that helped distinguish the firm?

A. This was the 1986 Chernobyl nuclear accident in the Soviet Union that attracted attention to One Lambda. Dr. Terasaki was one of only two American physicians allowed to help Soviet radiation victims. It was Armand Hammer of Occidental Petroleum who convinced the Soviet leadership to bring in Dr. Terasaki. Under the doctor's direction, One Lambda sent equipment, such as the Lambda Jet<sup>(6)</sup> and phase contrast microscope<sup>(7)</sup>, and typing supplies. He used this equipment to match bone-marrow donors with radiation victims. Dr. Terasaki's participation in this relief effort increased awareness of One Lambda's services and products.

### Q. As the market for organ transplantation supplies started to expand in the late '80s, how did One Lambda stay ahead of the competition?

A. First, by being at the cusp of technological change. For example, the '80s saw the introduction of monoclonal antibodies in diagnostics and therapeutics. This was one of the benefits of the biotechnology revolution. One Lambda was on the forefront of such technology, introducing the first monoclonal tissue typing tray in 1993. This test had advantages over the conventional microcytotoxicity test because it eliminated several steps in the process of tissue typing, and reduced assay time from 180 minutes to 60 minutes. As DNA started to shape the field, One Lambda introduced the Micro SSP kits, which provided detailed allelic typing. This assay provided allelic level results compared to serological testing. It also reduced repeat testing and minimized ambiguous HLA typings. We also were the first to introduce kits for HLA antibody detection using flow cytometry technology. Finally, we have recently revolutionized the technologies for DNA typing and antibody detection by introducing coded microspheres, which are used on a Luminex flow analyzer.

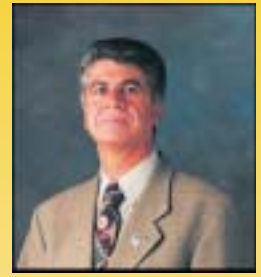
### Q. What is the main barrier to entry into this market?

A. We still don't understand the full functions of the HLA antigens. And because of their polymorphism, we are still uncovering new alleles<sup>(8)</sup>. So, standard, textbook knowledge of DNA won't give you an edge. There is subtle know-how that we gain by learning from customers and users. This is why One Lambda has continued the workshop mechanism started by members of the HLA research community in the '60s. In 1986, we offered our first HLA Technical Workshop. The meeting used hands-on study techniques to present and train professionals on the latest advances in tissue typing technology. One Lambda has hosted HLA Technical Workshops every year since, and has expanded its educational offerings to include wet workshops conducted in-house and across the HLA community worldwide.

### Q. One Lambda has been around for 20 years. What is your take on Los Angeles as a place to do business?

A. Because of the region's higher than average cost of living, it has been historically difficult to recruit people to Los Angeles. But once you get over this hump, the location works fine for us because of access to local talent, research institutions, and the large potential market. LA's diversity is also a key benefit. There are 17 languages spoken at One Lambda's corporate headquarters. This is good from an international marketing point of view, given that our customers are located all over the world, from China to the Middle East and from Europe to Latin America. Being in Los Angeles helps us find marketing and technical professionals who can respond in any language. You'd be hard pressed to

**George Ayoub**  
 President & CEO  
 One Lambda



- ♦ Was one of the original founders of One Lambda.
- ♦ Started as company's vice president and was named president in 1987.
- ♦ Was employed by the UCLA Tissue Typing Laboratory for ten years where his studies focused on improving and developing methodology for HLA typing.
- ♦ Authored and co-authored over 20 publications in the field of HLA research.
- ♦ Developed techniques that continue to be used today in laboratories performing cell subset separation for HLA serologic typing.
- ♦ Received his Bachelors of Science in biochemistry from UCLA in 1975.
- ♦ Received his Masters in business administration from Pepperdine University in 1983.

find this competitive edge anywhere else.

