NEWS ON DEVELOPMENTS
CURRENT DEVELOPMENTS AND ISSUES: A SUMMARY

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ABORTION

Further developments in RU 486 studies

Studies of RU 486 combined with prostaglandins to induce abortions show that the combination causes some problems. Aside from bleeding and abdominal cramps, the RU 486/prostaglandin combination has also been implicated in three cases of heart complications in which one case was fatal.

Two routes are being studied to reduce these problems. The World Health Organization (WHO) has shown that the dose of RU 486 "can be reduced by at least two-thirds without a fall-off of efficacy," *Science* reports. The WHO study included 1188 women from eight countries. The women from each center were divided into three dosage groups for RU 486, one with the standard dose and two others with lower doses. All women were given the same dose of prostaglandin. Complete abortions were induced in 95% of the women independent of the dose of RU 486.

The inventor of RU 486, Etienne-Emile Baulieu, thinks the problems with the combination stem from the prostaglandin used. Sulprostone is an injectable prostaglandin that is currently used. It is responsible for at least 80% of the abdominal cramps and may be implicated in the heart complications seen. He is currently testing safer prostaglandins that can be taken orally. One such is misoprostol, which, in combination with RU 486, produces abortion in 95% of the women treated, but with less incidence of cramps. Baulieu adds that an oral prostaglandin can be taken by women at home.

Roussel-Uclaf, the company that manufactures RU 486, has set its policy on where it will market the drug. It will sell it "where abortion is legal, where the social and political climate is favorable to abortion, and where distribution of the drug is tightly controlled," Science states. RU-486 will thus be available shortly in Scandinavian countries and the Netherlands. Third World countries such as India and China may be next in line, and Baulieu has been discussing the drug with the prime minister of Bangladesh. The United States is one country where RU 486 will probably never be marketed.

JOHN MAURICE, 1991. Improvements seen for RU-486 abortions. *Science* 254: 198–200.

Feminist critique of RU 486 published

Pro-choice feminists from the Institute on Women and Technology in Cambridge, Massachusetts have recently published a report that is critical of RU 486. The report, "RU-486: Misconceptions, Myths and Morals," was written by Janice Raymond, professor in medical ethics at the University of Massachusetts, Amherst; Lynette Drumble, physician in the Department of Surgery at the

University of Melbourne, Australia; and Renate Klein, biologist and Lecturer in Women's Studies at Deakin University, Victoria, Australia. The authors have studied the published data on RU 486 combined with prostaglandin and have concluded that using it is not as easy or safe as has been claimed. RU 486 "requires at least three visits to a clinic, whereas the conventional suction method used for most early-term abortions requires only two," *Science* reports.

The combination of RU 486 with prostaglandin is associated with "unnecessarily high levels of pain and bleeding, side effects that have been linked to prostaglandin use in the past," *Science* continues. The report also states that blood loss after using RU 486 and prostaglandin is twice that of conventional abortions, requiring transfusions in 1% of the women treated. Conventional abortions require transfusions in only 0.1% of the women.

MICHELLE HOFFMAN. 1991. Feminist group dissents on RU-486 use for abortion. *Science* 254: 199.

IN VITRO FERTILIZATION

Australian and New Zealand statistics on IVF success rates

The National Perinatal Statistics Unit at The University of Sydney, Australia has published (in 1991) the 1989 data from 25 clinics in Australia and New Zealand using IVF and other assisted conception techniques. The clinical pregnancy rate for IVF after transfer of fresh embryos was 13.9 per 100 egg-collection cycles. The live birth pregnancy rate was 9.0 per 100 egg-collection cycles. Frozen embryo transfers resulted in a live birth pregnancy rate of 9.9 per 100 egg-collection cycles. The live birth rate for GIFT (gamete intrafallopian transfer) was 20.9 per 100 egg-collection cycles. Frozen embryo transfer was associated with lower rates of spontaneous abortion and multiple pregnancies, and with a lower incidence of preterm birth and low birthweight in singleton pregnancies. The Fertility Society of Australia recommends that not more than three embryos be transferred in an IVF cycle, and therefore there was a reduction in the proportion of pregnancies occurring after transfer of four or more embryos. Fetal loss and other complications are more likely with artificial conception techniques when compared with natural conception. There were higher rates of ectopic pregnancy (7.7%), spontaneous abortion (22.9%), multiple pregnancy, preterm birth (17.8% in singleton pregnancies less than 37-weeks gestation), low birth-weight (34.8%, less than 2500 grams), and Caesarean section (41.7%). Major congenital malformations occurred in 2.2% of births and induced abortions after IVF and in 2.8% after GIFT. During 1989, the perinatal death rate for liveborn and stillborn foetuses and infants of 20-weeks gestation and over were 45.1 per 1,000 births for IVF and 43 per 1,000 births for GIFT. More than half of all perinatal deaths occurred in multiple pregnancies. Further details are contained in the National Perinatal Statistics Unit report. Write to Dr. Paul Lancaster, AIH National Perinatal Statistics Unit, Edward Ford Building A27, University of Sydney, New South Wales, Australia 2006.

AIH NATIONAL PERINATAL STATISTICS UNIT, SYDNEY. 1991. *Assisted Conception: Australia and New Zealand 1989.*

SEX SELECTION

Sex selection banned in India

"Use of prenatal diagnostic (PND) techniques to determine the sex of a fetus has been prohibited under legislation introduced in the Indian parliament," *Nature* reports. "It also bans advertisements of such tests and threatens violators with a fine of 10 000 rupees and a three-year jail term." The

legislation is hoped to control the increase in private clinics that offer PND and selective abortion of female fetuses. Such clinics have sprung up even in remote towns.

