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The winners of the European Inventor of the Year 2006 awards

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Part I

The winners of the European Inventor of the Year 2006 awards

An international jury chaired by former Netherlands Prime Minister Wim Kok has selected the first-ever winners of the European Inventor of the Year award from six different categories on the basis of outstanding technical inventions for which the European Patent Office granted a patent a patent between 1991 and 2000 (see [IP/06/558](#)).

The jury is composed of:

- **Wim Kok, Netherlands (chairman)** (Former Prime Minister of the Netherlands)
- **Gilles Capart, Belgium** (chairman of the board of PROTON Europe)
- **Dimitri F. Dimitriou, UK** (founder and CEO of DyoDelta Biosciences)
- **Leif Edvinsson, Sweden** (CEO of Universal Networking Intellectual Capital - UNIC)
- **Robert Peugeot, France** (Executive Vice President, Innovation and Quality at PSA Peugeot-Citroën)
- **Maive Rute, Estonia** (Deputy European Commission SME Envoy)
- **Paul Rübzig, Austria** (Member of the European Parliament since 1996)

More information on the **jury**:

http://www.european-inventor.org/european_inventor_of_the_year_jury.php

More information on the **18 nominees** for the awards

[IP/06/480](#)

The six winners are

Category "Industry"

Zbigniew Janowicz and Cornelius Hollenberg (Rhein Biotech, Düsseldorf, Germany)

Yeast Technology Helps Fight Against Hepatitis B

Scientists at Rhein Biotech invented a method for making proteins in Hansenula yeast, which is used as a key component in the production of an affordable Hepatitis B vaccine. More than 450 million doses of the WHO-qualified vaccine have since been sold in over 90 countries to date, helping combat the spread of the disease.

According to World Health Organization estimates, more than one third of the world's population is infected with Hepatitis B. Worldwide, 350

million people are chronic carriers of the virus. The disease can result in liver cirrhosis or cancer and in some cases, can be life-threatening. It can be transmitted by sexual contact, shared needles, or contaminated blood products. Doctors, or those working with blood, are at risk.

Prophylactic vaccination is generally considered to be the best means to control the spread of this severe, viral liver disease. However, existing recombinant vaccines were considered too expensive for mass vaccination programmes until scientists came up with a new, cost-effective vaccine technology.

The scientists, namely Zbigniew Janowicz, and Professor Cornelius Hollenberg, invented a process for the production of foreign proteins in *Hansenula* yeast. The technology allows for a high-yield production process. The result is a pure vaccine, which is free of pathogens and can be safely administered without using a needle. The method is deemed essential for the development of recombinant gene expression and processes for the production of proteins, especially active pharmaceutical ingredients.

The *Hansenula* technology was granted a patent in 1994. A number of commercial biopharmaceutical and biotech applications now use *Hansenula* polymorpha yeast expression technology. The method is acknowledged as an industrial standard for protein production.

The invention of *Hansenula* technology enabled the introduction of standard vaccination programmes to counter the spread of Hepatitis B disease worldwide. Rhein Biotech GmbH, a spin-off of the University of Düsseldorf, first developed a 3-dose Hepatitis B vaccine using the method at the start of the 1900s. The company then licensed the technology to Korea Green Cross, one of its subsidiaries. Korea Green Cross became the first company to offer an affordable Hepatitis B vaccine for mass vaccination programmes offered by international health organizations, such as UNICEF, for newborn children and infants.

In 1997, the World Health Organization (WHO) certified the Hepatitis B vaccine.

Rhein Biotech has granted numerous research licenses and commercial licenses for the use of its *Hansenula* technology to companies including Serum Institute of India, Wockhard Limited (India) and Aventis Pasteur.

On the basis of its 3-dose Hepatitis B technology, the biotech company additionally developed a 2-dose Hepatitis B vaccine with a much faster onset of immuno-protection. The new vaccine will enter clinical trials at the end of 2006.

Rhein Biotech has become the third largest global producer of Hepatitis B vaccines worldwide. The success of *Hansenula* technology enabled the company to list on the Frankfurt Stock Exchange in 1999.

In addition to Hepatitis B vaccines, Rhein Biotech has developed production technologies for three other biopharmaceuticals, all based on *Hansenula* technology: Interferon alpha-2a, human insulin and Hirudin. The company's licensees have successfully introduced the products into the market.

Further biopharmaceuticals may yet be developed using the technology. In the meantime, this invention has helped combat the spread of Hepatitis B worldwide through the development of a cost-effective vaccine production process, thanks to the work of scientists at Rhein Biotech.