### Q. What is your advice to public policy makers at the state and local levels to foster the life-science industry?

A. At the state level, more attention should be paid to the need to bring down the cost of doing business. This is key to keep manufacturing activities in California. Locally, more attention should be paid to area infrastructure, from roads and schools to housing affordability. One Lambda shares the concerns of many local businesses particularly with regards to transportation and housing. We continue to see an increase in traffic problems every year even with the introduction of new public transportation modes like the metro rail. Public transportation solutions are not keeping up with the population growth in Greater LA. Housing affordability is also a serious problem. The cost of owning a home in Southern California continues to skyrocket thus making it very difficult to attract people to the area. More and more residents continue to move farther out or leave the state.

### Q. What is your vision for One Lambda's future?

A. One Lambda seeks to expand by venturing into new markets for its HLA markers. We will continue to focus on patient care and those factors that promote long term graft survival. We are working with other companies and institutions to further define the role of HLA in disease associations. ❖

### Notes

(1) For an overview, see: Thomas M. Williams, "Human Leukocyte Antigen Gene Polymorphism and the Histocompatibility Laboratory," *JMD*, Vol. 3, No. 3, 2001.

(2) In early 1999, Dr. Terasaki retired from UCLA. However, he continues to serve as One Lambda's Chairman of the Board. He also founded the Terasaki Foundation Laboratory, a non-profit research organization in West Los Angeles, where he continues his interest in advancing transplantation research.

(3) Dr. Bernard Amos was one of the first researchers to identify the importance of the Major Histocompatibility Complex in transplantation immunology through work done on mouse models in the '50s. Dr. Amos passed away in 2003.

(4) Pel-Freez was acquired in 2003 by One Lambda's Norwegian competitor, Dynal Biotech.

(5) Cooper Diagnostics is now out of business.

(6) The Lambda Jet is a machine that accurately dispenses lymphocytes and other reagents into each well of the Terasaki tray to perform the serological HLA testing.

(7) The inverted phase contrast microscope is useful in examining the mixture of serum, cells, and complement from below the Terasaki Tray.

(8) Alleles are variant forms of the same gene. Different alleles produce variations in inherited characteristics such as eye color, blood type, or HLA antigens.

*Q/A with One Lambda was conducted on Dec. 7, 2004 by Ahmed Enany, editor-in-chief of SoCalBio Synergies (enany@socalbio.org) and Erik Deutsch, managing editor (erik@socalbio.org).*

## Prop. 71

Continued from page 1

grouping them into specialties. These traditional divisions have, in some instances, impeded the pace of scientific discovery.

Fortunately, a new interdisciplinary and collaborative research model is evolving that integrates the analytical strengths of two or more scientific disciplines in order to solve a given biological problem. By engaging seemingly unrelated disciplines, traditional gaps in approach and methodology can be eliminated. The scale and complexity of today's biomedical research problems demand that we break down barriers among disciplines in our own institutes, centers and even broad geographic regions.

Proposition 71 can be a true catalyst for this change. Cooperation between investigators on their own campuses and within their own regions using unique and complimentary expertise can help increase the flow of knowledge. This integrative approach to systems biology involves bringing together groups of researchers around a core theme, regardless of institutional loyalty. Applying seemingly unrelated disciplines and techniques can yield innovative approaches for the prevention, management, and treatment of medical disorders.

For example, here in Southern California we have world-class bioengineering expertise, but our bioengineers have little or no access to a substantial clinical patient population. Combining areas of expertise from different campuses and developing interdisciplinary coordinated regional research centers will solve such deficiencies and enable researchers to take full advantage of our regional strengths.

And there are many other areas in which we can be good stewards of the taxpayer's money. We can better prepare and retain our young scientists by further developing career pathways related to regenerative medicine and stem cell biology. It is our obligation to train a new generation of scholars and investigators so the whole world can benefit. Proposition 71 funding can also provide these scientists with much needed laboratory space that can be shared and used on a regional basis for years to come.

