

Who's who in biotech

K S Jayaraman, Sabine Louët, Kendall Powell, John Ransom, Cormac Sheridan, Brian Vastag & Emily Waltz

Nature Biotechnology's readers select some of biotech's most remarkable and influential personalities from the past 10 years.

As part of its 10th anniversary celebration, *Nature Biotechnology* has gathered here a gallery of portraits of the most notable personalities in biotech in the past 10 years. Rather than focusing on personalities that have commonly featured in the mainstream press, our intention was to identify thought leaders and technology pioneers known within the industry to have made significant contributions to the science and business of biotech. To accomplish this task, we turned to those who know best: our readers.

During the month of January, *Nature Biotechnology's* e-mail registrant list and website visitors were asked to vote for the people they viewed as most influential in eight categories of biotech. These categories were: society and ethics; policy and regulations; biopharmaceuticals; agricultural, environmental and industrial biotech; technology; US biobusiness; European biobusiness; and biobusiness in the rest of the world. The poll, posted online from January 12 to 31, 2006, included 291 nominees, short-listed by the editors of *Nature Biotechnology* (Box 1). In some cases, multiple individuals were grouped for a particular scientific contribution or business activity. Readers also had the opportunity to suggest additional nominees for inclusion in the poll.

Including people in the nominee's list was a question of definition and judgment. And

K S Jayaraman is Nature's India correspondent and is based in Hyderabad. Sabine Louët is the news editor at Nature Biotechnology and is based in Dublin, Ireland. Kendall Powell is a regular contributor to Nature based in Broomfield, Colorado. John Ransom is a freelance writer based in Lone Tree, Colorado. Cormac Sheridan is a regular contributor to Nature Biotechnology based in Dublin, Ireland. Brian Vastag is a freelance writer based in Washington, D.C. Emily Waltz is an intern within Nature Biotechnology's news section.



Burke/Triolo Productions/NewsCom

because it bears a certain level of subjectivity, the final list should not be scrutinized with the rigorous mind that our readers apply to peer-reviewed papers. Instead, it should be considered more like a very informal who's who of biotech.

Hence this list bears several caveats. Clearly, the shortlist was not definitive and the number of people suggested for each category is far from complete. Second, the shortlist highlights only those individuals considered by the editors to have made a 'positive' contribution to progress in the field (prominent opponents of biotech were not included, although their contribution to the debate about the use and uptake of new technology is a given). Many of the personalities were selected because they had been highlighted in *Nature Biotechnology's* pages over the past 10 years. What's more, because we considered only personalities who have made a contribution to the industry in the past 10 years, many of the founders—(e.g., Herb Boyer, Stanley Cohen, Concepcion Campa Huergo, Arthur Kornberg or Kary Mullis) of the field are not included. Lastly, the poll results themselves were influenced by the geographic location of our readers—the majority being located in the

United States, Canada and Europe. Nevertheless personalities appear on the list from territories, such as Japan, Israel, India, Australia and China. Curiously, the winner of the 'Biobusiness in the rest of the world' category, Biocon's CEO Kiran Mazumdar-Shaw, seems to be more popular on the global scene than she actually is at home.

Below, we profile those individuals voted by our readers the most influential in a particular biotech category; we also highlight those individuals who came close (in some cases very close) to winning a particular category. At the end of the article, we present a list of individuals nominated for their contribution to shape the world of biotech as we know it today (Box 1).

The diversity of personalities listed reflects what is unique about this industry: the mix of individuals across a wide range of expertise, and the importance of the interface between business and science. Indeed, biotech is a sector where it is not unusual for venture capitalist to discuss business models with a Nobel laureate over coffee.

Finally, you may feel that we omitted some people from the initial shortlist. Our readers already made some interesting suggestions for other nominees. Among them were Garth Cooper, discoverer of the recently commercialized synthetic analog of human amylin (pramlintide acetate) and a leading industry figure in New Zealand. Hiroshi Masumoto from Nagoya University in Japan was also nominated for his work on human artificial chromosomes. In the category 'US biobusiness,' we received several votes for Una Ryan, who is the longtime CEO of AVANT Immunotherapeutics and a central figure in Massachusetts biotech circles.

Nature Biotechnology would welcome further suggestions for additions to the list. We hope that in the next 10 years, the individuals highlighted here will inspire many of our readers to follow in their footsteps.

Sabine Louët, News Editor

Society and ethics

Individuals nominated for their contributions to biotech's public image or to the advancement of ethical debates about biotech applications

Winner:

Bill and Melinda Gates. Through their foundation, they promote biotech by funding research on neglected diseases and diseases affecting poorer countries.

Honorable mentions:

Christopher Reeve. The now-deceased actor who turned patient advocate and proselytizer for the use of stem cell research in biomedicine.

Michael Fernandez. Executive director of the Pew Initiative on Food and Biotechnology, which has sought to stimulate and showcase diverse viewpoints on the application of agbiotech.

Bill and Melinda Gates



Jim Roymen

Bill Gates is the kind of person who, when attending the World Economic Forum, will pass up a dinner with foreign dignitaries to sit down with a bunch of scientists. Although he sometimes contends that science research is only a hobby, the founder of Microsoft (Seattle, WA) is fascinated with biotech. And he has decided to spend some of the wealth he accumulated through his company to finance research for neglected diseases—an initiative that has inspired biotech companies to latch on to some of those development projects.

Since the creation of their eponymous foundation in 1995, Bill and his wife, Melinda, have strived to cure the maladies plaguing developing countries. But they realized their calling at different moments. For Melinda, it was during a vacation to Zaire, where she was struck by the extreme poverty of the women she met. For Bill, it was reading that millions of children die every year from preventable diseases.

“When we started to look at where the largest inequities are, global health really stood out, because by every measure, if you can improve people's lives through health, you improve all

measures of society,” Melinda told *Time* magazine in November 2005.

The couple used their knowledge and compassion to endow their foundation with \$29 billion. The Gateses specifically intended that the types of drug developed by the foundation would not be the typical blockbuster produced by the pharmaceutical industry. Large disease markets like obesity and heart disease don't particularly interest them. “The world is failing billions of people,” Bill said in a speech to the World Health Assembly in Geneva in 2005. “Rich governments are not fighting some of the world's most deadly diseases because rich countries don't have them.”

For this reason, their money targets neglected diseases such as malaria, HIV and tuberculosis. In fact, the Gateses will only sponsor research for diseases that meet three criteria: widespread, neglected and representative of the public health disparities between developed and developing countries. Over the past decade, their Seattle-based foundation has given more than \$6 billion in public health grants. So far, research programs for new vaccines, clinical drug studies and programs that try to prevent the spread of infectious diseases have benefited from the Gates' monies.

The couple often delves into the science behind projects and they personally approve every grant over a million dollars. Bill also taught himself some basic biology by talking with researchers and devouring books on science. Some of his light reading includes *AIDS in the Twenty-First Century* by Tony Barnett, and *Molecular Biology of the Gene* by James Watson.

Although Bill and Melinda are trying to tackle some of the world's most intractable public health issues, they take a business approach to their philanthropy. They know that third-world afflictions aren't the most attractive arenas for biotech. They also know that companies aren't exactly eager to roll out medicines for people who can't afford to buy them. So their idea is to use funding dollars to create leverage. Their money helps mitigate risk so that governments or biotech and pharmaceutical companies will take over development of drugs at later stages (*Nat. Biotechnol.* 21, 1254, 2003).

“[The Gates Foundation] has energized research into global health, made that work a credible career choice and attracted politicians to the cause,” wrote former president Jimmy Carter in a profile of Bill Gates in the *Smithsonian*. “Perhaps most important, the confidence Bill has brought to the field has stimulated much more funding.”

Emily Waltz

Policy and regulations

Individuals nominated for their contributions to legislation promoting biotech innovation/industry growth or to the debate about the regulation of biotech products

Winner:

Rita Colwell. Former president of the University of Maryland Biotechnology Institute and former director of the US National Science Foundation, who has long campaigned for the benefits of biotech, especially in environmental applications.

Honorable mentions:

Janet Woodcock. The US Food and Drug Administration's deputy commissioner for operations, and the brains behind the FDA's 'Critical Path' initiative to modernize tools and methods for evaluating biotech drugs.