PND will only be allowed for determining genetic diseases and only after medical consultation. "No doctor can conduct the tests on a pregnant women unless she is either above the age of 35, has a history of spontaneous abortions, has been exposed to radiation or teratogenic agents or has a family history of mental retardation," *Nature* states. All clinics that provide PND must register with a supervisory board appointed by the minister of family welfare within 6 months or close. Many will probably be forced to close.

K. S. JAYARAMAN. 1991. Saving female babies. *Nature* 353: 594.

Geneticist refuses to carry out sex tests at 1992 Olympics

"A prominent Spanish geneticist has refused to participate in a sex testing trial of women athletes participating in the 1992 Olympics in Barcelona, arguing that the simplicity of new testing methods, combined with their inherent fallibility, could lead to increased misdiagnosis of women athletes as men," *Nature* reports. The sex test uses the polymerase chain reaction (PCR) combined with a genetic probe that identifies the presence of Y chromosome genetic material, which is normally found only in males. 10% of the 3000 women athletes at the summer games are to be tested and the test is considered to be 98% accurate. The official Olympic policy defines a woman as a person having two X chromosomes.

But there are chromosomal variations that result in what society considers to be a woman even though she may carry some male-based genetic material. For example, some women have an inactive Y chromosome as well as an X chromosome or have bits of Y chromosome in their genetic makeup, neither of which give them any athletic advantage.

A major criticism of the test is that it is very easy to do and will thus lead to more and more women being tested. But what constitutes a female genetic makeup is still scientifically controversial and therefore the test will only confuse the matter.

CHRISTOPHER ANDERSON. 1991. Olympic row over sex testing. *Nature* 353: 784.

ORGAN DONATION

First "domino-donor" heart and lung transplantation in Australia

Australia's first "domino-donor" heart and lung transplantation has been carried out at the Alfred Hospital in Melbourne. According to the report of this operation, published in the *Medical Journal of Australia* (November 4, 1991), the increased demand for donor organs has placed importance on the efficient use of all available organs, and therefore the "domino-donor" operation was developed. A patient who has severe lung or heart and lung disease receives a heart-lung transplant from a brain-dead donor, and his or her own heart is then transplanted into a third person with heart disease. In this particular case, a 25-year-old man with cystic fibrosis received a heart and lung transplant, and his own heart was transplanted into a 20-year-old woman with end-stage cardiomyopathy, possibly associated with cocaine abuse. However, she had abstained from drug abuse for 18 months and was put on the transplantation list. At 8 months she rejected the heart and underwent another transplantation.

The first "domino-donor" operation was performed in 1987 in the United States.

ANDREW COCHRANE, JULIAN SMITH, and DONALD ESMORE. 1991. The "domino-donor" operation in heart and lung transplantation. *Medical Journal of Australia* 155:589-593.

ETHICS

"New" Australian health ethics committee

The membership of the "new" Australian Health Ethics Committee (AHEC), to replace the National Bioethics Consultative Committee (NBCC) and the Medical Research Ethics Committee of the National Health and Medical Research Council (NH & MRC). has been announced. The NBCC was disbanded by the Federal Health Minister, Mr. Brian Howe, after a joint meeting of the states' health and welfare ministers unanimously rejected the NBCC's proposals for the legalization of noncommercial surrogacy.

The AHEC is chaired by Robyn Layton (barrister), who was the chairperson of the former NBCC. The deputy chairperson is Professor Ross Kalucy (medicine/psychiatry). Members of the committee are: Prof. Max Charlesworth (philosophy). Prof. Don Chalmers (law). Prof. John Funder (medicine/endocrinology), Prof. Anne Woolcock (respiratory medicine). Dr. Heather Mitchell (medicine/epidemiology), Dr. Rob Simpson (chief medical officer. Health Department Victoria), Dr. Robin Watts (nursing education), Dr. Sandra Gifford (public health), Sister Regis Mary Dunne (bioethics), and Ms. Hilda Bastian (consumer advocate on health care). The first brief that the AHEC will address is the allocation of funds in medical research.

Seven members of the new committee were formerly on the NBCC. Critics have expressed concern that it is not a "new" committee, and that policy decisions on issues such as IVF, embryo experimentation, and genetic engineering have now been shifted back into a medical framework, as the AHEC is a subcommittee of the NH & MRC.

1991. *Australian Health Ethics Committee Newsletter* 1(1).

GENETIC ENGINEERING

Genetic survey of indigenous peoples gains support

Two scientists, Luca Cavalli-Sforza and Allan Wilson, issued a call for help during the summer of 1991 to collect DNA samples from as many remote indigenous populations as possible, before they die out. The idea is to better study human genetic diversity. The response has been overwhelming. Anthropologists are offering to collect blood samples from the tribes they are studying, and several U.S. agencies have offered to help fund parts of the study. Even the Human Genome Organization (HUGO) has jumped on the bandwagon and has written "a grand vision" of the project that is twice the size of the original proposal. Numerous experts are being consulted to determine which populations should be sampled first, before they disappear.

LESLIE ROBERTS. 1991. Genetic survey gains momentum. *Science* 254: 517

Controversy over gene patent application

On June 20,1991, Craig Venter of the National Institutes of Health dropped a bomb within the Human Genome Project by filing patents for 337 new human genes that his automatic gene sequencers had cranked out. The work took only a few months to do using a method that identifies only active genes using complementary DNA (cDNA). Venter is planning to file another patent for 2,000 more new genes. This is the first attempt to patent naked genes without knowing what they do.

The patent application immediately infuriated human genome project researchers all over the world. Venter doesn't know what the genes do, but his patent application covers the gene, its protein product, and the method used to obtain it. The controversy is whether such "naked DNA" is patentable or not, and if it should be. Until recently, patents were filed when a research group had identified and mapped a gene for a known protein or genetic disease.

