Clinton talks about science

Martian bacterial compass?

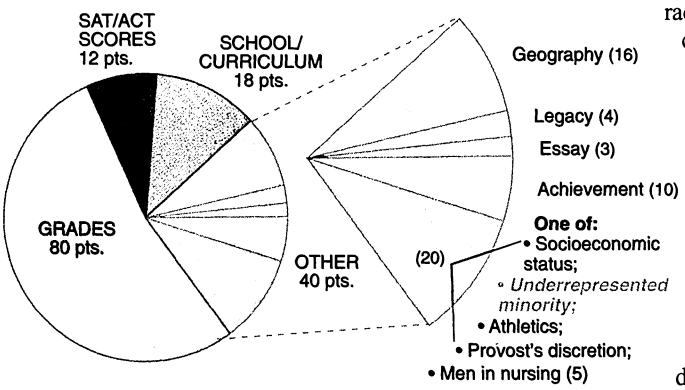
Models of infection

AFFIRMATIVE ACTION

Court Backs Michigan Policy on Diversity

A federal district court last week upheld the University of Michigan's race-sensitive admissions policies, pleasing advocates of affirmative action in higher education. The ruling was based in part on research showing that diversity enhances education, an argument that opponents of affirmative action reject as bad science. However, the ruling clashes with a 4-year-old decision by another federal court, opening the door to a possible review by the U.S. Supreme Court.

How Michigan Keeps Score



Numbers represent maximum points. A perfect score is 150. No more than 40 points may be awarded under the "Other" component.

SOURCE: UNIV. OF MICHIGAN

The Michigan case, *Gratz* v. *Bollinger*, was brought by Jennifer Gratz, a 23-year-old white woman who claimed she had been unfairly turned down as an applicant in 1995. Gratz was backed by the Center for Individual Rights (CIR), a Washington, D.C.–based group that has led attacks on affirmative action policies in three states and has another suit pending against Michigan's law school. Gratz won half of her case, with Judge Patrick J. Duggan ruling that Michigan's admissions policy then in force smacked of an unfair, racial quota system. But Duggan said that its current policy, adopted in 1997, is a valid attempt to achieve "a racially and ethnically diverse student body." Such diversity, he added, "produces significant educational benefits."

The ruling, expected to be appealed, is the second such decision in 2 weeks. In early December, a three-judge panel of a federal appellate circuit court in California upheld a now-defunct affirmative action program at the University of Washington, Seattle, law school. Both rulings conflict with *Hopwood*, a 1996 appeals court decision that outlawed race-sensitive admissions policies in universities in Texas, Mississippi, and Louisiana. Those conflicting rulings could set the stage for the Supreme Court to return to a topic that it has not visited since the historic *Bakke* ruling in 1978. In that decision, written by Justice Lewis Powell, the court struck down the two-tiered admissions system at the University of California, Davis, law school, but said that efforts to assemble a "diverse student body" were permissible.

Michigan's current system assigns applicants up to 150 points based on a variety of factors, including race (see graphic). "[T]his court is satisfied that ... the current [undergraduate] admissions program represents a permissible use of race ..." Duggan said.

In arguing for the benefits of diversity, the court cited work by University of Michigan psychologist Patricia Gurin. She has analyzed data from longitudinal surveys at Michigan and elsewhere to conclude that "students who experienced the most racial and ethnic diversity"—as gauged by social interactions and attendance at courses on multicultural matters—showed the greatest "engagement in active thinking processes, growth in intellectual engagement and motivation, and growth in intellectual and academic skills" (see www.umich.edu/~urel/admissions). A 1998 book by former Princeton University President William Bowen and former Harvard chief Derek Bok also cites the benefits of affirmative action for minorities.

Michael Martinson of the Washington, D.C., law firm Hogan and Hartson, which filed a brief for the defense representing several major educational associations, says that the diversity argument has replaced "remediation" as the central pillar supporting affirmative action. While remediation must be based on past discrimination, Duggan declared that "the need for diversity lives on perpetually."

Not everyone is impressed with the quality of diversity scholarship. Harvard historian Stephan Thernstrom calls Gurin's research "absolutely ludicrous as social science" and says her study measures "exposure to diversity courses, not exposure to diversity." Gurin says her methods are "absolutely standard" in social science, and that a high proportion of people in ethnic studies classes is nonwhite. Ultimately, though, opponents of affirmative action say that their argument rests on legal grounds. "Diversity is good, but lots of good things won't pass constitutional muster as justification for race discrimination," says CIR spokesperson Curt Levey.

