


RED HERRING
NEWSLETTERS
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BIOMEDICINE FOCUS

Personal Defense

IMMUNOTHERAPY SHOWS INCREASING PROMISE IN THE TREATMENT OF CANCER AND A WIDE RANGE OF OTHER DISEASES.

Breakthroughs are usually anything but. Most often, important innovations are the result of years of painstaking trial and error in the lab.

Case in point: transimmunization, a “new” immunotherapy that shows tremendous promise in the treatment of a wide range of cancers (see page 6). The story actually begins more than 20 years ago, when Richard Edelson, then a researcher at Columbia University, developed photopheresis, a treatment for a type of skin cancer called cutaneous T-cell lymphoma that used patients’ own malignant blood cells to boost their immune response against their cancer. The treatment showed startling success in early trials.

Photopheresis became the first FDA-approved selective immunotherapy for any cancer. It was covered in the *New York Times* and the *Wall Street Journal*. Johnson & Johnson licensed the therapy and built a company around it.

Trouble was, Edelson wasn’t sure exactly why photopheresis worked so well, and thus he had difficulty improving the treatment and applying it to other forms of cancer and immune-system diseases.

So Edelson, who is now at the Yale Cancer Center, went back to the lab. Only recently did he succeed in cracking the mechanism by which photopheresis works, which enabled him to aim the therapy at a number of diseases and start his new company, Transimmune. Nationwide clinical trials will begin within 12 months.

Edelson’s timing was good. Immunotherapies like transimmunization—which use the body’s own defense system to attack cancer and other diseases—are now the hottest field in biomedicine. At a recent JPMorgan Healthcare conference in San Francisco, the majority of companies presenting, 51, were based on immunotherapies of some kind or other. Only half as many were medical-device companies.

“There are a dozen products on the market and they promise to provide great benefits to patients,” says professor Larry Steinman, chair of the department of neurology and neurological sciences at Stanford University. “Research is starting to pay off after 20 years.”

And the payoff will likely be large. Pharmaceutical industry research firm IMS estimates immunotherapies for cancer will be a \$30 billion market by the year 2015 (see Metrics, page 3).

Immunotherapies based on monoclonal antibodies are already a lucrative market. Rituxan, a monoclonal antibody for the treatment of non-Hodgkin’s lymphoma, is now a \$1.6-billion-a-year therapy. The breast-cancer monoclonal antibody Herceptin generates annual revenues of \$450 million.

CONTINUED ON PAGE 2
WELCOME TO INNOVATION PIPELINE

Two forces drive technology in the world today: labs and markets. Innovation Pipeline brings them together in a newsletter that is current, candid and independent. Innovation Pipeline goes inside university labs, corporate research centers and early-stage startups around the world to tell readers what’s on its way to the market and what impact it will have when it arrives.

Innovation Pipeline offers business analysis of developments in seven key sectors: biomedicine, communications, defense and security, electronics, energy, nanotechnology and software. We explore promising technologies in each and give a clear picture of their applications, financing and competitive edge.

Innovation Pipeline profiles startups that show real-world promise. Their technologies are in various stages of development: some are already funded and in product stage; some are looking for capital; some are just out of the lab. None of them is a “science project.” All have the potential to alter the dynamics of their respective markets. ●



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ABOUT IP RATINGS

Each Innovation Pipeline technology profile includes an IP Rating of that technology's innovation, capitalization and market opportunity. The editors of Innovation Pipeline determine the IP Ratings by looking at each technology's fundamentals and potential. Innovation is a measure of the degree to which a new technology is different from existing technologies in its field. Capitalization is an appraisal of a startup's funding progress toward a marketable product. Market opportunity is an estimate of that product's five-year market potential.

COMING UP IN INNOVATION PIPELINE

Vol.3 No. 1: **Software**
Vol.3 No. 2: **Energy**
Vol.3 No. 3: **Nanotech**
Vol.3 No. 4: **Electronics**

Interest in immunotherapy is helping reinvigorate funding for biotech overall. Investment in 2004 was \$3.83 billion, up from \$3.53 billion in 2003, according to the MoneyTree Survey by PricewaterhouseCoopers, Thomson Venture Economics and National Venture Capital Assoc. Of the top 10 venture-backed IPOs in 2004, biopharma companies accounted for eight, raising \$550 million.

Among the venture capital firms investing in biotech, the most active is MPM Capital, which did 14 deals in 2004 worth a total of \$56.3 million, followed closely by Domain Assoc., with 11 deals worth \$39 million. Other leading investors were Burrill & Co., Alta Partners and Arch Venture Partners, each of which did 10 deals, according to the MoneyTree Survey.

Monoclonal-antibody therapies are artificial antibodies produced in a lab that selectively target cancer cells. Since Rituxan, Herceptin and other monoclonal-antibody therapies have shown to be useful—and profitable—researchers are now working to identify new diseases susceptible to immunotherapy.

The science of genomics holds promise for finding many targets for new therapies but early predictions of an explosion in therapies based on genomics have been toned down, as the process has proven far more complex than many first thought. Today there are roughly 370 therapeutic antibodies in development, around 75 of them in clinical trials.

To find out what's coming next, keep your eye on the nation's campuses, Steinman suggests. "The university labs is where the next wave of innovation will be born," he says. "And it will be at those academic institutions that are accepting of entrepreneurial activity."

But, as the story of Transimmune illustrates, the innovation is only the first step. "Bridging the university research lab and commercial markets is difficult," Steinman says. The biggest stumbling block is capital to run clinical trials. Transimmune had the advantage of federal and foundation grants. Others will need help from venture capitalists. "You can't make the discovery without the private sector," Steinman says. "Those who think you can do it without the private sector are fooling themselves."

There are considerable challenges inherent in the manufacture of immunotherapies. It's more difficult to produce large quantities of human cells than to produce vats of

There are considerable challenges in the manufacture of immunotherapies. "Frankly, it is rocket science," says Jon Mirsalis, of the SRI biosciences division. "But this has the most promise."

synthetic chemicals. Chiron was reminded of this last year, when contamination problems caused the quarantine of its flu vaccine at its facility in Liverpool.

"These are living systems that have a life of their own and it is, frankly, rocket science to do this work," says Jon Mirsalis, acting vice president of the SRI biosciences division and director of SRI's toxicology and pharmacology laboratory. "We're stumbling in fits and starts. But despite the number of impediments to overcome, this has the most promise." •

