It's a mad (cow) world

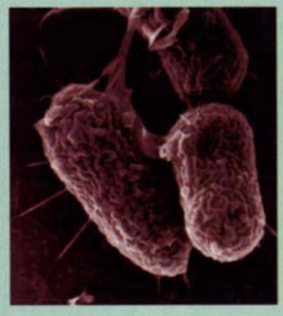
Reports by teams working in the United States (*New Engl. J. Med.* 335:924–930, 1996) and in Germany (*Lancet* 348:846–849, 1996) describe the first tests to accurately detect p130/131, a protein found in the cerebrospinal fluid of people suspected of having Creutzfeldt–Jakob disease (CJD) and cows with bovine spongiform encephalopathy (BSE). The new tests will enable scientists to track the BSE epidemic in live animals and will also allow farmers to distinguish BSE-infected cattle without having to kill the animals first.

Burger-loving UK residents fearing the onset of BSE-related CJD are turning to insurance companies for peace of mind. For about $150 a year, Goodfellow Rebecca Ingrams Pearson (GRIP), a British insurance company, will pay $150,000 to the beneficiaries of any insured person diagnosed with CJD. Despite the World Health Organization's incidence estimate of one case per million, 1300 panic-stricken people have stampeded to buy policies with the firm. When asked what he thought about the new tests, Simon Burgess, managing director of GRIP, was upbeat: "That's wonderful because we'll sell more policies. We're always interested in selling a few more policies."

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

The cows are mad as hell.

PCR-based *Salmonella* detection



Scientists at Applied Biosystems (Foster City, CA) have developed a polymerase chain reaction (PCR) method of detecting *Salmonella*-contaminated food products within 24 hours. Perkin Elmer (Norwalk, CT), the product's manufacturer, anticipates that the new one-step method will completely replace current laboratory methods for identifying *Salmonella* and other food-borne pathogens, which currently require four or more days to perform.

For Perkin Elmer, Applied Biosystem's TaqMan *Salmonella* PCR Amplification and Detection System could not have come at a better time. This past summer, President Clinton called for "more scientific" methods to examine meat and dairy products, which previously have only been checked by appearance, texture, and smell. The food industry balked at Clinton's tightening of controls, stating that the new regulations would greatly increase their labor costs. But Perkin Elmer insists that the new one-step method would be cost effective because it requires less time and equipment and is just as reliable as current methods.

The Centers for Disease Control (Atlanta, GA) estimates that approximately 1000 out of 4 million infected people die of *Salmonella* poisoning each year. The new government regulations finally acknowledge contaminated food as a major health hazard. With certain modifications, Perkin Elmer is confident that the procedure can also be applied to detect other menacing food-borne pathogens such as *Escherichia coli* 0157, *Campylobacter*, and *Listeria*.

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

US xenotransplantation guidelines released

A two-year consultation process at the US Public Health Service/Food and Drug Administration (FDA, Rockville, MD) on the risks and safety issues inherent to transplanting animal tissues into humans has now culminated in the release of the final draft of "Guidelines on Infectious Disease Issues in Xenotransplantation" (*US Federal Register*, Sept. 23, 1996). Several xenograft products are currently in the clinic, including fetal porcine neural cells for treating Parkinson's Disease (Diacrin, Charlestown, MA), encapsulated bovine adrenal cells for intractable pain (Cyto Therapeutics, Providence, RI), encapsulated porcine islet cells for diabetes (Divorx, Santa Monica, CA), baboon bone marrow for AIDS (University of California, San Francisco), and transgenic porcine liver perfusions, by which patients can be kept alive while waiting for human organs (Duke University, Durham, NC).

The guidelines are primarily concerned with preventing the transmission of any known infectious disease (or an emerging disease) from the animal to the graft recipient. Investigators must maintain extensive microbiology or virology facilities capable of identifying unknown or unusual pathogens. Both human and veterinary expertise is required for screening the herd, the donor animal, the xenograft recipient, and the health-care workers involved in the procedure. Specimens from the animal are to be banked for retrospective analysis. The document also deals with some ethical issues, such as the requirement for written consent from the donor recipient.

The government is currently accepting public comment and will issue the final guidelines after conducting a workshop in the first quarter of 1997.

