The Changing of the Guard

A rising cadre of scientists is focusing on detailed questions about HIV and—some believe—creating a more cooperative research culture

A decade ago, the world of AIDS research was more like a collection of fiefdoms than a typical field of science. The leading researchers were tumor virus hunters who had known each other for many years. They were split into camps whose leaders provided their collaborators—most of them tumor virologists—with viral samples, reagents, and the latest information. Early on, the different camps cooperated closely, even coordinating the publication of their findings, which sped the discovery of HIV and the proof that it caused AIDS. But, even before the discovery of HIV was announced, the harmony between the camps gave way to vicious feuds—feuds that earned the world of AIDS research a reputation for having a particularly nasty terrain.

Today, the landscape of the AIDS research world appears much different and, by most accounts, considerably less hostile. The field is now so large that no one lab controls anything. And the community itself has been transformed: The reign of the tumor virologists has been eclipsed by a younger generation of researchers who have spent their entire independent careers trying to tackle tough, detailed questions about HIV and AIDS. As Beatrice Hahn, 41, a molecular biologist at the University of Alabama, Birmingham (UAB), puts it simply: "The culture has changed."

The culture has shifted in part because this new guard of leading scientists has grown up together and seen the high cost of discord in the research community and the benefits of cooperation. "There is a younger generation at the forefront who don't have the egos, and it's very enjoyable," says Didier Trono, 39, a leading molecular biologist at the Salk Institute for Biological Studies. Richard Koup, 39, an immunologist at the Aaron Diamond AIDS Research Center (ADARC), has noticed the change, too: "It's really quite amazing how little real fighting or hatred there is, which distinguishes this era from the previous one." UAB oncologist George Shaw, 42, says his peers also have high regard for each other: "Many of the investigators of this era would not dream of doing anything to hinder even their fiercest competitor."

Scientifically, the ascendancy of this new generation of researchers is abundantly evident. The work of scientists in their 30s and 40s fills the top journals and is among the most frequently cited in the field. They are the foundation—and the soul—of world-class AIDS programs at places like ADARC and UAB. They are selected to give the choice talks at the biggest conferences, such as the upcoming international AIDS meeting to be held in Vancouver, Canada, next week, and they organize Keystone and other prestigious get-togethers. "The torch has been passed ... and that's how it should be," says UAB retrovirologist Eric Hunter, 48.

It's not just in the research arena that leaders of the new guard are making an impact: They are also helping shape the politics of the AIDS program. Most notably, these younger researchers, working with AIDS activists, played a pivotal role in persuading Congress in 1993 to revamp the Office of AIDS Research (OAR) at the National Institutes of Health (NIH). And they provided much of the muscle for a subsequent sweeping review of the NIH's AIDS research portfolio that OAR has just completed (see p. 1878).

These changes in the culture of the AIDS community reflect the maturing and expansion of the field itself. "There are not two or three major camps as there were before," says virologist David Ho, 43, who heads ADARC. "You could probably name a dozen groups" making major contributions. And the glory stakes are lower than they were when the virus was discovered: No longer is there any expectation that findings will quickly lead to effective vaccines or therapies. "I think everyone was trying to hit a home run in the beginning," says molecular biologist Steven Wolinsky, 43, of Northwestern University. "Quick answers just aren't going to be there any longer."

The realignment of the culture is less apparent to the old guard, however. "It happened without us thinking about it," says Robert Gallo, the tumor virologist whose former lab at the National Cancer Institute (NCI) first proved that HIV causes AIDS. Others, such as Duke University's Dani Bolognesi, a tumor virus veteran who became a leading AIDS vaccine researcher, say the lines between the eras are blurry. "I don't see the old passing into the new so much as it

The New Face of AIDS

The 11th International Conference on AIDS, to be held in Vancouver, Canada, next week, comes at a time of guarded optimism on some aspects of the 15-year battle against the disease. This represents a change from 3 years ago, when *Science* last did a special issue on AIDS, with a focus on European researchers (28 May 1993). This special section, focusing largely on the United States, looks at the changing culture of AIDS research; the AIDS marketplace (p. 1880); the story behind the discovery of a promising new class of drugs (p. 1882); and a surprising recent meeting on antiviral therapy (p. 1884). We also present the viewpoints of leading researchers on HIV pathogenesis (p. 1885), drug treatments (p. 1886), and vaccine research (p. 1888).

