Trip Report: The Future of Life Summit Monterey, CA February 19 – 21, 2003

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This event was sponsored by <u>*Time*</u> magazine to celebrate the 50th anniversary of the discovery of DNA by Francis Crick, James Watson (Cold Spring Harbor Laboratory), and Maurice Wilkins at Cambridge.

What was most fascinating about this conference was that it was not attended by a bunch of body-pierced, Birkenstock-wearing bozos blabbering about Web services, SOAP, UDDI, WSDL, WSFL...but a variety of academicians, biologists, engineers, ethicists, high-school teachers, IP experts, lawyers, physicians, policy makers, professors, and students. This gave a very broad perspective to such controversial issues as human cloning, embryonic stem-cell research, prolonged life spans, personalized medicines, and genetically modified (GM) foods.

Interview with Dr. James Watson

It was obvious after a few minutes of interview that Dr. Watson is neither religious nor a believer in God. He believes religion puts restrictions on one's imagination and you should learn nature by nurture. Here are some of his other observations:

- □ Crime is committed by people who are hungry. "If you are full, you go to sleep and not commit a crime in the street. So, to fight crime, we must fight hunger."
- Personalized medicine, despite the hype being created by pharmaceutical companies, will not be here anytime soon.
- Encourage embryonic stem-cell research, and don't let religious fanatics and ethicists discourage this.
- □ "I don't believe in truth by revelation. You need to constantly experiment."
- □ A well-lived life is good conversation, good books, tennis, and science.
- □ Abortion should be up to the mother and dangerous pregnancies should be terminated.
- Panels debating controversial topics such as stem-cell research should not have bio-ethicists and religious leaders as panelists. Instead, it should comprise parents and children with sick children and sick parents, respectively.
- □ President Bush was brought up by parents who made him believe in God. That is his biggest handicap. Why should you begin every staff meeting with a prayer?
- "I remember from my days in England that when a new school was about to be opened, Winston Churchill asked us for contributions towards a new chapel on the campus. Francis Crick (Watson's Professor at Cambridge who shared the Noble Prize with him) donated 10 Guineas and told Churchill that amount should go towards a brothel and not a chapel! Guys don't need God; they need gals!!

When ethicist Daniel Callahan insisted that bio-scientists didn't absolutely need embryonic stem cells in their quest to cure certain intractable ailments, Watson jumped from his seat shouting, "That's crap."

Business: Digital to Genomic and DNA

Prof. Juan Enriquez (Harvard Business School) presented a most provocative lecture on how nations flounder and prosper. He said that while genomics-based information would dominate the world economy in the next 50 years, only those countries that understand these developments and take advantage of them are going to be big winners. The rest, he said, are going to fall by the wayside, economically and otherwise.

For instance, from 1000 to 1850, China and India averaged a 0.1 percent annual growth. Yet, by 1840, these two countries accounted for over 40% of global economic output. Today, they produce 4.8 percent! Both these countries entered the Industrial Revolution too late. Commodities—be they oil, wheat, corn or soybeans—deplete over time. Natural resources are a curse—just follow Iran, Iraq, Saudi Arabia, and Venezuela. Countries need to produce knowledge to prosper. By the year 2020, China is expected to account for 50 percent of the world's manufacturing. Yet, will China be producing valuable knowledge or just be a home for tens of thousands of sweatshops?

In 1700, the GNP ratio of the richest country to the poorest was five to one; today it is 427 to 1. Poorer countries are getting poorer because of bad political decisions and still living in the past. Two-thirds of South Koreans that get their PhDs in the U. S. return to Korea, where as only 15 percent of Chinese and 20 percent of Indians return home. Sixty percent of PhDs in Saudi Arabia are awarded in Islamic studies and not science or mathematics! This doesn't create wealth. Great societies die because they get arrogant and complacent. You have to educate your kids in the language that creates wealth and knowledge. Look what cars did work for Japan, chips did for Taiwan, and transportation did to Singapore. Disruptive technologies can make or break nations.

You don't need 200 languages or 26 alphabets. In a digital world, you just need '0's and '1's. Information is growing too fast to keep up with: Twenty years ago, the pace of discovery was one fact per person per year. Today, you go to a website in the morning and you are bombarded with 100,000 facts. The Library of Congress has the largest collection of books and publications in the world. Yet, a pharmaceutical company in search of a new drug produces that much information in just one month!