Mark McClellan. FDA commissioner for a short stint between 2002 and 2004, who introduced an efficient risk-management approach to reduce delays and costs of product approvals.

Robert Klein. Instrumental in the introduction of Proposition 71 by which California was able to use its own taxes to finance stem cell research that is not allowed at the federal level.

Rita Colwell



University of Maryland Biotechnology Institute

As the US National Science Foundation's (NSF) first director with a life sciences background—as well as its first female head—Rita Colwell immediately set to work integrating far-flung fields. During her stint at the NSF in Washington, DC from 1998 to 2004, she wanted biologists to work with computer scientists, engineers with ecologists, and mathematicians with psychologists. Early in her tenure, she used the term 'bio-complexity' to push scientists to break out of their boxes and view the world more holistically. “The intersection of all of these fields is what I found most exciting,” says Colwell. “I would go so far as to call it bio-nano-info-cogno-geo-technology.”

A mouthful, to be sure, but Colwell backed it with action honed by experience

as a founder of the University of Maryland Biotechnology Institute in 1991. On her watch, the NSF's budget grew nearly 70%, to \$5.3 billion per year.

She championed international collaboration, doubled the math budget, established infotechnology, cyber infrastructure, and social and psychological science programs, and placed renewed emphasis on science education, where the US had been slipping for decades.

Further initiatives, such as an NSF bioengineering program she launched, aim to turn microorganisms into industrial recycling machines, generating fertilizer from toxic waste or hydrogen from sewage—a tantalizing solution for powering the next generation of clean vehicles.

Other high-profile projects advocated by Colwell sample DNA directly from seawater and other environments, skipping time and labor-intensive laboratory culturing to quickly produce a complete picture of the genetics of an entire ecosystem. This new field, which Colwell calls metagenomics, has led to discoveries of whole new classes of genes.

Colwell is also behind programs aimed at providing a clearer picture of how the health of the planet affects the health of its people. "This is a whole new area, the integration of environmental data, such as ocean circulation and seasonal patterns, with data on ecosystems and human health," she says. "You could call it cosmobiology."

One project in this realm, which Colwell works on now, as a distinguished professor of microbiology and biotechnology at the University of Maryland, tracks outbreaks of cholera—a disease she has been studying for 40 years. "We're using satellites to correlate sea height and sea temperature with cholera epidemics. It's proven to be uncannily effective because outbreaks are associated with plankton blooms.

"What we need to do now is model other infectious diseases and incorporate biological data into climate models," Colwell says. To that end, she recently secured computer time on the Japanese Earth Simulator, a project whose stated goals neatly parallel Colwell's, namely "to build a harmonious relationship between the Earth and human beings."

Despite all of her high-tech successes, Colwell is proudest of perhaps her simplest idea: using folded sari cloth to filter cholera from drinking water. She proposed the method 10 years ago, and a field trial published in 2003 proved the method effective, reducing the incidence of the disease 48% across 65 villages in Bangladesh. Colwell says, "That's the work that I feel best about, because it saves lives."

Brian Vastag

Biopharmaceuticals

Individuals nominated for their contribution to biopharmaceutical research and development

Winner:

James Shapiro and **Ray Rajotte**. Pioneers in islet transplantation for type 1 diabetes.

Honorable mentions:

Alain Fischer and **Maria Cavazzana-Calvo**. Pioneers in gene therapy for immunodeficiency disease.

Rudolf Jaenisch and **George Daley**. Pioneered the concept of therapeutic cloning.

James Shapiro and Ray Rajotte



In 1921, Canadian researcher Frederick Banting and colleagues discovered insulin, providing the first treatment for people with type 1 diabetes—a discovery that earned him a Nobel Prize. It's only fitting, then, that nearly 80 years later the next leap forward in diabetes treatment also originated in Canada; transplanting pancreatic islet cells has given the field of adult cell therapy one of its first tantalizing successes. In fact, much of the work was conducted in the same University of Alberta basement laboratory where Banting's colleagues pioneered insulin therapy.

The latest Canadian advance is also transforming the field of diabetes treatment. Called the Edmonton Protocol, the technique infuses purified donor pancreatic islet cells into the liver portal vein. There, the cells graft and function as a mini-pancreas, responding moment to moment to the patient's insulin needs.

Two Alberta clinical scientists, Ray Rajotte, professor of surgery and medicine and director of the Islet Transplantation Group, and James Shapiro, director of the Clinical Islet Transplantation Program, developed much of the protocol, which they published in the *New England Journal of Medicine (NEMJ)* in 2000 (343: 230–238). The article detailed the first seven Edmonton Protocol patients, who all became insulin independent after each receiving roughly 800,000 islet cells previously isolated from cadavers.

Before that landmark publication, researchers for years had tried, and failed, to implant islet cells in diabetes patients, filling a database with data from nearly 500 rejected or otherwise useless transplants. "I told myself I was going to give it one last try," Shapiro said in 2000, after the *NEJM* paper appeared. "At first, the researchers were quite resistant, and I managed to convince everybody to give it one more chance. That moment for me stands out."

Several innovations led to success. Instead of using steroids to try to ward off graft rejection, the team used the antibiotics Prograf (tacrolimus) and Rapamune (sirolimus), and the monoclonal antibody Zenapax (daclizumab), a combination never tried before. They harvested and infused more islet cells than had been done in previous attempts. And they infused the cells as quickly as possible, instead of incubating them for several days.

Rajotte, who had been working on islet-cell transplantation since 1972, said that the response from the diabetes community was overwhelming—calls jammed the university switchboard for days. At least 75 hospitals have adopted the Edmonton Protocol and a long-term clinical trial is underway.

But the technique is arduous, taking four technicians up to eight hours to extract and prepare the cells. Each patient requires cells extracted from two cadaveric organs, which makes the acute donor shortage even more severe. Thus, only a tiny percentage of type 1 diabetes patients have undergone the procedure; patients usually only need a day trip to hospital. And the latest report on the technique, a follow-up of the first 65 patients treated at Edmonton (*Diabetes*, 54, 2060–2069, 2005) proved somewhat disappointing. Forty-four of the patients achieved insulin independence—but not permanently.

However, the Edmonton Protocol proved the viability of cell therapy for diabetes and has spurred a large effort to improve and expand the protocol. Several teams are working on transforming embryonic stem (ES) cells into islet cells—a step that, if achieved, could render moot the organ shortage. And in industry, Menlo Park, California-based Geron Corporation, among others, is currently developing methods to differentiate islet cells from human ES cells for transplant purposes. Other approaches under study include living donor and xenotransplants.

Although Shapiro has written that injected insulin will be the 'mainstay therapy' for years to come, if any of the alternative islet cell sources pan out, expect a whole new biotech sector to spring up.

Brian Vastag

Agricultural, environmental and industrial biotechnology

Individuals nominated for their contributions to agricultural, environmental or industrial biotech research and development

Winners:

Ingo Potrykus, Golden Rice Humanitarian Board, Basel and **Peter Beyer**, University of Freiburg, Germany. Coinventors of Golden Rice and founders of the Golden Rice Humanitarian Project.

Honorable mentions:

Asis Datta. Pioneered the technique for nutritional enhancement of cereal crops using genes isolated from amaranth (*Amaranthus hypochondriacus*). His work led to India's first field trial of a GM crop potato.

Frances Arnold. For application of directed evolution to proteins for use in industry.

Ingo Potrykus and Peter Beyer



Ingo Potrykus and Peter Beyer met on a trans-Atlantic flight as they both headed to New York in the early 1990s for a rice biotech brainstorming meeting of the Rockefeller Foundation. The meeting would discuss the possibility of genetically engineering rice to include beta-carotene, or pro-vitamin A, to target malnutrition in developing countries.

A doctoral student working with Potrykus on rice genetics introduced them after he had sought out Beyer as an advisor on the beta-carotene biosynthetic pathway. Beyer's and Potrykus' matching expertise turned into a decade-long collaboration—resulting in the creation of Golden Rice in 1999 and the first genetically engineered product created specifically for humanitarian purposes.