There are many fears being voiced. One is that industry will shy away from investing money in genetic research. Anther is that commercialization will stop the free flow of information that has been promised by researchers within the human genome project. Many feel it just isn't fair. "The Genome Project was sold to Congress as a 15-year, $3,000-million effort to map and sequence the entire DNA molecule," *Nature* states. "Now Venter says he can get almost all the genes – the only part of the genome most congressmen care about – in a few years, for perhaps $10 million." Once the genes are found, getting money to sequence the other 97% of the genetic material will be difficult.

The controversy has led the British Medical Research Council to withhold its own cDNA sequences while it checks out the patenting options. Previously the MRC has made its cDNA sequences freely available to researchers but is now considering charging private companies for access to their gene data bank. Even the French Medical Research Agency, another cDNA research center, is worried about the development and is considering filing patents. The controversy has also prompted an editorial in the November 21,1991 issue of *Nature*, which questions both NIH and MRC for trying to cash in on their human genome data, thus putting the entire effort jeopardy. Everyone is now nervously awaiting the outcome of the U.S. patent office's deliberations.

CHRISTOPHER ANDERSON. 1991. US patent application stirs up gene hunters. *Nature* 353: 485–486; LESLIE ROBERTS. 1991. Genome patent fight erupts. *Science* 254: 184–186; PETER ALDHOUS. 1991. Tit for tat on patents? *Nature* 353: 785; CHRISTOPHER ANDERSON and PETER ALDHOUS. 1991. Secrecy and the bottom line. *Nature* 354: 96; CHRISTOPHER ANDERSON. 1991. More questions than answers. *Nature* 354: 174; 1991. Free trade in human sequence data? *Nature* 354: 171–172.

California antigenetic discrimination bill vetoed

A bill to prevent genetic discrimination by employers and insurance companies was vetoed by California's Governor Pete Wilson on October 14, 1991. The bill, passed by a majority of the state legislature, would have created an 8-year moratorium on using genetic tests to determine people's eligibility for health insurance, group life insurance, and disability insurance policies. The bill would also have stopped the use of genetic testing for employment purposes and made discrimination based on genetic characteristics illegal.

"Wilson, a Republican, said he supported the insurance provisions, as they would encourage people to take genetic tests needed to make important personal decisions," *Science* states. "But he balked at expanding the civil rights laws essentially because doing so would increase the cost of doing business." A new version of the bill addressing only the insurance questions is being planned.

CONSTANCE HOLDEN. 1991. California v. genetic discrimination. *Science* 253: 1484; CONSTANCE HOLDEN. 1991. Genetic bill vetoed. *Science* 254: 522; CHRISTOPHER ANDERSON. 1991. Privacy bill vetoed. *Nature* 353: 687.

Rifkin's heretical views becoming accepted by scientists

Jeremy Rifkin, of the Foundation on Economic Trends, is one of the more active critics of genetic engineering in the United States. Up to a few years ago scientists refused to talk to him, calling him and those who support him "modern-day Luddites," "nuts," "fearmongers," and countless other epithets. But "fifteen years of Rifkin's lawsuits, petitions, legislation, press-conferences and general harassment has finally made a dent on the gene scientist," *Nature* reports.

Recently, a congressional hearing heard about the dangers of misusing genetic

information from Bernadine Healy, director of the U.S. National Institutes of Health; Jame Watson, head of the U.S. human genome project; and W. French Anderson, gene therapy pioneer. The hearing was organized by Jeremy Rifkin. He has also lobbied Watson to support a genetic privacy bill that has been introduced to Congress.

Part of the reason these people were testifying at the hearing is that Rifkin has successfully lobbied Congress to force agencies involved in the human genome project to spend 4% of their budget on research on the ethical and social consequences of the project. This has forced the agencies involved to address such problems as genetic discrimination, eugenics, and other misuses of genetic information.

Rifkin states that although there is consensus on these issues, "There are still plenty of genetic issues on which he differs from much of the scientific community, including animal patenting and the release of genetically engineered organisms."

CHRISTOPHER ANDERSON. 1991. Evolution of a gadfly. *Nature* 353: 686–687.

Rifkin wins suit against U.S. Department of Defense

Jeremy Rifkin, president of the Foundation of Economic Trends, has won a lawsuit against the U.S. Department of Defense that will force the military to carry out an environmental impact assessment of their biological weapons research program. The assessment will have to cover the Biological Aerosol Test Facility at Dugway proving grounds in Utah, and five other laboratories where work on biological toxins is being performed.

CHRISTOPHER ANDERSON. 1991. Rifkin wins suit. *Nature* 354: 257.

New test could speed up genetic screening

"A new test could significantly speed up the mass screening of large numbers of people to see if they are likely to pass on genetic diseases such as cystic fibrosis and sickle cell anemia to their children," *New Scientist* reports. Developed in Australia at the Queensland University of Technology, the test takes 5 hours and can use DNA from the skin at the end of a single hair. "Once carriers of genetic diseases have been identified, their pregnancies can be more closely monitored and terminated if the fetus is found to be affected," *New Scientist* continues.

The test, called GeneCo Technology, is relatively cheap, costing about £25, and can be automated. The test can already be used to screen for hemophilia and phenylketonuria. It can rapidly be adapted to newly discovered genes. The method uses the fact that many genetic diseases are due to mutations in the affected gene.

A strand of DNA that codes for the gene up to the mutation is created. This so-called primer is then mixed with two separate samples of DNA from a person being screened. The primer then attaches to the person's gene up to where a mutation might be present. Two different bases are then added, one to each sample. One of these is the base that would add to the primer if the base in the person's own DNA is free of the mutation. The other is the base that would add to the primer if the defect is present. These bases have different radioactive labels. The primer is then removed from each sample and radioactivity measured to see if one or the other base attached to the primer.