The Southern California region is uniquely well positioned to spark the changes that must be made to transform scientific knowledge into tangible benefits for people. Ideally, the basic research discoveries on our campuses can be quickly transformed into diagnostics, drugs, treatments or methods for prevention. Such translation lies at the very heart of true collaborative research. ❖

*Kenneth Trevett is president & CEO of the Los Angeles Biomedical Research Institute (formerly known as Harbor UCLA REI) in Torrance, CA.*

## Big Pharma's Blues

Continued from page 1

### Current Difficulties:

Big pharma's current difficulties are best illustrated by figures for new drug productivity, which has declined steadily in recent years. In 2003, only 26 new molecular entities (NMEs – compounds not previously available as human therapeutics) were launched onto the world market, whereas in 1983 more than 40 NMEs were launched globally<sup>(1,2)</sup>. In addition, while new drug output has declined, R&D expenses have increased. In 2000, global pharmaceutical R&D spending was estimated at \$46 billion, with global biotech R&D expenditure accounting for a further \$11.2 billion<sup>(2)</sup>.

Clinical development accounts for a growing portion of overall R&D costs<sup>(2)</sup>. A 2002 US pharmaceutical industry survey showed that, on average, clinical trials account for 40% of total R&D costs<sup>(3)</sup>. As the complexity of trials and regulatory demands increase, the portion of R&D allocated to clinical trials will rise further. Yet with only 21.5% of drugs entering Phase I trials progressing to gain market approval, the pressure is intense on companies to improve success rates in clinical development<sup>(4)</sup>.

The Tufts Center for the Study of Drug Development (Tufts CSDD) has estimated the cost of successfully getting a drug to market at \$897 million<sup>(4)</sup>. Bain & Company has put the cost at \$1.7 billion by factoring in more of the commercialization costs than the Tufts CSDD estimate<sup>(5)</sup>. Both of these figures include a significant contribution from the cost of all new compounds that fail the R&D process. Furthermore, even if a company successfully launches a new drug, there is no guarantee that it will be a commercial success, and it is difficult to determine how much market exclusivity it will enjoy before competitor products appear.

### Facing Up to the Challenge:

Given the tremendous challenges facing companies that develop new drugs, one might wonder why any organization would seek to operate under such uncompromising conditions. Yet despite the daunting statistics and rising costs, there is no shortage of new entrants to the market, as the major companies continue to paint an optimistic view of the future. The fact is that even in these difficult times, there remains a high demand for new drugs. As long as there are areas of unmet medical need, companies will always have a market to aim for. In 2003, the global pharmaceutical market grew by 9%, with North American sales

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increasing by 11% over the previous year<sup>(6)</sup>.

Because most companies are unable to manage all drug development functions in-house, the trend has been to outsource such efforts. This strategy is particularly important given that many companies are expanding the therapeutic range of their R&D efforts in order to seek out new opportunities<sup>(7)</sup>.

The reasons for outsourcing vary from company to company. Larger companies, with in-depth experience in drug development seek to better allocate their resources. They look for the best combination of cost and quality that will drive productivity.

Smaller companies, in contrast, may lack necessary experience in drug development. Therefore, outsourcing allows them to overcome such limitations by harnessing external skills for drug development.

An analysis of the US pharmaceutical industry by UBS Warburg revealed that of the \$30 billion invested in R&D in 2001, around 20%-25% was spent on outsourcing<sup>(8)</sup>. The continuing success of the US pharmaceutical industry, which is responsible for approximately 20 of the world's best-selling drugs<sup>(3)</sup>, demonstrates that outsourcing plays a key role in R&D productivity.

Companies can also benefit from alliances that allow the parties to benefit from complementary commercial and technical strengths, as well as risk sharing. A good example is Roche's decision to buy exclusive worldwide rights to the portfolio of oncology drugs by UK biotech firm Antisoma<sup>(9)</sup>. This arrangement could net Antisoma \$500 million if all its products reach the market<sup>(9)</sup>. In turn, Roche has been able to supplement its existing oncology portfolio<sup>(9)</sup>.