Category "Small and medium-sized enterprises"

Stephen P.A. Fodor, Michael C. Pirrung, J. Leighton Read and Lubert Stryer (Affymax, Netherlands)

The Rosetta Stone of Functional Genetics: the DNA chip

While working at Affymax, a Dutch company, Dr Stephen P.A. Fodor shook the scientific community in the early 1990s with his invention of the DNA chip. Nothing short of a revolution in medicine, researchers are now able to look at genes tens of thousands at a time instead of just one at a time.

VLSIPS: A not-so-familiar abbreviation for Very Large Scale Immobilised Polymer Syntheses. Though few would recognise the invention by that name, few would fail to recognize it by its shortened, simplified name – the DNA chip. A breakthrough in the field of biochemical analysis, the theory behind the DNA chip is the notion that semiconductor manufacturing techniques could be united with advances in combinatorial chemistry to build vast amounts of biological data on a small glass chip.

Once on the chip, the data could then be used to identify susceptibility to diseases with a genetic component and to identify pathogens or other biological agents based on their respective genetic signatures. The DNA chip journey started at a European firm in the late 1980s, with Dr Stephen P.A. Fodor at the head of a team of scientists that included co-inventors Michael C. Pirrung, Leighton J. Read and Lubert Stryer. Fodor, a native of Seattle, Washington, received his PhD in Chemistry at Princeton University before joining Affymax, a Dutch company, in 1989. Fodor was recruited to work at the Affymax Research Institute in Palo Alto, California, a wholly owned subsidiary of Affymax, and it was there that he began

spearheading the research that eventually led to the invention of the DNA chip. At the core of the idea was the adoption of the same photolithographic technologies used by Silicon Valley computer chip manufacturers, but in this case used for the purpose of rapidly generating many different peptide or oligonucleotide compounds.

A single DNA chip measuring 1.28 cm by 1.28 cm, for example, can hold more than 400,000 of these "probe" molecules, allowing biologists to carry out huge numbers of experiments at the same time. Researchers are now able to ask questions across a whole genome at once instead of just a few genes at a time, and perform research in hours that used to take weeks, months – or even years. Commercial potential of the DNA chip was evident from the early stages, and Fodor quickly found himself entrepreneur in addition to scientist. In 1993, Affymetrix, a spin-off of Affymax, was created, and by 1994 manufacturing and sales were underway.

From its founding, Affymetrix relied heavily on government grants to secure funding for its research, taking in over \$30 million. The company also netted \$60 million in two rounds of private funding, and a further \$90 million through its initial public offering (IPO) in 1996.

Though revenues were still slim for Affymetrix in the year of its IPO, at just \$25 million, by 2001 the company was shipping between 5,000 and 10,000 DNA chips per month. Today Affymetrix employs around 1,000 people, and Fodor, now the company's CEO, can boast of global revenues nearing the \$400 million mark.

From the beginning, Affymetrix established a reputation for methodically and aggressively creating protection for its core technology through its intellectual property portfolio. By the end of 2000, it held 150 patents and earned ten percent of its income from license fees and royalties. The patent for the DNA chip was filed in Europe in August 1994 (EP0476014). It was a significant period in science: The Human Genome Project was in full swing, receiving considerable attention both in the inner circles of the scientific community as well as in the mainstream press.

Today Affymetrix's products are used by pharmaceutical, biotechnology, agrichemical, diagnostics and consumer products companies, as well as academic, government and other non-profit research institutes.

The chips are being utilised in a number of basic and clinical areas of research, including the detection of drug resistant mutations in infectious organisms, the monitoring of multiple human genes for cancer associated mutations, and for providing new insights into conditions ranging from diabetes to heart disease.

It's been called the "Rosetta Stone of Functional Genetics," and Fodor and Affymetrix have been credited with providing systems that enable scientists to improve the quality of life.

Category "Research Institutes/Universities"

Peter Grünberg (Jülich Research Centre, Germany)

Driving Into the New Millennium: the Giant- Magnetoresistance effect

An advancement of its predecessor, magnetoresistive head technology, Giant-Magnetoresistance Effect (GMR) vastly increases the data volume stored per square inch of hard drive. The invention enabled an up to fifty-fold increase in the hard drive capacity of typical workstations.

In 1988, Professor Peter Grünberg made a discovery that would go on to set a new standard for next-generation hard drive storage. In fact, the impact of his invention is omnipresent today, affecting numerous areas of everyday life, from computer use to mobile entertainment.

Grünberg, to this day a leading physicist at the Jülich Research Centre in Germany, saw his patent published in 1994. Four years later he was awarded the German Future Prize for his invention, which has in no small way gone on to revolutionize data storage.