Standing alone for Europe

Europe's biotechnology companies now have one voice—and a pronounceable epithet. The European Secretariat of National Biotechnology Associations (ESNBA) and the Senior Advisory Group Biotechnology (SAGB), which have been sharing premises in Brussels for over a year, have joined forces to become Europabio. Europabio—the European Association for Bioindustries—brings together both the smaller biotechnology specialist companies of ESNBA and the multinational interests associated with SAGB and now represents over 500 companies and their eight national industry associations. The two priorities of the new association are continued lobbying of European and national politicians and legislators, and the promotion of the bioindustry's image to the public.

BIO advocates genetic-testing privacy laws

The recent passage of the Kassebaum–Kennedy law in the United States prohibits insurance companies from denying coverage on the basis of an individual's medical history. Now BIO (Biotechnology Industry Organization, Washington, DC), wants to take this protection one step further—a federal privacy law covering medical information that would include results from diagnostics based on genetic testing. BIO says that only by Congress enacting such a comprehensive bill could the privacy of an individual's medical information be protected uniformly in the US. Otherwise, the organization claims, individual states may develop inconsistent policies that may jeopardize fair treatment under the law. BIO says that in enacting a federal law, it is important that genetic information be included as part of the medical history protected from the outset. Separating the privacy of genetic information from a patient's general medical history may allow loopholes for discriminatory use. The legislation BIO proposes would not allow the release of any medical information without an individual's written consent.

US science funding in the spotlight

To commemorate the 50th anniversary of the publication of Vannevar Bush's (Franklin D. Roosevelt's science advisor) "Science, the Endless Frontier," scientists, educators, and policy experts gathered at Columbia University (New York) on September 20–21 to discuss future US science policy. The current restrictive financial and social environment is very different from that of 1946, when Bush's policy paper defined the mechanisms for funding science, government funding pockets were deep, and the public offered carte blanche support for all research.

Most speakers conceded that scientists need to better convey the social benefits of supporting science (i.e., economic growth and improvement of public health) to the public, and cited biotechnology as a prime example of an area with a poor public perception. In addition, increasing collaborations between academia and industry were seen to be pivotal to meeting the shortfalls in funding resulting from shrinking public research budgets. One vocal opponent to such corporate funded research, John Holmfeld, former US House of Representatives Science Committee staff member, stated "Industrial liaisons have eroded collegiality." He called for a new science policy "restoring autonomy to academic institutions."

Cyclosporin fungus identified

Back in the mid-1970s, when Hoffmann-LaRoche (Basel, Switzerland) researchers isolated the immunosuppressant drug cyclosporin from a mold discovered in Basel, they hadn't a clue as to where it came from, or what the mold's natural substrate might be. Some 20 years later, a group of undergraduate students from Cornell University (Ithaca, NY) have serendipitously solved that mystery. Out on a "Field Mycology 319" collection foray, the students were sent out to gather "anything that looked like a fungus" as part of an identification exercise. One of the specimens collected grew out of the eviscerated shell of what appeared to be a dung beetle—a type of scarab beetle that feeds on organic soils and dung. The mold, in its so-called sexual state exhibited a yellow, finger-like, fruiting body that captured the attention of Kathie T. Hodge, then a Cornell graduate student.

Curious about the find, Hodge and coworkers determined that the fungus was the rarely seen *Cordyceps subsessilis*. The next step was to germinate the spores and identify the resulting mold. To Hodge's surprise, the spores not only germinated, the resulting mold turned out to be *Tolypocladium inflatum*—from which hundreds of thousand of cultures have been made to harvest cyclosporin. According to Hodge, the rarity of the fungus's sexual state is apparently tied to its ability to find a very special substrate—the dung beetle. It appears that once the fungus gains hold, it somehow influences the insect to climb any available vegetation to the highest point—an unnatural act for a dung beetle. Once the beetle dies at this lofty perch, it provides an ideal vantage point for the fungus to grow its fruiting body and distribute its spores.

Cornell's Thomas Eisner, an advocate of preserving biodiversity and the founder of the field of chemical ecology, sees this find as one more example of the untapped natural riches available for drug discovery. "This tells us to look at other related species of this fungus for potentially useful compounds," says Eisner. "At least 90% of the world's fungi have yet to be identified and examined."

And who exactly has been credited with bringing back the prized dung beetle? "No one knows, really," says Hodge. "We were just collecting fungi as fast as we saw them and no one remembers getting this one."