Each side also believes that the wind is blowing in its direction. That split ensures an attentive audience for the next battle: CIR's suit claiming racial preferences in the admissions policies of Michigan's law school. It's scheduled for trial next month.

–CONSTANCE HOLDEN

CELL BIOLOGY

Disease Genes Clarify Cholesterol Trafficking

For most of us, worries about cholesterol focus on whether this lipid is building up in the arteries of our hearts or brains, priming us for a heart attack or stroke. But for a small number of people suffering from a rare hereditary disease called Niemann-Pick C (NPC), cholesterol can cause even more serious problems. It so clogs their cells, particularly their brain cells, that the cells can't function normally and degenerate. Patients usually die in early childhood.

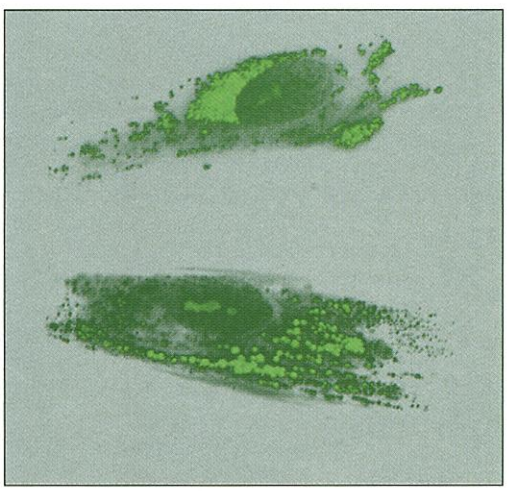
Now, two groups report results that should help explain what goes amiss in this devastating disease. Their findings should also help solve a long-standing mystery about how cells normally handle cholesterol, and they could eventually point to new ways to treat NPC patients as well as the much larger population with elevated blood cholesterol levels.

Researchers have known for about 7 years that NPC is caused by mutations in either of two separate genes. Mutations in both result in a massive accumulation of cholesterol in tiny sacs, called lysosomes, located in the cell cytoplasm. Something apparently blocks cholesterol's normal transfer to another cell structure, the network of membranes known as the endoplasmic reticulum (ER). Three years ago, a team led by Peter Pentchev and Danilo Tagle of the National Institutes of Health (NIH) identified one of the genes, *NPC1*, which causes 95% of NPC cases. Now two research teams have fingered its partner in crime, *NPC2*, and also discovered

the function of the normal NPC1 protein.

On page 2298, Peter Lobel of the Robert Wood Johnson Medical School in Piscataway, New Jersey, and his colleagues report that a previously identified gene that encodes a cholesterol-binding protein called HE1 is actually NPC2. And on page 2295, a team at Mount Sinai School of Medicine in New York City describes an unexpected function for NPC1. Work by Yiannis Ioannou, Joanna Davies, and Fannie Chen suggests that it is a permease that can transport lipids such as fatty acids, but apparently not cholesterol, across membranes.

The new work should help fill a major gap in current understanding of cholesterol transport in the cell. Researchers know how cholesterol gets into the lysosomes. And they know a great deal about what happens after the lipid reaches the ER. But, says cholesterol expert Joseph Goldstein of the University of Texas Southwestern Medical Center in Dallas, "the black box is that we never knew how it gets out of the lysosome" and into the ER—a critical step, given the severe pathology that results when it's blocked.



Cholesterol depots. In this human cell, shown from two angles, the green color marks the lysosomes, which are loaded with the dye acriflavine.

CREDITS (TOP TO BOTTOM): J. P. DAVIES, F. W. CHEN, Y. IOANNOU; L. N. SANCHEZ/LANL

Because mutations in the two NPC proteins can produce that blockage, researchers suspect that in their normal form they play a role in transporting cholesterol from the lysosomes to the ER. The current work does not yet explain how they do that, but it may open the door to finding the answer. "It's the beginning of a whole new way of looking at the trafficking of cholesterol in the cell," says Goldstein.