The pharmaceutical industry invests \$40 billion in R&D annually and IT spending in this segment is growing at 20% per year. On the subject of new-drug development, it is well known that, on an average, bringing a new drug to the market takes 10 to 15 years at a cost of over \$800 million. Is there any way to make this cheaper and faster? IBM Life Sciences division was started three yeas ago. IBM's Caroline Kovac described how Big Blue is helping drug companies mine, dig, search, slice, and dice vast amounts of data generated during drug discovery and thus help them bring new drugs to the market sooner. As we digitize biology gradually, is it possible that the IBMs of the world will soon become drug companies? Kovac contended, "I don't think so, but we will play a major role and help drug and pharmaceutical companies succeed." The genetic revolution happening today will eventually become the most profound one in history. It will be a long time before *in silico* (vis-à-vis *in vitro* and *in vivo*) models become a reality. However, there is unbelievable convergence of pharmaceuticals and IT. As we move from blockbuster drugs to designer, personalized medicine, IT companies will play a major role in the drug and pharmaceutical industry. Preventive, predictive, and personalized medicine is worth looking into.

Weapons of Mass Destruction (WMD)

<u>Raymond Zilinskas</u>, Director of the Chemical and Biological Weapons Non Proliferation Program at the <u>Monterey Institute of International Studies</u> presented a fascinating lecture on the WMD programs in the former Soviet Union and Iraq. The USSR had the most successful bioweapons program in the world. Soviet researchers were highly successful in creating huge quantities of super-virulent bacterial agents that resisted vaccines and treatments. Although the program's infrastructure collapsed with the demise of the Soviet Union, Russian researchers continue to guard their biowarfare agents closely, refusing to allow the United States to test vaccines against them. We do not know why, but Zilinskas believes, "They think, 'We have more knowledge and more sophistication with biological weapons than anyone has ever had, so let's keep that intact," he said. Russia and the rest of the former Soviet republic hold strains of smallpox, anthrax, and

other bacteria that resist U.S. vaccines and antibiotics. The Russians transferred genes from the Ebola virus into smallpox, but found that it wasn't any more deadly. Eventually they succeeded at producing several super-virulent agents including what Zilinskas called a "devilish little machine"—Yersinia pestis, also known as the black plague. They added a touch of Venezuelan equine encephalitis to make it even more resistant and deadly. He said ethics training is even more important, considering that many of the brilliant and talented Soviet scientists who worked on these bioweapons projects are now in the U.S., Israel, and the

Iraq's declared biological weapons include:

just want to be scientists."

- □ 25 Al Hussein Missiles (13 botox; 10 aflatoxin; two anthrax)
- □ 157 R400 bombs (100 botox; 50 anthrax; 7 aflatoxin)
- □ MIG-21 with 2,200-liter belly tank
- □ Bulk formulations (8,000 liters botox; 2,000 liters anthrax)

We have absolutely no idea what China and other countries on the 'Axis of Evil' have. So, can the United States defend itself against such a threat?

United Kingdom doing regular science. "These people don't want their colleagues to know their past, they

Not with duct tape, rhetoric, and plastic sheeting, according to Zilinskas. He criticized the Bush administration's emphasis on stockpiling supplies to try to block contamination from a biological attack. Such advice might be helpful for peace of mind, he said, but it is useless for actual safety because it's not likely the public would find out about a bioterror attack until three to six days after it hits. Muin Khoury, director of the Office of Genomics and Disease Prevention at the <u>Centers for Disease Control and Prevention</u> agreed that the U.S. government's focus is non-sensical. "Public health is in disarray, and this emphasis on terrorism is eroding the public health infrastructure even more," said Khoury, who spoke as part of a panel on the use of DNA information.

Genomics, Genetically Modified Foods, and Designer Babies

Ecologist <u>Thomas Lovejoy</u> estimated that loss of species was occurring at an alarming rate of 100,000 a year, mainly because of the destruction of habitat. During the last 200 years about 1.2 million to 1.3 million species have been found. There are anywhere from 3.5 million to 100 millions of species on our planet. In a handful of soil, you have about 6,000 types of bacteria. We have barely identified all the species on earth. There are 400 types of bacteria in the mouth alone. The average life span of a species is one million years. He and his fellow panelists, Harvard's <u>E. O. Wilson</u> and <u>Ryan Phelan</u> of the <u>All Species Foundation</u>, described themselves as guardedly optimistic. Said Wilson, "The world is beginning to wake up to the loss." He predicted that the cataloging of the planet's still-uncounted millions of species would become a major scientific effort, especially in the developing world, but added that it would require "education, education."