Plastic surgeons turn to biotechnology

The American Academy of Facial Plastic and Reconstructive Surgery (AAFPRS, Washington, DC) recently held its first biotechnology forum, at which presentations of preclinical and clinical trial results were interspersed with panels featuring representatives of biotechnology companies developing new therapies for use by surgeons nationwide. Among the topics discussed were surgical tissue adhesives, bone replacement materials, and wound healing and tissue engineering. Program chair Dean M. Toriumi of the University of Illinois at Chicago said that the forum was important because surgeons need to "communicate to biotechnology companies that they are going to be increasingly dependent on new technologies," with traditional materials like silicone losing favor with safety-minded patients because of its deleterious effects on health. Toriumi's own research, in conjuction with Genetics Institute (Cambridge, MA), focuses on mandibular reconstruction in dogs using recombinant human bone morphogenic protein type 2 (BMP-2) in a carrier made of demineralized dog bone powder matrix. The technique is capable of inducing host bone formation across a 3 cm gap in the lower jaw and the new bone is stable after more than 2 years. Toriumi foresees the technique in clinical use within 5 years.

Sections of the 3 cm gap with control carrier (left), and carrier with BMP-2 (right), with resultant bone growth. Mineralized bone is stained black.

Cistron and Immunex fight on

Unable to settle out of court, the battle between Cistron Biotechnology (Pine Brook, NJ) and Immunex Corporation (Seattle, WA) over the patent rights to interleukin 1β (IL-1β) continues as the two parties await judgment by a jury. The trial, previously scheduled to begin on September 24 and postponed, is now scheduled to begin November 5. In 1993, Cistron filed a suit against Immunex for allegedly misappropriating the DNA sequence of IL-1β during peer review of a scientific manuscript, and then using it fraudulently to gain access to funding sources (*Nature Biotechnology* **14**:275–279, 1996). The case raises important ethical and financial issues associated with the review of scientific papers.

FDA looking into regulating the Internet

Recognizing that nearly every drug-development company now has a Web site where it disseminates information about its products, the US Food and Drug Administration (FDA, Rockville, MD) says it is going to look into what's being said about therapeutics on the Internet. At present, the agency has "statutory provisions, regulations, and policies concerning advertising and labeling" in traditional media, and it wants to be sure that those same standards are being applied on the Web as well. Under these rules, companies are barred from promoting any unapproved uses of drugs and devices by the FDA. But when advocacy groups post information about a drug being approved overseas or a new unapproved use for a drug and link that information to the manufacturer's web site, what—if anything—should the drug developer do? The FDA also wants to take up the question of "fair balance." Manufacturers are currently required to provide information about a drug's effectiveness as well as its potential side effects in any advertisement. If a Web page falls into the category of an "advertisement" does this require manufacturers to provide "fair-balance" information on every screen? So far, the agency has not reprimanded any drug makers for their Internet activities. However, medical device manufacturers have been "warned" about their promotional activities on the Internet.

Another microbial genome sequenced

Human Genome Sciences (HGS, Rockville, MD) has completed sequencing the entire genome of *Streptococcus pneumoniae*. Streptococcal pneumonias, responsible for 15–20% of community-acquired pneumonias in the United States, currently have a 5–7% mortality rate even after antiinfective treatment, and multidrug resistant strains are on the rise. HGS has strategic alliances to develop new antibiotics against streptococci with Hoffman-LaRoche (Nutley, NJ) and to provide candidate proteins for vaccine development by MedImmune (Gaithersburg, MD).

The *S. pneumoniae* genome sequence is the latest addition to the expanding portfolio of microbial genomes completed by HGS, including *Staphylococcus aureus* and pathogenic *Escherichia coli*. HGS also has commercial rights to three genomes sequenced by The Institute for Genomic Research (TIGR, Rockville, MD): *Haemophilus influenzae*, *Mycoplasma genitalium*, and *Methanococcus jannaschii*. In addition, TIGR has completed sequencing *Archeobacter globus*, *Treponema pallidium*, and *Helicobacter pylori*. Genome Therapeutics (Waltham, MA) has sequenced the genomes of *H. pylori* and *S. aureus*.

Gene of the month

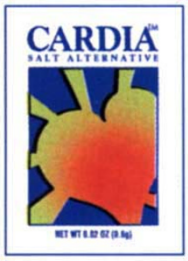
Researchers at the University of Pittsburgh (*Nature Genetics* 14:141–145, 1996) have been able to identify and sequence the gene responsible for hereditary pancreatitis (HP) and hypothesize a mechanism through which it may operate. The disease gene, which encodes the pancreatic digestive enzyme trypsinogen, contains an arginine to histidine substitution at residue 117. The HP gene had previously been mapped to the long arm of chromosome 7. Fortuitously, it resides in the vicinity of the β T-cell receptor locus, a region that has been the subject of extensive sequencing. By analyzing this region, the Pittsburgh team were able to fish out the disease gene from eight other trypsinogen-like genes.

