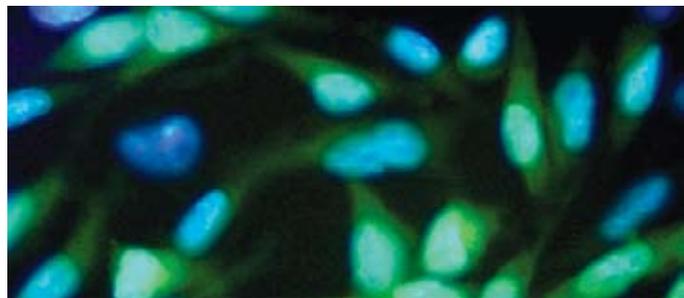


35 YEARS

OF TECHNOLOGIES THAT MADE A DIFFERENCE



OTL AT A GLANCE

CUMULATIVE INCOME

\$1,027,658,000

CUMULATIVE U.S. PATENTS ISSUED

1,518

CUMULATIVE AMOUNT GIVEN TO:

OTL RESEARCH INCENTIVE FUND

\$37,115,000

INVENTORS

\$114,300,000

DEPARTMENTS

\$129,300,000

SCHOOLS

\$127,400,000

ABOUT THE OTL STAFF

AVERAGE AGE

42

AVERAGE YEARS AT OTL

7

CUMULATIVE EXPERIENCE

327.5 YEARS

NUMBER OF EMPLOYEES

29

OFFICE OF TECHNOLOGY LICENSING

ANNUAL REPORT 2005

What have we learned in the past 35 years?

More than anything, we have learned that technology transfer is rarely easy — it takes creativity and time and tenacity. Although we have undoubtedly become more adept at transferring Stanford technology through the years, it remains a challenge to evaluate promising technologies, market them to appropriate potential licensees with the hope of finding a committed licensee, license them and then manage the long term, often unpredictable relationships between Stanford and industry. In spite of the complexities of

this work, something all of us at OTL share is the feeling of satisfaction that comes from knowing that we have helped to bring a new technology to market.

Our office mantra — “doing what’s best for the technology” — guides every step we take, every decision we make. It’s easy to become distracted by visions of financial windfalls, nightmares of litigation, political pressures, or challenging relationships. To be sure, dealing with all of these issues is part of our job. But

at the end of the day, we've learned that by fostering and valuing long-term relationships with faculty and industry, by devising the right licensing strategies, and by taking an open and flexible approach, we will always do what's best for the technology. And most of the time, the money will follow — rewarding the inventor, the inventor's department, and the inventor's school.



GENSCAN

Genscan was one of the popular software tools to aid scientists around the world in the task of gene mapping and sequencing for both human and plant genomics. Developed by former Stanford student Christopher Burge while in the research group of Dr. Samuel Karlin of Stanford's mathematics department, the software was licensed to over 80 companies, including pharmaceutical companies, biotechnology companies, and bioinformatics companies.

Our office mantra - “doing what is best for the technology” - guides every step we take, every decision we make.

MICROARRAYS

In 1994, Professor Pat Brown and graduate student Dari Shalon invented an arraying technique that became the basis of spotted DNA microarray technology. Although OTL initially marketed the technology widely, no company expressed interest. In 1995, Dr. Shalon founded Synteni, Inc. to exclusively develop the technology. Eventually, Synteni was sold to Incyte Pharmaceuticals and Incyte became the exclusive licensee.

The patented technology became embroiled in a long-running dispute with Affymetrix, but in 2002, Affymetrix, Stanford, and Incyte resolved patent oppositions and interferences, making way for unfettered commercialization by both companies. Stanford now licenses the technology on a non-exclusive basis.

NUMBER 1

In these pages, we describe 35 technologies that have made, or will make, a difference. All of these technologies have been licensed; some have reaped significant royalties while others have served a useful purpose but made less of a financial impact. We believe that what is most noteworthy is the range of innovations that have emerged from the work of Stanford researchers and the fact that we have been able to help turn them into successful products.

We couldn't publish our 2005 annual report without noting the liquidation of equity received from our license agreement with Google. At \$336 million, this is by far the most lucrative invention we have ever licensed. While we did not necessarily expect the technology to be a big winner at the outset, we did think it had merit — even when other

NUMBER 4

INSULATED GATE BIPOLAR TRANSISTORS

Invented in 1976 by current Dean of Engineering James Plummer, Insulated Gate Bipolar Transistors (IGBTs) are high power switching devices for switching large currents in applications ranging from washing machines to power plants. Stanford completed licenses with more than seven companies, including International Rectifier, Harris Semiconductor, Motorola, Mitsubishi Electric, IXYS, Hitachi, and Toshiba.

What have we accomplished in 35 years? We have evaluated over 6,000 inventions, obtained 1,500 U.S. patents, entered into 2,500 licenses and option agreements, and brought in over one billion dollars in licensing revenue.

PHYCOBILIPROTEINS

Phycobiliproteins, proteins that occur naturally in algae, have been extensively used in the biotechnology research community as fluorescent tags for the tiny beacons of light they emit. Invented by Professor Lubert Stryer of Stanford, Professor Alexander Glazer of the University of California, Berkeley, and Dr. Vernon Oi of Stanford, the technology was licensed exclusively in 1982 to Applied Biosystems (then a fledgling company that hoped to make phycobiliproteins a major product) and Becton Dickinson and Company for various fields of use.

