STANFORD TECHNOLOGY BRAINSTORM

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"Giant Fish Tank Filter" Coming to a Gas Station Near You

Stanford has licensed an inexpensive groundwater remediation apparatus and method invented in 1989 that cleans up "Volatile Organic Compounds" (VOCs), organic chemicals that are toxic in high concentrations and carcinogenic in any amount, to NOVOCS (from "No VOCs"), a Sunnyvale start-up company.

Inventors Steve Gorelick and Haim Gvirtzman hope the patented technology will be used to reduce the estimated $752 billion required to clean up polluted soil and groundwater nationwide.

Half the drinking water in Santa Clara Valley and 40% nationally comes from underground sources. VOCs, which include industrial solvents, gasoline, and kerosene, leak from everything from storage tanks at the local gas station to government weapons development installations.

"There are two and a half million underground storage tanks in the U.S., and a good fraction of those leak," says Gorelick, an Associate Professor in the Department of Geological and Environmental Sciences.

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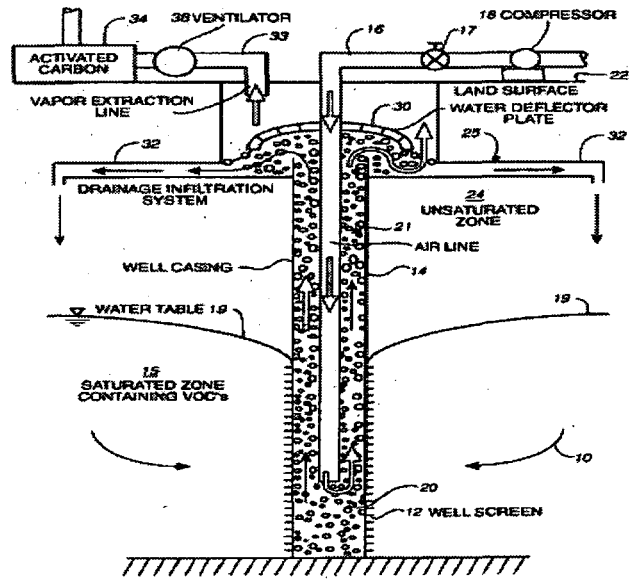

Schematic structure of a well: Air (hollow arrows) is injected into the well. Bubbles rise, become saturated with VOCs, and are collected at the top. Water (solid arrows) is lifted in the well, forced to the unsaturated zone, and eventually flows back to the well.

Phycobiliproteins Light the Way for Research, Diagnostics

They are older than the dinosaurs in *Jurassic Park*, but the technology they now make possible is licensed to 45 companies worldwide and brought Stanford and the University of California over $2 million in royalties last year.

They are "phycobiliproteins," light-harvesting and fluorescent proteins found in blue-green and red algae and now, thanks to three scientists at Stanford and UC Berkeley, used widely for the analysis of molecules and cells.

From Molecular Biology to High Technology

Lubert Stryer, the Stanford professor of cell biology in whose lab the technology was invented, describes the concept as "very bright lanterns that are hooked up to molecules which recognize important cells we want to study."

That's the simple explanation. The other is so complex that Alex Glazer has built his career as a biologist at UC Berkeley studying and describing the basis for it: the mechanisms by which algae gather light deep under water.

It was known by the late 1970s that the phycobiliproteins in algae — phycoerythrin (PE), phycocyanin (PC), and allophycocyanin (APC) — are organized in a complicated pigment-protein complex that transfers energy from light to the algae's chlorophyll for photosynthesis.

What was not known was how this complex is organized, and Glazer set out to map it.

Each phycobiliprotein absorbs light along a different range of wavelengths, and Glazer found that in the complex, energy from the light absorbed by each phycobilprotein is passed on unidirectionally (unusual for a biological system) via electron flow.

Thus energy from the light absorbed by PE is transferred to the PC, where it joins the energy from the PC's own absorption, and so on to the APC and, finally, to the chlorophyll.

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Stanford University
Technology Transfer Through Licensing
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STANFORD TECHNOLOGY BRAINSTORM

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STANFORD TECHNOLOGY BRAINSTORM is published quarterly by Stanford University's Office of Technology Licensing (OTL) to provide information about OTL and general information of interest to the licensing community, both within and outside Stanford.

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OTL's services are available to any Stanford faculty, students, or staff who invent technologies which may benefit the public or be of commercial value.

To find out about a specific technology, or to disclose one of your own, contact us at the above address.

Phycobiliproteins Light the Way...

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Thus algae can absorb light along a broad spectrum of wavelengths and make all its energy available for use in photosynthesis. Glazer also found that PE, PC, and APC exist in different concentrations at different ocean depths, allowing maximal light absorption and, ultimately, the algae's survival.

Meanwhile, back at the Farm, Lubert Stryer was hard at work on a problem: how to simultaneously identify the presence of more than one surface antigen on a cell.

The person who had helped pose this problem was Vernon Oi, a postdoctoral fellow working in both Stryer's lab and the lab of Leonard Herzenberg, another Stanford biologist who was developing a device to separate cells according to various properties (the "cell sorter," another important and successful Stanford invention.)