The British writer and author (*Genome: The Autobiography of a Species in 23 Chapters*) Matt Ridley argued that the early fears about tinkering with genes had proved to be groundless. "I am an optimist, because I believe in technology. What we are afraid is that we may know too much that we will be scared. But knowledge gives us evitability. If we discover something, will we become fatalistic? Transgenic mice are proving gene transplants are indeed possible. Yet, about 30% of animal cloning has organ defects. Cloning is dangerous. He dismissed the current concerns of many of his fellow Europeans about GM foods. Mother Nature, he said, had been engaged in such crossbreeding experiments for millions of years. "She's got a huge research budget and the chances of us beating her at that game seem to me rather remote," he added. He saw no moral arguments against human cloning it if it turned out to be a safe. He even suggested that something good might be said for the atomic bomb: "Maybe MAD (mutually assured destruction) did indeed prevent great wars between East and West." We tend to underestimate the impact of technology in the long run, and overestimate in the short term, he concluded, quoting Arthur C. Clarke.

Harvard's <u>Rudolph Tanzi</u> predicted that, with recent identification of more genes associated with Alzheimer's, substantial progress would be made in the search for a treatment for this devastating disease. "The news is good," he said. "We're well on our way to new leads in the development of drugs for Alzheimer's." Ms. <u>Bartha Knoppers</u>, University of Montreal law professor pointed out that advances in genomics could lead to greater mutual understanding among peoples by illuminating how narrow our genetic differences really are. "We could finally realize our ideal of the family of man," she said.

Are GM foods bad? There is hysteria in Europe on this issue. Every year 500,00 die worldwide of Vitamin A deficiency and every day 24,000 die of malnutrition. GM crops need lesser amount or fertilizers, but aren't *we* putting pesticides in the first place?

If gene typing and designer babies become commonplace:

- □ Is a gene patentable? There are many countries in the world that do not accept patenting genes. Human genome belongs to humanity.
- □ What about loss of privacy?
- □ Who owns our genes—we?
- □ Isn't the actual discovery intellectual property? Does it belong to the creators or the created?
- □ Does this lead to the advent of a genetic caste system where the wealthy can afford super babies and the poor excluded from such genetic perks?
- □ Will this take us back to Hitler's days of creating a super race?
- □ They will not end diversity. Not every parent wants a seven-foot tall blonde blue-eyed Arnold Schwarzenegger!

So, is bioethics a failure? Yes and no. Many ethicists are front-end people for drug companies. Many things have gone wrong in science, but we haven't given up on it. Similarly, we will not give up on bioethics. The shadow of Hitler falls on all of us; he killed 70,000 psychiatric patients performing gruesome tests on them. Man also has made many animals dumb by domesticating them. Is playing with genes always safe? Not necessarily. In fact, if you take away the gene that causes anxiety and depression, it also makes you lose interest in sex!

Columbia University's neuropsychologist <u>Nancy Wexler</u> provided a different viewpoint. Dr. Wexler has done extensive scientific studies among clusters of families around Venezuela's Lake Maracaibo afflicted with Huntington's disease. This has paved the way for the identification of the gene for the fatal ailment and a test for its detection. She emphasized that treatment for the disease is no better now that it was when her mother died of it in 1978. She claimed this is at least partly because drug companies are interested in mass-producing blockbuster drugs (such as Viagra and Prozac) and not in developing "orphan drugs" for diseases with a relatively low incidence of occurrence. Thus, few people get tested for the gene, and those who do, face the added burden of possibly being denied health insurance should the test turn out to be positive. Her messages: New social policies are badly needed to protect such people. We will find cures to diseases, but the critical obstacles are anonymity and privacy.

If Genetics is a goldmine, where is all the gold?

There are over 5,000 biotech companies in the world, half of them in the U. S. Yet, the market capitalization of public biotech companies (~\$150 billion) is one-half of that of Pfizer and Merck combined!

Paul Gelsinger (<u>CIRCARE</u>), whose 18-year-old son Jessie died during a gene-therapy trial at the University of Pennsylvania in September 1999, made a plea to drug and pharmaceutical companies. He noted that several children in France have come down with leukemia in gene therapy. He said doctors painted a beautiful picture of the benefits of the treatment without a full explanation of the risks. Why? <u>Dean Hamer</u>, chief of the <u>National Cancer Institute</u>'s Gene Structure and Regulation Section, argued it is because too often the protocols used in clinical trials are hidden at the insistence of drug companies eager to protect their patent rights. Calling for more transparency in such experimental procedures, he said there was a simple explanation for why there aren't tougher federal regulations on informed consent: "Just follow the

money," said Hamer, "and you'll get the answer." He cited treatment of AIDS as a prime example of economics-driven medicine. "There are great drugs for HIV," he said, "but only three percent of the people affected get them."