In 1986, Stanford filed a patent infringement suit against Coulter Corporation for selling phycobiliproteins without a license, but the lawsuit was subsequently settled and Coulter became a long-time licensee. After the respective exclusive terms expired, Stanford licensed the phycobiliprotein technology to 73 companies. Although the patents have expired, the technology is still used extensively by researchers all over the world.

existing search engine companies dismissed it. Certainly, Larry Page and Sergey Brin deserve all the credit for making Google the company it is today. Our role was to find the very best licensee, and Google was it!

What have we accomplished in 35 years? We've evaluated over 6,000 inventions, obtained 1,500 U.S. patents, entered into 2,500 licenses and option agreements, and brought in over one billion dollars in licensing revenue. The University used a portion of OTL royalties

NO. 5

FUNCTIONAL ANTIBODIES

A process for generating functional antibodies, developed by Stanford inventors Leonard Herzenberg and Vernon Oi in collaboration with Sherie Morrison, formerly of Columbia University, is currently OTL's highest royalty producer.

Originally invented in the early 1980s, functional antibody products and other chimeric antibodies have

been used to produce drugs to treat a wide variety of diseases. Products include Remicade (from Johnson & Johnson) for rheumatoid arthritis and Crohn's disease and Synagis (from MedImmune) for respiratory syncytial virus — a major cause of respiratory illness in young children. Other licensees currently have antibody drugs in the FDA pipeline.

to fund 35 Graduate Fellowships, 376 seed research projects, and 68 Birdseed grants. We have reluctantly instituted four lawsuits in order to protect the University's intellectual property assets. We established the OTL-LLC to enable Stanford to help other sister institutions license their technologies. We received the Licensing Executives Society (LES)

Achievement Award. Never content to simply continue as we have always done, we have often asked the GSB Alumni Consulting Team (ACT) to help us improve our operations.

My colleagues at OTL join me in saying that it's been a terrific 35 years. All of us hope — and believe — that the next 35 will be as promising and productive.

GLOWING MICE

Nicknamed "glowing mice," this technology uses bioluminescence to detect and track pathogens in living hosts. The inventors (Professor of Pediatrics David Benaron and post-doctoral fellows Chris Contag and Pamela Contag) discovered that bioluminescent microorganisms inside a living animal were observable with a digital camera. By adding bioluminescent genes to bacteria, the inventors were able to non-invasively follow the course of infection in a live animal.

OTL licensed the invention to Xenogen, an inventor-affiliated start-up in 1996. Xenogen, which went public in 2004, sells biophotonic real-time in vivo imaging technologies and has extensively sublicensed the Stanford patents to pharmaceutical and biotech companies.



Katharine Ku, Director

YEAR IN REVIEW

PAST SUCCESSES AND NEW EFFORTS

ADVICE FROM OUR FRIENDS AT THE GSB

Started in 2004, the Graduate School of Business Alumni Consulting Team (ACT) finalized its recommendations on two projects for OTL: 1) improving OTL's marketing efforts to find more licensees and 2) identifying new initiatives for the Stanford OTL-LLC, the division of the office that works with non-Stanford entities. GSB alumni Dave Plough and Marc Canabou led both teams.

With respect to the first project, OTL markets its inventions broadly to ensure fair access and wide dissemination of Stanford technology. Most importantly, marketing helps us to assess the commercial interest for an invention and find potential licensees. With more than 400 inventions a year, however, the marketing effort takes a significant amount of time and resources. The ACT team recommended that we adopt a "customer relations management" approach to

NUMBER 8

cMUTS

Capacitive Micromachined Ultrasonic Transducers (cMUTs) are electrostatic-driven transducers micromachined into silicon. These transducers and their arrays, developed in the lab of Professor B.T. Khuri-Yakub, have attracted immense interest from across the corporate spectrum. The keenest interest has come from the medical imaging industry, where the standard transducer used in ultrasonic imaging, the piezoelectric transducer, is severely limited in comparison to the potential of the cMUT. In addition to the possibility of enhanced performance in medical imaging, the cMUT is also opening up a world of commercially viable 3-D imaging. OTL has already licensed the cMUT technology nonexclusively to several players in the \$2 billion medical imaging industry.

NO. 7

MEDICAL IMAGING TECHNOLOGIES

Stanford's long relationship with General Electric (GE) began in 1978 when GE commercialized a Computerized Axial Tomography scanner (CAT scanner) that included inventions developed by a team of Stanford physicists, radiologists, and electrical engineers headed by physicist Doug Boyd.

Years later, Professor Albert Macovski and his colleague Professor Dwight Nishimura developed technologies in the field of Magnetic Resonance Imaging (MRI), also licensed and commercialized by GE. To

date we have licensed over 150 inventions to GE, encompassing both hardware and software technologies from MRI to CT to X-Ray.

Siemens and Phillips Electronics have also licensed many of these technologies. "Molecular imaging," in particular, is one of the fastest growing areas in medical imaging research, both in the corporate and university arenas. We receive many invention disclosures in this field and expect to see many new products commercialized in the future.