"If, as a basic scientist, you find out that you could make a contribution to the real world, that you have some tools in hand that might make a change, you go for it," Beyer recalls thinking after the meeting. Vitamin A deficiency (VAD) results in about 6,000 deaths per day worldwide and 500,000 cases of blindness per year. It predominantly affects

young children in poor areas of Asia with rice-based diets.

In 1999, the duo finished the first proof-of-concept Golden Rice strain (*Science* **287**, 301–305, 2000). The spotlight on Golden Rice as a cure for VAD made it both the champion genetically modified (GM) product and the chief target of anti-GM critics. The media attention and the nearly universal adoption of precautionary European agricultural biotech regulations made the trip from bench to field much tougher than either Potrykus or Beyer anticipated.

The invention also signaled a move into a product development phase—a phase not supported by traditional public research funding. "We would have quickly run into a dead end road if we had not been able to create an alliance with the private sector," notes Potrykus. The team brokered a unique agreement with Zeneca (now Basel-based Syngenta) in 2000. The company would shepherd the development of a second generation Golden Rice containing higher levels of beta-carotene as well as provide know-how on advancing through regulatory hurdles.

The key to the agreement, Potrykus says, was drawing the line between the company's commercial interests and the humanitarian efforts—farmers with an annual income of \$10,000 or less would be given the seed for free.

With Syngenta's help, a new strain, dubbed Golden Rice 2, was created that could provide the daily recommended allowance of vitamin A with a 70-gram portion of rice (*Nat. Biotechnol.* **23**, 482–487, 2005). Potrykus and Beyer also oversaw the first field trial in Louisiana in 2004 to show that Golden Rice grows like conventional rice.

Although that was a major milestone, Beyer and Potrykus both express frustration that Golden Rice seeds are not already in farmers' hands. Both say current regulation is unreasonably cautious and not scientifically based. Potrykus' view goes even further and he notes that even if the deregulation process goes smoothly, Golden Rice won't reach the fields until 2010, representing a six-year delay of the technology.

"By an extremely conservative calculation, this delay is responsible for 67,500 deaths. If our society does not change GM [organism] regulation, then our society is responsible for crimes against humanity," Potrykus argues. But Potrykus remains both optimistic and obstinate—two qualities he says carried him through the past 16 years of the project.

In five years, Potrykus expects the first Golden bananas, Golden sorghum and Golden cassava to be produced. Genetically engineered crop varieties to address drought, poor soil, pests and other nutritional deficits

are in laboratory pipelines all over the world. In 2005, Beyer headed up a consortium funded by \$11.2 million from the Bill and Melinda Gates Foundation to develop rice that, in addition to high beta-carotene, also includes vitamin E, zinc and iron. These products will take the dedication and ingenuity of researchers like Beyer and Potrykus. But, the duo points out, these products will also need changes in the regulation of GM organisms to become realities.

"All technology needs development," says Beyer. "The first airplane didn't go very far. All we are asking is for the same right to develop the technology."

Kendall Powell

Technology

Individuals nominated for their contributions to the development of key biotechnologies

Winner:

Ian Wilmut and Keith Campbell. Pioneers of somatic cell nuclear transfer, creators of Dolly in 1997. Wilmut is a founder of PPL Therapeutics.

Honorable mentions:

Leroy Hood. Long-time inventor of automated sequencing but lately a pioneer of systems approaches in biology; cofounded the Institute for Systems Biology in Seattle in 2000. Founder of numerous biotech.

Andrew Fire, Craig Mello and Tom Tuschl. For invention and application of RNAi in mammalian cells.

Ian Wilmut and Keith Campbell



The birth of Dolly, the sheep cloned from the DNA of an adult cell, triggered an extraordinary worldwide reaction. This global frenzy overshadowed the fact that this work was part of a continuum of experiments in animal reproduction that had stretched back to the beginning of the 1990s. In the rush to speculate about where the pioneering work of Ian Wilmut and Keith Campbell would go next, the media circus largely ignored where it had come from.

Far from being a singular event, their report from the Roslin Institute in February 1997 of the birth of a viable cloned lamb, whose genetic material was obtained from a mature, differentiated somatic cell derived as described in *Nature* (385, 810–813, 1997), had followed several significant studies.

The previous year, Wilmut and Campbell had reported on the birth of two other cloned lambs, Megan and Morag, baptized with Celtic names in honor of their Scottish birthplace. Both lambs were derived from DNA obtained from cultured lines of quiescent, embryo-derived cells that had already differentiated into epithelial cells (*Nature* 380, 64–66, 1996). This work was noteworthy as previous nuclear transfer procedures could only employ either early embryos or embryo-derived cells as donors. Campbell and Wilmut were able to demonstrate successful nuclear transfer of genetic material obtained from cells that had been in culture for up to 13 passages.

This held out the prospect of genetically engineering the DNA contained in those cells, before transferring it to an enucleated immature egg or oocyte. Previously, engineering transgenic animals relied on random insertion of DNA into the pronuclei of fertilized eggs (at a stage before the parents' genetic material has fused)—a haphazard procedure, rife with failures and inconsistencies.

The nascent technique that Wilmut and Campbell developed offered the prospect of far greater precision and predictability, with immediate application in the production of biopharmaceutical proteins and in the engineering of farm animals with improved traits. This work also supported a key insight of Campbell's: that cellular differentiation did not involve irreversible genetic modification. The birth of Dolly on July 5, 1996, confirmed this hypothesis. She had been cloned from DNA isolated from a cell taken from the udder of a six-year-old ewe.

In the following year, the arrival of the transgenic clones Polly and Molly during the lambing season demonstrated that the techniques of somatic cell nuclear transfer and genetic engineering could be combined, confirming the feasibility of the scheme Wilmut and Campbell had outlined just two years previously. The two lambs were engineered

to express the human blood clotting protein Factor IX in their milk (*Science* 278, 2130–2133, 1997).

Wilmut's and Campbell's success in the laboratory has not, however, been replicated in the commercial marketplace. PPL Therapeutics, an Edinburgh-based biotech company that had rights to the Roslin Institute's intellectual property (IP) burned through around £85 (\$148) million of investors' cash before it closed business. The decision was made after a move by its strategic partner Bayer, of Leverkusen, Germany, not to

proceed with development of its lead product candidate recombinant α -1-antitrypsin.

Its assets were put up for sale at the end of 2003, the same year in which Dolly was put down; she had developed ovine pulmonary adenocarcinoma.

Longstanding Dutch rival Pharming of Leiden, the Netherlands, which had itself narrowly avoided collapse a couple of years previously, picked up the last of the Roslin Institute's IP portfolio in August 2004.

Neither Wilmut nor Campbell is now based at the Roslin Institute, but each continues to make important contributions to academic research. As head of the Center for Regenerative Medicine at the University of Edinburgh, Wilmut is back in the headlines, following his receipt in February 2005 of the second-ever license to undertake human therapeutic cloning experiments in the United Kingdom. Wilmut and colleagues aim to study the mechanisms underlying motor neuron disease by examining the differentiation into neurons of embryonic stem cells derived from disease patients. Meanwhile, Keith Campbell, now based at the University of Nottingham, remains focused on teasing out the key steps in embryonic development and improving nuclear transfer techniques.

A decade on from Dolly, the whole field of cloning research has been clouded by recent revelations of scientific fraud and ethical misconduct on the part of Woo-Suk Hwang, the Korean scientist who falsely claimed to have developed a technique for generating patient-specific stem cells. Perhaps, this episode highlights even more the scrupulous attention that the Roslin Institute duo paid to the ethical dimensions of their work.

Cormac Sheridan

Wilmut's and Campbell's success in the laboratory has not been replicated in the commercial marketplace

US biobusiness

Individuals who have distinguished themselves in business activities related to biotech in the United States

Winner:

Arthur Levinson. CEO Genentech.

Honorable mentions:

Stanley Crooke. Founder, chairman and CEO of antisense company Isis Pharmaceuticals, which shepherded the first antisense product, Vitravene to FDA approval.

Alejandro Zaffaroni. Serial entrepreneur and founder of ALZA, DNAX, Affymax, who was still going strong in the nineties founding Affymetrix, Symyx, Maxygen, SurroMed and Alexza.