An advancement of its predecessor, magnetoresistive head technology, Grünberg's Giant-Magnetoresistance Effect (GMR) vastly increased the data volume stored per square inch of hard drive. The invention enabled an up to fifty-fold increase in the hard drive capacity of typical workstations (from approximately 10 GB in 1997 to between 100 and 500 GB today). But Grünberg's invention also paved the way for the commercial production of hard drive video recorders and the ongoing development of MRAM, a technology that will enable computers to boot instantly.

The emergence of lightweight miniature hard drives also ushered in a new epoch for compact mobile devices, such as MP3 players and digital cameras. Take, for example, the pocket generation and the transformation of sales at Apple, manufacturer of the world's best known MP3 player, the hard drive-based iPod. In Q1 of Apple's 2006 fiscal year, the iPod generated revenues of \$2.9 billion, a 51 percent share of the company's total revenue.

So how does the underlying technology work? Data on a hard drive is layered onto hard drive platters and stored as a consecutive sequence of magnetised areas, each of which has one of two possible polarisations which constitute the smallest unit of digital data – the bit.

The sequence of the polarisations on the rotating platter represents the data's digital code, which is accessed by a read head, a process resembling a stylus playing a record on a record player.

The read head works by measuring the voltage of the electric current induced by the bits. The easiest way to improve a hard drive's storage capacity is to use smaller magnetised areas, but these have weaker field strengths and corresponding voltages which are more difficult for the read head to detect.

This is where GMR comes into play as an affordable new method for detecting even very small magnetic fields. With GMR, the read head consists of a sandwich of two ultra-thin ferromagnetic layers with a third non-ferromagnetic layer in the middle. When the first of the two magnetic layers comes into proximity with the bit on the platter, the pole of the magnet of the layer is realigned so that its polarisation is changed according to the polarisation of the bit.

Meanwhile, the second ferromagnetic layer is permanently magnetised and detects the magnetic field direction of the magnet in the other layer which is reading the bit. An electric current then passes through the two magnetic layers. When the two magnetic layers have the same magnetic field direction, resistance is low and voltage is high; when they have opposing magnetic field directions, resistance is high and voltage is low.

With previous technologies, smaller bits were unable to be read because the magnetic field was too weak for the read head to detect. GMR, however, enables the measurement of weaker magnetic fields and thus a decrease in the size of the magnetised area.

IBM became the first licensee of GMR in 1995 and launched its first product in 1997. This new technology caused the price of 1 MB memories to plummet, from 20 cents in 1997 to less than half a cent in 2001. During that same period, the global revenue for hard drives grew by 66 percent, from \$126 million to \$209 million.

Today more than 90 percent of all hard drive read heads are based on Grünberg's discovery. However, this versatile technology has also been successfully used in devices other than hard drives, notably non-volatile memory chips and a variety of sensors ranging from ABS brake systems to currency handling applications and medical implants.

Category "new EU member states"

John Edward Starrett, John Martin, David Tortulari, Joanne Bronson and Mutzamil Mansurin (Academy of Sciences of the Czech Republic, Prague)

Easing the Pain: prodrugs of phosphonates

These chemical compounds have novel anti-viral properties which can be administered orally, thereby increasing their effectiveness against viruses such as HIV or hepatitis B.

These days there is seemingly no getting away from the importance of producing and stockpiling antiviral drugs for a plethora of existing and future diseases and viruses. For a while it was SARS, currently we're in the grip of a mounting panic over the H5N1 strain of bird flu, and HIV/AIDS continues to devastate lives around the world.

As a result, scientists are constantly trying to find new and innovative ways of dealing with such infectious diseases. One key aspect of their work is the development of drugs that can effectively help body cells affected by a disease while at the same time remaining benign to healthy cells. This is where a breakthrough on the so-called prodrugs of phosphonates by John Starrett and others has made significant inroads. What's novel about the work of these scientists, which was patented in 1998, is that it enables the activation of some phosphonates, or chemical compounds, by placing chemical groups on the administered drug which then activate the desired effect. In short, Starrett and his team managed to change the building blocks of the natural molecules setting free anti-viral properties. The patent is now held by the US pharmaceuticals firm Bristol-Myers Squibb, and Starrett works for the company as a research fellow in the Neuroscience Chemistry group. Indeed, while the virus may still be able to recognise the drug that is making its way into the bloodstream, the different makeup of the building blocks means the virus can no longer replicate and spread. While that sounds simple enough, it's actually a highly skilful process.