Sufferers of a number of genetic diseases have two copies of the mutated gene. But carriers have a copy of the normal gene and a copy of the mutated gene. In the GeneCo test, sufferers of the disease will have radio-activity found only in the sample where the defect-related base was added. Carriers will have radioactivity found in both samples.

The test has been through clinical trials and was found to be 100% accurate. Patents on the method are now being sought internationally

and negotiations to market the test kit are being conducted in the U.S.

IAN ANDERSON. 1991. Simple test screens genetic disease. *New Scientist*. October 26:25.

DNA testing by a hair's breadth

Scientists at Queensland University of Technology (QUT) have developed a test that can detect recessive genes in a single hair root cell (Collins, *The Australian*, October 16, 1991; O'Neill, *The Age*, October 19, 1991). This genetic screening technique can detect recessive genes in prospective parents and determine whether there is a risk of passing on genetic conditions to their children. Recessive genes do not cause disease in the carriers, but in individuals who inherit two copies of the recessive gene. The QUT scientists say this test can be used to detect aberrant genes responsible for cystic fibrosis, haemophilia, phenylketonuria, and some forms of muscular dystrophy. One specific "mutation" accounts for 70% of cystic fibrosis cases, and six other genetic irregularities account for another 15% of cases. The researches claim that seven tests should reveal most individuals who carry a recessive gene for cystic fibrosis. In Western populations about 1 person in 20 carries such a gene, and 1 couple in 400 may be at risk of having a child with cystic fibrosis. Professor Dale of the QUT team said it would be feasible to screen couples with family histories of particular disease. Given that most people are carrying recessive genes for genetic diseases, the QUT team has considered the idea of mass screening populations as a way of reducing the high social and economic costs of genetic disease in the general population.

The test uses the polymerase chain reaction (PCR), which can multiply a selected DNA fragment into millions of copies, starting from a single copy present in a human cell. The PCR gene-amplifying technology was originally developed by the Cetus corporation in the U.S. This technique is used in forensic science, particularly in rape and murder cases. The test will be patented and marketed worldwide by Geneco, a private company set up by QUT.

CAROLYN COLLINS. 1991. DNA testing by a hair's breadth. *The Australian,* October 16; GRAEME O'NEILL. 1991. Test identifies silent genes of genetic disease. *The Age* (Melbourne). October 19: 25.

Cystic fibrosis – future prospects for screening and gene therapy

When the genetic defect for cystic fibrosis (CF) was identified in 1989, there was an almost immediate cry for widespread screening to detect carriers of the gene. CF is one of the more common inherited diseases in white people, affecting 1 in 2000 children. About 1 in 25 white people in the U.S. and England are carriers, meaning they have one normal copy and one defective copy of the gene. They themselves do not get CF, but they can pass it on to their children.

Now researchers are learning more about the protein that the gene codes for and what goes wrong when it is defective. The protein controls chloride transport across cell membranes, and this no longer occurs in cells with two copies of the CF gene. This is leading to speculation that CF may be treatable by gene therapy in the future. Researchers have successfully inserted normal copies of the gene into cells from CF patients and restored chloride transport.

The organ that is most affected by CF is the lungs. Researchers are now working with possible ways to insert normal genes into the cells in the lungs using viruses that are inhaled in an aerosol.

But gene therapy lies far in the future. Screening is already possible and is causing much controversy. A number of questions are being posed about testing for CF carriers in Great Britain.

How will the results be interpreted? So far only 85% of carriers can be identified, so it is impossible to know if a negative result really

means that the person does not carry the gene. Does everyone want screening? "An ongoing study at Cambridge of 1700 pregnant women showed that a third said they would not consider terminating a pregnancy on grounds of fetal abnormality, 7 per cent felt that nobody should be allowed to, and 10 per cent agreed with the statement 'If there is something wrong with my baby I'd rather not know,'" *New Scientist* states.

When is prenatal testing justified? Many feel that CF is not a serious enough genetic disease to warrant testing and termination of a pregnancy. Does screening make pregnancy more stressful? Previous studies have shown that prenatal diagnosis using other methods causes anxiety in pregnant women. There will always be a certain percentage of "false positives," women whose fetuses test positive but that later are shown not to have the disease. Women who have had false positive results have been found to be more anxious and have more negative attitudes towards the baby.

What happens if the screening shows that the woman's partner is not the child's biological father? Infidelity may also be suspected in cases where the father is not a carrier but the child has CF due to a new mutation.

KEVIN DAVIES. 1991. Cystic fibrosis: The quest for a cure. *New Scientist*. December 7:

30–34; GAIL VINES. 1991. The social dilemmas of screening for CF. *New Scientist*. December 7: 32.

Mice immunized against cancer with genetically engineered vaccine

"A vaccine based on genetically engineered tumour cells can seek out and destroy small cancers in mice," *New Scientist* reports. Cells were removed from tumours in the mice, and a gene for interleukin-4 (IL-4) was added to them. The cells were then injected back into the mice. IL-4 stimulates killer T cells that are known to inhibit and reduce tumours. The reinjected cells led to the complete disappearance of the tumours in the mice tested. A similar vaccine for humans could be used to treat patients who have had a major tumour surgically removed but who run the risk of recurrence or spread of the cancer.

PHYLLIDA BROWN. 1991. Gene-spliced tumour cells immunise mice against cancer. *New Scientist.* November 9: 22.