METRICS

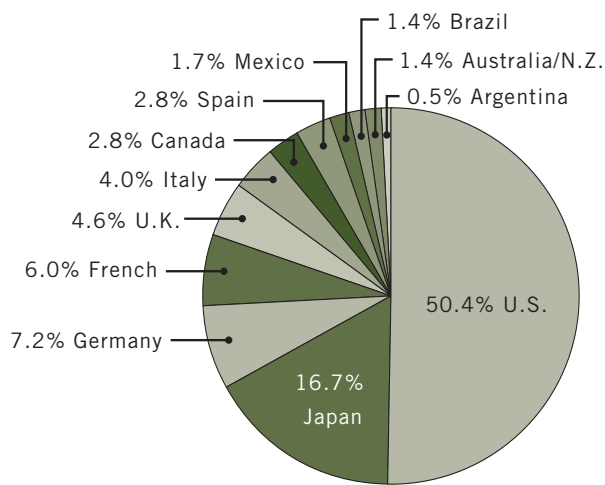
A recent study commissioned by the National Venture Capital Assoc. measured the impact of venture investment on the life sciences industry. The upshot? NVC estimates one in three Americans has been positively impacted by venture-funded medical innovations over the past 20 years. That includes 70 million people who have had their lives extended and 25

million people who have had their quality of life improved by venture-backed diagnostic and therapeutic treatments. The study says that for every venture dollar invested, recently launched life sciences products have returned \$50, while products launched 10-15 years ago have returned \$750 on each dollar invested. Venture-backed innovations also come to market three times faster than innovations

that receive no venture funding, which is part of the reason why immunotherapies for cancer could be a \$30 billion market as soon as the year 2015. Based on that rate of growth, the \$1.4 billion in venture capital invested in therapeutic biotech products last year could deliver big impact soon.●

2004 RETAIL PHARMACEUTICAL SALES IN 12 KEY MARKETS

The U.S. accounts for half of pharmaceutical sales in 12 leading nations, though Latin American countries saw greater growth.

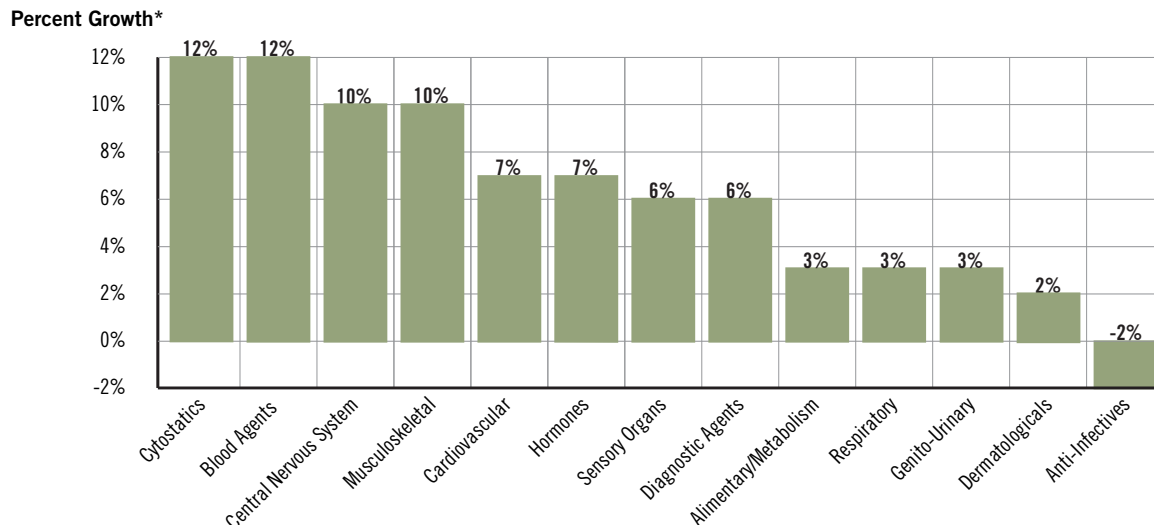


| | Sales (billions) | Percent growth* |
|--------------------------|------------------|-----------------|
| U.S. | \$175 | 8% |
| Japan** | \$58 | 1% |
| Germany | \$25 | 1% |
| France | \$21 | 5% |
| U.K. | \$16 | 7% |
| Italy | \$14 | 3% |
| Canada | \$10 | 9% |
| Spain | \$10 | 7% |
| Mexico | \$6 | 9% |
| Brazil | \$5 | 21% |
| Australia/N.Z. | \$5 | 9% |
| Argentina | \$2 | 16% |
| Total selected countries | \$374 | 6% |

*From 2003 to 2004 at constant exchange rates. ** Includes hospital sales. Source: IMS Health Retail Drug Monitor

2003–2004 PHARMACEUTICAL SALES GROWTH BY THERAPY

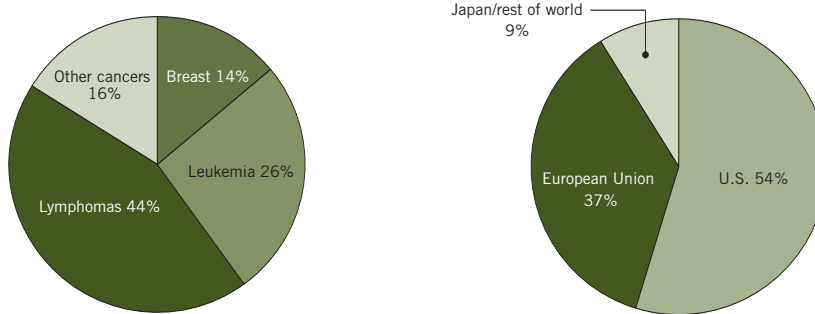
Blood agents and cytostatics registered the largest sales increases worldwide; sales of drugs for the central nervous system grew most in North America.



* At constant exchange rates. Source: IMS Health Retail Drug Monitor

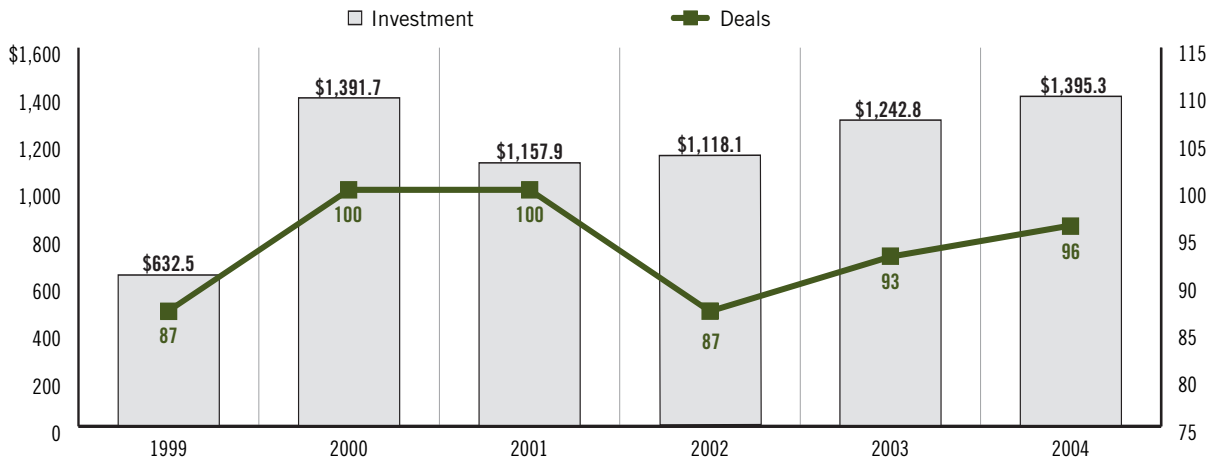
2004 BIOTHERAPY AND IMMUNOTHERAPY CANCER-TREATMENT REVENUE BREAKDOWN

Most products are sold to treat lymphomas and their high cost means the developed world accounts for the majority of sales.