"The art is to put the right entity of the prodrug on the right side of the drug," said Jan Balzerini, professor of virology and chemotherapy at the Rega Medical Institute in Leuven, Belgium.

In the past, doctors have struggled with the fact that some drugs also displayed distinct anti-tumour activity and a broad spectrum of antiviral possibilities. This required several metabolic steps to make them efficient. But doctors faced another problem: How to administer the drug.

"Not many patients like injections, and the effect is counter-productive," said Patrick Chaltin, technology officer at the Rega Medical Institute. "But

this patent, this so-called prodrug, can be given orally and it has a high solubility. And that's what makes it innovative."

Balzerini agreed that the novel orally active prodrugs turn it into a different ballgame altogether: "In the past, the problem was that only a few percent of orally absorbed phosphonate drugs filtered through to the area of the malignant cells they were supposed to get to. The development of this prodrug, however, increases that selectivity ten- or even twenty-fold."

Not only does the theory sound great, but the invention also works in practice. In 2001, US biopharmaceutical company Gilead Sciences launched the drug Hepsera, a prodrug to treat chronic infection with hepatitis B virus (HBV) in adults. And it seems to be doing exactly what the patent's inventors – one of whom is John Martin, now CEO of Gilead – had anticipated: Blocking an enzyme that is necessary for the virus to replicate in the body helps stop the hepatitis B virus from multiplying.

"Previous medicines used to treat chronic hepatitis B were largely ineffective due to their poor toleration or the fact that the virus became resistant to them," said Professor Stephanos Hadziyannis, MD of the Medical Department at Henry Dunant Hospital in Athens. "However, with Hepsera we've noticed a marked improvement in efficacy against the virus and a distinct slowdown of the infection." Sales and revenue figures for 2004 also show that this particular prodrug is making an impact.

In the United States, Hepsera achieved annual revenue of almost \$56 million, a 61 percent increase over 2003. Worldwide the product achieved revenue of \$113 million, an increase of 12.3 percent over the previous year. According to Gilead Sciences, more than 400 million people worldwide suffer from chronic hepatitis B. An estimated one million die each year as a result of the infection.

This means that for many patients, the breakthrough on prodrugs will help ease their suffering.

Category "Non-European inventors"

Larry Gold and Craig Tuerk (NeXstar Pharmaceuticals, Boulder, USA)

Getting a Grip: the SELEX-technology

The inventors discovered that nucleic acids can bind to a protein to potentially intercept proteins that cause disease

For sufferers of age-related macular degeneration – the leading cause of blindness in people over fifty – the discovery American scientists Larry Gold and Craig Tuerk made in a Colorado University laboratory in 1989 may be life altering. Gold and Tuerk developed a process which they would name Systematic Evolution of Ligands by Exponential Enrichment. SELEX (Patent EP0533838, date of publication and mention of the grant of the patent December 3, 1997) was the discovery that nucleic acids could bind to any protein, and therefore potentially bind to and intercept proteins that cause disease.

Sixteen years later, Macugen (pegaptanib sodium injection) was launched in the US, and as of February 2006 it is legally deliverable as an approved drug in Europe. The drug – which uses Gold and Tuerk's discovery – slows or sometimes even halts "wet" age-related macular degeneration by blocking an essential signal that causes abnormal blood vessels in the eye to grow and leak. It is these leaking, or "wet," blood vessels around the centre of the retina that cause blind spots and blurred vision in AMD sufferers.

"It's a very significant step forward because it treats a patient group for which there is no currently recommended treatment," said Adnan Tufail, a consultant ophthalmologist at Moorfields in the United Kingdom, the largest specialist eye hospital in the world. He noted that the closest existing treatment, Verteporfrin, works for only one quarter of the sufferers whereas Macugen could potentially treat everyone.

While there is much interest in the drug from eye doctors, it was initially hoped – back in that Colorado laboratory, and in the companies which Larry Gold subsequently formed – that SELEX would lead to drugs to treat cancer and AIDS. However, scientists working at Gold's NeXagen company (which later became NeXstar Pharmaceuticals) found it difficult to create an aptamer (a molecule that can bind to another molecule) that was both cost-effective and would behave as they wanted.

Meanwhile, venture capitalists Warbug Pincus pressured Gold to develop applications which could potentially yield greater returns, and that meant high-profile diseases such as cancer.