Arthur Levinson



Genentech CEO, Arthur Levinson, has not cured cancer. Yet. But under the leadership of the research-driven CEO, Genentech has fundamentally changed the treatment of some types of cancer through the use of targeted drugs that offer to better control tumors; with the hope that these drugs will also change some cancers from a sometimes death sentence to a manageable chronic disease.

Although Levinson thinks of himself as a scientist first and foremost, his rare ability to make a success of scientist-as-chief-executive, and balance the roles appropriately, makes the Genentech story compelling. Levinson hopes that balance serves as a roadmap for biotech success well into the future. "Our goal at Genentech is to discover and develop drugs that dramatically improve the treatment options for patients with life-threatening and serious diseases," says Levinson, adding, "We are not looking for an incremental change in existing therapies. We aim to develop genuine breakthroughs."

Levinson's accomplishments as a scientist often obscure the fact that he's a charismatic CEO that sits astride a \$92-billion biotech powerhouse—a phrase once considered oxymoronic—who started as a research scientist for the company back in 1980.

His background in science has given Levinson an often unique insight into biotech research. Hence, his bet on the theory of angiogenesis in controlling tumors, and his commitment to building a company that produces long-term results, make Genentech is different from competitors. Those companies often have small product pipelines and hope that success with one product will produce a buy-out by a large pharmaceutical company. Thus, since its creation in 1976, Genentech has stood out among scores of rival companies that have been shuttered on account of failed research, poor financing and flawed business models.

"We believe that strong basic research is the key for identifying breakthrough drug candidates for development in the clinic," Levinson points out.

As fruit of this vision, Genentech now markets several products with revenues of over \$6.5 billion that treat a variety of medical conditions, such as heart attack, allergic asthma, psoriasis, stroke, growth hormone deficiency and cystic fibrosis. These products represent a pipeline that was created, in part, under Levinson when he took over as research chief for the South San Francisco-based company in 1990.

Levinson has since made quite a mark on the company. Consider this: when he joined in 1980, fresh from a postdoctoral fellowship with the University of California's microbiology department, Genentech offered \$35 million in stock to the public and had 166 employees. Today, the company has net annual income of \$1.4 billion and 9,500 employees.

In 1995, when Levinson took over as CEO from Kirk Raab, the company produced revenues of around a billion dollars with a stock price of about \$6.00 on a split-adjusted basis. On January 10, 2006, the company released results for the full year of 2005 with \$6.63 billion in operating revenue, a 44% increase over 2004, whereas its stock traded at over \$85 per share. In a mature biotech industry where the 'D' in R&D can often stand for 'dollars,' numbers like these garner respect from scientists and financial analysts alike.

To date, Levinson and his company have received quite a bit of positive attention. Disparate publications, such as *Fortune*, *Science Magazine* and *The Scientist*, recently named Genentech the top company to work for in the United States. The company has also received recent awards from *Working Mother* for making it into its top 100 companies. *Wired* voted the company number 7 for innovation, technology and strategic vision.

John Ransom

European biobusiness

Individuals who have distinguished themselves in business activities related to biotech in Europe

Winner:

Dan Vassella. CEO Novartis, a company which has been very proactive in partnering with biotech companies over the last decade and made big plays in gene therapy.

Honorable mentions:

José María Fernández Sousa-Faro. Chairman of PharmaMar, the first large Spanish biotech company focusing on active compounds extracted from the sea.

Ernesto Bertarelli. CEO of Europe's largest biotech, Serono, succeeding his father and grandfather Fabio and Pietro.

Dan Vassella



Novartis chairman and CEO Dan Vasella is unusual among his big pharma peers in having spent several years as a practicing physician before entering the business world. Still only 52, Vasella seems like a fixture atop Europe's drug industry. He is now credited for his active deal making with the biotech industry, after a decade at the helm of Novartis, the Basel-based company formed in 1996 via a \$41-billion stock merger between Sandoz and Ciba-Geigy.

His progress from the bedside to the boardroom was swift. He quit medicine in 1988 and moved to New Jersey, where he initially took up a trainee post in the US headquarters of Sandoz, before becoming product manager for a newly approved pancreatic cancer drug, a somatostatin analog called Sandostatin (octreotide).

By 1993, Vasella was back in Switzerland, as head of corporate marketing at Sandoz, and, less than a decade after entering the pharmaceutical industry, he presided over one of the biggest mergers in that sector's history. It took several years for the company to prosper under its new identity, but under Vasella's leadership Novartis has succeeded in breaking away from the rigid, conservative ethos that had prevailed at both Sandoz and Ciba-Geigy. Instead, Vasella introduced a more aggressive and less

risk-averse culture with performance-based, American-style remuneration packages and bonus schemes.

For Vasella, the company's biggest achievement over the past decade has been the successful transformation of Novartis' culture. "We have succeeded in creating a climate where it was possible to be successful in the sense of discovering and developing new compounds and marketing new compounds," he says.

Novartis established its credentials for innovation—and for speed—by its rapid, in-house development of the breakthrough chronic myeloid leukemia drug (CML) Gleevec (imatinib mesylate). The compound clocked up almost \$2.2 billion in sales during 2005.

Vasella has also transformed the company's research infrastructure into a global network of institutes led from Cambridge, Massachusetts, in the United States, rather than from the company's headquarter in Basel.

Under the leadership of Vasella, Novartis partnered with 200 biotech companies last year, thus spreading its wings across many therapeutic areas. These include the rapidly growing vaccines market, following the acquisition of Chiron, of Emeryville, California. And although its extensive investments in genomics and gene therapy, like those of many other big pharma companies, have so far failed to bear fruit, Novartis has over the past year entered major alliances in emerging areas, such as RNAi and toll-like receptors.

Alone among its top 10 big pharma peers, Novartis is also building a large presence in the generics market by an aggressive acquisition strategy. And its generics unit Sandoz is on track to gain approval for the first ever biosimilar drug to be approved in Europe—a version of human growth hormone called Omnitrope—already launched in Australia. "I don't think the financial advantage for one industry player is what matters," Vasella says. The fact that biotech cannot have a "lifelong monopoly" on certain products is more significant.

As president of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), a Geneva-based global lobby, Vasella is now a senior—if not an elder—statesman within the pharmaceutical industry. Although admitting that the industry has long been "reactive" in dealing with criticisms of its poor record in making medicines available to patients in less developed countries, he claims that industry has improved its performance, while political corruption and poor governance within developing countries remain real obstacles to progress. "The primary responsibility lies with governments, and the primary failing parties are local governments."

Cormac Sheridan

Biobusiness in the rest of the world

Individuals who have distinguished themselves in business activities related to biotech in the rest of the world

Winner:

Kiran Mazumdar-Shaw. CEO of biopharmaceutical company Biocon, the first Indian biotech to go public.

Honorable mentions:

Philip Yeo. Chair of Singapore's Agency for Science, Technology and Research (A*STAR) and one of the key players in the development of Singapore into a hub for biomedical and biotech research that includes Biopolis.

Eli Hurvitz. Chairman of Israeli generics company Teva since 2002. Previously, he was Teva's President and CEO for over 25 years.

Kiran Mazumdar-Shaw



Kiran Mazumdar-Shaw, India's icon of woman entrepreneurship, entered biotechnology quite by accident. When she could not break into the male-dominated brewing industry—in spite of an Australian degree in malting and brewing—she decided to launch her own company on "an impulse."

Like in all good biotech stories, she started her company by renting a garage in Bangalore. And with just \$10,000 in hand and a staff of two she started using her knowledge of fermentation to produce enzymes for the food and beverage industry. It was 1978 and she was 25.

Today, the company of which she is chairman and managing director, Biocon, is one of India's premier biotech companies with 2,000 employees. In 2004, Mazumdar-Shaw became India's richest self-made business woman when Biocon went public—the first Indian biotech company to do so. She owns 39% of the stock and her Scottish husband John Shaw has 26%. Overall, she is worth about \$440 million.

And last year she made it to *Fortune's* list of the 50 most powerful women in international

"I was just lucky to have arrived at the biotech scene at the right time," Mazumdar-Shaw explains

business. Although titles like 'biotech queen' and 'India's richest woman' make her feel uncomfortable she cherishes the civilian 'Padmabhushan' award bestowed on her by India's president A.P.J. Abdul Kalam in 2005. She has also been inducted into the Prime Minister's business advisory council—a vast difference from the initial Biocon days when banks would not give her a loan because of her gender.