The section, including links to other AIDS sites, is available on the World Wide Web at http://www.sciencemag.org.

HEAVY HITTERS 1993–95

Rank	Name (Number of Papers)	Cites/Paper
1	Jan Orenstein (25) George Washington University	28.96
2	Giuseppe Pantaleo (37) NIAID	27.16
3	Michael Saag (30) Univ. of Alabama, Birmingham	19.80
4	George Shaw (38) Univ. of Alabama, Birmingham	18.11
5	Yunzhen Cao (29) Aaron Diamond AIDS Res. Ctr.	18.03
6	Donald Kotler (42) Columbia University	16.98
7	Anthony Fauci (83) NIAID	16.89
8	Beatrice Hahn (36) Univ. of Alabama, Birmingham	16.61
9	Gene Shearer (57) National Cancer Institute	15.81
10	Mario Clerici (58) San Raffaele Scientific Inst.	15.74
11	David Ho (77) Aaron Diamond AIDS Res. Ctr.	14.26
12	Stephen H. Hughes (25) National Cancer Institute	11.88
13	Martin Hirsch (28) Harvard University	11.32
14	Jay Levy (51) Univ. of California, San Francisco	11.31
15	John Moore (44) Aaron Diamond AIDS Res. Ctr.	11.05

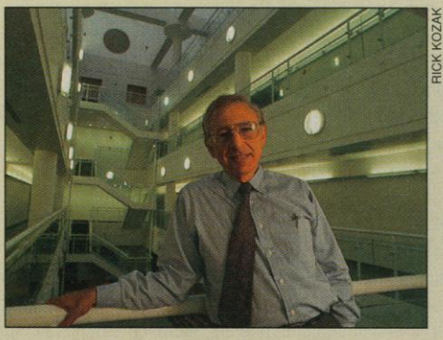
SOURCE: INSTITUTE FOR SCIENTIFIC INFORMATION

The Rebirth of Robert Gallo

BALTIMORE—An area at the center of this city, called the Inner Harbor, is often cited as a model of urban renewal. Once in dire straits, it has been reborn as Harborplace, a mecca for natives and tourists alike. Robert Gallo is hoping that it will be a fitting venue to launch a second career. The retrovirologist recently ended a 30-year stint at the National Cancer Institute (NCI)—where his lab first published convincing evidence in 1984 that HIV causes AIDS—to run a brand-new institute just a few blocks from Harborplace. Known as the Institute of Human Virology (IHV), its launch, combined with a recent landmark paper Gallo co-authored, provides ample evidence that at least some old-guard researchers are still a force to be reckoned with.

"I have a desire to leave something behind when I die," says Gallo, 59. That's an odd thing for Gallo to say, considering that he has been credited with speeding the development of the HIV blood test, which has saved lives. His NCI lab was also celebrated for discovering the chemical messenger interleukin-2 and the two human tumor leukemia viruses—the first of which proved that a human tumor virus really exists. If that weren't enough, Gallo and Fiorenza Cocchi, working with Paulo Lusso from Italy's San Raffaele Scientific Institute, on 15 December 1995 published in *Science* (p. 1811) a discovery about the role natural anti-inflammatory chemicals called chemokines play in the suppression of HIV—a finding that has opened up the hottest new area in the field (see p. 1885 and 21 June, p. 1740). But Gallo, a man who attracts scientific controversy in almost equal measure to his scientific achievements, is restless to prove himself once again. And IHV is the vehicle.

Set in a refurbished department store warehouse that boasts 100,000 square feet of usable space framed around a giant atrium, IHV—which will focus on battling AIDS and other viral diseases—is Gallo's dream come true. He has shed the bureaucratic shackles of the NCI, where he was the subject of a long-running scientific misconduct investigation into his role in the discovery of HIV. Among the material benefits of relocation: IHV will soon have its own clinic, so Gallo will no longer be forced to rely on clinical specimens from chance collaborations. The center is part of the University of Maryland (UMd), which will allow Gallo to interact with students—another plus, he says. Because IHV will have its own biotech partner, Omega Biotherapies, investigators will be able in theory to develop new treatments quickly (and also make money). "It's one of the most impressive facilities I've ever seen," says Dani Bolognesi, a Duke University AIDS vaccine researcher. Gallo has "an opportunity there to do wonders."



