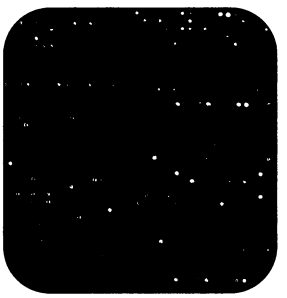
POTENTIAL TARGETS

Aspergillus fumigatus; Bacillus anthracis; Borrelia burgdorferi; Yersinia pestis; Burkholderia mallei; Chlamydia pneumoniae; Entamoeba histolytica; Enterococcus faecalis; Group B *Streptococcus; Mycobacterium smegmatis; Mycobacterium tuberculosis; Neisseria meningitidis; Plasmodium falciparum; Pseudomonas aeruginosa; Rickettsia prowazeki, R. conorii, R. typhi; Salmonella typhimurium; Staphylococcus aureus; Streptococcus pneumoniae; Vibrio cholerae*



Candidate list. A new center will pick three organisms to start from a pool of pathogens for focused work, including microarray preparation.

valis's genes and proteins behave during infection. "We've got just basic equipment, [so to be able] to use microarrays is a big step up," she says.

Many other disease researchers soon will be joining Baker in benefiting from TIGR's expertise. Last week the institute announced that it has signed a 5-year, $25 million contract with the National Institute of Allergy and Infectious Diseases (NIAID) to help scientists expose the inner workings of at least 10 human pathogens whose genomes have been sequenced. The new Pathogen Functional Genomics Resource Center will exploit the growing sequence archive by "making some essential tools more easily available to microbial researchers," says TIGR's Robert Fleischmann, one of the center's leaders.

Scientists have sequenced the genomes of more than two dozen pathogens over the last 7 years, including killers such as cholera and syphilis, with more pending. But putting all that information to use in understanding infections or developing drugs is difficult. It takes expertise and money to make the specialized reagents, gene clones, and microarrays—chemically treated glass slides or silicon wafers that can detect the activity of hundreds of genes at a time—that researchers need. To avoid funding duplicate requests, NIAID officials 2 years ago began looking at ways to centralize some toolmaking and training activities, and last year they announced a competition to select a host for the new center.

As the winner, TIGR is moving quickly to outfit labs and recruit a staff of 25 and a 10-member advisory committee; it hopes to have the center humming by spring. A first task will be to select three target pathogens from a short list of hot candidates (see table), with at least another seven coming by 2004. Then TIGR can begin making and distributing materials, processing samples, and analyzing data for needy labs.

Some offerings, however, will be rationed because of their high cost. Microarrays, for instance, may initially be available to just 10 selected labs per pathogen, says Fleischmann, with each lab getting about 150 of the glass slides. The center also has to work out data-sharing and patenting policies. In both cases, Fleischmann says the intent is to share information and materials as widely as possible, particularly with labs at smaller institutions such as Bates.

Eventually, organizers hope TIGR will help the research community solve two long-standing problems: training talent and establishing workable, accepted standards for various lab techniques and data-storage methods. Says Fleischmann: "We want to be more than a factory for pumping out reagents."

–DAVID MALAKOFF

PATIENT PRIVACY

Researchers Say Rules Are Too Restrictive

A coalition of biomedical societies and research universities is mounting a major assault on a new rule covering the privacy of health records, arguing that the regulation will stifle research. However, patient rights groups say that scientists are overreacting to needed reforms.

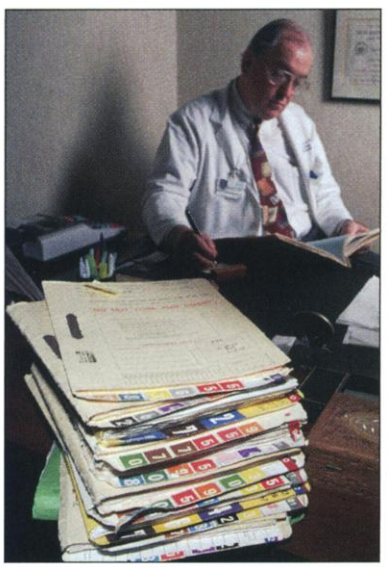
The Privacy Rule sets out new procedures for handling patient records, including a requirement that certain information be stripped from records that researchers can use without prior permission. It also gives patients the right to see their records and to find out if they have been made available to a public health or law enforcement agency, or for research.