The honors and wealth have only made Mazumdar-Shaw more humble. "I was just lucky to have arrived at the biotech scene at the right time," she explains. But even her rivals admit that her unique vision and ability to seize opportunities had steered Biocon's transition from an enzymes company to an integrated biotech enterprise specializing in biopharmaceuticals, custom research and clinical research focused on health care.

Biocon and its two subsidiaries—Syngene International Pvt and Clinigene International Pvt—had \$160 million in revenues in the year ending March 2005, a big jump from \$13 million in 1997. The challenges for the Biocon chief are not over, however. With about two-thirds of its revenue coming from exports, Biocon is facing tough competition, especially from anticholesterol statins made in China.

Her latest venture is in the diabetes segment. She is hoping that the first blockbuster drug—an oral insulin pill—will come from her company. In October 2004, she partnered with Nobex, a North Carolina company, to develop such a pill. Confirming her optimism, the product is about to start human trials in India, despite a recent bankruptcy filing by Nobex. And she is multiplying collaborations to diversify her pipeline. In June 2004, she established a joint venture with Cimab, a Cuban biotech research institute that develops monoclonal antibodies and vaccines against certain cancers.

Mazumdar-Shaw is also excited about the future of the biotech industry in India as a whole. "The stage is certainly set for exponential growth in the biotech sector," she writes. "India already ranks among the top 10 biotech hubs in the world. The aim is to be amongst the top five by 2010 and the top three by 2015."

K.S. Jayaraman

Box 1 The *Nature Biotechnology* shortlist of nominees

We present below the 291 nominees, shortlisted by the editors of *Nature Biotechnology*, as personalities who have made the most significant contribution to biotech in the past 10 years.

Society and ethics

Andrew Baker. Chairman and CEO of Huntingdon Life Sciences, the British contract research organization, who has led the company forward despite personal attacks from animal-rights activists.

Ronald Bailey. Science correspondent for *Reason* magazine, and a keen proponent of the integration of new biotechnologies.

Karen Bernstein and David Flores. Founders of the biotech industry's foremost newsletter *BioCentury*.

Arthur Caplan. Perhaps one of the most visible and accessible bioethicists in debates about biotech applications.

Greg Conko. A commentator on public health and consumer safety issues in biotech.

Gordon Conway. As president of the Rockefeller Foundation, Conway has been a proponent of public-private partnerships to resolve some of the barriers to developing world farmers gaining access to new technologies.

Carl Feldbaum. Former BIO chairman, who sought to unify and improve the public face of the biotech industry.

Michael Fernandez. Executive Director of the PEW initiative which has sought to stimulate and showcase diverse viewpoints on the application of agbiotech.

Bill and Melinda Gates. Promote biotech by providing funding for research on neglected diseases and diseases affecting poorer countries through their foundation.

Richard Jefferson. Leader of the open-source biology movement that attempts to circumvent problems with traditional patenting.

Eduardo Kac. Perhaps the most well-known proponent of the bioart movement, which attempts to use art to challenge our perceptions of biotech applications.

Evelyn Fox Keller. A science historian and MacArthur Fellow who has authored several books, including the *Century of the Gene*, that challenge common assumptions about genetics and genetic engineering and argue for scientific and political realism.

Robert Klein. As chairman of the 'YES on Californian stem cell research initiative, Proposition 71,' spurred embryonic stem cell research in 2004.

Cardinal Renato Martino. A religious leader who has supported the use of agbiotech for hunger and health.

Henry Miller. Former founding director of the FDA's Office of Biotechnology who in his position at the Hoover Institute is a vocal proponent of the free market and opponent of biotech critics and regulatory proliferation.

Miyata Mitsuru. General manager of the Tokyo-based financial publisher Nikkei Business Publications.

Thomas Murray. A bioethicist, president of the Hastings Center.

Dorothy Nelkin. The now-deceased sociologist and professor at NYU School of Law whose eloquence and insights highlighted how biotech is perceived—and, often, misperceived—by the public.

Paul Rabinow. An anthropologist, author and popularizer of the personalities behind biotech innovations that have had a profound impact on society.

Christopher Reeve. The now-deceased actor who turned patient advocate and proselytizer for the use of stem cell research in biomedicine.

Cynthia Robbins Roth. Founder of *BioPeople* and *BioWorld*. Expert commentator on the biotech industry.

Florence Wambugu. CEO of the A Harvest Biotech Foundation International (AHBFI), who campaigns for the use of biotech in developing countries.

Mike Ward. Expert commentator on European biotech, who is on the staff of *BioCentury*.

Policy and regulations

Alexander Berghout. Head of clinical development and regulatory affairs at Swiss generics company Sandoz, he was the first to file for approval of the first follow-on biologics of human growth hormone in Europe, the US and Australia.

George W. Bush. His Aug 2001 decision to deny federal funds to research on new embryonic stem cell lines put moral and ethical debates center stage and spurred international competition.

Rita Colwell. Former president of the University of Maryland Biotechnology Institute and former director of the US National Science Foundation, who has long argued for the benefits of biotech, especially in environmental applications.

Dan Glickman. Former US Department of Agriculture secretary who oversaw the implementation of a regulatory framework for genetically modified crops that includes voluntary labeling.

Willy de Greef. Consultant, former Head of Regulatory and Governmental Affairs at Novartis Seeds, who has sought to fight the implementation of non-scientific regulation in Europe.

John Doll. Director of Technology Center 1600 of the US Patent and Trademark Office, responsible for examining biotech patents, who updated examination procedures and criteria to keep up with the onslaught of biotech patents.

Carl Feldbaum. Former BIO chairman. Contributed to the recognition of biotech among policy makers.

David Kessler. FDA commissioner from 1990 to 1997, who oversaw the introduction of the Prescription Drug User Fee Act (PDUFA).

Robert Klein. Instrumental in the introduction of Proposition 71 by which the State of California was able to use its own taxes to finance stem cell research that is not allowed at the federal level.

Marc Cantley. Adviser in the Directorate for Life Sciences in the EU's Directorate-General for Science, has long raged against proliferation of non-scientific biotech regulations.

Mark McClellan. FDA commissioner between 2002 and 2004, who introduced an efficient risk-management approach to reduce delays and costs of product approvals.

Fernand Sauer. First EMEA executive director, who oversaw the development of European regulations for biotech medicines.

Janet Woodcock. The US FDA's Deputy Commissioner for Operations, the brains behind the FDA's 'Critical Path' initiative to modernize tools and methods for evaluating biotech drugs.

Erik Tambuyzer. Founding board member and treasurer of EuropaBio, the European Bioindustry Organization, which is active in helping to shape European policy.

Peter Heinrich. President of industry group Emerging Biopharmaceutical Enterprises, part of the European pharmaceutical federation EFPIA, which helps shape European policy. He is also a cofounder of the German company MediGene, focused on cancer and cardiac drugs.

Biopharmaceuticals

Abe Abuchowski. CEO of Prolong Pharmaceuticals, who developed the concept of pegylation of biopharmaceuticals.

Julian Adams. Discoverer of Velcade (bortezomib), a first-in-class drug targeting the proteasome.

Frank Bennett, Stan Crooke and Arthur Levin. Developers of the first antisense drug Vitravene (fomivirsen) approved in 1998.

Paul Carter, Leonard Presta and Mark Sliwowski. Contributors to antibody humanization and the development of Herceptin (trastuzumab).

Robin Coombs, Herman Waldmann, Alun Munro, Mike Clark and Timothy Springer. Pioneers in the development of Campath (alemtuzumab).

Tse-Wen Chang and Nancy Chang. Discoverers and developers of anti-IgE antibody Xolair (omalizumab).

Mac Cheever and Patricia Stewart. Key developers of the anti-lymphoma drug Bexxar (tositumomab) which was approved by the FDA in June of 2003.

Brian Druker, Nick Lydon, Alex Matter and Juerg Zimmermann. The codevelopers of Gleevec (imatinib) who started in the early 1990 at Ciba-Geigy (now Novartis).