NO. 9

MEDIPHOR

Developed in 1973 by Professor Stanley Cohen, Mediphor is a database for informing patients, pharmacists, and doctors about drug interactions. The database describes the characteristics of prescription drugs and their interactions with other prescription drugs to help patients avoid toxic events. The technology, licensed by Facts and Comparisons, continues to generate royalties.

marketing – particularly for large companies with many areas of interest.

Toward this end, we will ask companies interested in university licensing to indicate their areas of interest and provide specific contacts for new technologies in these areas. We will then be able to notify companies of inventions they may be interested in licensing more easily and efficiently.

Based on ACT's recommendations, we are investing in a major upgrade of our database, which will greatly improve our marketing and administrative capabilities. In addition, the ACT team recommended that OTL centralize some functions, develop more defined roles for its staff, and streamline the administrative and clerical tasks through information technology. GSB alumni on this project were Aydin Koc, Kathryn Bowsher, Pam Versaw, Patti Fry, Roy Vella, and Tony Seba.

The second project involved the OTL-LLC, which was incorporated on September 1, 2002. OTL asked the ACT team to think strategically about future initiatives for the OTL-LLC, if any. The ACT team made a bold and intriguing recommendation: that OTL establish a relationship with one or more premier universities in China, Russia, or India to license their technologies in the U.S. Stanford administration was supportive of the idea for some future time, suggesting

that the OTL-LLC follow the academic lead as faculty and students develop relationships with universities in these countries. GSB alumni on this project were: Andres Wydler, David Ai, Jerry Huang, James Canizales, Nancy Spangler, Skip Fleshman, and Yvonne Nomizu.

SELF-IMPROVEMENT

Licensing sometimes feels like a “contact sport,” but there is no question that personal contact is one of the most effective ways to foster technology transfer, especially in the age of email. One of the specific recommendations of the ACT team was that OTL should make more targeted phone calls to potential licensees in order to receive real time feedback about our inventions. In keeping with this recommendation,

FM SOUNDS AND PHYSICAL MODELING

Between 1971 and 1975, OTL tried to interest one U.S. company after another in Professor John Chowning's FM Sounds, an invention that would soon revolutionize the electronic music industry. But not a single one could be persuaded. It was an engineer from Yamaha who immediately understood its potential. Professor Chowning then spent seven years collaborating with Yamaha to develop a new music synthesizer using FM synthesis, and OTL's relationship with Yamaha has flourished ever since. The Yamaha FM chip became the de facto standard for sound synthesis for music synthesizers, personal computers, and cell phones, and five amendments to the license were made.

In 1989, Yamaha licensed second generation music synthesis technology based on Physical Modeling, which is used to create realistic synthesized sounds based on physical parameters. And Stanford and Yamaha agreed to pool their portfolio of patents to form the Sondius-XG program. Sondius represents Stanford's trademark while XG represents Yamaha's trademark — and the combined trademark reflects the close Stanford-Yamaha relationship. Stanford and Yamaha licensed Korg, an existing musical instrument company, and Staccato Systems, a start-up that was eventually acquired by Analog Devices, which uses Physical Modeling for PC music-audio products. Yamaha and the other Sondius-XG licensees have gone on to incorporate the Stanford/Yamaha portfolio of technologies into a variety of royalty-bearing products including electronic keyboards and computer chipsets.

NUMBER 11

HIV DIAGNOSTICS

An HIV-mutation diagnostic technology, now FDA-approved, was developed by Professor Thomas Merigan and licensed to several companies including Affymetrix, Specialty Labs, Quest Diagnostics, LabCorp, Bayer, and Celera Diagnostics. This technology is used to determine whether an HIV patient's antiretroviral therapy is effective by using assays that detect mutations in certain HIV codons — providing an indication of a patient's imminent immunological decline or improvement under certain antiretroviral therapies.

we had two sales training seminars so that the staff could learn some of the sales methods used by sales professionals.

We had an office retreat to spend dedicated time to think and talk about our core competencies, as well as ways we could improve. It is clear that it would benefit all parties if licensing transactions were more efficient and effective. We continue to put “ready-to-sign” licenses on the Web site and post template agreements so that our potential partners are familiar with the kind of license terms typically used by Stanford. We were inspired to think about industry-university relations in the broadest sense, fostering and facilitating

interactions when possible, whether or not directly licensing or sponsored research related. Good relationships start with the first encounter.

FRESH FACES

Change is inevitable, and this year seven new people joined OTL, a 25 percent infusion of new ideas about how we do our work. New staff present both a challenge and an opportunity: the challenge is bringing them up to speed as quickly as possible and the opportunity is the new perspectives they bring to our organization.

COMPLIANCE

Our compliance manager hosted the first ever “Compliance Meeting” attended by compliance officers from Yale, MIT, Massachusetts General Hospital, and the University of California, Office of Technology Transfer. The responsibilities of the compliance manager involve reporting inventions and patents to the sponsors, in particular the U.S. government as required by the Bayh-Dole Act. The U.S. regulations governing the administration of government-funded inventions are very explicit, and failure to comply can result in lost patent rights. We hope that from this initial meeting will emerge a semi-formal organization through which universities can share best practices in order to do a better job of meeting our obligations to sponsors.