Before phycobiliproteins, Oi explains, there were only a couple of dyes for sorting. "It was like telling how many people in a crowd have red hair and are right handed," he says, adding that it required two lasers to do even that.

More dyes were needed, Oi says, that would allow one "to tell which of those people are also wearing brown shoes and like chocolate ice cream — all at the same time."

In 1980, Glazer, having met Stryer in 1962 while

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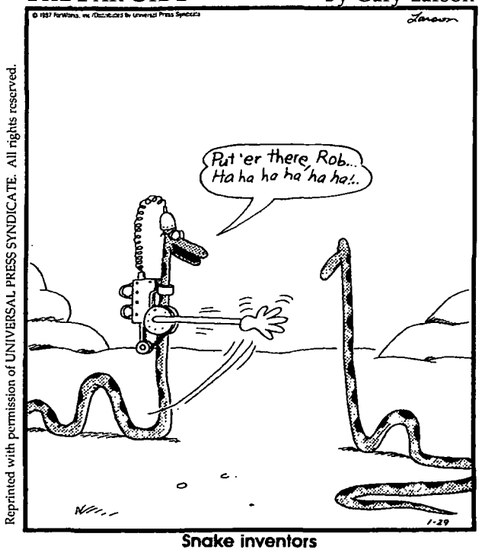
License Agreements Signed by OTL in the Last Quarter

Docket(s)	Title(s)	Uses	Company(s)	License Type
S74-043	"Cohen-Boyer Recombinant Technology"	DNA Cloning — Production of proteins	Cytogen, Inc. GroPep Pty. Ltd. Jackson ImmunoResearch Mitotix; Procept, Inc Triplex Pharmaceutical Tularik, Inc. Ambico, Inc. Interneuron Pharmaceuticals	Non-exclusive
S79-066	"Mouse Anti-Human Hybridomas"	Human therapeutics	Celltech	Exclusive
S81-026	"Fluorescent Conjugates for the Analysis of Molecules and Cells"	Tagging and tracking molecules and cells	Mallinckrodt	Non-exclusive
S85-043, et.al.	"Physical Modeling Sound Synthesis"	Electronic music & sound synthesis	Atari	Non-exclusive
S88-118	"The Correlation Microscope"	Quality control in semiconductor manufacturing	Prometrix	Non-exclusive
S91-140	"Application of Data Clustering Technique to Optical Metrology"		Prometrix	Non-exclusive

THE FAR SIDE by Gary Larson



Snake inventors

Uncle Leland Wants *Your* Biological Materials

BY HANS U.D. WIESENDANGER, SENIOR ASSOCIATE

Many Stanford researchers in the biological and medical sciences may not be aware that OTL can license many of the biological materials developed in the course of their research, thereby generating welcome research funds through royalties.

Biological materials are typically licensed for three different fields of use. The first is for sale as *research reagents*. Such reagents usually generate a large number of relatively small sales and, therefore, relatively few royalties.

However, royalties of tens of thousands of dollars per year are not unusual, and some licenses for only the research market generate as much as $200,000 per year — a nice bit of research money!

A practical advantage of such licensing is the liberation of the researcher from having to provide samples to colleagues who request them, as they become readily available from the licensee.

Another benefit is that the sale of a reagent in the research market will sometimes lead to other specific uses that might not be developed were the reagents not so readily available.

A second area for which biological materials can be licensed is in *diagnostics*, either *in vitro* or *in vivo*. Such materials may, for example, find use in new assays or in imaging applications. Presumably these markets offer a higher potential for sales – and, therefore, royalties – than the research market, but in most cases they also take longer to develop.

Finally, many biological materials can be licensed for *therapeutic* and *prophylactic uses*. These uses are likely to produce the highest royalties, but they typically take the longest to develop, and royalties are often many years in the coming.

Be that as it may, the important point is that *the potential is there for many biological materials to be licensed*. Suspecting that our researchers may have many freezers full of such materials, we believe it's likely that we have received disclosures of only a small fraction of them. We also believe many of those still out there could be licensed.

All researchers are therefore invited to send OTL disclosures of available biological materials they have developed. Disclosure forms are available from OTL on request.

Disclosures should contain accurate descriptions and designations of the materials, as well as any available information about potential uses. Publications or manuscripts (marked "Confidential", if necessary) should also be attached .

Please send us disclosures of YOUR biological materials!

'Giant Fish Tank Filter' Coming to a Gas Station Near You

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The invention was spawned when Gorelick met Gvirtzman, a post-doctoral fellow visiting from Israel. Gvirtzman says he had a problem in that he had no background in microbiology, whereas most American research in groundwater hydrology was concentrated in bioremediation (using waste-consuming organisms to clean up contamination).

"I had in mind to enter the remediation field from the avenue of the simple physics and chemistry of groundwater," Gvirtzman says. "When I met Steve Gorelick — it was BINGO!"

The two began discussing in-situ (within the ground) remediation and, eventually, air-lift pumping. The technology they came up with is called "in-situ vapor stripping," but both describe it as basically a "giant fish-tank filter in the ground" (see diagram).