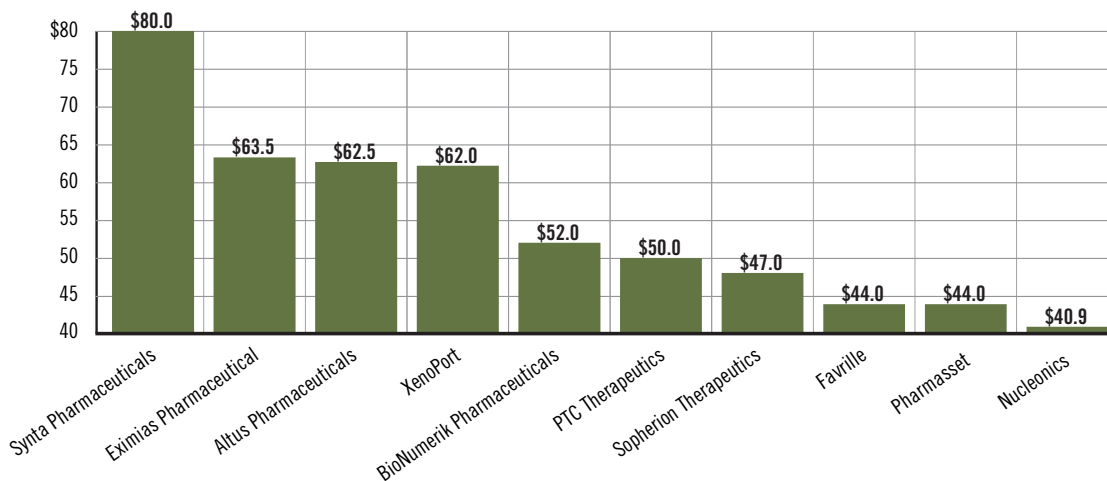
THERAPEUTIC BIOTECHNOLOGY VENTURE INVESTMENT TREND

2004 investment in biotechnology startups eclipsed even 2000 investment.



Investment in millions. SOURCE: PricewaterhouseCoopers, Thomson Venture Economics, National Venture Capital Assoc. MoneyTree Survey

TOP THERAPEUTIC BIOTECH VENTURE DEALS IN 2004



Investment in millions. SOURCE: PricewaterhouseCoopers, Thomson Venture Economics, National Venture Capital Assoc. MoneyTree Survey

LAB SPOTLIGHT

Department of Biomedical Engineering at UC Irvine

LOCATION

Irvine, California

FOUNDED

1998

URL

www.bmc.uci.edu

FOCUS

Biophotonics, biomedical nanoscale systems, biomedical computational technologies, tissue engineering.

BACKGROUND

The world-renowned researchers at Irvine's Biomedical Engineering Department work in areas including biomedical photonics and optoelectronics, biomedical nanoscale and microscale systems and fabrication, and biomedical computation and modeling.

Among the resources available to researchers are major campus facilities like the Beckman Laser Institute, for biophotonics, and the Integrated Nanosystems Research Facility, for nanofabrication and microfabrication. Additional research partnerships are available at the Center for Biomedical Engineering.

Faculty members involved in tissue engineering are exploring implantable prevascularized tissues and neural tissue.

MAJOR PROJECTS

Optical biopsy device: a rapid, 3D, non-invasive device to image the larynx and other areas, which will accelerate early detection of cancerous or abnormal cells using optical coherence tomography.

Cochlear implant technology: a cost-effective sound chip based on cellphone technology that improves ability to understand speech and music.

High-speed cell analyzer: a microtechnology-based system to grow living cells in a proprietary cassette and automati-

cally analyze and manipulate them at very high speeds while maintaining viability.

Dental device: a noninvasive testing instrument to increase dental-implant success, detect internal fractures in natural teeth and detect mobility associated with periodontal disease even in very early stages.

Stent-sizing instrument: for use by interventional cardiologists with standard guidewires or catheters in cardiovascular procedures for instantaneous arterial sizing.

Lab on a chip: a device for uniform generation of small particles tagged with molecular keys enabling consistent and efficient drug delivery to a diseased site.

Bioengineered nerve tissue: biodegradable nerve conduits to transfer growth factors and regenerate nerve function in 40 million injuries each year, in tumor resections or in congenital defects.

DEPARTMENT CHAIR

Steve George, William J. Link professor and chair of the Biomedical Engineering Department: George's work focuses on understanding the biology and physiology of the human lung as an integrated whole organ. Within this context he's pursuing two overarching areas of research, both of which combine cellular and whole-organ studies and experimental as well as theoretical techniques: one, nitric-oxide metabolism; and two, wound healing and tissue remodeling.

George and his group are working toward an understanding of what changes in the local biochemical environment affect exchange dynamics at the cellular and whole-organ level. The project involves an understanding of the fluid mechanics of the bifurcating tubes, mass transfer coefficients and lung mechanics. Current research projects include: a characterization of endoge-

nous and exogenous nitric-oxide exchange in the lungs; wound healing and extracellular matrix remodeling in the lungs; drug delivery of nitric oxide, nitric-oxide donors and peptides; and cytokine-induced production of nitrous oxide in the lungs, particularly in response to exercise.

KEY RESEARCHERS

Michael W. Berns, professor of biomedical engineering and cofounder of the Beckman Laser Institute. Berns' research is focused on the study of how the body's cells and tissues respond to light. This includes basic research into the interaction of light and tissue at the subcellular, cellular and tissue levels and the application of the findings in clinical research.

Tibor Juhasz, professor of biomedical engineering. Juhasz has developed a highly successful research program centered on femtosecond-laser applications for ophthalmologic problems. His discoveries led to the formation of Irvine-based IntraLase—a company whose laser technique is the base technology used to create the corneal flap in the Lasik procedure.

Ghassan Kassab, professor of biomedical engineering. Kassab's work focuses on understanding the biomechanics and adaptation mechanisms of the coronary circulation system in order to predict its response to such diseases as hypertension and hypertrophy. Under the tutelage of Y.C. Fung, he developed the first mathematical model of the entire coronary vasculature.

SPINOFFS

Tamar Technology (2000), Robomedica (2001), Cell Biosciences (2001), CODA Genomics (2004).

BIOMEDICINE

SECTOR OVERVIEW A handful of biomedical startups announced huge funding rounds earlier this year but Wall Street has yet to show equal enthusiasm. In March, Targacept pulled its IPO registration, citing “difficult market conditions in the life-science industry.” Three other biotech firms have gone public this year—Threshold Pharmaceuticals, Favril and Icagen—but all reduced their listing price by as much as 50 percent before going to market. There are now 19 venture-backed healthcare companies in registration and it is a safe bet that not all will make it out of the starting gate. The concern is that some biotech startups will be denied future financings by skittish VCs. Transimmune, featured here, is currently financed by federal grants. But VCs would be well advised to take a close look at immunotherapies like this one.

TRANSIMMUNE

Immunotherapy
New Haven, Connecticut
www.transimmune.net

| IP RATING (scale 1–10) | |
|------------------------|---|
| INNOVATION | 9 |
| CAPITALIZATION | 2 |
| MARKET OPPTY | 8 |

A frequent problem with cancer treatments is that they damage healthy cells as much as cancer cells. One solution: help the body cure itself. The approach is called immunotherapy and it’s growing fast. Immunotherapies of all types now account for about a third of all clinical trials.

