STANFORD TECHNOLOGY BRAINSTORM

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OFFICE OF TECHNOLOGY LICENSING
STANFORD UNIVERSITY

OTL Honors the Inventors of Stanford's Most Successful Inventions

John Cioffi's group were among the inventors recognized by OTL

On February 26, 2002, over cheese and crackers, some of the most innovative people in the world made cocktail party chatter, discussed the intricacies of their world-changing inventions, and toasted each other's contributions to Stanford and to society. They also tried to understand their colleagues' inventions. Electrical engineers struggled to grasp how Phycobiliprotein Conjugates work, and biotechies wondered just what the heck a Tiny Tera is. While these innovators may have worked in vastly different areas of research, they did have something in common; they were responsible for the most successful inventions to be licensed by Stanford, and they were attending a ceremony hosted by OTL to honor them.

OTL's mission is to transfer Stanford technology for society's use and benefit, and to generate income to support future research and education. In our office's 33 year history, we've received over 4,850 invention disclosures, executed 1,956 licenses and brought in over $550 million. Not including our biggest winner, our average license generates $153,000 cumulative. This number is low, because most

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OTL OFFICE OF TECHNOLOGY LICENSING
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Stanford Technology BRAINSTORM is published to provide information about OTL and general information of interest to the licensing community, both within and outside Stanford.

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 learn about a specific technology or to disclose one of your own, contact us by any of the above means.

Inventor Party... *Continued from page 1*

of our inventions are very early stage, and many do not make it to a commercial product. However since OTL began operating, 21 inventions have generated between $1 and $5 million, and 10 have generated $5 million or more.

The ceremony's 100+ attendees represented all aspects of the licensing process, including inventors, patent attorneys, licensees, and OTL staff. The program included the presentation of plaques to the inventors of the technologies that grossed over $5 million from the OTL associate who handled the licensing.

A Selection of Recent Licenses Granted by OTL

Docket(s)	Title(s)	Uses	Licensee(s)	License Type
S02-164	"Identity Based Encryption From the Weil Pairing"	Encryption	Voltage Security	Field Exclusive
S03-087	"Improved Methods for Ranking Nodes in Large Directed Graphs"	Personalized Web Searches	Kaltix	Option
S02-193	"Bi-directional Synthesis of Oligoguanidine Transport Agents"	Drug Delivery	CellGate	Exclusive
S92-053	"HIV PCR Analysis Directs Drug Use"	Monitoring HIV Therapy	Celera Diagnostics	Non-Exclusive
S96-103	"Isozyme selective inhibitors and activators of protein kinase C"	Development of Cardiovascular Therapeutics	Anchora	Field Exclusive

A Selection of Inventions that were honored

Tiny Tera
Inventors: Nick McKeown, Rolf Muralt, Ken Kun-Yung Chang, Shang-tsê Chuang, Pankaj Gupta
Use: Very high speed data switching technology utilized primarily in telecommunications applications.
Licensee: Abrizio, acquired by PMC Sierra

Amplification of Eukaryotic Genes
Inventor: Gordon Ringold
Use: Enhanced production of proteins
Licensee: Widely non-exclusively licensed

Discrete Multitone Modulation for DSL
Inventors: John Cioffi, Jacky Chow, Peter S. Chow, Minnie Ho, Huiling Lou
Use: High speed data transmission over phone lines
Licensee: Amati Communications, acquired by Texas Instruments

Fiber Optic Amplification
Inventors: H. John Shaw and Michel Digonnet
Use: Amplification of fiber optic signals
Licensee: Litton, acquired by Northrop Grumann

Other honored inventions:
Functional Antibodies (Leonard Herzenberg, Vernon Oi, Sherie Morrison), Computer X-Ray Scanner (Doug Boyd), TRIMOS Device (James Plummer)

Transfering Tech Transfer to Finland

By Daniel W. Weinstein

The big boom of technology transfer in the United States began with the Bayh-Dole Act in 1980. Since then, technology licensing offices have been popping up at universities all over the country. Stanford's OTL is among the oldest offices at 33 years old, but the average age of a US office is around 15. In Finland, tech transfer is barely 10 years old, and licensing activity has been very low. Many efforts have been made to help accelerate the success of university technology licensing in Finland, and Stanford's OTL is now playing a part. OTL has established a relationship with two Finnish licensing organizations, Hermia and Finn-Medi, in which we provide assistance and guidance to aid them in establishing their licensing program. In return our office is gaining a presence in Europe and the occasional box of Finnish chocolate.