Many industry observers see smaller organizations as the source of future innovation in drug development, with larger companies turning to them for new ideas. A growing criticism of big pharma is that its preoccupation with the market leads to the launch of products that represent incremental improvements of older versions of medicines, rather than innovative new compounds. As the public takes a greater interest in drug pricing, it becomes difficult for the industry to justify the expense of new drugs that do not represent any sort of scientific breakthrough.

In many countries, governments operate a range of pricing systems that restrict what companies can charge. Only companies that develop a truly innovative product are able to charge a high price. The price of a new product not considered to be a major

advance is typically forced down using a series of measures that categorize it alongside older and perhaps similar products.

Once on the market, companies must maximize all available commercial opportunities in the face of fierce competition. Although 88% of global pharmaceutical sales come from the US, Europe and Japan, emerging markets such as Asia and Latin America are growing in importance<sup>(2,6)</sup>. Many large and small companies have established themselves in these regions, or have partnered with local companies in order to benefit from improving conditions. With large populations, growing spending on healthcare and stronger economic prospects, these countries represent lucrative future markets. Similarly in Europe, companies are gaining new markets through the 2004 expansion of the European Union.

### Outlook:

Even pharmaceutical and biotech companies with years of experience can no longer guarantee success for their next new product. In order to remain innovative and productive, companies must explore new approaches to the technical and commercial obstacles that stand in their way, while forging partnerships with organizations that can help them realize their goals. ❖

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*Dr. Faiz Kermani serves as budgets, proposals and marketing executive at Chiltern International, Slough (UK).*

# Transplantation

Continued from page 1

marketplace wouldn't have been possible without the introduction of enabling technologies that solved, or at least eased some of the nagging problems faced by transplantation surgeons. These technologies include:

- ◆ Methods to detect the HLA genes, and thus determine the best possible match between transplant donors and recipients<sup>(6)</sup>. HLA typing techniques were pioneered by researchers such as Paul Terasaki, Ph.D., at the UCLA Tissue Typing Laboratory during the '60s and '70s (see *Interview with One Lambda* on page 5).
- ◆ Identification of drugs to suppress the recipient's immune system, and thus decrease the likelihood of organ rejection. One notable example is Cyclosporin, which gained FDA approval in 1983<sup>(7)</sup>.
- ◆ Improved techniques to preserve donor organ viability until transplantation. This includes the development of UW solution by Folkert Belzer and James Southard of the University of Wisconsin in 1986, which increased organ storage time from six to 36 hours<sup>(8)</sup>.
- ◆ Development of novel surgical techniques -- from suturing to laparoscopy -- that increased transplant effectiveness while reducing surgery pain and hospitalization time<sup>(9)</sup>.

Also, worthy of mention are the public policy initiatives sought to facilitate organ donation and matching, and subsidize the cost of transplantation. These include:

- ◆ The *Uniform Anatomical Gift Act* which authorized the organ donor card. This legislation was enacted in August 1968 and revised in 1987 to establish comprehensive and uniform laws regarding organ and tissue donations. All 50 states adopted the act, with some making minor variations<sup>(10)</sup>.
- ◆ The passage of legislation allowing Medicare coverage of transplantation starting in 1973 with the development of the *Medicare End Stage Renal Disease* (ESRD) program. Coverage for other organs began in 1986.
- ◆ The 1984 *National Organ Transplant Act*, which authorized the establishment of an Organ Procurement and Transplant Network to provide a central registry linking donors and potential recipients<sup>(11)</sup>.
- ◆ The 2001 *Gift of Life Donation Initiative* by the Department of Human Health Services, a national program seeking to increase organ donation for transplantation<sup>(12)</sup>.

## A Sizeable Industry:

All these factors have contributed to the creation of a sizeable human organ and tissue transplantation market including diagnostics, organ procurement, surgery, immune-suppressing drugs, and hospitalization. The size of this market in the US alone was about \$11 billion in 2002 (see Table 1 below)<sup>(13)</sup>.

A March 2003 report by the Business Communication Company (BCC) claims that it is an even bigger market -- valued at \$17 billion -- if one factors in the cost of animal and synthetic tissues used in place of human bone, heart valves, and skin<sup>(14)</sup>.