Yale School of Medicine spinoff Transimmune has developed an immunotherapy to treat some of the most deadly forms of cancer, including colon, prostate, breast and lung. The startup is led by Richard Edelson, director of the Yale Cancer Center.

In 1982, Edelson pioneered an immunotherapy called photopheresis to treat non-Hodgkin’s lymphoma, the first immunotherapy approved by the FDA to treat a specific cancer. Johnson & Johnson built a company, Therakos, around photopheresis, which is now also used to treat autoimmune diseases and organ-transplant rejection.

Tumor cells cause cancer because they don’t present on their surface the antigens that would normally provoke the immune system to attack them. Photopheresis induces the transfer of cancer cells’ antigens to healthy white blood cells, which then present them on their surface and provoke an immune response against the body’s cancer.

It works this way: the patient is hooked up to a machine that withdraws blood and separates out the white blood cells, including the malignant T-cells. Doctors add methoxypsoralen, a drug derived from plants that, when exposed to ultraviolet light, binds to the malignant T-cells’ DNA and kills them while leaving other white blood cells unharmed. The unharmed cells then absorb the dying cancer cells and begin to present their tumor antigens. Returned to the body, these cells work as a vaccine, provoking an immune response that fights cancer.

In the last 10 years Edelson and his Yale team—Carole Berger and Douglas Hanlon—have refined photopheresis into a new treatment called transimmunization. Transimmunization has proven so effective that it’s now being tested in the treatment

of a variety of the most deadly cancers.

While Edelson is reluctant to estimate how successful the treatment will be until clinical trials are complete, early tests have indicated that transimmunization could be several orders of magnitude more successful than chemotherapy, which has around a 40-percent success rate.

Better still, the process is a great deal less damaging to the patient than most cancer treatments because it’s entirely organic. So far there are no cases of patients sickened by the treatment.

Transimmune is now entering clinical trials at the Yale University School of Medicine. Nationwide trials will begin in 12 months. “If clinical trials go as well as early preclinical tests, then we’ll have a responsibility to make the treatment available as soon as possible,” Edelson says.

To date Transimmune has been wholly funded by federal and foundation grants and has exclusive rights to the patents, which are held by Yale University.

ANALYSIS: In the past few years immunotherapy has become one of the most prominent—and promising—fields of cancer research. Industry watchers say Transimmune has several advantages over competing approaches. Its therapy is tailored to individual patients and is based on methods already known to have clinical efficacy. Christopher Kersey, managing director at Cogene Biotech Ventures, says he’s very intrigued by new cancer treatments like Transimmune but says venture capitalists need to see some successful medium-term clinical trials before they invest. •

COMMUNICATIONS

SECTOR OVERVIEW Has the wireless industry reached bubble stage? VCs invested roughly \$1 billion in wireless startups last year, inflating valuations and attracting plenty of marginal business ideas. Still, most industry watchers are not yet ready to declare the second coming of the dotcom bust. “By the end of this year an estimated 2 billion people worldwide will have a wireless connection and device, and the market will continue to grow, with the total wireless market approaching \$1 trillion by 2010,” says an ebullient Roman Kikta. Kikta just launched Mobility Ventures, a VC firm dedicated to wireless investments. But even if we are in bubble, innovative startups like Silvus Communication Systems, featured here, will likely survive and thrive, especially with the imminent arrival of converged services.

SILVUS COMMUNICATION SYSTEMS

Gigabit Wireless Networks
Los Angeles, California
www.silvuscom.com

| IP RATING (scale 1–10) | |
|------------------------|---|
| INNOVATION | 8 |
| CAPITALIZATION | 2 |
| MARKET OPPTY | 7 |

Nobody can accuse Babak Daneshrad of underselling his second startup, Silvus Communication Systems. “We’re going to be the next Broadcom,” says the UCLA electrical engi-

neering professor. Broadcom is a \$6.5 billion chip company. And, if Silvus' technology operates as promised, Daneshrad may be right.

Silvus is working on the hottest technology problem in communications today: how to make gigabit-speed wireless devices without significantly increasing the size of their battery or their physical dimensions. Even with overhead, Daneshrad says he'll deliver a usable bandwidth of 250 megabits per second per link.

That would be a vast improvement on today's wifi networks, the best of which toddle along at 54 megabits per second—a speed few users actually enjoy, since distance, overhead and additional devices drop real throughput to a fraction of that.

If Daneshrad can deliver, the transformative effect would be enormous. Such speeds would be fast enough to replace in-building wiring, enable wireless devices to receive DVD-quality streaming video and supply enough bandwidth for almost any application on the market today.

Daneshrad and his team have developed a chip programmed with algorithms for MIMO, multiple-input multiple-output technology that enables a device to send different signals to different antennas on the same frequency band. Normally, such signals are treated as interference. But with a Silvus receiver chip, all of these signals can be recovered, enabling linear improvement in performance with each antenna added, at no cost in power or bandwidth.

Silvus isn't the only company working with MIMO technology. With IEEE specifying that the emerging 802.11n high-speed wireless standard will use MIMO, many chip vendors are getting into the act. So far, Airgo Networks is the only vendor offering a MIMO chipset. Atheros Communications has just announced one and Broadcom is hard at work on its own MIMO chipset.

Those companies, though, are focused on delivering MIMO into 802.11n. Silvus wants to take MIMO horizontally and enable all wireless technologies to benefit from it. The Silvus algorithms enable MIMO to be adapted to any wireless technology. Silvus is creating the patent and intellectual property portfolio.

MIMO is a broad term for a group of four technologies: spatial multiplexing, space-time coding, smart antenna processing and diversity processing. Each uses unique algorithms. Elements of smart antenna processing and diversity processing can be found in a number of existing systems targeting the 802.11n space.

However, Silvus intends to deliver algorithms that will enable all four MIMO technologies to work across all wireless systems. That means vendors producing wifi, wimax or any other wireless equipment will be able to leverage MIMO to improve their devices' performance by buying the Silvus field-programmable gate array chip.

Daneshrad has raised \$1.5 million from DARPA, the Office of Naval Research and the National Science Foundation and is hoping to double that this year. He claims he's already secured a number of commercial contracts to deliver MIMO capabilities. With enough money in the bank, he might even be able to attract his old Ph.d. adviser, Henry Samueli, the founder and CTO of Broadcom.

ANALYSIS: Market research firm ABI Research says vendors like Silvus are getting an important headstart on the competition by offering MIMO-based devices even before standards fully mature. ABI analyst Philip Solis says MIMO will play an important part in future wireless standards and that late arrivals to the market will have a hard time securing customers for their chipsets. Quickest from the gate has been Airgo, which has already sold more than 1 million MIMO chipsets, according to Solis. •

DEFENSE & SECURITY

SECTOR OVERVIEW The security sector shows no sign of cooling off. Morgan Keegan projects the market for IT security will be \$25.1 billion in 2005, up from \$7.3 billion in 2000, and the monitoring and identification segment to be \$27 billion this year, up from \$15 billion in 2000. In March a new \$12 security surcharge was added to the fee for U.S. passports and renewals. The charge is intended to fund biometric features to be added to passports this year. The new biometric passports will contain a digital image of the bearer's face and biographic information on an electronic chip that can be read by a scanner. Biometric technologies of all stripes are gaining traction in the marketplace. A startup called Privaris, featured here, has developed a biometric fingerprint scanner on a keyring that guards access to everything from cars to computers.