More gene therapy trials receive approval

Two research groups received approval for three gene therapy trials, two for cancer therapies and one to treat high cholesterol levels in the blood. A fourth application, to treat ovarian cancer, was not approved.

The U.S. National Institutes of Health (NIH) recombinant DNA advisory committee (RAC) approved two trials from Steven Rosenberg of NIH's National Cancer Institute, where patients will be immunized against their own cancers. In one trial, the tumor cells will be genetically engineered to contain the gene for tumor necrosis factor, and in the other the cells will contain the gene for interleukin-2. In the third trial, James Wilson of the University of Michigan Medical Center will insert a gene into liver cells that is hoped to correct a genetic defect leading to high cholesterol levels.

The fourth application was first approved by the gene therapy subcommittee of the RAC. But the full RAC rejected the application, stating that more animal research data was needed. The disagreement is leading to discussions of phasing out the subcommittee. Researchers find the two-tier system of approval at NIH to be burdensome, unnecessary, and confusing.

Gene therapy experiments in humans now total 6 gene-transfer and 5 gene-therapy studies. Seven additional applications are expected in early 1992.

DIANE GERSHON. 1991. Cracks in the RAC. *Nature* 353:591; CONSTANCE HOLDEN. 1991.

Gene therapy trials on the move. *Science* 254: 372; BARBARA J. CULLITON. 1991. Gene therapy on the move. *Nature* 354: 429.

Gene for alcoholism called into question

Two conflicting articles have been published in the same issue of the *Journal of the American Medical Association (JAMA)* claiming and disproving the existence of a gene for alcoholism. A previous study claimed to have found a link between a marker for a dopamine receptor gene and severe alcoholism. In a study by the (U.S.) National Institute of Mental Health this correlation was not found.

The two *JAMA* articles add fuel to the controversy. One study, by David Comings of the City of Hope National Medical Center in Duarte, California, finds the link between the marker and alcoholism, as well as a number of other disorders thought to be caused by abnormal dopamine receptors. The other study, by Joel Gelernter at Yale University School of Medicine, finds no such link. The major difference in the two studies is the number of controls who have the marker. Both studies found the marker in about 43% of the alcoholics. But in the Comings study, only 15% of the control group had the marker, whereas in the Gelernter study 35% of the controls had the marker.

These results immediately resulted in arguments between the two groups about the differences in their control groups. Gelernter believes that there may be differences in the frequency of the gene based on ethnic origin. All the subjects were white but were not categorized by ethnic origin. Comings argues that Gelernter did not do a good enough job to sort out alcoholics from his control group.

CONSTANCE HOLDEN. 1991. Alcoholism gene: Coming or going? *Science* 254:200.

Researchers fail to replicate studies linking gene to schizophrenia

Several years ago, two reports were published claiming to have found a genetic marker for certain types of schizophrenia. But no one has been able to repeat these results, including those who carried out the first studies.

JULIAN LEFT. 1991. Schizophrenia in the melting pot. *Nature* 353: 693–694.

Researchers in U.S. searching for intelligence genes

Researchers at Pennsylvania State University have started a three-year project to screen 100 genetic markers in 600 children to look for genes that are linked to intelligence. The children are between the ages of 6 and 12 and range from being mildly retarded to extremely "gifted." The children will go through a battery of cognitive tests. The researchers say that they expect "the real payoffs of the study to come from 'the really smart kids,'" *Science* reports. "The only way to get high scores is if you've got everything going for you, including the positive alleles [genes]."

CONSTANCE HOLDEN. 1991. On the trail of genes for IQ. *Science* 253: 1352.

Gene for specific form of deafness being tracked

A syndrome that leads to deafness is being studied in the village of Cartago in Costa Rica. The syndrome has been common in the area for over 200 years and leads to hearing loss of low frequency sound at first. The loss begins in adolescence and leads to complete deafness by the age of 30 or 40. Families in the village are being studied using molecular biology methods, and a genetic marker has been found on chromosome 5. Researchers hope to have identified the gene within the next year. The genetic deafness seems to be inherited as a dominant trait, that is, requires only one copy of the defective gene to result in deafness.

CHRISTOPHER JOYCE. 1991. Gene hunters close in on cause of deafness. *New Scientist.*

October 19: 12.

New improved DNA fingerprinting technique developed

Alee Jeffries, the British scientist who developed the method used for DNA fingerprinting, has now developed a more foolproof version. The method compares the variations in a person's DNA instead of the length of the pieces that are obtained when the DNA is cut with.molecular scissors. In the latter method, the pieces were then separated in a gel using an electric current that caused small pieces to move faster. This led to a pattern of bars that could be compared to another sample to determine if they came from the same person. But this system is not as foolproof as was thought.

The new method, called minisatellite variant repeat (MVR) mapping looks at stretches of DNA where certain bases repeat themselves in a unique pattern for each individual. For each short repeat, there are three possible combinations that can occur. These repeats can then be coded using digital coding (e.g., using a 1 for one combination, a 2 for the second combination, and a 3 for the third type). This results in a long stretch of DNA with many such short repeats that can be easily recorded using ones, twos, and threes. Such a digital number would be unique for each individual and would make possible the creation of large databases containing genetic fingerprints from millions of people.

The method has its own internal control, is reliable and sensitive, and can be carried out on degraded DNA, a necessity if it is to be used in forensic work. The new method will intensify the debate about the use of DNA fingerprinting and will spur the idea of creating data bases. For example, a British parliamentary committee has been discussing recommendations to have all male adults genetically fingerprinted and the data placed in a data base to help trace rapists.

PHYLLIDA BROWN. 1991. 'Foolproof' DNA fingerprints within grasp. *New Scientist*. November 23: 14; C. J. FARR and P. N. GOODFELLOW. 1991. New variations on a theme. *Nature* 354: 184; PAULINE LOWRIE and SUSAN WELLS. 1991. Genetic fingerprinting [Special insert]. *New Scientist*. November 16: 1–4.