Traditionally, contaminated water has been cleaned by being pumped above ground, treated, and then reinfiltrated or, since regulations often prohibit the reinfiltration of partially treated water, stored above ground.

The vapor stripping technology functions by pumping air or some other gas down a well, accomplishing two things. First, bubbles are forced up through the water, collecting the VOCs and carrying them up to be pumped off as a gas and treated.

Second, the air forces water upward and outward into unsaturated soil outside the well, where it flows downward into the water table and eventually back into the well.

Thus an entire area is stripped of VOCs, and the costs of above-ground water treatment and storage are eliminated. And the more times the water circulates, the cleaner the area becomes.

The procedure also works quickly, according to Gorelick. At a test site in Hanford, Washington, which currently has a clean-up bill estimated at $36 billion, one cycle should take a week to 2 months, and contamination should be decreased by a factor of 10 after six months to a year.

Another advantage of the technology is that it can be combined with other technologies in a single borehole, according to Gvirtzman. For example, in a second major pilot test in Israel, Gvirtzman hopes to introduce a new gasoline-eating bacteria into the well that devours contaminants ten times quicker than previous bacteria.

Other important advantages of the technique are that it is scalable — from the local gas station to a major installation such as Hanford — and that it can clean deeper than other methods, because air can be forced as deep as can be drilled and rises without assistance.

NOVOCS has already had success in sublicensing the technology to ICF Kaiser Engineers, a large engineering company operating in the United States, Europe, and Asia. And Stanford is already collecting royalties from the license — an unusually quick turnaround for a four-year-old technology.

The Environmental Protection Agency has also been very supportive of the technology and its tests, says Gorelick.

As for problems with the technology itself, Gorelick says simply, "It's the laws of nature — not much can go wrong." It's as simple as, well, feeding fish.

Notice to Department Heads

Distributions of royalties from OTL to departments and schools will appear on the 8/33 Fund Statements, which your administrators should receive around mid-September.

Phycobiliproteins Light the Way for Research, Diagnostics *Continued from page 2*

both were post-doctoral fellows in England, visited Stanford, and Stryer asked his advice on the problem.

Glazer's answer was simple: phycobiliproteins. "They have a unique combination of physical and spectroscopic properties that make them exceptionally well-suited for use as fluorescent tags," he says.

Per molecule, they absorb light many times more strongly than simple organic dyes. They have a high quantum field of fluorescence — that is, they very efficiently convert the excitation energy produced by the light they absorb into fluorescence.

Senior Associate Luis Mejia (right) and his trusty assistant (a.k.a. your trusty Brainstorm *editor) Eric Grunwald, hard at work tracking the nearly $2 million from Stanford's third all-time most successful technology. The story begins on page 1.*

And, like the surfaces of living cells, they carry a negative charge under physiological conditions, so they don't bind arbitrarily to any cell.

"And this is far from a complete list of their favorable features," Glazer hastens to add.

So Stryer, Glazer, and Oi were off and running, testing their innovative concept of attaching ("conjugating") the proteins to monoclonal antibodies — cells that search out other cells based on a particular characteristic, such as an enzyme on the surface of the target cell.

Stryer credits the "wonderful partnership" in coming up with the invention, saying, "It really required three people — no two of us could have done it. Alex understood the biology, Vernon understood the need, and I knew of both their work and made it click."

Stryer did this, adds Oi, in an unusual way: "He put on a lab coat, rolled up his sleeves, and went back into the lab. That's unusual when you consider he's a full professor. Full professors normally sit behind a desk and analyze data — that's how much Lubert believed in the concept." (Stryer describes it simply as "great fun.")

The result, according to Oi: "[Fluorescent conjugates] have permitted a lot of science to be done that previously wasn't doable."

Licensing Success and the Future

Despite its multicolored splendor ("wonderful oranges, reds and greens," Stryer says), the conjugate technology is not a "glamorous" invention like recombinant DNA, according to Luis Mejia, the Senior Associate at OTL responsible for its licensing. "It's a workhorse," he says – a very useful and successful workhorse, however.

Mejia gives much of the credit for that success to Applied Biosystems, one of the first two licensees, which signed up over 25 sublicensees before transferring control of their agreements to Stanford at the end of 1988.

Oi also credits Stryer, who in his view "was one of the few professors who understood the mechanisms and the value of patenting."

What's more, the technology's full potential has yet to be reached. Until now, the market for phycobiliprotein conjugates has been mainly in research reagents – substances used by companies and researchers to do basic science such as determining whether cancer cells are present in a rat.

But the inventors agree the technology has great potential in diagnostics (assays), such as determining whether tumor cells are present, counting the number of white blood cells in the body, or most any other test one might have done in a hospital.

Most such tests are now performed with radioisotopes, which are accompanied by the dangers of radiation. However, replacing them, Oi says, will require great capital investment.

Glazer, meanwhile, sees nothing new on the horizon that might replace the conjugate technology, explaining, "When you are fortunate enough to find a naturally occurring class of molecules that are singularly effective in a fundmental application, you are hard pressed to do better with a [genetic] engineering technique."

Phycobiliproteins may be natural, but as Stryer adds, "Nature never figured we'd be doing the kinds of things we're doing with them."

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