PRIVARIS
Identity Authentication
Fairfax, Virginia
www.privaris.com

| IP RATING (scale 1-10) | |
|------------------------|---|
| INNOVATION | 7 |
| CAPITALIZATION | 6 |
| MARKET OPPTY | 6 |

Ensuring the identity of people accessing networks and facilities has become a critical security issue for government agencies and businesses. Making a reliable device that people can carry with them is one of the long-sought goals.

In 2001 entrepreneur David Russell and University of Virginia computer science professor Barry Johnson set out to solve the problem. Their solution: a keyring-size fingerprint scanner called the BPID Security Device, a wireless gadget that uses fingerprint-based biometrics to authenticate users of everything from cars to computers.

Users log in by placing their thumb on a pad. The print is scanned and matched to prints stored on the BPID. Once verified, the user presses a button to send an encrypted signal, either Bluetooth or RFID, to the accessed device.

The BPID is designed to be backward compatible with existing RFID access systems so companies can replace anonymous card-access devices with BPID fingerprint scanners.

The keyring also stores up 400kb, so it can be used to hold electronic passports, corporate ID cards, medical records, even driver licenses.

Privaris is not the only company with a fingerprint-authentication device. Similar solutions are available from LG

Electronics, Microsoft and other firms, which offer everything from a fingerprint USB dongle to a biometric mouse. But Privaris has the only fingerprint-ID product that is small, battery-powered and wireless.

“We don’t consider other devices to be a competitive threat because our intellectual property covers biometrically authenticated wireless transactions,” says Privaris CEO Barry Johnson.

Privaris has sold BPID keyrings to government and corporate customers. The Transport Security Administration is assessing the device for use by airport workers. Employees will press the RFID button to gain physical access to the building and press the Bluetooth button to access their computers.

Privaris has 12 patents (four secured and eight pending) that cover biometric wireless transactions.

While the company and its manufacturing partners now sell a \$179 biometric keyring device, Privaris’ real growth opportunity likely will be in the licensing of its technology to cellphone, auto and computer manufacturers. It recently did license its technology to a mobile-phone maker. Users will have their thumbprint scanned by their phone, which can then carry out a secure wireless transaction with another device. This could be used for electronic payments.

The greatest obstacle, according to Johnson, is competition from companies like Precise Biometrix, which has similar offerings. But the potential market size is large. Morgan Keegan estimates the IT security market will grow to \$25.1 billion in 2005, up from \$7.3 billion in 2000. It says the monitoring and ID product market will be \$27 billion in 2005, up from \$15 billion in 2000.

Privaris has 15 employees and has raised \$12 million from angel investors. It has contracts to supply its device to U.S. government agencies and is now licensing its technology to auto, cellphone and computer manufacturers.

ANALYSIS: Privaris is pursuing an intriguing partnership strategy that could help raise its profile. For instance, it has teamed up with transportation company TransCore to develop an access-control system that combines RFID and biometrics to identify both vehicles and drivers as they enter high-security facilities like military bases and nuclear plants. VCs say they’re always interested in startups with a strong partnership strategy because it opens multiple streams of revenue.●

ELECTRONICS

SECTOR OVERVIEW The disaster-recovery market made headlines in March with the news that a consortium of private equity firms led by Silver Lake Partners are in talks to acquire SunGard Data Systems for \$10 billion. Among other things, Sungard provides disaster-recovery services for corporate IT systems. Disaster recovery is all about protecting a company’s data and internal systems and a perfect storm of factors has recently driven the sector into the limelight, chief among them is compliance laws like Sarbanes-Oxley, which demands more rigor in data storage and recovery. Illuminator, profiled below, is bringing a fresh approach to this increasingly important market sector.

ILLUMINATOR

Application-Recovery Software
San Mateo, California
www.illuminator-sw.com

| IP RATING (scale 1–10) | | |
|------------------------|--|---|
| INNOVATION | | 6 |
| CAPITALIZATION | | 4 |
| MARKET OPPTY | | 6 |

Businesses large and small live in fear of catastrophic system failure. Traditionally they’ve protected themselves by investing in powerful servers and storage devices to back up all critical information and applications. One-year-old Illuminator is taking a different approach. Instead of backup, it focuses on recovery.

Illuminator says that, contrary to popular belief, conventional file backup does not ensure application recovery after a system failure. In 2001, Enterprise Storage Group estimated that 60 percent of attempts to recover data were unsuccessful.

Illuminator claims its flagship product, Restore-Illuminator, finds the gaps in a company’s data-recovery process. It identifies servers on a network that are not being backed up and all objects—including file systems and directories—that are on unprotected servers. Illuminator then compares this information to the backup software’s indexes and policies to find inconsistencies in policies and to determine vulnerabilities. Essentially, the system provides an ongoing audit, marking those applications and files that are recoverable and those that are not sufficiently backed up and offering suggestions to fix deficiencies.

Illuminator says it’s one of the first companies in the market to focus exclusively on recovery-management tools. Larger firms like Veritas have staked out the backup market but have not made a big push into recovery. Illuminator’s key selling point is that by providing advance warning of which applications are unrecoverable the system reduces the need for expensive disaster-recovery drills.

Illuminator is still in stealth mode and declines to talk in detail about its technology. However, the company reveals that it employs a repository that consolidates all backup policies in a single location. These backup policies are automatically imported from various backup servers found within an organization.

Restore-Illuminator also features a discovery engine that scours the network for new servers that have not been added to the backup policy and then generates a list of storage objects that could have recovery problems. Finally, the company says, its system has the ability to quickly analyze tens of millions of files on servers, storage devices and backup clients, which allows for quicker recovery if disaster strikes.

Illuminator’s founders developed EMC Legato Systems’ NetWorker Operations product and have deep roots in the storage and recovery space. CEO Yoav Boaz previously founded Integrity Systems, an Israeli infrastructure company. VP of R&D Rami Katz was a senior executive at Magic Software Enterprise, a maker of application development tools. The Restore-Illuminator technology was developed at Integrity Systems and spun off.

ANALYSIS: Illuminator recently raised \$5 million in series A funding from Greylock Partners and Evergreen Partners. That

money will be used to relocate from Israel, where the technology was built, to Silicon Valley and hire sales, marketing and product-development staff. “Disaster recovery is a market that has been underserved for many years, yet is growing in importance,” says Moshe Mor, general partner at Greylock. “We really like the domain expertise of the Illuminator founders and believe they’ve developed a solid product with a direct link to real customers.” Illuminator could make an acquisition target for the likes IBM or EMC Legato, which could gain a competitive edge by integrating application-recovery technology into their product portfolios.●

ENERGY

SECTOR OVERVIEW The landscape is littered with innovative fuel-cell companies that failed to bring their technologies to market. Like Metallic Power, which raised \$40 million to develop zinc-based fuel cells—and shut down in January. But the technology rolls on. A new wave of fuel-cell companies are focusing on targeted markets, better designs and reduced production costs. PowerGenix, for instance, recently raised about \$14 million for its rechargeable nickel-zinc fuel-cell battery for the cordless-tool market. INI Power, featured below, is another fuel-cell startup fresh from the lab with an intriguing technology.