The 32-page rule was hammered out by the Department of Health and Human Services (HHS) in response to a 1996 health insurance law; it was published in final form in December 2000 as one of the Clinton Administration's final acts and goes into effect in April 2003. But the Bush Administration decided to review portions of the rule after concerns poured into HHS over how it will work. Health care organizations and researchers have taken advantage of that opportunity to make their case.

The new rule "will seriously impair our ability to conduct clinical trials" as well as pathological, epidemiological, and genetic studies, says a 20 November letter to HHS Secretary Tommy Thompson, signed by more than 60 professional societies and 110 universities. David Korn, senior vice president for biomedical and health sciences research at the Association of American Medical Colleges (AAMC), which has spearheaded the campaign, says that changes the biomedical groups have proposed would not weaken patient privacy.

The letter urges HHS to pare down the amount of data cleansed from patient records before they are made available to researchers. Removing even data such as zip codes and birth dates, says Korn, makes the data "useless" for research that requires such "identifiers." Researchers who want to use identified data without a patient's permission can apply for a waiver from an ethics board. But the rule lays out fuzzy review criteria, such as weighing whether a privacy risk is "reasonable." The research community urges HHS instead to leave the decision in the hands of the ethics review panel that assesses the original study. Other recommendations include easing restrictions on access to existing archives.

The researchers have found receptive ears for some of this: In a 21 November letter to Thompson, an advisory committee to HHS that has been tracking the rule says it "detected a high level of anxiety" from researchers in recent public hearings and recommends reconsidering a few sections, including the rules for stripping identifiers. But other complaints result from a "misunderstanding" of the rule, says panel member Mark Rothstein, a bioethicist at the University of Louisville School of Medicine in Kentucky. Angela Choy of the consumer-oriented Health Privacy Project at Georgetown University in Washington, D.C., says the rule offers researchers "lots of ways to get" the information they need.



Eyes only. Access to patient data sparks renewed debate.

Biomedical groups worry that some hospitals may decline to share any data to avoid the cost of compliance and to steer clear of criminal penalties

CREDITS: (ARRAY) NIH; (PAPERS) TIM WRIGHT/CORBIS

for any violations. Some hospitals in Minnesota, which passed a law 5 years ago that imposes strict rules for releasing records, have banned external researchers—those not on hospital staff—from using their databases, Korn says. Having more health care systems put their databases off-limits, the AAMC letter warns, could "paralyze vital public health research." –JOCELYN KAISER

OBESITY RESEARCH

Pot-Bellied Mice Point To Obesity Enzyme

Words linking fruit and the human anatomy have long sweetened sonnets and love letters. But lately the term "apple-shaped" has gained renown on the pages of medical texts. People who carry excess fat around their waists—the so-called apple-shaped body type—are more prone to obesity-related maladies than their equally overweight but pear-shaped counterparts, who pack weight around their hips. Physicians have observed the connection for decades, but no one could explain it, let alone search for a therapy to right the scales.

Now on page 2166, researchers at Beth Israel Deaconess Medical Center in Boston suggest a reason for the disease–body type relationship, and a possible new target for treatment. The culprit is an obscure enzyme that works to recycle a steroid stress hormone called cortisol. Through delicate genetic engineering, endocrinologist Jeffrey Flier and his colleagues overexpressed the gene for this enzyme solely in the fat of mice. These rodents look and act a lot like overweight apple-shaped people: They eat more than normal mice and gain fat disproportionately around their middles. As adulthood sets in, the animals develop the early biochemical symptoms of heart disease and diabetes. Blocking the enzyme in people, the researchers suggest, might thwart obesity-related illnesses.

"This was really the first proof that manipulating steroid conversion in fat alone is enough to lead to all these abnormalities," says endocrinologist Stephen O'Rahilly of Addenbrooke's Hospital in Cambridge, U.K., who studies the genetics of obesity and diabetes. "I wish I'd done the experiment myself."