Biotechnology has yet to produce the promised pot of gold. Venture capitalist <u>G. Steven Burrill</u> (<u>Burril &</u> <u>Co.</u>) estimated that investors had poured some \$220 billion in biotechnology startups in the past two decades and still haven't made any money. But that could soon change and many speakers urged the U.S. not to let this opportunity slip by such shortsighted policies as curbing stem-cell research, a decision that has led at least one prominent scientist to move his laboratory out of the country. "When you see whole groups of scientists move to take advantage of new opportunities," said Juan Enriquez, director of the Harvard Business School's life science project, "you can make a country rich or poor very quickly." As for genomics, he said, "This is the sort of technology that leads to the rise and fall of nations."

Ralph Merkle, vice president of technology assessment for the <u>Foresight Institute</u>, heralded the great promise of nanotechnology in medicine—the development, for example, of tiny molecular computers that could work inside the body—but was quite pessimistic on the idea of any quick profits from such innovations because we are still many years from the technology being turned into a practical reality.

Although they avoided a face-to-face meeting, the audience heard from both Francis Collins (<u>National Human Genome Research Institute</u>, <u>National Institutes of Health</u>) and <u>J. Craig Venter</u> (<u>The Center for the Advancement of Genomics</u>), the rival leaders of the public and private human genome projects. Collins announced his ambitious new goals that include sequencing all 23 pairs of human chromosomes, applying genomics to the treatment of specific diseases, developing gene-spotting systems for early detection of disease and expanding genome studies to larger populations so as to pinpoint the role of genetic differences in disease.

Venter suggested that the sequencing effort was just a starting point for much more science. He said an immediate target should be reducing the cost of sequencing an individual genome to \$1,000 or less in the next decade or so. This would be a powerful tool, he added, to catch diseases like colon cancer years before the onset of observable symptoms when there is a 90 percent or better chance of curing them. "We would give power to the individuals to know their own risk of disease," he concluded. Now heading up four nonprofit genomics groups, <u>Celera Genomics</u>' former CEO discussed his latest interests, most notably the development of synthetic microbes that could be used to produce inexpensive, nonpolluting alternatives to fossil fuels like hydrogen. Asked if it was really true, as one magazine recently reported, that his ambition was nothing less than to save the planet, Venter replied, "Well, we want to make a start."

Perhaps the most exciting discussion centered on using the new findings from the revelation of the human genome to lengthen our productive lives. Susan Greenfield, director of the Royal Institution of Great Britain, speculated that soon women would be able to have their eggs fertilized while they were still in their normal childbearing years, store them, and then bear the child whenever they choose. "People of all ages will be having children," she said. Inventor of the first reading machine for the blind and many other amazing things, <u>Raymond Kurzweil</u>, made a prediction that left even his fellow panelists gasping. Asked how long he expected to live in light of all these advances, he replied without hesitation, "1,000 years. My kids, too." He also predicted that, ten years from now, we would be adding one year to our life every year. Finally, he boasted we could produce one million vaccines against smallpox and anthrax per hour. <u>Bill Joy of Sun Microsystems</u> retorted, "But we can't distribute and inject one million per hour." He also noted that a calculation that takes a year today would take eight hours in a few years with improved hardware and software. Soon, a million-fold improvement in computing and algorithms will see a trillion-fold improvement, helpful to both the good and terrorists.

Conclusions

Overall, this was a fascinating conference. There were a lot of predictions, some real—such as being able to conquer some diseases—and some highly speculative—such as living to be 1,000 years old. A hundred years ago, the killer diseases were typhoid, malaria, plague, and influenza; today, they are cardiovascular diseases, cancer, AIDS, diabetes, and stroke. A hundred years ago, the average life expectancy in the U. S.

was 48 years; today it is 60 percent higher at 77. Does it mean that it will be 124 years in the year 2100? What will be the 'new' diseases then? Are bacteria getting so smart that they are resisting penicillin? Today, there are over 200 anti-bacterial antibiotics and scores of anti-viral medications. But, bacteria and viruses are smart and become resistant over time to cures we develop. So, it is a constant battle of nature versus humankind. Who will win the battle? Well, nature is millions of years older than mankind is. And, whereas mankind has been here for a little over 100,000 years, cockroaches and sharks have been here for over 300 million years. So, you be the judge.