INI POWER SYSTEMS

Portable Fuel Cell
Cary, North Carolina
www.inipower.com

| IP RATING (scale 1–10) | |
|------------------------|---|
| INNOVATION | 7 |
| CAPITALIZATION | 3 |
| MARKET OPPTY | 6 |

Extending laptop battery life has been a goal of the computer industry for years. INI Power Systems, a spinoff from the University of Illinois, claims to have come up with a solution.

Its INI Personal Power Plant fuel cell is about the same size and weight as a conventional rechargeable battery but runs up to five times longer. Under optimal conditions, it can power a note-

Under optimal conditions, the INI fuel cell can power a notebook for up to 24 hours without recharging, the company says.

book for up to 24 hours without recharging, the company says.

The problem with most fuel cells is power loss due to a common problem called crossover, which is when fluids get caught on the wrong side of an electrolyte membrane, resulting in increased energy consumption and a loss of capacity.

INI’s Personal Power Plant incorporates a dynamic microfluid system that eliminates the electrolyte membrane,

meaning less power loss and longer battery life, claims the company. The patented laminar-flow fuel cell operates like the capillaries in a human body, allowing ions to migrate freely without mixing.

“You can make batteries better by trying to erase the limitations with electrolyte membranes or you can come up with an entirely new design,” explains INI founder Larry Markoski. “My inspiration for this design came from photosynthesis and its ability to separate two things without having a physical barrier between them.”

Like most other fuel cells, the Personal Power Plant is fueled by methanol. Unlike most other cells, it’s not limited to methanol and can use a variety of different fuels, including formic acid and inorganic fuels.

For the time being, INI is not focused on powering laptops but on building a portable 20-watt fuel cell for the Army to power telecommunications devices and global positioning systems.

Until last summer, Markoski was working as a research specialist in chemistry at the University of Illinois Beckman Institute. INI’s intellectual property includes an exclusive license to a University of Illinois patent covering the methanol laminar-flow fuel-cell concept, as well as design and component improvements developed and owned by INI. (Markoski borrowed the name from a chant popular at Illinois football and basketball games: “I-L-L-I-N-I!”)

As for competition, there are currently scores of fuel-cell companies entering the market. The challenge for INI will be demonstrating to the world that its products work as well as advertised and are indeed a leap forward in the portable-power arena. INI says it plans to have a working fuel cell for laptops by early 2007. INI says manufacturing should not be especially expensive because it will employ the same processes and materials used to manufacture flexible circuit boards.

If INI succeeds it could secure a foothold in a portable-device battery market that generates nearly \$8 billion annually.

ANALYSIS: INI recently raised \$3 million in series A funding from Morrissey Hawthorne, MHI Energy Partners and IllinoisVentures. The money will be used to continue the development of the company’s fuel cells. INI also received a \$750,000 development contract from the Army Research Office. “We were attracted to INI because they were working to solve a significant problem in the fuel-cell space,” says John Regan, a senior director at IllinoisVentures. “The company has made tremendous progress from the time we first looked at them, almost two years ago, to today. I really believe they could be in the right place at the right time as we start to see real products come to market.”●

SOFTWARE

SECTOR OVERVIEW The web is not yet fully spun. The latest version is coming soon to a screen near you: the semantic web. Championed by web inventor Tim Berners-Lee, the semantic web

is like the traditional web on Red Bull. It will present data understandable not only by people but by machines as well. And it's closer than most people think. Late last year Berners-Lee's W3C consortium announced final approval of the key standards for the semantic web. Now a number of visionary startups are going to work to take advantage of the new, improved web. Fetch, profiled here, is an emerging leader in the field.

FETCH TECHNOLOGIES

Web-Data Extraction
El Segundo, California
www.fetch.com

| IP RATING (scale 1-10) | | |
|------------------------|--|---|
| INNOVATION | | 6 |
| CAPITALIZATION | | 5 |
| MARKET OPPTY | | 7 |

Businesses are getting much better at consolidating information across multiple internal databases—such as finance and sales—to get a clearer picture of performance. But when it comes to the internet, accurately extracting information from an almost endless series of databases powering billions of web pages is infinitely more complex.

That's where Fetch Technologies enters the picture. It has developed a suite of software tools to extract and integrate

Southern California. Artificial intelligence is key because the software works by making decisions and learning on its own.

This is critical when it comes to data extraction because very few databases label their information the same way. For instance, the same product—say, a raincoat—might be labeled “trench-coat” in one database and “anorak” in another. The Fetch algorithms are programmed to learn extraction rules by example and make common-sense judgments as they go. In essence, the company says, its system can connect the dots between data points, then build knowledge from those connections.

“Eventually we'll be able to take humans out of the loop,” Minton says.

To date, a handful of companies have licensed the Fetch technology. JD Power uses Fetch to retrieve pricing information in the used-car market. Other customers include Infotriever, BizRate and Sony. The potential is huge. By 2010 the market for intelligent web-data retrieval software and services could exceed \$60 billion, according to a study by research firm TopQuadrant.

Fetch's most noteworthy competitor is an Austrian company called Lixto Software. Fetch says its advantage is the ability to extract semistructured data from websites, whereas Lixto

Late last year Tim Berners-Lee's W3C consortium announced final approval of the key standards for the new, improved semantic web. A number of startups, Fetch included, are already going to work to take advantage of the semantic web.

semistructured information from multiple web sources.

An online retailer, for instance, could use Fetch to gather market intelligence on its competitors. Fetch's so-called Web Agents can be programmed to scour hundreds of competitors' sites for pricing information on thousands of products. This information typically resides in underlying databases and using manual methods to retrieve it might take weeks or months. Fetch says it can extract and integrate the same information automatically and update price and product information in near realtime.

Fetch claims this is far different from the everyday search engine that retrieves web pages without any concept of what it's bringing back. “With a search engine, there's no understanding of what is on the page, whereas with our technology there is,” explains Steven Minton, chairman and CTO of Fetch.

At the heart of the technology are advanced artificial-intelligence algorithms originally developed by the company founders—Minton, Craig Knoblock and Yigal Arens—at the University of

can only extract more rigid structured data, requiring less artificial intelligence.

Fetch is a spinoff from the research labs at the University of Southern California's Information Sciences Institute. Fetch's founders were faculty members in the computer science department when they developed the core AI algorithms behind the Fetch Agent Platform. Knoblock and Arens are still at the university.

ANALYSIS: Fetch has raised about \$3 million from private investors and has received another \$5 million in government grants from the likes of DARPA, NASA and the National Science Foundation to further develop the technology. The company admits the technology is still evolving but says it's not currently looking for venture capital. Still, Fetch is starting to play an important role in a new category called the semantic web, a framework for linking data now being championed by web creator Tim Berners-Lee. •

Q&A



Little Man on Campus

TOM KALIL WAS POINTMAN ON PRESIDENT CLINTON'S NATIONAL NANOTECH INITIATIVE. NOW HE'S LEADING UC BERKELEY'S PUSH TO MAXIMIZE THE IMPACT OF ITS NANO RESEARCH.

Collaboration is a key to the innovation process at any university research lab. Great minds working together produce landmark technologies.