For a small country, there is quite a bit of high-tech innovation in Finland. Much of that innovation is taking place in universities, and Hermia and Finn-Medi were established to enable the commercialization of university intellectual property. They both have well established incubator programs, and are now trying to establish a licensing business. Hermia is a company of 18 people that was established in 1992 to handle inventions from the Tampere University of Technology. Over the last 10 years, more than 200 startups have been created there. Finn-Medi handles life science inventions from the University of Tampere, Tampere University of Technology and Tampere University Hospital, and works in cooperation with Hermia. They were both among the first university technology licensing organizations in Finland.

The first attempts of technology transfer from university to industry began in Finland as part of a nationwide initiative in 1992. In 1999, after years of slow progress, the Finnish government started a project in the 6 main universities to increase the volume of deals. The main goal of the 3 year project was to strengthen international licensing know-how in Finland. Hermia and Finn/Medi decided that a very important step in meeting this goal was to have a presence in the United States, and they began reaching out to American university tech transfer organizations. In 2000, at the annual meeting of AUTM (Association of University Technology Managers), Antti Juva of Hermia met OTL director Kathy Ku, and a relationship between our offices began.

As part of the collaboration, Antti and Reijo Itkonen, a licensing professional from Finn-Medi, each spent 12 weeks living in Palo Alto and working in our office. They worked along side us and observed how our office operates, learned how we evaluate and market technologies and how we negotiate licenses. Together we determined marketing and licensing strategies for their wide variety of (30) technologies (see back page for some of their more unique inventions).

Antti and Reijo face many of the same issues we do, but because of different laws regarding intellectual property, they also face different issues, or deal with them differently than we do. For instance, in Finland, the inventors own the patents, and often a deal will involve a sale of patent rights. In the US, the university owns the patents, and we license the right to use the patented technology. Ownership of patents almost always stays with the university. Also, the patent process in Europe is different than in the US. In Europe, a patent application must be filed before any publication describing the invention is made (in the US you have

Finland... *Continued on Outside Flap*

OTL 2001-2002 Fiscal Year Numbers

Total royalties received from *Licensees*:	$52.7M
Amount distributed to *Other Institutions*:	$2.5M
Amount distributed to *Departments**:	$13.5M
Amount distributed to *Schools**:	$13.1M
Amount paid to *Inventors* (Individuals)*:	$11.3M
Patent expenses:	$4.9M
Royalties from new licenses:	$1.4M
Number of inventions producing income:	385
Number of new invention disclosures:	315
Total new licenses:	112
Companies Stanford took equity in:	13

* Royalty Income is divided among the inventor, the inventor's department, and the inventor's school. Some inventors designate a portion of their royalty income to their laboratories.

In Other News...

OTL has begun assisting other non-profit institutions with their technology transfer needs. We have formed an LLC to support these collaborations.

Organizations that OTL LLC is partnering with are:

- The Monterey Bay Aquarium Research Institute (MBARI, see Fall 2001 Brainstorm)
- Oceanic Institute (see insert)
- Hermia/Finn-Medi (see page 3)

BRAINSTORM SPECIAL ARTICLE:

Building the Marine Technology Alliance — The Oceanic Institute and Stanford University OTL LLC Form Technology Licensing Partnership

By Luis Mejia and Janet Crawford

Advancing its initial effort to create an international marine technology alliance, the Stanford University OTL, LLC has entered into a technology licensing partnership with the Oceanic Institute, a private not-for-profit research organization dedicated to marine aquaculture, coastal resource management and biotechnology.

The genesis of the partnership began when Martin Anderson, a past Trustee of Stanford University and a current Trustee of Oceanic Institute, visited OTL to plant the seeds of the idea. "We were quite open to Mr. Anderson's idea because of the caliber of OI's scientific staff as well as their important technological achievements", said Luis Mejia, an OTL LLC board member. The partnership further embellishes the nucleus of the marine technology alliance formed when Stanford and MBARI entered into a similar pact in 2001.