The NIH team spent years searching for the *NPC1* gene, first mapping its location on chromosome 18 and then sorting through the DNA there until they found a gene mutated in NPC1 patients. By contrast, Lobel and his colleagues discovered NPC2 while looking for proteins that might be defective in the broader class of so-called lysosomal storage diseases. When they came upon HE1, its cholesterol-binding ability and its lysosomal location raised the possibility that it might be involved in NPC. It was. "We lucked out," says Lobel.

Using antibodies to the protein, the New Jersey team found that it is present in normal skin cells but not in skin cells from NPC2 patients. The researchers also found that adding the normal protein to cells derived from NPC2 patients reduced the cells' lysosomal cholesterol content. "When you add [the protein] back, it restores function," Lobel says. Cinching the case, sequencing studies showed that the gene from NPC2 patients, but not from controls, carries mutations that inactivate it.

Still unclear is exactly how NPC2 contributes to cholesterol transport out of the lysosomes, or how its role meshes with the newly discovered function of NPC1. Researchers had expected the NPC1 protein, which is located in lysosomal membranes, to be a cholesterol transporter, but that's not what Ioannou's team found. Instead, it resembles a family of bacterial permeases that transport various substances, including fatty acids, through the bacterial cell membrane. "Based on this structural homology, we reasoned that NPC1 is the first eukaryotic member of this family," Ioannou says.

To test whether it is a permease, the researchers exposed both normal and NPC1 cells to the fluorescent dye acriflavine—one of the molecules transported by the bacterial permeases. The dye ended up in the lysosomes of both cell types. When Ioannou and colleagues then removed acriflavine from the cell culture fluid, the lysosomes of the normal cells gradually lost the dye, while those of the NPC1 cells didn't. This indicates that the normal cells, but not the mutant ones, have a pump for transporting acriflavine out of their lysosomes.

More direct evidence that NPC1 functions as permease came when the researchers engineered cells of the bacterium *Escherichia coli* to make the protein. They found that NPC1 production greatly increased the bacterial cells' uptake of acriflavine and also of oleic acid, a long-chained fatty acid. It did not transport cholesterol, however, leaving unclear how it moves the lipid out of the lysosomes. As Ioannou says, "we have a lot to do in dissecting the functions of these proteins."

But now that both have been isolated, researchers expect that the contents of the "black box" will be revealed. "It is likely," Pentchev says, "that these contributions will … raise our scientific understanding of one of the critical issues in cellular cholesterol metabolism."

–JEAN MARX

ScienceScope

Doing Well by Doing Good? National Science Foundation (NSF) director Rita Colwell is gearing up for a big increase in public outreach that she hopes will also benefit the agency's bottom line. An advisory panel headed by PR honcho Frank Mankiewicz last week called for at least doubling the agency's $2.5 million public affairs budget as part of a major campaign to inform the public about the scientific underpinnings of today's economy. "NSF needs to be the place that the scientific media calls" on any breaking science story, Mankiewicz told the National Science Board, NSF's overseer. Such one-stop shopping would not only improve public understanding of science but also raise NSF's profile, said several panelists, who asserted that other agencies—in particular NASA—do a much better job of publicizing discoveries they have funded.

Board members embraced the panel's message, as did Colwell. "If I understand you correctly," said John White, chancellor of the University of Arkansas, "a $15 million increase in the agency's PR budget could give us a chance to increase NSF's budget by $15 billion ... a pretty good rate of return." One sour note: For all its visibility, NASA's budget has stalled in recent years, while NSF's has grown steadily.

Voicing Support A troop of arms-control experts is planning to ride to the aid of the Department of Energy's embattled national laboratories. The new U.S. Committee for the National Laboratories, announced this week, hopes to help the labs restore their reputation as guardians of national security in the wake of a string of espionage and mismanagement scandals.

"The labs have been subject to a lot of attacks, and not enough people are coming to their defense," says national security consultant Bill Courtney of DynMeridian in Alexandria, Virginia, one of the organizers of the committee. In contrast, he notes, flocks of outside supporters rally to the Pentagon's side in times of need.

Courtney says the nonprofit group—led for the time being by attorney and former government arms-control expert Thomas Graham—has been blessed by lab officials and expects to raise funds from corporations, foundations, and individual members. Among its first tasks, he says, will be "to acquaint people with some of the good things the labs are doing."