Like Unix, the graphics-based web browser and, more recently, the world's first nanoscale motor—small enough to fit on the back of a virus. All were developed, in large measure, by grad students and faculty on the Cal campus.

What's next? We asked Tom Kalil, special assistant to the chancellor for science and technology at UC Berkeley. His job is to develop new multidisciplinary research initiatives combining Cal expertise in nanotechnology, information technology, microsystems and biology.

Before Berkeley, Kalil worked in the Clinton administration, “those dark days of peace and prosperity,” as he calls them. He was the president's deputy assistant for technology and economic policy and deputy director of the White House National Economic Council. He was pointman on a number of technology fronts, including allocation of spectrum for new wireless services and the National Nanotechnology Initiative.

Innovation Pipeline: What's going on in the area of nanotechnology here on campus?

Tom Kalil: We can create all of these really interesting “nanoblocks,” which have novel and potentially useful properties, but there aren't a whole lot of examples where we've been able to take those building blocks and integrate them into functional systems. Most people believe creating those functional systems is going to require tools and techniques from multiple disciplines. So learning the tools and techniques of multiple disciplines is going to be very important in training the next generation of scientists, entrepreneurs and engineers.

IP: What about intellectual property? How do you deal with the issue in industry collaborations?

TK: The Berkeley philosophy is to maximize the impact of our research rather than maximize our revenue. We're not in the business of doing research to make money, we're doing research to have an impact on the world. Our IP strategy flows from there.

IP: How does that compare to IP policies in the IT industry?

TK: In the IT industry IP is primarily used defensively. Whereas the way to have impact is achieve ubiquity and oftentimes the way to achieve ubiquity is not to be encumbered by intellectual property. That's why we're not patenting TinyOS. That way it might become the de-facto standard.

IP: What are some of the ways you're trying to build multidisciplinary lab environments?

TK: There are several approaches. One is using architecture—buildings that are not allocated to departments. In every lab there's a space where students hang out and drink coffee and read journal articles. When you hear people talk about Bell Labs you hear them talk about how important the cafeteria was, because you'd run into some Nobel laureate and have an opportunity to explain what you were working on and get some valuable insight into the problem.

IP: Is Berkeley interacting with industry in new ways?

TK: I'll give you a good example. Intel has decided that no matter how big a company they are they can't hire all the smart people in the world. So they've decided to locate a series of labs on the periphery of what they consider the leading research universities. They're called lablets. It's codirected by a Berkeley professor and an Intel research employee. And it has both Berkeley students and Intel research employees doing experiments and collaborating in the open. Everyone is working on the same floor. If we were aggressive about asserting our intellectual property in that context you could imagine it would not be an environment conducive to research.

IP: Talk about some of the current collaborative research efforts being done in conjunction with the federal government.

TK: One we're working on now is with the National Cancer Institute, which is very interested in nanotechnology for cancer. Typically only one in 10 molecules in a cancer drug goes to the tumor. We're working on more efficient targeting. Another front is early detection.

IP: What about the collaboration between Lawrence Berkeley Lab and UC Berkeley. How does that foster innovation?

TK: There's a huge amount of cross-fertilization. The DOE is giving UC Berkeley \$85 million to construct a molecular foundry, which will also have an \$18 million-a-year operational budget. Under one roof you'll have all of the facilities for nanoscale fabrication—synthesis of inorganic nanostructures, organic and biopolymers, top-down nanolithography, biological approaches to making things at the nanoscale, imaging, modeling and simulation. The foundry will be a place where you can learn state-of-the-art process and bring that back to your institution.●

Science Isn't Everything

KODIAK VENTURE PARTNERS GENERAL PARTNER CHRIS GREENDALE SAYS MARKET APPLICABILITY IS A KEY FACTOR IN VC FUNDING DECISIONS.



It's no secret that many of the great technology advances of our time originated in university research labs and served as the foundation for some very big companies. Labs foster the risk taking, entrepreneurial spirit and vision necessary to develop breakthrough innovations.

But these days labs hoping to launch startups to transfer their technologies to the marketplace have to do more than dazzle investors with their scientific genius. To succeed, entrepreneurs must capably demonstrate that their technologies have real-world applications.

Technologies that spring from university labs typically have a number of advantages over those developed in business settings. Labs furnish high levels of investment, they often offer the support of researchers who are luminaries in their fields, they enable years of research free from the rush-to-market pressures that businesses force, and thus typically yield technologies that are sound and highly differentiated. As a result, startups built on lab technologies have a high degree of credibility and are well-equipped to defend their differentiation.

But VCs also know that lab technologies are often anchored in pure research rather than applied research and, unfortunately, pure research is rarely marketable. Because it's not aimed at businesses and customers, pure research can be a solution looking for a problem, a technology-driven rather than a market-driven innovation.

Before today's more cautious VCs are convinced that a technology has market applicability, they usually want several things. First and foremost, VCs want access to the lab—generally through an ombudsman from the lab—so that they can take an early look at the technology and have a sense for what's being researched.

How do they decide which technologies are worth a first-hand look? There are a number of ways VCs monitor university labs and stay apprised of the latest developments. They go to lab seminars and conferences, they subscribe to lab newsletters, they read analysis from industry pundits, and work their personal and business contacts. By maintaining close connections this way, VCs not only stay aware of the latest advances at labs, they guarantee themselves an "in" should a technology be of interest. If they're interested in a technology, VCs will usually ask associates from their firms to investigate further or ask a graduate assistant from the lab to provide them with more information on the technology. With access to the lab early on, VCs can evaluate the potential market viability of the technology and decide whether to fund the venture.

Due diligence is the next step. VCs assess the viability of a potential deal by answering the following questions, among others:

- What's the market for the technology?
- What's the value proposition for the startup?
- What's the competitive advantage?
- How will the technology be applied?

Intellectual property issues play a key role in the funding process as well. VCs need to know the nature of the intellectual property and how the lab intends to build a company around it. But, most important, VCs must know the terms under which the intellectual property will be released. Some universities want to keep an equity percentage, some want royalty deals, others have no preference.

Once VCs make the decision to fund a lab-based company, it is important that they immediately begin networking for the right people to form a management team. VCs will need to determine the type of involvement the lab research team will have in the startup moving forward. In general, the professor involved in the project will join the startup's board of advisers. A graduate student instrumental in the technology will often play a significant role in the new company, perhaps as chief technology officer or as an adviser with equity in the startup. Because CEOs with prior business experience are preferable, VCs usually bring in outside executives for this position. While lab researchers who develop technologies tend to be a bit more entrepreneurial and visionary than others, their vision generally is highly influenced by technology. For this reason, VCs often augment the lab team with business-oriented managers who have relevant domain expertise and industry backgrounds.

Finally, VCs will want to work with entrepreneurs to understand the level of financial investment the startup will need. Once VCs decide to back a new startup, the funding and growth prospects do not differ widely from other types of investments.

University research labs will continue to be the source of technology breakthroughs that attract investor interest. There is every good reason for VCs to reach into labs and for labs to look for relationships with the investing community. Working together, university labs and the venture community form the winning combination for effectively transferring the benefits of technology advancement to the marketplace.