NO. 12

PROTEIN DETECTION FOR RESEARCH, DRUG DISCOVERY, AND DIAGNOSTICS

Professor Helen Blau, Research Associate Tom Wehrman, and investigators in Stanford's Baxter's Laboratory have developed a new technology that is particularly advantageous for drug screening and validation. The technology allows comparisons of the effects of drugs on heart disease, cancer cells and inflammation by monitoring protein movement in live cells in a quantitative manner previously not possible. Licensed

to DiscoverX and Vivios, this technology has applications in many diagnostic and therapeutic areas.

Another Baxter Laboratory invention involves the use of the E. coli lacZ gene to measure expression of proteins in cells. This activity can be detected using quantitative biochemical assays, flow cytometry or microscopy and permits simultaneous microscopic visualization of other fluorescent markers. Licensed by Applied Biosystems, PanBio and Vivios, the technology will be used to screen for potential drug candidates, diagnostics and basic research.

INVENTION UPDATE

Functional Antibodies

As has been the case for several years now, Functional Antibodies is again the biggest royalty generator – save for Google, which is discussed earlier in this report.

This invention from the early 1980s, a process for making functional antibodies, covers such antibody products as:

- Remicade for the treatment of Crohn’s Disease and rheumatoid arthritis
- ReoPro, an anti-clotting agent
- Synagis, a drug for the treatment of respiratory syncytial virus (a major cause of respiratory illness in young children).

Professor Sherie Morrison, formerly of Columbia University, and Professor Leonard Herzenberg and Dr. Vernon Oi of Stanford are joint inventors.

Functional Antibodies is jointly owned with Columbia University, with Columbia taking the lead in licensing. The technology is licensed exclusively to Johnson & Johnson, which is being sued (as are Stanford and Columbia) by sublicensee MedImmune. The lawsuit was recently dismissed by the district court judge, but MedImmune has asked

RECOMBINANT DNA

The fundamental inventions underlying biotechnology — the gene splicing and cloning techniques known as recombinant DNA — were developed in 1973 by Stanford Professor Stanley Cohen and University of California Professor Herbert Boyer, who conceived of the idea while having lunch at a delicatessen on Waikiki Beach during a meeting on bacterial plasmids.

DNA cloning is a method to splice DNA from two or more sources, which become incorporated into a single recombinant molecule. It is used to produce drugs such as insulin, for diabetes; erythropoietin, a protein that stimulates the production of red blood cells and is used in the treatment of anemia; tissue plasminogen activator, a clot-dissolving enzyme used to prevent damage to heart muscle following a heart attack; and human growth hormone.

Stanford University, which managed the three basic DNA cloning patents on behalf of the two universities, granted a total of 478 non-exclusive licenses, which contained reasonable royalty rates (e.g., 1/2% on end product sales.) Royalties on the patents exceeded \$255M, a portion of which has been used to support research and education at both universities.

the Supreme Court to review the case. We believe that the Supreme Court will turn down the request.

This invention has been the center of attention for several companies that are in the business of buying royalty streams.

Fiber Optic Amplifier

The Fiber Optic Amplifier is yet again the biggest royalty-producing invention in the School of Humanities and Sciences, and the second largest royalty producer this year. This invention, licensed exclusively to Litton Systems, Inc., a wholly owned subsidiary of Northrop Grumman, has generated over \$32M in its lifetime and is our fifth largest income-producing invention to date. It is particularly noteworthy because it is the one of the few physical science inventions that has generated such significant royalties.

**NO.
3
1**

GREEN FLUORESCENT PROTEINS

Green Fluorescent Proteins (GFPs) are proteins naturally occurring in jellyfish that emit a bright green light. Professor Stanley Falkow and his colleagues modified the already known proteins to make it a much more useful tool. GFPs are widely licensed and used by scientists around the world to peer into cells and track their inner workings.

**NO.
15**

DSL

In 1992, many people were touting fiber optic cables as the answer to growing consumer demand for bandwidth. At the same time, Professor John Cioffi and graduate students Jacky Chow, Peter Chow, Minnie Ho, and Hailing Lou were developing technology related to Discrete Multi-Tone (DMT) technology, the technology that came to be used in Asymmetric Digital Subscriber Line (ADSL), which provides broadband Internet access to homes and businesses around the world. ADSL was revolutionary because it enabled use of the common tele-

phone line to transmit large amounts of data quickly — at rates 30 to 100 times faster than the 56K analog modems.

In 1992, OTL issued an exclusive license to four patents to Amati Communications Corporation, which was founded by Professor Cioffi. In 1995, Amati merged with ICOT, which was then acquired by Texas Instruments in 1998. Stanford's exclusive licensee, Texas Instruments has been broadly sublicensing the Stanford patents.

Selective Amplification of Polynucleotide Sequences

Selective Amplification of Polynucleotide Sequences broke the \$1M mark last year and continues to grow. The technology – an alternative to Polymerase Chain Reaction – was invented in 1987 by Professor John Boothroyd, Dr. Philippe Pouletty, and Dr. J. Lawrence Burg. The technology, licensed by Gen-Probe and Biomerieux, is used in several diagnostic tests.

FACTS AND FIGURES (2004–2005)

OTL received gross royalties of \$384M. More significantly, Stanford retained \$382.5M of gross royalties. We distributed \$1.5M to other organizations for their share of royalties. Of the 428 technologies that generated income, 44 generated \$100,000 or more each, and of those 44, seven produced \$1M or more each.