"We are extremely pleased to be allied with Stanford's OTL and look forward to a mutually beneficial relationship in such an important area for human kind," said Dr. Thomas E. Farewell, President and CEO of the Oceanic Institute. "We want to make our inventions available to industry quickly and effectively through OTL."

With Oceanic Institute as an Alliance member, the SU OTL LLC is now on its way to building a critical mass of marine technologies. By leveraging its experience, contacts and infrastructure, the OTL LLC's licensing activities will not only contribute to the Alliance members' missions, but also to the greater public good by transferring the technologies for society's use and benefit.

More about the Oceanic Institute...

Adopting innovative technologies

Competitive edge may be gained by adopting innovative technologies that revolutionize industry practices and government policies, bring forth new products, and provide assurance for commercial success. As a generator of cutting-edge marine science technologies, the Oceanic Institute, with its 105 scientific and professional staff, is poised to transfer the findings of its research to private industry.

The Oceanic Institute develops leading technologies through its research in aquaculture, stock enhancement, environmental science, and marine biotechnology. As a tax-exempt corporation, the Institute fulfills its public obligation by helping U.S. firms improve their productivity and profitability in concert with environmental sustainability. The Institute conducts collaborative research with universities, research organizations, and firms of all sizes and also provides professional training and educational programs. The Oceanic Institute is affiliated with Hawaii Pacific University, Hawaii's largest private university.

Extensive R&D facilities

Established in 1960, the Oceanic Institute is headquartered between the mountains and the sea at Makapuu Point, Oahu, Hawaii. This location provides an abundant supply of high-quality seawater in a mild, tropical climate. The Institute's 56-acre, Oahu site includes: modern research laboratories; maturation and hatchery facilities for marine finfish; biosecure breeding and growout facilities for marine shrimp; large-scale algae, copepod, rotifer, and *Artemia* food-production facilities for larvae; an analytical laboratory for water quality and biochemical analyses; and laboratories for aquatic feeds formulation and testing. Located on the island of Hawaii is an isolation facility for marine shrimp.

The stage is set

Around the world fishery harvests have reached a plateau while increases in population and per capita consumption of seafood have intensified the demand. At present aquaculture contributes roughly one-third of the world's edible seafood supply. To meet the projected demand, worldwide aquaculture of fish and shellfish needs to triple 2000 production levels by the year 2015.

U.S. fishery and aquaculture production lag worldwide production, amounting to a $7 billion trade deficit in edible seafood products in 2002, the second largest trade deficit next to oil. Facing seafood supply deficits similar to the worldwide pattern, the urgency to expand the nation's aquaculture industry is manifest.

A key challenge facing the U.S. aquaculture industry is the need for its products to be competitive with low-cost imports. U.S. farmers are faced with limited land and water resources; strict environmental and governmental regulation; and high production costs, labor and feeds in particular. And, as is the case throughout the world, they are faced with an increasing number of diseases that threaten their crops.

Biotechnology advances aquaculture

Biotechnology advances aquaculture and the Oceanic Institute is poised to move technology in this sector to a higher plain that not only assures sustainable operation, but also compatibility with the environment. The application of biotechnology and modern scientific tools to the culture of marine shrimp and fish results in a competitive edge for the U.S. aquaculture industry. Seafood that is plentiful and of superior quality can be produced economically.

Biotechnology provides the means to develop disease-resistant aquatic animals, manage the health of cultured animals, perform molecular breeding of commercially important species, maintain genetic diversity of captive broodstock, improve spawning of cultured animals, enhance the efficacy of feeds, maximize the usefulness of naturally occurring microbes, and minimize environmental impacts.

The future holds great promise

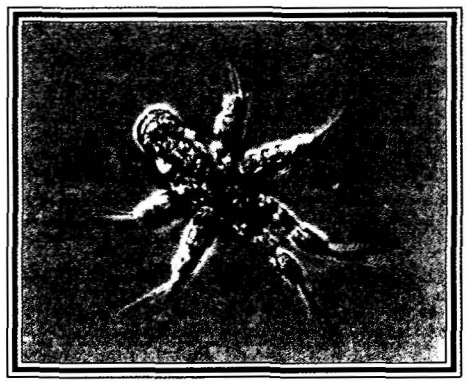
Exciting opportunities on the horizon hold great promise for the aquaculture industry. New laboratory discoveries have the potential for vastly improving the quality, quantity, and nutritional value of aquacultured products, farm productivity, and industry profitability. Current research at the Institute provides an insight to future successes.