Inspiration for the study came indirectly from a rare illness called Cushing syndrome. Its sufferers have too much cortisol coursing through their bloodstreams and become diabetic and severely obese. For decades, endocrinologists hypothesized that common forms of obesity may represent very mild cases of Cushing syndrome. If so, most obese people should have higher than normal blood levels of cortisol—but researchers found that they don't and discounted the hypothesis.

The theory was resurrected by Paul Stewart of the University of Birmingham in Edgbaston, U.K., whose group found that people have pockets of high cortisol activity. The team compared stress hormone production in two types of fat in 16 patients undergoing surgery, most of whom were of normal weight. One sample came from underneath the skin, the other from adipose tissue in the abdomen. In the belly fat, the researchers found higher activity of an enzyme called 11β hydroxysteroid dehydrogenase type 1 (11β HSD-1), which regenerates active cortisol from its inactive form, cortisone.

Flier read a 1997 paper in *The Lancet* on the research and thought, "If we could make a mouse that overexpresses the enzyme only in fat, we could ask the question, 'Will that mouse get the apple-shaped body type and all its ill effects?' " he recalls. Visiting scientist Hiroaki Masuzaki engineered the mice; he linked a rat 11β HSD-1 gene to a promoter that turns on only in fat. The mice had 2.4 times more enzyme activity in their belly fat than did normal mice. Stress hormone levels in stomach fat tissue rose by 15% to 30%, but, as in most obese humans, bloodstream levels of the hormone were normal. As adulthood set in, the transgenic mice ate more, got fatter than normal mice, and carried the fat in their abdomens. Even when fed low-fat diets, the transgenics carried a spare tire that accounted for 37.9% of their total body fat compared with 27.5% in normal mice. The mice showed the hallmarks of early diabetes and hypertension: insulin resistance, renegade blood glucose levels, and other biochemical abnormalities. And a high-fat diet accelerated the pot-bellied rodents' downward spiral.

"It is really the whole picture of what we refer to as the metabolic syndrome," says Flier, citing a term now in vogue in en-

Belt loosener. Activating an enzyme in fat gives mice a syndrome seen in apple-shaped people.

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ScienceScope

War's First Casualty The British government wants to stop publicizing the locations of U.K. labs working with genetically modified (GM) organisms. In October, the government's Health and Safety Executive (HSE) temporarily stopped releasing a list that pinpointed government, university, and commercial labs doing GM research on grounds that terrorists might use the list to locate ready sources of virulent superbugs. And last month, the HSE proposed to permanently strike labs working with potential bioweapons from the public list. If parliament agrees, the agency would release a sanitized version in January.

Observers disagree on whether the censorship is a good idea. "Any other position would be irresponsible," says Tom Loeffler of the Biotechnology and Biological Sciences Research Council, a grant-giving body. But because "GM organisms currently pose little more threat than existing ones," delisting the labs does little to improve security, says Alastair Hay, a bioweapons expert at the University of Leeds. Clever readers, he adds, can discover out what labs are doing by trolling through journals.

Wayward Brains? Scientists at the U.K.'s Institute for Animal Health (IAH) have come out swinging against two government-sponsored audits that conclude that they mixed up cattle and sheep brains in a high-profile study. The IAH had carried out a 4-year investigation into whether Britain's sheep flock was infected with "mad cow disease." But last October, an independent laboratory reported that sheep brain samples used in experiments actually came from cows, calling the study's results into question (*Science*, 26 October, p. 771).

The audits, made public last week, blame the fiasco on IAH's poor sample labeling and record keeping. But they produced "no clear evidence" for mistakes at IAH, argues institute chief Chris Bostock. The samples originally came from another government facility, he notes, meaning a mix-up or contamination could have occurred either before the IAH took custody or after it sent out the tissues for independent analysis.

IAH researchers complain that auditors spent just 1 or 2 days visiting their lab in Edinburgh, where much of the work was done, and did not interview the scientists who first worked with the samples. Says one IAH staffer: "Everybody is furious at the way this has been handled."

Contributors: Andrew Lawler, Richard A. Kerr, John Pickrell, Michael Balter