## The Future:

Keep in mind that only a small fraction of the potential demand for organs is satisfied. In 2004, only 22,545 solid organ transplantation procedures were performed in the US. At the same time, there were more than 78,000 patients on the waiting list.

Table 1

### 2002 Human Tissue & Organ Transplant Surgery Cost in the US<sup>(1)</sup>

Transplantation Procedure	Number of Cases	Average Cost Per Patient	Total Cost (Million)
Autologous Bone Marrow	10,468	\$243,800	\$2,552
Kidney	14,883	\$143,300	\$2,133
Allogeneic Bone Marrow (related)	4,976	\$362,100	\$1,802
Liver	5,462	\$313,600	\$1,713
Heart	2,220	\$391,800	\$870
Allogeneic Bone Marrow (Unrelated)	1,716	\$447,300	\$768
Cornea	34,265	\$14,200	\$487
Lung	1,054	\$343,000	\$362
Kidney-Pancreas	921	\$195,500	\$180
Pancreas	680	\$148,900	\$101
Intestine	96	\$814,500	\$78
Heart-Lung	48	\$504,400	\$24

\* Cost includes evaluation, organ procurement, surgery, hospitalization, immunosuppressants, and follow up for one year after the surgery.



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## VIOXX Score

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seems justified in its approach to protect consumers. But the fact is the FDA has become completely consumed with safety issues to the potential detriment of consumers, and the latest events with Vioxx and the influenza vaccine are likely to make the situation worse. The FDA is so focused on the economic risks of approving an unsafe drug, that it risks overlooking the equally significant problem of delaying or altogether denying approval of lifesaving drugs.

If we look a little deeper, we can see another very interesting trend developing. The combined costs of drug development, manufacturing and distribution have made bringing a new drug to market increasingly expensive. The risk-adjusted cost of taking a drug from identification of a new chemical compound to FDA approval is estimated at approximately \$800 million. This means that drug companies can only afford to invest in a drug if they think it could be a so-called "blockbuster," with projected revenues exceeding \$2 billion a year. This is why we've seen the rise of so many specialty pharma companies in the past few years, a \$50 million or even \$100 million drug is simply not sufficient to affect the bottom line of a large pharmaceutical company.

In the '80s and even early '90s, applications for new drugs tended to focus on narrow indications and high efficacy. Once it was approved, the manufacturer would try to expand the drug's use to other indications, or introduce new methods of drug delivery. Now, the only drugs pharmaceutical companies can realistically afford to invest in are major blockbusters such as Viagra, Celebrex and Prozac. The inherent problem with the status quo is that in order to become such a blockbuster, a drug must be both expensive and prescribed for a very large population. Such drugs tend to be "life-style" drugs, not smaller-market life saving drugs. Perhaps not coincidentally, decisions about which drugs to submit to the FDA are increasingly being made by overwhelming financial considerations.

One problem with developing life-style drugs is that clinical trials must be directed toward symptomatic patients, as opposed to

those with a definable, easily diagnosed disease. As the population sample grows larger and the patients with a certain symptom become more diluted, the efficacy of a drug becomes greatly reduced, which increases its chances of failure in the eyes of the FDA. This is also consistent with the fact that more and more drugs are failing later rather than sooner, in late stage (Phase IIB/III) clinical trials, where the costs of drug approval are greatest.

So it becomes a vicious cycle: as pharma companies continually look for even bigger blockbuster drugs, they increase the likelihood of failure because of the necessity to broaden the sample of the population in the clinical trials. This tends to reduce efficacy and ultimately increases the risk-adjusted cost of the drug.

The bottom line is, if the cost of bringing a new drug to market keeps increasing while the FDA continues to be so risk averse, the drug approval processes will slowly bog down. This will drive people with Alzheimer's, cancer and other life-threatening illnesses to go outside the US to get the life saving drugs they need.