L-tryptophan linked to deaths

In 1989, a link was found between deaths caused by eosinophilia-myalgia syndrome (EMS) and the intake of L-tryptophan, an amino acid dietary supplement. The L-tryptophan implicated had been produced by genetically engineered bacteria at the Showa Denko company in Japan. An immediate investigation was begun to determine if there was a causal effect and if genetic engineering was implicated.

The new data seem to show that L-tryptophan, independent of origin, may be dangerous. What seems to be the major problem is a particular from of L-tryptophan where two molecules bind together to create a dimer. The dimer is not present in the fermentation broth with the genetically engineered bacteria but shows up later in the production process during purification. But laboratory tests on rats using the single L-tryptophan also produce similar, though less severe, symptoms of EMS.

These results have led the U.S. Food and Drug Administration (FDA) to conclude that, although the product may be implicated, the process of using genetically engineering bacteria is not at fault. Thus, biotechnology poses no unique hazards and therefore does not need to be regulated differently than other drug-making processes.

PETER ALDHOUS. 1991. Yellow light on L-tryptophan. *Nature* 353: 490.

Japanese court clamps down on patent infringement

The Osaka District Court sent bailiffs to shut down production of tissue plasminogen activator (TPA) by Toyobo Ltd., stating that

Toyobo was infringing on Genentech's patent for TPA. Japan awarded Genentech a patent for TPA in January of 1991.

Genentech has licensed TPA production to Mitsubishi Kasei Corporation in partnership with Tanabe Seiyaku and Kyowa Hakko. Toyobo has a partnership with Dai-chi Pharmaceutical and Genzyme Corporation. The court ruled that the Genzyme technology infringes on Genentech's patent. Toyobo plans to appeal the decision.

DAVID SWINBANKS. 1991. Genentech wins in Japan. *Nature* 354: 4.

European Patent Office okays first animal patent

The European Patent Office (EPO) changed its mind and decided to approve the patent for a genetically engineered mouse. The "oncomouse" was developed at Harvard University in the U.S. and has been genetically engineered to get a human cancer. The U.S. Patent Office granted a patent for the mouse in 1988, the first ever for an animal. Harvard then applied to the EPO for a similar patent, but the application was rejected on the grounds that the European Patent Convention prevented the patenting of animals or plants.

The application was appealed and the appeals board told EPO to reconsider the application. The appeals board considered the mouse to be "something created using a microbiological process, a category of invention which is patentable under European Convention," *New Scientist* reports. They told the EPO to also consider if a patent on the oncomouse would be a "threat to public morality," which would make it unpatentable.

The criteria suggested for this judgement were whether the benefits of using the mice for cancer research outweighed any suffering of the mice or any environmental threat they might pose. The EPO's decision was that "the onco-mouse's purpose of facilitating cancer research and treatment was of paramount importance for the welfare of mankind" and outweighed any negative effects. However, EPO has made it clear that this is not an approval of animal patents per se, only the Harvard patent. New applications for animal or plant patents will be treated individually. The staff of the EPO are tired of the whole thing. "We wish someone would invent a transgenic cat to eat this transgenic mouse," a patent officer in Munich exclaimed. "Then we could go back to ordinary work."

The patent ruling may influence the outcome of a directive being considered by the European Parliament that would allow patenting of transgenic animals within the EEC. The Parliament's Agriculture Committee rejected the directive and sent it back to the European Commission for further study, stating that the directive was being rushed through with "social, ecological and ethical aspects . . . deliberately played down as a tiresome afterthought," *New Scientist* states.

But the directive still has a chance, since Parliament's Legal Affairs Committee has jurisdiction on patenting and is planning to support it.

Susan Mayer and Daniel Alexander discuss the issue of challenging animal patents on moral grounds in an article in *New Scientist*. Although the oncomouse patent was approved, another transgenic mouse patent has been rejected by the EPO on moral grounds. The mice were engineered to study hair growth. The EPO ruled that the mice were of limited use and that this did not justify animal suffering.

Thus Mayer and Alexander state that "challenging patents on moral grounds is thus very far from being a lost cause." It can also lead to the rejection of patents for transgenic organisms to be released into the environment, especially if alternatives already exist. However, the authors see problems with allowing EPO to solely decide these issues. They call for a wider public debate before the EEC directive is decided upon.

DEBORA MACKENZIE. 1991. Europe

rethinks patent on the Harvard mouse. *New Scientist*. October 19: 11; PETER ALDHOUS. 1991. Europe approves first transgenic animal patent. *Nature* 353: 589; DAVID P. HAMILTON. 1991. Europe's bio-patent dispute. *Science* 254: 19; SUSAN MAYER and DANIEL ALEXANDER. 1991. Mice, morals and the environment. *New Scientist*. November 23: 12.

Controversy over patenting seed banks' genetic resources

"Directors of the international agricultural research centres [IARCs], trustees of the world's most valuable collections of crop genes, are discussing whether they should establish intellectual property rights over the material stored in the centres' gene banks," *New Scientist* reports. Such patents would protect genes from crop plants in the Third World by preventing industry from misusing them. The directors plan to have the profits channeled back into Third World countries, for example, via the United Nations International Fund for Plant Genetic Resources.

"The arguments have been roundly criticised by Genetic Resources Action International (GRAIN), a nongovernmental organisation campaigning on behalf of Third World farmers," *New Scientist* states. Patents would hinder the free exchange of plant material and genetic resources needed in plant breeding.