STANFORD'S PATIENT EDUCATION RESEARCH CENTER

Over the past 25 years, Stanford's Patient Education Research Center (SPERC) has developed, tested, and evaluated self-management programs for people with chronic health problems ranging from arthritis to HIV/AIDS. SPERC focuses its research and development efforts on those programs that can be tested for effectiveness with randomized, controlled trials that span two to four years. The aim of all SPERC programs is to improve the physical and emotional health of participants while reducing health care costs. Under Professor Kate Lorig's direction, SPERC has done just that. The flagship program, "The Stanford Chronic Disease Self-Management Program," has been licensed to over 500 organizations throughout the world. Currently health organizations, state health departments, national voluntary organizations, community based organizations, and hospitals in 17 different countries and 40 states in the U.S. offer the program. Dr. Lorig's group is now researching and launching a Web-based version of the program to provide even broader access.

NUMBER 17

LASERS

Professor Robert Byer has devoted over 35 years of his career to conducting research in lasers and nonlinear optics. He has disclosed more than 45 technologies — over half of which have been licensed. The diode end pumped laser and harmonic generator is a particularly lucrative laser invention that improves the efficiency and changes the output color of a laser by using a semiconductor to "pump" the laser, and a nonlinear element to generate visible light. His inventions, which have been licensed to more than 20 companies, are used in a variety of markets including materials processing, semiconductor fabrication, and biotechnology.

FY04-05 ROYALTY PAYMENTS TO STANFORD SCHOOLS

School of Medicine	\$10,512,031
School of Humanities and Sciences	\$1,303,533
School of Engineering	\$828,715
Dean of Research	\$169,079
Graduate School of Business	\$3,429

NUMBER 18

ACOUSTIC MICROSCOPE

The acoustic microscope, invented by Professor Calvin Quate and his colleague Ross Lemons in 1973, enables the imaging of elastic properties with a resolving power similar to the optical microscope. The technology was originally licensed to American Optical in 1974, but the company was not able to create a product. Leitz (now Leica) in Germany and Olympus in Japan subsequently became co-exclusive licensees in 1980 and both companies developed licensed products that have generated over \$600K in cumulative royalty income for Stanford.

ROYALTY DISTRIBUTION

Stanford’s royalty-sharing policy provides for the distribution of cash net royalties (gross royalties less 15% for OTL’s administrative expenses, minus direct expenses) to inventors, their departments, and their schools. In FY04-05, inventors received personal income of \$12.7M, departments received \$13.5M, and schools received \$12.9M*.

We contributed \$1.5M to the OTL Research Incentive Fund, which is administered by the Dean of Research for the support of early-stage, innovative research ideas, cost sharing of shared instrumentation, and similar research items. In addition, we contributed \$111,000 to the OTL Research and

Graduate Fellowship Fund; this \$111,000 was a portion of the liquidated equity. Stanford also paid the University of California and other organizations \$1.5M for jointly-owned technologies for which Stanford has licensing responsibility.

EXPENSES

We spent \$4.4M on legal expenses, of which \$1.6M was reimbursed by licensees. We have an inventory of \$6.9M, which represents patent expenses for unlicensed inventions. Our operating budget for the year (excluding patent expenses) was \$3.6M.

NO. 19

FIBER OPTIC AMPLIFIER

The fiber optic amplifier, invented in the early 1980s by Professor John Shaw and Dr. Michel Digonnet, enables light signals to be transmitted over long distances, allowing data and voice transmissions to be sent over fiber optic cables. It was developed in a research program in fiber optics research originally sponsored by Litton Systems, Inc.

Litton Systems, Inc., under exclusive license from Stanford University, has sublicensed the fiber optic amplifier to major telecommunications and CATV companies in North America, Europe, and Japan.

In addition to the fiber optic amplifier, numerous other pioneering inventions have resulted in products including the fiber optic gyroscope, fiber optic gratings, fiber optic sensors and arrays, polarization controllers and others.

* While net royalties are divided evenly between the inventor, the inventor’s department, and the inventor’s school, some inventors designate a portion of their royalty income to their laboratories, hence the discrepancy in income.

**NO.
20**

GOOGLE

When Larry Page came into the OTL office to talk about a new Internet search technology he had developed, there were already many search engines for the World Wide Web vying for a seemingly saturated market. But Larry and fellow Stanford graduate student Sergey Brin were convinced that the Page-Rank algorithm was a better technology — though most companies that OTL contacted were outwardly unimpressed with this.

The OTL licensing associate who met with Larry and Sergey thought their idea of placing the technology into a startup had merit, and the rest, as the saying goes, is history. Today Google is Stanford's best known licensee and the patented technology plays a key role in the world's most popular search engine.

NEW LICENSES

In FY04-05, we concluded 84 new license agreements totaling \$1.2M in up-front license fees. We received equity from 12 start-up companies. The average upfront royalty was more than \$14,000. Forty-nine of our 84 licenses were nonexclusive; three of these nonexclusive licenses were “ready-to-sign” agreements (i.e., downloadable from the OTL Web site, set price and no negotiation).

EQUITY

As of August 31, 2005, Stanford held equity in 80 companies as a result of license agreements. The market for initial public offerings was dismal this year and share prices were down. For institutional conflict-of-interest reasons and insider trading

concerns, the Stanford Management Company sells our public equities as soon as Stanford is allowed to liquidate rather than holding equity to maximize return. This year, we received \$336M in liquidated equity from seven companies.