Larval rearing technologies: a critical link

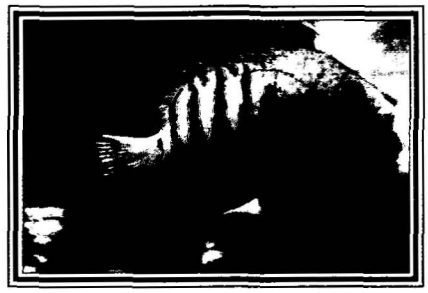
Groundbreaking advances in the culture of commercially promising, yet difficult-to-rear, marine food fish and marine ornamental fish are being made at the Oceanic Institute. Among the technologies that show great potential are those supporting the critical first feeding of small, rapidly growing, predatory larvae that actively consume microscopic, live prey. If these larvae do not eat the right food, they die, and the link to maturity is broken.

A variety of single-celled marine plants (microalgae) and small invertebrate organisms (zooplankton) are used to create the food chain necessary to sustain marine fish larvae. Microalgae nourish the zooplankton on which the fish larvae feed and provide a healthy environment for the fish larvae. Unfortunately, zooplanktonic prey that are conventionally used in aquaculture are unsuitable for the first feeding of small larvae.

In a major breakthrough, scientists successfully isolated a particular zooplankton directly from the local reef environment—a type of copepod—that is small enough and that provides the proper nutrition for the difficult-to-rear species. The critical process developed at the Institute, now under patent-pending status, is the mass culture of this copepod to ensure the availability of live prey in quantities large enough to feed hatches of thousands of eggs, thus yielding high survival production rates.



Copepod nauplius cultured at the Oceanic Institute to provide nutrition for the critical first feeding of marine food fish and marine ornamental fish



Flame angelfish broostock used for pioneering research at the Oceanic Institute that successfully reared juvenile angelfish in captivity

Marine ornamentals: an immediate application

Playing a pivotal role in warm-water aquaculture development in the United States, the Oceanic Institute is achieving major advances in culture techniques for small, sub-tropical, marine ornamental fish. These ornamental fish are prized for their colorful beauty and are now removed

from the wild by collectors and dealers, thus destroying the biodiversity of the reefs and the sustainability of the species. There is a great need for the culture of these ornamentals.

Researchers have progressed in the domestication of spawning populations of several, signature, Hawaiian reef fish species (pygmy angelfish and yellow tang), and the Institute has documented the first natural spawning of yellow tang under aquaculture conditions. Greater success in rearing ornamental fish larvae was achieved by using the recently isolated and cultured copepod. The Institute's researchers reared the world's first juvenile flame angelfish in captivity, an achievement that will pave the way for the commercial culture of other marine ornamental fish.

Microbial biocomplexity

There is great promise in current research that provides an understanding of microbes and their effect on the complex balance of the marine aquaculture environment. Research underway on the production of marine shrimp is yielding technologies that are revolutionizing the shrimp industry and that are applicable to the culture of similar marine crustaceans, bivalves, and mollusks.

Proper balance of a beneficial microbial consortium that occurs naturally in pond water maintains acceptable water quality in a production facility, enhances rapid marine animal growth, and supports high survival rates. The microbial consortium is comprised of phytoplankton, bacteria, and protozoa that fluctuate throughout the shrimp growout period in response to environmental changes such as amount of light, level of aeration in the water, and protein content of the formulated feed.

In research trials, controlling the synergistic effect of specific algae and bacteria in a closed, recirculating, super-intensive, shrimp growout raceway has produced shrimp that grow twice as fast as those grown under traditional farming methods and has produced ten times the amount of shrimp as traditional shrimp farms.

Diatoms are an example of the potentially beneficial microorganisms for shrimp production that are under research by the Oceanic Institute

Sustainable, environmentally responsible shrimp production: BioZEST™

The vision of developing a shrimp production system that is environmentally responsible and economically viable has become a reality at the Oceanic Institute. Scientists have developed a unique process for the production of shrimp in a system that excludes pathogens, has low water usage, is environmentally friendly, and has high yields.