IARCs were developed to help Third World farmers but have been criticised for using technology to solve Third World problems. The Green Revolution was one example, where new hybrid crop varieties developed by the IARCs to increase yields benefited only those farmers who were rich enough to buy pesticides, fertilizers, and machines that were necessary to obtain the higher yields. IARCs are mostly run by researchers from the North. Patenting is seen "as a move that strengthens the influence of the North over organisations whose only concern should be how best to serve the interests of the South."

OMAR SATTAUR. 1991. Will Third World lose out if crop genes are patented? *New Scientist*. November 2: 12.

Drugs from milk on verge of commercialization

Ever since researchers succeeded in creating transgenic mice that produced human proteins in their milk, companies have been trying to scale up the process in larger animals such as goats, sheep and cattle. The major problem has been low yields of the proteins in the milk from larger animals. Three different research groups now report that they are overcoming these problems and may soon be able to start commercial production. For a few years people had their doubts, "but now the work shows that the mammary gland can be used as an impressive bioreactor," Robert Bremel of the University of Wisconsin says.

Pharmaceutical Proteins, Ltd. in Scotland, together with the Agricultural and Food Research Council's Institute of Animal Physiology and Genetics Research, has produced sheep that produce human alpha-1-antitrypsin (AAT). The yields are up to 35 grams per liter of milk. AAT is used to treat a type of lung emphysema.

A second group from Tufts University School of Veterinary Medicine and Genzyme Corporation, both in Massachusetts, have developed transgenic goats that produce tissue plasminogen activator (TPA). TPA is used to treat heart patients. They have a yield of 3 grams per liter of milk. Both groups are looking for more powerful gene regulators to improve the yields.

The third group is a collaboration between Dutch researchers at Gene Pharming Europe BV, the Research Institute for Animal Production, the University of Leiden, and U.S. researchers from GenPharm International in California. They are trying to develop cattle that produce human lactoferrin in their milk. Lactoferrin transports iron and fights bacteria, and is hoped to be used as a supplement in baby formulas.

Another hurdle exists before proteins produced in milk will be on the market. The proteins have to be shown to be safe and effective with no toxic effects.

ANDY COGHLAN. 1991. Making drugs the milky way. *New Scientist*. October 19: 22; ANNE SIMON MOFFAT. 1991. Transgenic animals may be down on the pharm. *Science* 254:35–36.

Plants engineered to kill insects

"Genetic engineers have discovered a natural protein with the potential to kill aphids, plant hoppers, whiteflies and other insects that damage plants by sucking their sap," *New Scientist* reports in its December 14 issue. The gene for the protein has been identified from snowdrop flowers, and researchers now plan to put the gene into commercial crops to protect them from such insects.

And Agracetus, a U.S. biotechnology company, is creating transgenic plants that produce scorpion venom. The venom kills any animals that eat the plants.

1991. Gene transplants to zap sap-suckers. *New Scientist.* December 14: 24; 1991. Killer plants. *New Scientist*. October 26: 28.

Transgenic potatoes

Calgene Pacific, an Australian biotechnology company, has found a gene that makes potato plants produce twice as many tubers. They are now planning field trials of the transgenic potato they have produced using the gene. The potatoes are grown in 130 countries and are one of the major food sources internationally, so the economic impact of higher yields could be large.

1991. Potatoes-a-plenty. *New Scientist*. October 26: 19.

Transgenic tomato ripens on demand

Researchers at Plant Gene Expression Center in California have created a genetically modified tomato with a slowed down ripening process. They have inserted an anti-sense gene that blocks the tomato's normal production of ethylene, a gas that causes the tomato to ripen. The researchers can then cause the tomato to ripen on demand by spraying it with ethylene. The method could be developed for use on fruits that could be kept from ripening on long journeys.

1991. Tomatoes that ripen on demand. *New Scientist.* October 26: 27.

New genetic gun developed to create transgenic rice

A new version of the genetic gun has been used by researchers at Agracetus Company in the U.S. to create transgenic rice. The method shoots small gold beads with new genes into rice cells. Agracetus is working on introducing resistance to tungro virus and certain insects in Indica rice varieties. The researchers are hoping to be able to make the new rice varieties available to Third World farmers for little or no cost and are negotiating with the Rockefeller Foundation for help.

ANDY COGHLAN. 1991. Genetic gun makes rice growers' day. *New Scientist*. November 2: 23.

Insects developing resistance to biopesticides

Toxins from a bacteria called *Bacillus thuringiensis*) (Bt) have been used as a biopesticide since the 1950s. The usual method was to spray crops with the bacteria itself. The action of the bacteria was short-lived and it disappeared rapidly; beneficial insects were not affected. The only drawback was that the fields had to be sprayed frequently if there were major insect infestations.

Genetic engineers have been trying to use other methods to increase the efficacy of Bt toxins. The genes for specific toxins (called Bt-endotoxins) have been isolated and placed in other bacteria that produce the toxins. The toxins are thus usable as biopesticides. Recent

developments include placing the gene for Bt-endotoxin in the plants themselves, so that insects die when they try to eat them.

Biologists were certain that insects would never be able to develop resistance to all of the toxins produced by Bt, but they are now being proved wrong. In 1986, researchers in Hawaii began to receive reports from farmers using Bt on their crops that the biopesticide was not as effective in controlling insects-as before. Other reports of Bt-resistant insects began to surface from Thailand, the Philippines, Japan, and other parts of the U.S.

It was found that insects exposed to high doses of Bt produced offspring that were more resistant to Bt. The development of Bt resistance in insects is sure to hit the industry hard. Many companies planning to market plants and biopesticides based on Bt-toxin may find that they have no effect on insects.

ANN GIBBONS. 1991. Moths take the field against biopesticide. *Science* 254: 646.