Jay Leno joked on *"The Tonight Show"* that President Bush was happy to visit Canada because he could get all his prescriptions filled -- but this is no laughing matter. The problem of prescription drug costs will exacerbate the creation of a two-tiered health care system in the United States, in which only the rich can afford to get the drugs they need.

Merck's problems with Vioxx may not impact many of us directly today, but we will certainly feel their effects in the not too distant future. Solving the drug industry's larger problems and saving the future of our healthcare system will take visionary thinking from policy leaders in the public and private sectors. ❖

*Richard C. Hsu is a partner at the law firm of Townsend and Townsend and Crew LLP in Palo Alto (CA). Edwin P. Ching is a patent attorney in Woodside (CA).*

Efforts made to close the gap between organ demand and supply, as in the case of the federal government's "Gift of Life Donation Initiative," are expected to increase the size of the transplantation market<sup>(15)</sup>.

But, the BCC report also detects another important market growth driver in the US: the "quality-of-life transplantation" sought by aging baby-boomers. This is distinct from the old-fashion transplantation targeting life-threatening conditions. The new boomer-driven demand is about procedures involving tissues, such as body fat, collagen, cartilage, bones, and even hair used in 'fixing' aging-related conditions, from wrinkles and sagging breasts to chronically-aching knees and baldness. The boomers will help expand the human organ and tissue transplantation market, which is projected to reach \$20 billion by 2007. ❖

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*Ahmed Enany is president and CEO of the Southern California Biomedical Council; Lee Goodglick is assistant professor at the UCLA School of Medicine and co-director of the UCLA Early Detection Research Network, and Gary Lazar is a medical oncologist and managing director of CT Venture, a Pasadena (CA)-based venture fund focusing on technology and life-science investment opportunities.*

## Opportunities for Biotech Companies

Continued from page 1

almost any clinical trial is unlikely to reveal a serious effect that occurs in just a small percentage of users – even if that effect is potentially lethal (witness Vioxx).

### Personal Convictions:

Instead of facing up to the consequences of its “bigness,” the pharmaceutical industry relentlessly consolidates. This trend continues while companies should be dividing down into smaller entities that would be more efficient, less voracious, and ultimately more profitable.

The widely ballyhooed \$800 million-plus cost of getting a drug to market is a self-serving and misleading figure. It includes the costs of all the failed R&D chasing the limited number of indications that pharma judges to be sufficient to satisfy its revenue requirement. It is not an indicator of what money can buy when the objective is treating human disease that is less than ubiquitous.

There are countless opportunities to “do good” and make money developing drug products to treat less common conditions. Targeting such conditions is, in reality, a lower risk, higher return strategy.

The continuing elucidation of the human genome enables us to identify subsets of the population that respond to highly specific therapeutic interventions. It is increasingly clear that even large populations that appear to be suffering from the same condition may require different compounds to get maximum therapeutic effect. For example, one of our most promising biotechnology investments is based on the

genomic differences among patients with multiple sclerosis, and the company’s plan to design compounds specific for each patient subset.

### One Answer:

Many early stage biotechnology companies are likely to profit in this environment. By their very nature, biotechnology companies are aware of the relationship between genomic information and the mechanisms of action of the drugs they are developing. The notion that a compound may treat only one subset of a disease population is not a deterrent, but rather a catalyst to develop alternatives for the other subsets.

In my experience, biotech start-ups seek to focus on conditions for which there are no (or plainly inadequate) alternatives, rather than waste precious resources on modest improvements to widely available products. Their revenue targets are not counted in the billions (though some may ultimately meet this milestone). Their R&D is substantially more cost effective than big pharma. And big pharma is standing by, checkbook in hand, to handsomely reward these companies when they achieve their objectives.

As a physician, I respect and admire the approach of these more narrowly-focused biotech companies. As a patient, I’m grateful for their achievements. And as an investor, I like their odds. ❖

*Dr. Wolfe serves as general partner at UV Partners (Salt Lake City, UT & Manhattan Beach, CA), a venture capital fund investing in technology and the life-science industry.*

## ABOUT SYNERGIES

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