The Institute holds a patent on its innovative "Biosecure Zero-Exchange System for Maturation and Growout of Marine Animals." The process takes advantage of the synergistic effect of specific-pathogen-free shrimp; in situ microorganisms; specially formulated feeds; disinfected culture water; and an enclosed, biosecure, zero-water-exchange growout facility.

The facility recirculates salt water rather than using a traditional flow-through system. Due to its drastically reduced requirement for water, the system can be adapted for operation inland, away from environmentally sensitive coastal areas.

Optimal aquatic feeds

The development of optimal aquatic feeds is key to the success of commercially sustainable aquaculture, not only from the standpoint of providing requisite nutrition, but to minimize waste, reduce cost, alleviate reliance on fishmeal proteins, and function synergistically with in situ microorganisms.

The "Tropical Aquaculture Feeds and Culture Technology Development Project II: Development of Shrimp Feeds" stresses the importance of the interactions between the cultured animal and the culture system. The major areas of research include shrimp nutritional requirements, nutrient flow and sinks within pond systems, feeds and ingredient processing technology, ingredient characterization, feeds management, pond management, statistical and economic modeling, and production system models.

Economic and environmental benefit can be attained for the seafood harvesting industry by using fish by-catch and fish processing waste. Within the cooperative project "Alaska Fisheries By-Product Utilization," the Oceanic Institute will be devising processes that convert fisheries by-products into higher-quality, secondary products such as fishmeal, fish oil, bone

meal, stickwater, and hydrolysates in order to incorporate these secondary products in innovative feeds and other products for agriculture and aquaculture.

Selectively bred, marine shrimp

Selective breeding strategies for marine shrimp produce genetically improved lines, thereby promoting the expansion of a sustainable shrimp aquaculture industry in the U.S. Using artificial insemination, families of shrimp are bred for specific traits such as resistance to disease (Taura Syndrome Virus), rapid growth, and tolerance to low-salinity environments.

Working in collaboration with the U.S. Marine Shrimp Farming Consortium, the Institute developed and continues to produce selectively bred, specific-pathogen-free (SPF) Pacific white shrimp. The SPF shrimp bred at the Institute are certified to be free from nine different pathogens, principally viruses that are harmful to shrimp. The next step is the development of SPF cold-water tolerant shrimp for farming as a winter crop or for farming in northern regions.

Offshore, submerged-cage culture

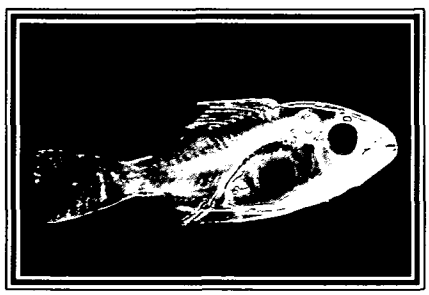
Research projects to examine the biological, environmental, and economic feasibility of open-ocean, submerged-cage aquaculture in Hawaii using Pacific threadfin, an indigenous species, have yielded the first such commercial venture in the United States. Following on that success, the Institute plans to research a second foodfish species in the summer of 2003. The new project will focus on the use of greater amberjack, another indigenous and highly desirable species.

Applied research conducted at the Institute on marine fish reproductive development and captive spawning is leading to these advances in commercial aquaculture. Changes in fish physiology are documented to allow scientists to resolve biological, chemical, or environmental issues that may be blocking the reliable spawning of fish in captivity. Pilot-scaled research facilities onsite will enable scientists to perfect the technology for large-scale amberjack production, thereby removing the risk of failure from the commercial sector.

Fisheries restoration

The Institute is conducting one of the most documented research programs in the U.S. designed to develop and demonstrate technologies that can be used by appropriate state or federal agencies as options for the restoration of depleted fisheries and the management of wild stocks. Using Pacific threadfin as a test species, the "Hawaii Stock Management Program" emphasizes six major areas of research: culture technologies, release optimization, ecosystem interactions and habitat utilization, behavior and conditioning, genetic management, and the ecological basis of fisheries production.

A collaborative research project in the U.S. coastal waters of the Gulf of Mexico aims to develop stock enhancement and habitat restoration resource-management tools that can be employed by appropriate state or federal agencies as options for the restoration of depleted fisheries. Working with red snapper, the "Gulf of Mexico Marine Stock Enhancement Program" examines demographics and ecology, genetics, animal health and disease, culture methods, behavior and conditioning, release and recovery strategies, fish tags and tagging procedures, cost benefits, and experimental releases.