Marc Feldmann and Ravinder Maini. Pioneer in the development of anti-TNF therapy Remicade (infliximab).

Napoleone Ferrara. Developer of humanized anti-VEGF antibody Avastin (bevacizumab), which received FDA approval in February 2004 for treatment, joined Genentech in 1988.

Alain Fischer and Maria Cavazzana-Calvo. Pioneers in gene therapy for immunodeficiency disease.

Mark I. Greene. University of Pennsylvania, described the first monoclonal antibodies against the Her2/Neu oncogene that was to become Herceptin (trastuzumab) approved in 1998.

Geoff Hale and Herman Waldmann. University of Oxford, discoverer and developer of Campath, a monoclonal antibody for the treatment of B-cell chronic lymphocytic leukemia.

Peter Hudson and Phillip Holliger. Pioneered the development of antibody fragments.

Rudolf Jaenisch and George Daley. Pioneers for the concept of therapeutic cloning.

Doug Lauffenburger. Professor at MIT, pioneer in rational cytokine design via protein engineering.

Lars Peterson. Pioneer in autologous chondrocyte transplants, leading to Genzyme's Carticel, the first FDA-approved cell therapy.

William Rastetter, Dennis Slamon and Greg Winter. Pioneers in the development of antibodies as biopharmaceuticals.

James Robl. CSO and director of Hematech, pioneer in the production of human polyclonal antibodies in large animals.

James Shapiro and Ray Rajotte. Pioneers in islet transplantation for type 1 diabetes.

Peter Senter. Pioneer in the development of conjugated antibodies.

Agricultural, environmental and industrial biotechnology

Frances Arnold. For application of directed evolution to proteins for use in industrial applications.

Charles Arntzen. Pioneer of transgenic plant vaccines.

Roger Beachy. Pioneer in creating new virus-resistant crop varieties; now as president of the Donald Danforth Plant Science Center, a vocal critic of patent/license stacking.

Peter Beyer and Ingo Potrykus. Coinventors of Golden rice; first showcase GM plant for 'saving' the world and heavily used by the industry for publicity; also, founders of the Golden Rice Humanitarian Project.

Nam-Hai Chua. Responsible for characterization of cauliflower mosaic virus 35S promoter, which has been used in the vast majority of transgenic plant lines; more recently the developer of alternative selection strategies to antibiotic resistance markers.

Asis Datta. Pioneered the technique for nutritional enhancement of cereal crops using genes he isolated from Amaranth plant (*Amaranthus hypochondriacus*). His work led to India's first field trial of a GM crop potato. Now the director of the National Center for Plant Genome Research, in New Delhi.

Luis Herrera Estrella. Head of the National Laboratory of Genomics for Biodiversity of the Center for Research and Advanced Studies of the National Polytechnic Institute, Irapuato, Mexico, who has worked on plants better adapted to growth in acidic or suboptimal soils.

Neal First. Pioneered research in the reproductive biology and cloning of livestock.

Richard Flavell. Instrumental in creating agbiotech research center John Innes Institute in Norwich, UK; later to become CSO of Ceres, a California-based plant genomics company.

Jikun Huang. Director of the Center for Chinese Agricultural Policy at the Chinese Academy of Sciences, he is developing genetically modified rice in China.

Derek Lovley. Pioneer in microbial energy fuel cells and environmental biotech.

Pal Maliga and Henry Daniell. Developed the technology for plastid transformation in higher plants.



Box 1 The *Nature Biotechnology* shortlist of nominees (continued)

Melvin Oliver. USDA scientist who was inventor of so-called "Terminator" technology making crops sterile to ensure containment and the need to buy new transgenic seeds each season.

C.S. Prakash. Director of Center for Plant Biotechnology Research at Tuskegee University; through AgBioForum has unified international agbiotech community.

Roger Salquist. As CEO of Calgene of Davis, California, until 1996, oversaw the development of Flavr Savr, the first transgenic tomato product to reach the supermarket with longer shelf life.

David Salt and Richard Meagher. Pioneers in the development of phytoremediation strategies.

Jay Short. Cofounder, former president and CEO of Diversa, a company exploiting living organisms for industrial applications.

Greg Stephanopoulos. Pioneered work on *in silico* modeling and metabolic engineering of industrial strains of bacteria.

Bob Wall. USDA scientist who has pioneered large animal transgenic research; created animals expressing proteins in the bladder and antimicrobial proteins in the mammary gland.

Technology

Rüdi Aebersold. Inventor of the mass spectrometry method of isotope-coded affinity tags (ICAT).

Victor Ambros. Of Dartmouth College, considered the discoverer of microRNAs (lin-4 described in 1993 *Cell* article; the term microRNA was coined in 2001).

Rudi Balling. German Research Center for Biotechnology in Braunschweig, pioneer of large-scale ethylnitrosourea (ENU)-mutagenesis as a tool for functional genome analysis and a coordinator of the German Human Genome Project.

David Baltimore, Srinivasan Chandrasegaran and Matthew Porteus. Coinventors of zinc finger chimeric endonuclease technology for gene repair.

Eugene Bell. Pioneer in tissue engineering, MIT emeritus professor and founder of Organogenesis.

Charles Cantor. In the 1990s refined mass spectrometry methods for large-scale genotyping. He is currently CSO, Sequenom.

George Church. For contributions to novel high-throughput sequencing approaches and integration of 'omic data.

Calvin Chow, Michael Knapp and Wallace Parce. Cofounders of Caliper (now Caliper Life Sciences), specialist of advanced liquid handling and lab-chip technology.

Daniel Cohen. Of the Center for the Study of Human Polymorphisms in Paris, produced a rough map of all 23 pairs of human chromosomes and became CSO at Genset, later acquired by Serono.

Philip Cohen. A leading figure in research on protein kinases, which have become preeminent drug targets, particularly in biotech oncology research.

Francis Collins. Director of the National Human Genome Research Institute at the US National Institutes of Health and head of the public Human Genome Project.

Daniel Erlanson, James Wells and Andrew Braisted. Inventors of tethering: fragment-based drug discovery.

Stan Fields and Roger Brent. Developed the yeast two-hybrid system, which over the past 10 years has become a bench standard method for proteomics.

Andrew Fire, Craig Mello and Tom Tuschl. For invention and application of RNAi in mammalian cells.

Stephen Fodor/David Lockhart and Pat Brown/Ron Davis. Codevelopers of photolithographically synthesized oligonucleotide chips and cDNA microarrays, respectively. Together with genome sequencing launched a new era of 'omics-based research.

Árpád Furka. Inventor of the principles of combinatorial chemistry, which blossomed in the mid-1990s, including both synthesis and the iteration screening strategy.

Tilman Gerngross. Developer of strains of yeast capable of human-type glycosylation.

David Haussler. University of California at Santa Cruz, introduced hidden Markov models (HMMs) for protein sequence analysis, developed a kernel function from the profiles to be used in support vector machine training, and produced the first public, large-scale rough draft assemblies of the entire human genome sequence.

Sam Hanash. Chair Human Proteome Organization (HUPO) and a pioneer in cancer proteomics.

Leroy Hood. Long-time inventor of automated sequencing but lately a pioneer of systems approaches in biology; cofounded the Institute for Systems Biology in Seattle in 2000. Founder of numerous biotech.

Aaron Klug, Carl Pabo and Jeremy Berg. Pioneers of zinc finger technology, which has recently gained momentum with chimeric endonuclease technology.

Ashok Kolaskar. University of Pune, laid the foundation for much of bioinformatics work going on in India.

Fred Kramer and Sanjay Tyagi. Developer of molecular beacons.

Eric Lander. MIT & Whitehead Institute; named first author when the draft of the human genome was published in 2001. One of the cofounders of Millennium.

Robert Langer. MIT; pioneer in the fields of drug delivery systems and tissue engineering. His research laboratory is the largest biomedical engineering lab in the world, maintaining about \$6 million in annual grants and over 100 researchers.

Robert Lanza. Pioneer in human somatic cell nuclear transfer.

Paul Lizardi and David Ward. Inventor of isothermal rolling circle amplification 1999.