It wasn't until Gilead acquired NeXstar in 1999 and teamed up with (OSI) EyeTech that the push to use the breakthrough as the basis for an AMD treatment really began. During its first ten weeks on the American market (OSI) EyeTech was showing a gross product revenue for Macugen of \$25.4 million. "In just ten weeks, we believe that Macugen has changed the treatment paradigm for neovascular age-related macular degeneration," claimed Eyetech CEO David Guyer in the company's 2005 (first quarter) financial report. The Bull Market Biotech Investor, which publishes long-term investing advice, is slower to jump on the bandwagon, stating: "Some analysts have projected that Macugen sales may reach \$1 billion per year, which appears to be an aggressive estimate for a drug that only addresses the wet form of AMD."

With Macugen trials across Europe now complete and its EMEA approval secured, it is now down to local agencies in each European country to decide whether the costs and benefits of the drug make it feasible for their particular territory.

"Various (European) countries at various points over the next year will gain access to Macugen," said Elisa Artime, a Macugen representative in the UK.

And with the first patients in Britain already receiving treatment, it looks as though Europeans will soon know whether Macugen really is the revolution in AMD treatment that many hope it will be.

Meanwhile, the two inventors have taken very different career paths since their discovery: Tuerk left NeXagen in 1994, many years before his invention would ultimately lead to Macugen. He currently teaches biochemistry and genetics at Kentucky's Morehead State University.

His colleague, Gold, is the founder of SomaLogic, where he continues his work on aptamers. Dr. Gold was made a member of the American Academy of Arts and Sciences in 1993, and the National Academy of Sciences in 1995.

Lifetime achievement

Federico Faggin (Italy) - the father of the microchip

"A work of intellect and love"

A small chip with a huge impact: without Federico Faggin's contribution to microelectronics, there would be no PCs and no modern cars. The engineer fought tenaciously for his idea.

By the time he appeared on the scene, everything – in a sense – was already too late. In 1970, Intel's developers had fallen behind in the microchip stakes, and catching up seemed almost impossible. One colleague claimed that the development of a microprocessor had been completed, and disappeared on a business trip, although in fact nothing was finished. A Japanese client, seeing that the chip would not work in his pocket calculators, became furious and, abandoning Japanese decorum, noisily accused his business partner of incompetence. That was the starting signal for Federico Faggin, who had only just joined the company. Working 12 to 16 hours a day, he struggled heroically to carry out his mission. He had invented the metal-on-silicon microprocessor some years before when working for Fairchild Semiconductors. But no one had yet managed to fit an entire CPU on a single chip.

Clearly, however, it was only a question of time before someone succeeded in doing just that. So Faggin went for the prize. Inventing, he says today, is "a struggle between the believers in an idea and those who have something to lose by it. You have to believe in the idea passionately enough to carry on. It is a work of intellect and love." Six months later he had found a way of accommodating microcircuits on a chip, and Intel was soon able to produce the first wafers for its 4000 chip family. But the first run was a disappointment: one of the masking layers had been omitted in the wafer processing, and the chip did not work. Faggin's hands were trembling when the next batch arrived. He tested the wafers one by one in the lab until three o'clock in the morning, his excitement mounting as he gradually found that nearly all of them were usable. He remembers exactly how he felt: "I went home in a strange state of exhaustion and excitement. All that work had suddenly paid off in a moment of intense satisfaction." In March 1971, when the first microprocessor was shipped to Japan and became a commercial reality, Faggin already realised that the new chip had many other potential applications. But it would need to be mass-produced, cheaply and not just for one manufacturer. Others took a different view: the single-chip CPU was not greeted with enthusiasm. "Engineers who designed the early microprocessors fought technical battles and management indifference. Nevertheless, I persuaded Intel's president to market the 4004."

Even the critics now see the microchip as the most important invention of the twentieth century. Without it, there would be no computers, no calculators, no modern cars. Billions of the miniature digital helpers are in circulation. The legendary 4004 and its successor were only the start of the revolution, and the real breakthrough for Intel and the industry as a whole came later, with the next generation of chips developed by Faggin as Intel's head of R&D. But the inventor was not content to rest on his laurels. The physics PhD and electronics expert is a typical engineer – never satisfied with the finished product and always on the lookout for ways of improving it. The logical next step was to set up his own company, Zilog, in 1974, which was totally dedicated to the microprocessor market. Zilog filed 27 patent applications, and its Z80 CPU outperformed the subsequent range of chips from Faggin's previous employer, but also put an end to his career as an engineer. When Zilog set up as a rival to Intel, Faggin moved away from R&D to become an entrepreneur and CEO. He has headed three start-ups, and recently became chairman of the board of his latest venture, Synaptics, a developer of user interface solutions for mobile computing and entertainment devices. His native country has paid tribute to him with honorary doctorates in computer science and electrical engineering from the universities of Milan and Rome – and his pioneering work has earned him a place in the National Inventors' Hall of Fame.