Australia markets transgenic biopesticide

"Australia is the first country to allow the sale of a genetically altered living organism for general commercial use," *Nature* reports. Biocare Technology Pty Ltd. is selling a biopesticide called Nogall, which protects plants from crown gall disease. They are now applying for registration of the product in the U.S. and Japan.

MARK LAWSON. 1991. First to market. *Nature* 353: 687.

Transgenic virus planned as rabbit contraceptive

Rabbits are serious pests in Australia. Researchers at the Division of Wildlife and Ecology, CSIRO (Australia's national research organisation) are planning to create a contraceptive vaccine for rabbits that may control their population growth. The researchers have previously studied mating behavior among rabbits after sterilizing (tubal ligation) the dominant females, which are the only ones that mate with males. Sterilization did not change their status, even though they did not produce young. As long as their hormonal system is intact, they still remain dominant and continue to mate.

The researchers plan to create a contraceptive by adding to the myxoma virus, which is common among rabbits, genes that code for proteins found on the surface of the sperm. The virus would then be used to immunise the females against sperm, making them sterile.

TIM THWAITES. 1991. Rabbit virus could carry contraceptive. *New Scientist*. October 19: 18.

U.S. grapples with genetically engineered food questions

The Environmental Defense Fund (EDF) is petitioning the U.S. Food and Drug Administration (FDA) "to apply its rules for chemical additives to any food that has been altered by genes made in the laboratory," *New Scientist* reports. At the moment, the FDA has no system for judging if genetically engineered food is safe. Such food can be considered a new food, a food assumed to be safe, or a food additive. EDF wants all genetic engineering products that end up in the food to be considered food additives, which require the most stringent regulation.

Genetically altered foods have not been proven to be safe, EDF contends. But the Industrial Biotechnology Association states that no one has proven them to be unsafe either. Examples of genetically altered foods being discussed are transgenic fish with mammalian growth hormone genes, bread baked with engineered yeast, and cheese made using enzymes produced by genetically engineered bacteria. The FDA will decide its policy on genetically engineered foods in January 1992.

CHRISTOPHER JOYCE. 1991. Fresh battle over safety of altered food. *New Scientist*. November 2: 15.

Biotechnology investors' dream for quick profits once again

During 1991 financial investors invested in biotechnology companies at a rate not seen since the mid-1980s. A major reason is that several biotech companies are beginning to show profits, especially those in the health care sector. There are currently 750 biotechnology companies in the U.S. Fifteen drugs and biological products developed using genetic engineering have been approved by the Food and Drug Administration (FDA), and over 100 others are being developed.

The Office of Technology Assessment in the U.S. has published a report on U.S. competitiveness in biotechnology called *Biotechnology in A Global Economy* (OTA-BA-494, Washington, DC, U.S. Government Printing Office, October 1991). They emphasize the need for a strong research base to keep the U.S. first in commercial exploitation of biotechnology.

Meanwhile, the FDA is trying to deal with an increase in applications for registration of drugs developed using genetic engineering. The FDA predicts that it will need 100-180 more scientists to handle the future load, but they actually have a smaller staff now than in 1979. And many research areas are on the cutting edge of their fields, which means that the scientists competent to review the applications are the ones doing the research.

ANN GIBBONS. 1991. Biotech pipeline: Bottleneck ahead. *Science* 254: 369; MARK CRAWFORD. 1991. Wall Street takes stock of biotechnology. *New Scientist.* November 23: 36-37; DIANE GERSHON. 1991. US biotech in good health. *Nature* 353: 785.

French biotechnology initiative

Rhone-Poulenc, a French pharmaceutical company, plans a joint government-industry biotechnology initiative over the next 5 years to be called Bio-Avenir. The project will receive $170-340 million in funds over the 5-year period.

CHRISTOPHER ANDERSON. 1991. French drug industry initiative. *Nature* 353: 487.

Canada aims to strengthen biotech research

The Canadian government plans to strengthen Canada's research in biotechnology. In the report *National Biotechnology Business Strategy: Capturing Competitive Advantage for Canada,* the government points out the obstacles that are hindering biotechnology development. These include "a lack of risk capital, trained managers and technicians, delays and uncertainties in governmental regulatory procedures, and a patent system that has produced a backlog of nearly 2,500 patents pending as far back as 1979," *Nature* reports.

The report comes with recommendations to deal with these problems, including "streamlining regulations and patent laws and harmonizing them internally and with those of other countries." The report states that there are at least 200 companies in Canada that use biotechnology, and the report "identified four areas in which significant market opportunities are matched by Canadian strengths: waste management, forestry, food and agriculture and human biopharmaceuticals."

DAVID SPURGEON. 1991. Canada targets biotech. *Nature* 354: 423.

British biotech companies worried about regulations

"British biotechnologists are concerned that proposed genetic engineering regulations published last month by the UK government, will place British companies at a competitive disadvantage within the European Communities (EC)," *Nature* states. The regulations stem from two EC directives on the contained use and environmental release of genetically engineered organisms. "Among other things, the directives say that no environmental releases of engineered organisms will be allowed without the prior

approval of national authorities, and propose that, once a product containing an altered organism is approved in one member state, it can be marketed throughout the EC," *Nature* continues.

Industry is worried because the British regulations will charge companies and researchers wanting to market products to help

pay for the costs of implementing the regulations. For example, applications for deliberate release permits will cost between £2,000 and £4,000, but the cost may go up if the permit has to be reviewed more carefully by the Advisory Committee on Releases into the Environment. Several other countries, such as Denmark and Germany, have come up with similar proposals for charging for permits.

PETER ALDHOUS. 1991. Regulation cost concerns. *Nature* 354: 5.