Matthias Mann. Contributor to the creation of the first algorithm for peptide identification in sequence databases and invention of the mass spectrometry method 'stable isotope labeling of amino acids in cell culture' (SILAC).

Chad Mirkin. Pioneer in nanotechnology applications.

Eugene Myers. Contributor of algorithms used in computational biology who was involved in decoding of the shotgun human genome sequence. Former vice president of informatics research at Celera Genomics.

Shuming Nie and Paul Alivisatos. Developers of biological application of quantum dots.

Peter Nielsen. Pioneer in the development of peptide nucleic acids.

Maynard Olson. Inventor of yeast artificial chromosomes, or YACs, expression vectors for large proteins. Currently at Washington University Genome Center.

Bernhard Palsson. Pioneer of novel approaches for *in silico* model building and metabolic engineering; cofounder of several biotech companies in the nineties.

Yves Poirier. Pioneer in developing and refining the production of biodegradable plastics in bacteria.

Stephen Quake and Michael Ramsey. Pioneers in the miniaturization of fundamental biochemical experiments and microfluidics.

Nadrian Seeman. Contributor to nanobiotech development.

'Pim' Willem Stemmer. Inventor of gene shuffling; currently with Maxygen and Avidia.

James Thomson and John Gearhart. Inventors of methods used for isolation and culture of human embryonic stem and germ cells.

Joseph Vacanti. Massachusetts General Hospital, tissue engineer who grafted a human ear onto the back of mouse.

Ham Smith and J. Craig Venter. Pioneered shotgun sequencing approach at the Institute for Genomic Research (TIGR). Venter, currently the president of the J. Craig Venter Institute and former president and founder of Celera Genomics, also devised the express sequence tag method.

Bert Vogelstein and Ken Kinzler. Inventors of serial analysis of gene expression (SAGE).

Teru Wakayama. Pioneer in mouse cloning who worked with nuclear transfer embryonic stem cells.

Irving Weissman. Stem cell pioneer actively involved in the founding of cell therapy biotech in 1990s.

James Wells. Coinventor of the 'tethering' approach, a screening method to identify small organic compounds that inhibit protein-protein interactions used to identify small molecules that bind interleukin 2. Also a cofounder of the San Francisco-based biotech company Sunesis Pharmaceuticals.

Ian Wilmut and Kevin Campbell. Pioneers of somatic cell nuclear transfer, creators of Dolly in 1997. Wilmut is a founder of PPL Therapeutics.

Greg Winter and Hennie Hoogenboom. Developers of phage display technology for isolation and engineering of antibodies.

US biobusiness

Moshe Alafi. Founder of Alafi Capital Company and an investor for over 25 years in biotech. He was a seed investor in Cetus, Biogen, Applied Biosystems and Amgen.

Frank Baldino. Founder and CEO of Cephalon.

Gordon Binder. Former president, CEO and chairman of Amgen.

Joshua Boger. President and CEO of Vertex Pharmaceuticals.

Brook Byers. Investor at Kleiner Perkins Caufield & Byers, venture capital investor since 1972; formed the first Life Sciences practice group in the venture capital profession in 1984.

Steven Burrill. CEO, Burrill & Co., a life science investment company, which produces an annual snapshot of the industry.

John Clarke. Managing General Partner, Cardinal Partners; founder of Alkermes and Cubist Pharmaceuticals, founder and chairman of Alnylam.

Lisa Conte. CEO of PS Pharmaceuticals and founder and CEO of now-defunct Shaman Pharmaceuticals, a natural product pharmaceutical company.

Stanley Crooke. Founder, chairman and CEO of Isis Pharmaceuticals, a company focused on antisense oligonucleotides, which has built a formidable patent portfolio.

Julian Davies. Former head of Biogen now at the University of Vancouver. Has formed company around metagenomics.

Jean Deleage. Founder of venture capital firm Alta Partners.

Juergen Drews. Former president for global research a Hoffman-LaRoche, now at investment firm Bear Stearns Health Innovations Management. A high-profile proponent of genomic medicine and the need for pharma to adopt genomics-based drug discovery to address shortfall in products.

Stephen Evans-Freke. Former investment banker at PaineWebber and former CEO of Sugan, a company that pioneered the pursuit of kinase inhibitors, now on the board of Cambridge in America, the development arm of Cambridge University.

Stephen Fodor. As chairman and CEO of Affymetrix, oversaw the growth of technology platform company in the 1990s, also cofounder, in 2001, of Perlegen.

Steven Gillis. Venture partner at Arch Venture partners in Seattle, founder and former CEO of Corixa and also a founder and director of Immunex from 1981 until 1994.

William Haseltine. Ex-chairman and CEO of Human Genome Sciences, the biotech that clinched the first deal with a pharma company, validating genomics.

Kevin Hrusovsky. President and CEO of Caliper Life Sciences, previous CEO of Zymark.

Michael Hunkapiller. Former president of Applied Biosystems and a founder of its sister company Celera Genomics.

Mark Levin. Founder of Millennium Pharmaceuticals whose business acumen is widely regarded as the secret of the company's success.

Arthur Levinson. CEO Genentech.

James Mullen. President and CEO of Biogen Idec.

Thomas Okarma. President, CEO of Geron.

Stelios Papadopoulos. Vice chairman of investment bank SG Cowen Securities Corporation focusing on the biotech and pharmaceutical sectors.

Alan Patricof. Cofounder of Apax Partners in the United States.

Ed Penhoet. Founder and CEO of Chiron until 1998. Now president of the environmental conservation funding organization Gordon and Betty Moore Foundation in San Francisco.

Tom Perkins. Investor at Kleiner Perkins Caufield & Byers and venture capitalist since 1972. Founding chairman of Genentech.

George Poste. As former president, R&D and chief science and technology officer at SmithKline Beecham, first to take the leap into genomics. Now CEO of Health Technology Networks, a healthcare consulting group and on several biotech boards.

Dennis Purcell. Senior Managing Director, Perseus-Soros BioPharmaceutical Fund who was managing director Life Sciences Investment Banking at Hambrecht & Quist.

Box 1 The Nature Biotechnology shortlist of nominees (continued)

William Rastetter. Recently retired executive chairman of Biogen IDEC and former CEO of IDEC.

George Rathmann. Former president, CEO, chairman of Amgen. Also a founder of ICOS Corporation.

William Rutter. Cofounder of Chiron.

Ivor Royston. Founder of IDEC, now a partner with the venture capital firm Forward Ventures.

George Scangos. President and CEO Exelixis.

Hubert Shoemaker. Cofounder Centocor (now part of Johnson & Johnson).

Richard Seldon. Founder of Transkaryotic Therapies (now part of Shire), which invented gene-activated erythropoietin, a competitor to Amgen's erythropoietin.

Dale Stringfellow. Former CEO and president of Berlex Biosciences, a research, development and manufacturing organization. Founder Myriad Genetics, Cognetix and Acacia Biosciences.

Henry Termeer. Chairman, president and CEO Genzyme, has been with the company since 1983.

Lyle Turner. Founder, chairman and CEO Invitrogen Corporation until 2002.

Roy Whitfield. Cofounder and former CEO Incyte Pharmaceuticals.

Axel Ullrich and Joseph Schlessinger. Cofounders of kinase inhibitor company Sugen.

Alejandro Zaffaroni. Serial entrepreneur and founder of ALZA, DNAX, Affymax, who was still going strong in the nineties founding Affymetrix, Symyx, Maxygen, SurroMed and Alexza.

Vincent Zurawski. Cofounder Centocor (now part of Johnson & Johnson) as well as numerous other companies including DNA vaccine company Apollon and oncology play Auburn Pharmaceuticals.

European biobusiness

Goran Ando. Former CEO Celltech Group in the UK.

Lucas Benatti. Founder and CEO Newron Pharmaceuticals, an Italian company focusing on the central nervous system.

Ernesto Bertarelli. CEO of Europe's largest biotech Serono, succeeding his father and grandfather Fabio and Pietro.

Joel Besse. Senior partner Atlas Venture, a founding investor in Swiss biotech Actelion.

Simon Best. Founder and Chairman of UK-based Ardana Bioscience, specializing in human reproductive biology now head of EuropaBio.

Stephen Bunting. Partner at UK-based venture capital firm Abingworth.