Joint ventures

Company 1	Company 2	Company 3	$ Million	Details
Genetics Institute (Cambridge, MA)	Chiron (Emeryville, CA)	Genentech (S. San Francisco, CA)		Chiron and Genentech have joined Genetics Institute's DiscoverEase protein development platform. DiscoverEase is based on the "signal sequence trap" that rapidly identifies and isolates genes coding for secreted proteins.
Monsanto (St. Louis, MO)	Asgrow Agronomics (Kalamazoo, MI)		240	Monsanto has signed a letter of intent to acquire Asgrow Agronomics from Seminis, a subsidiary of Empresas La Moderna.
Genzyme (Cambridge, MA)	Diacrin (Charlestown, MA)		40	Have formed a 50:50 venture to develop and commercialize Diacrin's NeuroCell porcine neural cell products for Parkinson's and Huntingdon's disease. Genzyme will provide $20 million funding initially.
Elan Corp. (Athlone, Ireland)	Cytogen Corp. (Princeton, NJ)		20	Will form a new company, Targon Corporation, as a wholly owned subsidiary of Cytogen to develop Elan and Cytogen's differentiated oncology products. Elan has invested $20 million in Cytogen and will have equal ownership with Cytogen.
Antisoma Ltd. (London)	Imperial Cancer Research Technology (London)			Antisoma and Imperial Cancer Research Technology, the commercializing arm of the Imperial Cancer Research Fund, have formed a company called Cancer Therapeutics Ltd. to develop anticancer products.
Visible Genetics (Toronto, Canada)	Univ. of Pittsburgh (Pittsburgh, PA)	Univ. of Pittsburgh Medical Center (PA)		Will form a joint venture company called the Genetic Foundry, which will develop DNA-based diagnostic tests.
NV Organon (Oss, NH)	Anergen (Redwood City, CA)		2	NV Organon has licensed Anergen's AnergiX peptide for $2 million. AnergiX, an MHC-derived protein complexed to a disease-specific autoantigenic peptide, will be developed for use in rheumatoid arthritis therapy.
Tripos (St. Louis, MO)	Panlabs (Bothell, WA)	Bristol-Myers Squibb (New York)	1.5	Tripos and Panlabs will receive $1.5 million from Bristol-Myers Squibb in exchange for designing and synthesizing combinatorial libraries for Bristol-Myers Squibb's screening program for new drugs.
Incyte Pharmaceut. (Palo Alto, CA)	Monsanto (St. Louis, MO)			Incyte will detemine sequences and gene expression information for various plant species for Monsanto in exchange for licensing fees and potential royalties on products developed.

Tasty medicine

A routine trip to the doctor may soon land you a grocery list: Foods with medicinal properties, so-called nutriceuticals, are now coming to market.



Applied Microbiology, a New York based company, has been pitching its salt substitute, CARDIA, to primary care physicians, stating that the product reduces dangerous high blood pressure. IVAX Corporation (Miami, FL) makes a chocolate-flavored candy bar called Zbar for diabetics. The chocolate bar, made from uncooked cornstarch, is intended to replace late-night snacks that diabetics are required to eat to prevent their blood sugar from falling while they sleep. IVAX is also touting its product to doctors, hoping that they will recommend it to their diabetic patients.

The therapeutic effectiveness of these food products, however, is controversial. "Food substitutes are totally unnecessary," says Marion Nestle, chair of the Department of Food Studies and Nutrition at New York University, "Until I see a study that links the decrease of a disease in a population to a food substitute, I'm going to remain skeptical."

Quote of the month

"As a researcher in the pharmaceutical industry, collaboration seems like the most unnatural act I can think of."

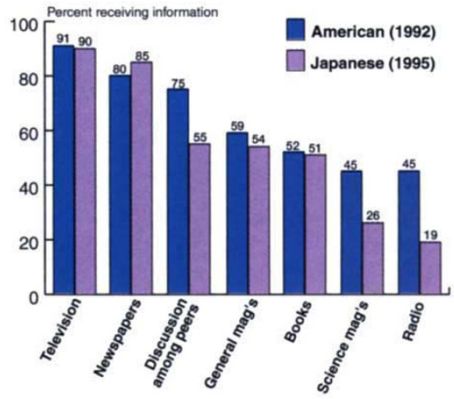
Anonymous

Association of German biotech companies launched

Following in the footsteps of the US Biotechnology Industry Organization (Washington, DC) and the UK's Biotechnology Industry Association (BIA, London), 55 start-up German biotechnology companies launched a national "Association of German Biotechnology Companies." Known as the Vereinigung deutscher Biotechnologie-Unternehmen (VBU, Frankfurt, Germany), its declared goals are to eliminate the obstacles to biotechnology growth and to promote its economic potential. The group wants to work to increase a positive public perception of biotechnology and to serve as a central exchange for national and international contacts. Its initial agenda will focus on finding partners to help young entrepreneurs launch new startup biotechnology businesses.