START-UPS

While Stanford entrepreneurs are still starting companies, the economy clearly has negatively affected the Silicon Valley entrepreneurial ecosystem. Venture capital investments dropped dramatically and investors are becoming more stringent. Yet licenses to 12 companies involved equity: 4Cyte, Athenagen, Cellerant, DK Spine, EIFaMed, Fluid Medical, Fundamental Applied Biology, SaraTech, Spinal Modulation, StemCells, Stream Processors, and VIA Pharmaceuticals.

**NO.
12**

ATOMIC FORCE MICROSCOPY

Professor Calvin Quate and his research group began much of their pioneering research in atomic force microscopy (AFM) in the mid-1980s, inventing more than 40 technologies. AFM is a powerful tool for characterizing surfaces with a resolving power sufficient to image single atoms. Commercial AFMs are sold for use in many markets from semiconductor to materials research to life sciences. AFM cantilevers based on this research have been licensed to more than eight companies.

GRATING LIGHT VALVE (GLV)

Invented in 1991 by then Stanford Professor David Bloom, this invention consists of microfabricated silicon ribbons that leverage the wave-like properties of light. This approach provides for high resolution, robust, and low cost solid-state light beam modulation that can be used in displays, communications, and other optical apparatus such as printers.

Licensee Sony is currently developing a commercial display product using the “Deformable Grating Modulator.” Earlier this year, Sony demonstrated the technology on a gargantuan 100m screen using grating light valves (GLV). The size of the display, resolution, and the colors displayed were impressive. Another licensee, Light Connect, has launched two successful products based on the GLV for use in the optical networking industry.

NEW DISCLOSURES

In calendar year 2005, we received over 400 new technology disclosures. Approximately 48% were in the life sciences and 52% were in the physical sciences, including computer science technologies. Our work with the Stanford Biodesign Network's Biomedical Technology Innovation Program class generated 14 disclosures from students as part of their coursework.

STANFORD TRADEMARK ENFORCEMENT FUND

The Chief Financial Officer and General Counsel of Stanford recommended that Stanford provide a permanent source of funding for extraordinary cases associated with the protection of the Stanford name and associated logos and trademarks. Based on their recommendation, the President and Provost approved the creation of the Stanford Trademark Enforcement Fund (STEF). Initial funding for the STEF comes from 1% of the department and school shares of net revenue OTL receives. For FY04-05, we transferred \$265,123 to STEF.



NUMBER 23

SELECTIVE AMPLIFICATION OF POLYNUCLEOTIDE SEQUENCES

The newest invention to generate over \$1,000,000 in royalties for Stanford, "Selective Amplification of Polynucleotide Sequences," offers an alternative to Polymerase Chain Reaction — once thought to be the only approach for nucleotide amplification. Invented in 1987 by Professor John Boothroyd, Dr. Philippe Pouletty, and Dr. J. Lawrence Burg, it is now being used in several diagnostic tests, including those for tuberculosis and chlamydia. The technology is licensed by Gen-Probe and Biomerieux.

BIRDSEED FUND

The OTL Birdseed Fund, administered by the Dean of Research, has provided small amounts of money (typically up to \$25,000) to fund prototype development or modest reduction-to-practice experiments for unlicensed technologies. This year, the Birdseed Fund funded ten new projects, for a total of 68 projects funded to date. The rate of licensing of Birdseed funded inventions is about the same as unfunded inventions (20-30%) but without this funding, many of these inventions would likely have remained unlicensed.

RESEARCH INCENTIVE FUND

The Dean of Research has used the OTL Research Incentive Funds to fund 376 seed research projects cumulatively in all parts of the University. Primarily intended for assistant professors, research grants of \$11,000 to \$40,000 were used to fund 24 projects, including Scott Klemmer's (computer science) *Rapid Interaction Prototyping for Information Appliances*, Rebecca Sandefur's (sociology) *Social Class and the Use of Law*, and Karl Sylvester's (surgery) *Mechanisms of Hematopoietic Stem Cell Therapy for Liver Disease*.

INDUSTRIAL CONTRACTS OFFICE

ANNUAL REPORT 2005

In its eighth year of operation, OTL's Industrial Contracts Office (ICO) negotiated more than 625 sponsored research and other research-related agreements. Among these, just over 400 were material transfer agreements with industry and nonprofit organizations worldwide, for incoming and outgoing research materials ranging from human and mouse embryonic stem cells to microfluidic chip systems.

ICO negotiated agreements with companies in industries ranging from therapeutic drugs to semiconductors, to microarrays and consumer electronics, for studies performed by faculty and student researchers from the Schools of Medicine, Engineering, Humanities and Sciences, Education, and Earth Sciences, and the Independent Laboratories. The agreements describe the research plan, funding, and publication terms, and set forth ownership of and licensing options for intellectual property created in the course of the research.

NUMBER 25

ADRENERGIC RECEPTOR GENE DISRUPTION MICE

Adrenergic receptors are plasma membrane proteins that mediate cellular responses to the hormone/neurotransmitters adrenaline and nonadrenaline, which are released from sympathetic nerve terminals or the adrenal gland. The receptors mediate a variety of physiologic functions regulating blood pressure, heart rate, cardiac contractility, carbohydrate and fat metabolism, fluid and electrolyte balance. Professor Brian Kobilka's lab has developed a number of mice models for testing new drugs (activators or agonists, and inhibitors or antagonists) that act on alpha 2 adrenergic receptor subtypes. The mice have been licensed to several companies for research use.