David Chiswell. Founder Cambridge Antibody Technology.

Jean-Paul Clozel. CEO and Founder of Actelion, in Switzerland.

Ronald Cohen. Cofounded venture capital firm Apax Partners, formerly known as MMG.

Jeremy Curnock-Cook. Investor, chairman of Bioscience Managers, formerly at Rothschild Asset Management where he created and led the Rothschild Bioscience Unit in the UK.

Host Domdey. Managing Director of BioM, a technology transfer and seed-capital company based in Munich.

Chris Evans. Founder UK venture capital firm Merlin Bioscience.

Lisa Drakeman. CEO of antibody company Genmab located in Copenhagen.

Paul Drayson. Founder and former CEO drug delivery company PowderJect.

Glyn Edwards. CEO UK oncology company Antisoma, known partner of Roche.

Chris Evans. Founder UK venture capital firm Merlin Bioscience.

Peter Fellner. Executive chairman of Vernalis, former chairman and CEO of Celltech Group in the UK.

José María Fernández Sousa-Faro. Chairman of PharmaMar, the first large Spanish biotech company focusing on active compounds extracted from the sea.

Bernard Gilly. Former president and CEO of Transgene, previously a gene therapy company, now a therapeutic vaccines and immunotherapy products company.

Alan Goodman. Cofounder of biopharmaceutical companies Medeva, Chiroscience and Peptide Therapeutics, now known as vaccine company Acambis, and of venture capital firm Avlar BioVentures.

Michel Gréco. Deputy CEO and member of the Board of Aventis Pasteur until 2003. He is a board member of several public and private biotech companies.

Franck Grimaud. Founder and CEO vaccine platform company Vivalis, France.

Joern Aldag. CEO of German company Evotec, focused on the central nervous system, since 2001.

Ian Harvey. Former CEO of technology transfer company BTG in the UK.

Paul Haycock. Former CEO of vaccine company Cantab, former director of venture capital firm Apax Partners, now a board member of investment boutique Ferghana group in the UK.

Alan Kingsman. Cofounder and CEO Oxford BioMedica in the UK.

Denis Lucquin. Managing partner at venture capital firm Sofinnova Partners in Paris.

Keith McCullagh. Founder, British Biotech in the UK who led the fight to make the LSE change its rules for listing young companies, allowing biotech companies to grow through capital markets and venture capitalist to consider them as lower risk investments.

Simon Moroney. CEO of German antibody company Morphosys.

Jean-Yves Nothias. Managing director of Société Générale Asset Management Alternative Investments, where he leads the Biotechnology Team. SGAM is one of the largest investor in the life science in France.

David Oxlade. Former CEO of biopharmaceutical company Xenova Group, now part of Celtic Pharma Development UK.

Raj Parekh. Founder and former CSO Oxford GlycoSciences, proteomics platform-based drug discovery company, which was acquired by Celltech in the UK.

Fredrik Paulsen. CEO Ferring of Sweden, one of the first European companies developing and selling pharmaceutical products based upon natural, pituitary-produced peptide hormones.

Jos Peeters. Cofounder of the Easdaq stock exchange in Brussels, which was Europe's answer to Nasdaq.

Philippe Pouletty. Founder, Clonatec, SangStat, Conjuchem, DrugAbuse Sciences. Chair of the French bioindustry association France Biotech.

William Powlett-Smith. Partner & UK Health Sciences leader at consultancy Ernst & Young in Cambridge, UK.

Claudio Quarta. Cofounder and CEO Biosearch Italia, who became COO of Vicuron Pharmaceuticals when Biosearch was acquired in 2003; now Pfizer owns the company.

Jürgen Rüttgers. Former German Minister of Science, who launched the BioRegio funding scheme in 1996.

Steen Riisgaard. President & CEO, Novozymes, a specialist in enzymes and microorganisms production in Denmark.

Spiro Rombotis. CEO of oncology company Cyclacel in the UK.

Christopher Samler. CEO of drug delivery company Weston Medical, former CEO of xenotransplantation company Imutran, now part of Novartis.

Helmut Schühler. Managing partner of German venture capital firm TVM in Munich.

Bernd Seizinger. CEO of German oncology company GPC Biotech since 1998.

Francisco Sinigaglia. Founder and CEO of Italian biotech BioXell, spin off from Roche, focused on urological disorders and inflammatory diseases.

Lars Rebieb Sørensen. President and CEO Novo Nordisk since 2000, a company specialized in enzyme and hormone production based in Denmark.

Gerard Soula. Founder Flamel Technology, a French companies listed on Nasdaq.

Silvano Spinelli. Cofounder of Novuspharma and CEO between 1999 to 2003 until it was acquired by US company Cell Therapeutics, now its executive vice-president.

Kari Steffanson. Founder and CEO of population genomics company deCODE Genetics.

Harry Stratford. Executive chairman of Prostrakan and the founder and former CEO of Shire Pharmaceuticals.

Carl-Johan Sundberg. Investment Director, Karolinska Investment Fund in Sweden.

Jean-Noël Treilles. CEO Biopartners, a Swiss company developing follow-on biologics in partnership with Korean company LG Life Science.

Gerard van Beynum. Chairman of Dutch biotech think tank Biopartner also a former vice president for strategy and communication at transgenic animal company Pharming.

Dan Vassella. CEO Novartis, a company which has been very proactive in partnering with biotech companies over the last decade and made big plays in gene therapy.

Friedrich von Bohlen. Former CEO of bioinformatics company LION Bioscience, located in Germany.

Alexander von Gabain. CEO Austrian vaccine company Intercell.

Biobusiness in the rest of the world

Katsuhiko Asano. President of Kirin's Pharmaceutical Division and also served as chairman of the Board of Kirin-Amgen from 1996 to 2001.

Greg Collier. CEO of Geelong, Victoria, Australia-based genomics drug discovery company ChemGenex Pharmaceuticals.

Krishna Ella. Chairman and managing director of Bharat Biotech International. A pioneer who, upon his return from the US in 1995, chose to build a vaccine plant in a barren area 40-km from Hyderabad in India, that eventually became the genome valley of today.

Martin Godbout. President & CEO, genomic fund Genome Canada since 2000.

Fang Hu. President of Sunway Biotech, Chinese biotech company developing second generation gene therapy for cancer.

Eli Hurvitz. Chairman of Israeli generics company Teva since 2002. Previously, he was Teva's President and CEO for over 25 years.

Kiran Mazumdar-Shaw. CEO of biopharmaceutical company Biocon, one of India's most dynamic biotech.

Brian McNamee. CEO of the largest listed Australian biotech CSL, based in the state of Victoria.

Eli Mintz. A cofounder of Israeli drug discovery platform company Compugen.

K.K. Narayanan. Managing director of METAHELIX Life Science Private, Bangalore, homegrown company developing products in the agbiotech sector.

Seung-Kwon Noh. CEO Korean company Eugene Science that developed a cholesterol-lowering food additive sold through the US market through a deal with food giant ADM.

Hyunseok Park. CEO MacroGen, first Korean company to list on the Seoul stock exchange.

Zhaohu Peng. CEO Shenzhen SiBiono GenTech, China The CEO of the company who brought the first approved gene therapy to the world.

Cyrus Poonawala. Chairman of Serum Institute of India, Pune.

Varaprasada Reddy. Chairman and managing director of Shantha Biotechnics, Hyderabad, which made, in 1997, India's first recombinant healthcare product, an hepatitis-B vaccine.

M.K. Sharma. CEO of Mahyco-Monsanto Biotech (MMB) in Jaina marketing of *Bacillus thuringiensis* (Bt) cotton hybrid seeds (Bollgard) developed by Mahyco since 2002.

Shinichi Tamura. Cofounder, president, CEO of Sosei, a company identifying new uses for established drugs.

Ei Yamada. President and CEO Japanese gene therapy company AnGes.

Philip Yeo. Chair of Singapore's Agency for Science, Technology and Research (A*STAR) and one of the key players in the development of Singapore into a hub for biomedical and biotechnological research that includes Biopolis.

Weidong Yin. Founder and CEO of Sinovac Biotech, a Chinese biotech company developing a SARS vaccine.