Chris Greendale is a general partner at Kodiak Venture Partners, a Waltham, Massachusetts-based firm providing seed and early-stage funding for communications/IT, semiconductor and software companies. He focuses on software and services investments.●

IP MARKETPLACE

A new technology isn't like a new baseball field. Build it and, often, they won't come.

Researchers in labs around the world are working on innovations with the potential to fundamentally alter their prospective markets. But that's the easy part, many would say. The real job is attracting the interest of investors.

To help get the word out, we've developed a new feature: IP Marketplace. It's a short list of technologies eligible for investment and licensing at university and research labs in the U.S. and abroad.

This first edition of IP Marketplace features biomedical innovations from the labs of the Southeastern Universities Research Association. SURA spans an area from Texas to Massachusetts. Members include Rice, Florida, Georgia Tech, Duke, Georgetown, MIT and over 50 other schools.

CLEMSON UNIVERSITY

Technology: a stabilizing multiwell-plate insert for biomaterial testing

Application: better assessment of cell-material interaction

More information: www.clemson.edu/curf/techshowcase

Contact: Matt Gevaert, business development manager, mrg@clemson.edu, (864) 656.1140

Many new products depend on accurate testing of the interaction between the product materials and mammalian cells. But existing test methods often fall short. Clemson researchers have developed an insert to position and stabilize material samples in commercially available multiwell plates for the study of cell-material interactions. The insert is similar to commonly used sterile, disposable polystyrene cell-culture products and can be used with standard in-vitro equipment and procedures. It allows precise control of cellular contact with the material being tested—better than current methods, Clemson says—and thus enables standardized, repeatable, quantitative analysis of cell-material interactions. Widespread use of the technology could reduce or eliminate the need for animal testing.

DUKE UNIVERSITY

Technology: nonfouling oligoethylene glycol polymer brushes

Application: improved diagnosis and disease screening

More information: www.cbimms.duke.edu

Contact: Ashutosh Chilkoti, associate director, Center for Biologically Inspired Materials and Materials Systems, chilkoti@duke.edu, (919) 660-5373

Self-assembled monolayers of oligoethylene glycol make a dense “nonfouling” brush that’s possibly the best such system now available. But its robustness is limited. Duke has developed a method to synthesize nonfouling coatings that combine the advantages of self-assembled monolayers with the benefits of more robust films containing polyethylene glycol, which prevent

nonspecific protein adsorption and cell adhesion and are used in many biomedical applications. Duke says it can make polymer brushes of tunable thickness in the 5nm-50nm range, which is not achievable in self-assembled monolayers or polymer grafts alone. Duke says its brushes are easily synthesized, exhibit no detectable adsorption of proteins and are cell-resistant for up to a month under typical conditions. The synthesis method is compatible with a range of patterning techniques, from the nanoscale to the microscale, which enables the patterning of cells in a biologically relevant milieu over long periods of time.

UNIVERSITY OF MARYLAND

Technology: preparation and use of berry extracts and other berry-based edible products

Application: prevention and treatment of obesity

More information: www.otc.umd.edu

Contact: Gayatri Varma, senior technology manager for life sciences, gayatri@umd.edu, (301) 403-2711

Obesity is the major risk factor for cardiovascular disease, which is the leading cause of death in the U.S. An estimated 52 percent of all adults in the U.S. are overweight or obese and a large number of them use at least one alternative treatment to assist weight loss. But none of these currently available alternative treatments has been demonstrated effective and safe. Researchers at the University of Maryland College Park and the University of Maryland Baltimore have developed a procedure to prepare natural extracts that they say inhibit gut mucosal growth and aid in the prevention and treatment of obesity.

UNIVERSITY OF TEXAS

Technology: MEMS/NEMS-based drug-delivery device

Application: enhanced drug delivery and targeting of diseased cells and tissues

More information: www.otc.utexas.edu

Contact: Brian Cummings, licensing associate, bcummings@otc.utexas.edu, (512) 475-7659

Current drug-delivery technologies rely on diffusion and degradation and are neither targeted nor stimuli-responsive. Several MEMS-based devices have been formulated but they leave much to be desired. Current technologies require direct injection of a contrast agent, which can result in poor targeting of tissues and noise in the subsequent image. Most MEMS-based devices must be surgically implanted and removed, which can cause inflammation and complicate drug release, are too large for systemic delivery and lack stimuli-responsive mechanisms. Texas says its device simultaneously releases drugs and contrast agents in response to stimuli, providing accurate drug delivery and noninvasive monitoring of both therapeutics and the device, allowing easy evaluation of delivery, intracellular uptake and release. Because the device is injectable, no surgery is required.

TULANE UNIVERSITY

Technology: biventricular pacemaker-implanting device

Application: improved access to the coronary sinus and cardiac veins for left-heart pacing

More information: www.som.tulane.edu/techdev

Contact: Harl Tolbert, senior licensing associate, htolbert@tulane.edu, (504) 988-6962

Congestive heart failure afflicts almost 5 million people in the U.S., with 500,000 new cases each year. Therapy for heart failure has been pharmaceutical-based but a promising new treatment involves implantation of a new type of pacemaker into both ventricles of the heart, which resynchronizes the left and right ventricles and improves the heart's pumping efficiency. But positioning pacemaker leads for placement into the left ventricle of the heart is technically challenging: a surgeon must maneuver a lead through the major vessels, and gaining access to the coronary sinus and cardiac veins for implantation is difficult. Tulane's device, which is under development, enables identification of landmarks in the heart blood vessels and facilitates precise placement of left ventricular leads. Tulane says the device will dramatically simplify the implanting of leads for left heart pacing.

UNIVERSITY OF VIRGINIA

Technology: receptor-selective mimetics of sphingosine and sphingosine 1-phosphate

Application: immune system-modulating drugs

More information: www.uvapf.org

Contact: Alan Bentley, assistant director, University of Virginia Patent Foundation, arb3u@virginia.edu, (434) 982-1615

Virginia researchers have synthesized and characterized agonists and antagonists selective for the five sphingosine 1-phosphate receptors (S1P1-5). S1P is a lysophospholipid mediator that evokes a variety of responses from cells and has been implicated in angiogenesis. There has been speculation that an S1P1 receptor antagonist would be an effective antiangiogenic agent but it is S1P1-receptor agonists, acting to modulate the immune system, that are the most promising drug candidates now. S1P-receptor agonists disrupt normal lymphocyte trafficking to direct effector T-lymphocytes away from sites of inflammation. S1P1 agonists prolong transplant survival and show potential against many autoimmune diseases. The University of Virginia Patent Foundation currently has patents pending on various S1P analogs, their synthesis and therapeutic applications. •



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50 of the most innovative companies in Southern California and companies funded by the Advanced Technology Program of the National Institutes of Standards and Technology (NIST).

Dear Readers,

When an innovation leaves the lab and begins life as a startup, it takes the first step in a difficult and exciting journey: from science to technology, from campus to commerce. Reporting on that journey is what this newsletter is all about.

To better convey this focus to our readers, we recently decided to change our name. ICC Report is now **Innovation Pipeline**.

Other than that, our commitment remains the same. We'll continue to apply the highest journalistic standards to the coverage of ideas on the move from lab to market.

Thanks for your ongoing interest in Innovation Pipeline. If you have any questions or comments, please get in touch at ipipeline@redherring.com.

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