Red snapper juvenile reared at the Oceanic Institute from domesticated broodstock that spawn naturally, year-round

All photos courtesy of Oceanic Institute

Finland... *Continued from page 3*

a year after publication to file). Therefore a decision must be made very early on whether or not to file any patent applications. And because Finland is a small market, foreign patent applications are typically necessary. Filing many foreign applications can be very expensive, which makes the decision that much more important.

There is also a difference in culture. Antti was shocked at the casual dress in our office, and how expensive the Bay Area is. On his first trip he brought nothing but suits, and spent his first night at the Stanford Mall trying to find more casual Silicon Valley-wear. Business in Finland tends to be very formal. As one who pushes our office's casual dress code to the limits, I was a little embarrassed to learn that what I wore every day would have been found offensive in Finland (it's rude to have your undershirt showing). The Finn's style of communication is also different. Small talk is usually avoided in Finnish business interactions, which means many OTL associates wouldn't do very well there.

The experience has been a great one for both US and Finnish tech transferrers alike. Antti and Reijo have each expressed how helpful they thought this experience was. In addition to getting help with their inventions, they made many contacts with venture capitalists, potential licensees and other parties involved in tech transfer, which they felt was invaluable. Likewise, we feel fortunate to be collaborating with Reijo, Antti and their organizations. Several OTL staff members have visited Finland to learn more about their process, and to educate others there about ours. We have established both an important working relationship and friendship with Antti and Reijo, and we're excited to see the progress they've made. Since their visits, Hermia has become a private company, and has successfully negotiated its first license.

OTL's Mary Watanabe and Daniel Weinstein (right) try to recreate the Finnish Midsummer Holiday for Antti Juva (center) who was visiting Stanford during this special Finnish Holiday in June.

Technology Spotlight: Finnish Inventions

By Jacqueline Tay

The following are a selection of inventions handled by Hermia and Finn-Medi.

Every inch counts

The world's first automated long jump landing pit, the AccuLevel, promises to put pit-rakers out of work. Currently, competitive track meets use a two-man team of rakers to even the sand in the pit after someone has jumped. Used in the 1996 Olympics, the automated pit-raker/smoother can smooth the sand to the same exact level after every jump with a level of precision far beyond that of raking by hand. The evenly packed sand is a softer target for jumpers, making injury less likely. The improved accuracy of this rake in combination with its speed promise to make it a valuable commodity at future track meets. Stanford installed two of these landing pits in February, just in time for the NCAA Championships, the US Open and the US ATF Junior/Senior Nationals.

Micro-movements

From molecule to atom to subatomic particle, the shift in focus from the macro to the micro scale has resulted in a demand for more accurate visualization and manipulation of smaller objects. This micromanipulator facilitates the automatic handling of microscopic objects via computer controls. The object of interest can be either biological or mechanical in nature, for example, injecting a single biological cell with a drug or assembling hybrid micro-electro-mechanical (MEMS) devices. Its unique design allows it to be used in conjunction with other devices attached to the end of a microscope or with additional micromanipulators to manipulate various objects simultaneously. The nanometer resolution on all three axes allows for accurate visualization of the object and the use of injection pipettes allows less frequent cleaning or changing compared to using a single micromanipulator. Due to its efficient and innovative design, this micromanipulator is also cost-efficient.

Walking through walls

This new invention called WAVE uses fog to create a physically penetrable walk-through display. The fog screen is made up of a laminar airflow created by fog particles injected from nozzles. Images from a projector can be cast from the front or the rear onto this fog screen to create walk-through or large-scale screens for indoor and outdoor uses. Among the possible uses for a screen like this are the creation of virtual rooms, simulators for military exercises, walk-thru advertisements, public presentations, museums, theaters, amusement parks and sporting events. To see how the fog-screen works, please visit:

http://www.cs.tut.fi/~ira/wave.html
and
http://www.abc.net.au/science/news/stories/s696846.htm

For more information on these technologies please visit www.hermiayrityskehitys.fi/english/offers.html or contact Antti Juva (antti.juva@hermia.fi).

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