Prime time TV: A good source of science?

A random telephone survey of approximately 1,200 US and 1,000 Japanese citizens, conducted by Thomas J. Hoban, associate professor of sociology at North Carolina State University, ranked television as their primary source of information on science and technology. Even though science represents a relatively small percentage of all print news coverage and a minute percentage of television coverage, the majority of people rely on both mediums for all of their science and technology information—a reality that, Hoban says, clearly shows "that scientists need to first educate reporters about science and technology." *Nature Biotechnology* reporting staff have taken note.



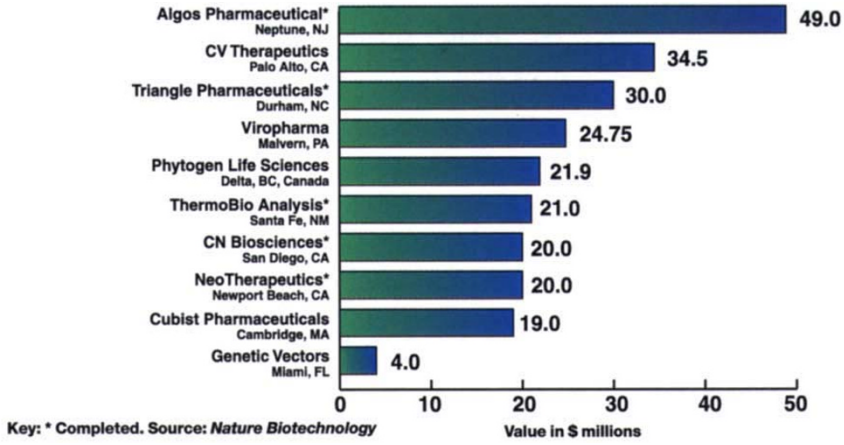
Recombinant vaccines inch closer to clinic

Fourteen biotechnology-derived vaccines are now approaching the clinic (see table) and, according to a new survey by the Pharmaceutical Research and Manufacturers of America (Washington, DC), a total of 62 vaccines are under development for diseases as diverse as AIDS, cancer, genital herpes, sickle cell anemia, osteoporosis, and multiple sclerosis. Out of the legion of human immunodeficiency virus (HIV) vaccines in phase I and preclinical research a few years ago, only Remune, an inactivated gp120 HIV antigen from The Immune Response Corporation (Carlsbad, CA), has made it through to phase III trials. In the area of bacterial infectious disease, several pertussis vaccines are now in late-stage trials, notably Chiron's (Emeryville, CA) DTaP vaccine (see "WHO and UNICEF find vaccines too costly," p. 1532), and two vaccines against Lyme disease are also in multicenter trials. Cancer continues to be a major focus for research, with 4 out of a total of 27 anticancer vaccines now in phase III trials.

Recombinant vaccines in phase III trials.

Indication	R&D Company	Product	Licensee
Bacterial disease			
Lyme disease	Connaught/RP	Innoculyme	
Lyme disease	SmithKline Beecham	OspA antigen	
Pertussis	SmithKline Beecham	Pertussis vaccine	
Pertussis	Chiron	Modified holotoxoid	Ciba-Geigy
Pertussis	Chiron	DTaP	
Cancer			
Melanoma	Progenics	GMK	
Melanoma	Ribi	Melacine	Schering-Plough
Melanoma	Ribi	Melacine	Biomira
Ovarian	OncoTech	Allogenic tumor cells /IL4	
Viral disease			
Hepatitis B	Medeva	Hepagene	
HSV2	Chiron	HSV2 gB2&gD2	Ciba-Geigy
HSV2	SmithKline Beecham	HSV gD2t	
HIV seropositive	Immune Response	Remune	
Rotavirus	Wyeth-Ayerst	Rotashield	

Initial public offerings



Key: * Completed. Source: *Nature Biotechnology*