NO.
24

FLUORESCENCE-ACTIVATED CELL SORTER

Developed in the early 1960s by Professor Leonard Herzenberg and colleagues, the Fluorescence-activated Cell Sorter (FACS) is a widely used instrument that separates cells according to fluorescent-tagged antibodies. The FACS allows scientists to quickly characterize, count, and sort thousands of individual cells per second. Originally commercially produced by Becton Dickinson and later by other companies,

the FACS is now used around the world for a variety of applications ranging from cancer detection, to treatments for autoimmune and infectious diseases, to stem cell research. Its first major clinical application was counting the number of T-cells in patients with AIDS, which allowed physicians to monitor the progression of the illness in their patients.

NO.

20

DHFR

Invented in 1982 by then Stanford Professor Gordon Ringold, this patent describes a way to increase protein production in mammalian cells using the dihydrofolate reductase (DHFR) gene. Today it is used in the production of biotechnology therapeutic products such as Campath (for lymphoma and leukemia), erythropoietin (which increases red blood cell production), and Herceptin (breast cancer treatment). To date, the technology has generated a cumulative royalty of about \$30M.

PROTEIN KINASE C

Professor Daria Mochly-Rosen's research focuses on protein kinase C (PKC), a family of closely related enzymes, or isozymes, that are involved in normal signal transduction and disease. PKC functions include regulation of gene expression, response to ischemic injury, regulation of hormone responses and ion channels. Earlier attempts to create drugs to modulate a specific PKC isozyme have stumbled because of the similarity of the isozymes and the drug's lack of specificity.

Stanford licensed several of its PKC patents to KAI Pharmaceuticals, a company founded by Professor Mochly-Rosen and one of her students. KAI recently initiated a clinical trial of an inhibitor of delta PKC for the treatment of reperfusion injury associated with acute myocardial infarction (AMI) — or an acute heart attack. Because AMI is a leading cause of morbidity and mortality in the United States, with approximately 1.3 million cases of nonfatal AMI reported each year, the drug could prove to be a significant therapy in the future.

During the year, ICO negotiated a Master Research Agreement with Amgen designed to cover a variety of research projects within the School of Medicine, and focused particularly on supporting research at the new Neurosciences Institute.

ICO also finalized a research project agreement for Professor Garry Nolan's microbiology and immunology lab and Bristol Myers Squibb. The purpose of the research program is to characterize cellular signaling events in immune cells and to correlate those events to anti-tumor efficacy. The study's goal is to define pharmacodynamic endpoints potentially applicable in clinical trials. Pharmacodynamics pertains to the action of a drug on the body.

In the School of Humanities and Sciences, ICO negotiated a multi-year agreement for Intel to sponsor research in Professor Hongjie Dai's lab in the Chemistry Department. The project is focused on carbon nanotubes and semiconductor nanowires, quasi one-dimensional materials that are likely to be used in future electronics and computer chips that provide much higher performance than current semiconductor devices. Also in Chemistry, the Korean company LG Chem is sponsoring research in Professor Bob Waymouth's lab that is designed to develop new classes of polymerization catalysts. If it is successful, the research program should pave the way

NUMBER 27

for new classes of plastics that combine the useful physical properties and processing characteristics of polyolefins with the functional properties of polyamides (nylons), polyesters and vinyl polymers.

In another research program initiated last year, Professor Zhenan Bao from the School of Engineering is researching the use of organic electronic materials and carbon nanotubes in electronic devices such as flexible displays, nonvolatile memory and flexible sensor arrays. Samsung is sponsoring the research in her chemical engineering laboratory.

For information on Stanford's policies on intellectual property and industry-sponsored research, please visit www.stanford.edu/group/ICO

THE NEXT GENERATION

A SAMPLING OF 2005 INVENTION DISCLOSURES

Use of electro-osmotic pumps together with wicking structures for water management in fuel cells

Worlds Apart documentary

Ubiquitous e-commerce platform based on Smart Mouse, 2d/3d barcode and camera phone

Fabrication of multilayer nanoparticles

3-D models from data

Vehicle position estimation

Multi perspective panoramas

Amplification and probe dissociation assay for quantitative detection of JAK2 mutation

A vision-based full-body interface

H.264 SI picture regeneration

Technique for sorting carbon nanotubes

Data delivery for multiple peer-to-peer distribution trees

Convex parimutuel call auction mechanism

New device for mechanically fastening tissue

Design and synthesis of inhibitors for cancer chemotherapy

Fetal diagnostics

High-yield expression of membrane proteins using cell-free protein synthesis

Microfluidic sample stacking method using single-interface isotachopheresis

Scatter-Add in data parallel architectures

Self replicating shRNA molecules

Hydrogel intraocular lens

CARDIAC OUTPUT MONITOR

A persistent and entrepreneurial inventor, then Stanford Professor Mark Yelderman convinced a major pharmaceutical company, Baxter Healthcare Corporation, that a 1982 cardiac device he had developed could save lives in the emergency room. The cardiac output monitor measures the flow of blood through the heart.

Used for the continuous monitoring of the cardiac output of critically ill patients, this device was first licensed to Interflow, a venture-based start-up in Texas. Baxter acquired the license in 1988 and introduced its product in 1991. The patent has expired but the device is still an integral part of emergency care. It generated over \$5.9 million in cumulative royalty income for Stanford.

NUMBER 28

CHEF ELECTROPHORESIS

In 1987, Bio-Rad licensed two inventions from Professors Gil Chu, Ron Davis, and Douglas Vollrath related to a gel electrophoresis device that manipulates the electric fields for the separation of molecules, such as DNA. Their inventions improved the separation of molecules by altering the shape and orientation of the electric fields. Today, gel electrophoresis is an important tool in molecular biology and provides insight into many aspects of genetics. To date, these inventions have generated over \$2 million in royalties.

NO.

0

M

COMPACT X-RAY SOURCE

A compact x-ray source invented by Professor Ron Ruth and graduate student Zhirong Huang at the Stanford Linear Accelerator Center (SLAC) is the basis for a start-up company, Lyncean Technologies, and may generate significant royalties someday. The prototype development and testing is supported by the Small Business Innovation Research Program from the National Institutes of Health's Protein Structure Initiative. If it works as planned, it will address a wide variety of applications, including protein structure analysis and soft tissue imaging.

NUMBER 31

HEARTBAR™

Developed by Associate Professor of Cardiovascular Medicine John Cooke, the HeartBar™ contains L-arginine, which eases the symptoms of cardiovascular disease by relaxing the arteries and increasing blood flow. Improved circulation reduces angina pain and gives patients more stamina.

MINOS

A very popular suite of optimization software developed in 1981 by Professor Michael Saunders and Professor Bruce Murtagh, MINOS (Modular In-core Nonlinear Optimization System) is still generating significant royalties. This software program has been widely distributed to academicians and research labs all over the world through our licensee Stanford Business Software. In addition, over 40 companies have taken licenses for commercial uses ranging from the electric power industry to yacht design, financial asset optimization, portfolio management, and chemical process control. A robust and versatile invention, it continues to withstand the test of time.

A semi-rigid method for lung nodule registration

MCV difference method of indexing plasma hypertonicity

Double check verification system

Arrayed primer extension (APEX) mutation detection assay

Light field microscope

Anatomy labeling on PACD to enable voice navigation

Trojan Horse immunotherapy

Method for solid phase synthesis

Self-assembly of semiconducting pigment single crystals for field-effect transistors

A method for diagnosing prostate cancer

Early disease detection through ultrasensitive high-throughput assays

Use of HIF-1 inhibitor and hypoxic cytotoxin in the treatment of solid tumors

Biomarkers of human aging

High time resolution Bradbury-Nielson gates

Needles for sampling tissue fluids

PDMS surface modification

Method to detect defibrillation and increase pacemaker threshold

Progenitor profiling in hematologic malignancies

Imaging pain

Multi-layered tubular structures

Flow-based detection of rod-like barcoded particles

System for measuring clinical status of subjects

Susceptibility imaging

Liposome mediated tissue regeneration

Bone void filler

An efficient imaging sensor architecture for vision-based applications

Algorithms for optimizing dialysis
Determining L-Arginine in biological samples

Biomarkers for inflammatory diseases

Knock down of a gene using a novel siRNA TAG

Bonding substrates at low temperatures

Method to measure color image density of digitized photographs

Surface parallel modulator

Surgical gamma camera adaptive exposure using optical flow

Briefcase personal computer

NO. 32

IDENTITY-BASED ENCRYPTION

Identity-Based Encryption (IBE) is a new and more efficient approach to encrypting and protecting email. Current popular encryption techniques require dependence on both a public and private key. For example, Sender A cannot encrypt a message for Recipient B without knowing B's public key. Invented by Stanford Professor Dan Boneh and U.C. Davis Professor Matt Franklin, IBE creates a public key based on a simple text string, like an email address — allowing Sender

A to encrypt a message using Recipient B's email address, without the time-consuming and costly process of looking up a public key.

The IBE patents have been licensed to Voltage Security, a company originally founded by Stanford E-challenge winners, which provides solutions for secure communication to leading financial services, healthcare, government, and pharmaceutical companies.

NUMBER 34

OLIGONUCLEOTIDE SYNTHESIZER

This invention by Professor Thomas Brennan is an apparatus and method for synthesizing sequence-defined polymers using arrays for a much lower price than previously possible. These polymers can be used in gene probe assays for the detection of specific nucleic acid sequences.

This invention has had a complex licensing history: We originally licensed the invention to Protogene, which changed its name to Custom Primers. Life Technologies then bought Custom Primers, and Invitrogen eventually bought Life Technologies.

NO. 25 3

ANTIBODIES

Antibody producing cell lines (12E7, L243, L368, L17F12 and 4G7) were developed in 1979 and 1983 in the laboratory of Professor Ron Levy. Licensed as Tangible Research Property, these cell lines are used extensively for research and in vitro diagnostic purposes. With relatively straightforward license agreements and few expenses, they continue to generate significant royalties.





OFFICE OF TECHNOLOGY LICENSING
STANFORD UNIVERSITY
1705 EL CAMINO REAL
PALO ALTO, CA 94306-1106
650.723.0651
[HTTP://OTL.STANFORD.EDU](http://OTL.STANFORD.EDU)