RICK KOZAK

New digs. Gallo launches a second career as head of the Institute of Human Virology.

IHV is still in its infancy. But 12 scientists have already come on staff in four areas: Gallo is overseeing basic researchers, former NCI researcher William Blattner heads the epidemiology division, ex-Army AIDS researcher Robert Redfield heads the clinic, and Ed Tramont, the one-time head of the U.S. military's entire AIDS program, leads the vaccine division.

In addition to spending $52 million on the building and equipment, the state of Maryland has promised IHV $13 million over 4 years. "These became the carrots to attract [Gallo], Redfield, and Blattner," says Tramont, who heads UMd's Medical Biotechnology Center and put the deal together. Another new hire is Mikulas Popovic, a virologist who aided Gallo's discovery of HIV and, likewise, was a subject of the misconduct investigation. (Both Gallo and Popovic were cleared of wrongdoing.)

Gallo, being Gallo, is not content with simply starting IHV, which he hopes will employ about 500 people. He's already thinking about expanding to a second IHV in Pasadena, possibly affiliated with the California Institute of Technology. "What attracts me is it opens up many more clinical possibilities and goodwill between the West Coast and East Coast," says Gallo. Clearly, some of the old guard in AIDS research are ready for anything but retirement. –J.C.

all being better integrated," says Bolognesi. He points out, for example, that Gallo, who recently left NCI to run a new Institute of Human Virology at the University of Maryland (see box above), is still making discoveries that shape the field. Jay Levy of the University of California, San Francisco, another tumor virologist who independently discovered HIV, says "AIDS is still an area where there are camps. Unfortunately, I don't see any difference."

Ho and others are quick to acknowledge that competitive juices still flow strongly when different groups home in on the same target—such as the race to unravel the connections between HIV and chemokines (*Science*, 21 June, p. 1740). But the rivalries that clouded the field for a decade have dissipated. James Mullins, 44, a molecular biologist at the University of Washington, Seattle, who got caught in some of the early storms, has much enjoyed the climate change over the past few years. "I started sleeping a lot better," says Mullins, "and I know many people did."

The Birmingham and Manhattan projects

The new guard of AIDS researchers, who started out when the epidemic was first recognized 15 years ago, have climbed their way through the hierarchy and are now making their mark in many institutions. Nothing exemplifies the shift in the world of AIDS research so much as the new prominence of ADARC and UAB. These two powerhouses have become "remarkable forces" in AIDS research, says Bolognesi.

One gauge of just how remarkable they have become is their impact on the AIDS literature. A database of AIDS research papers put together by the Institute for Scientific Information in Philadelphia assesses impact by tallying the number of citations authors receive per paper. The database shows that for authors publishing 25 or more papers between 1993 and 1995, six of the top 15 researchers come from ADARC and UAB (see table). And their rise has been rapid: If the same analysis is done for publications in an earlier slice of time, 1988 to 1992, none of them even ranks in the top 25.

In parallel with their meteoric rise in the citations index, ADARC and UAB have displayed many other similarities. Both strongly link clinical and basic research, focusing on pathogenesis (how HIV causes disease). They both embrace a wide range of expertise, allowing clinicians to team up with primatologists, molecular biologists, immunologists, vaccinologists, retrovirologists, and, in the case of UAB, epidemiologists and behavioral scientists. And, although everything isn't lovey-dovey at both institutions, success has

OAR Gets by With a Little Help From New Guard Friends

In October 1994, a group of leading young investigators attending the Cent Gardes AIDS colloquium near Paris had a heart-to-heart talk with Anthony Fauci, head of the National Institute of Allergy and Infectious Diseases (NIAID), in a challenge to the old ways of doing business. David Ho, head of the Aaron Diamond AIDS Research Center (ADARC) in New York, recalls that he and a dozen others told Fauci they felt that his staff at NIAID, the hub of AIDS research at the National Institutes of Health (NIH), was too heavily directing their research. "We sat with Tony and said, 'It's rather unusual for so many middle officials at NIH to dictate to us what to do. Let more of the science be driven by extramural scientists,' " says Ho. "It was a great meeting," says Fauci. "Ten, 20 years from now when people talk about how things evolved, that meeting has to come down as important."

One reason Fauci describes the meeting as "pivotal" is because it led him to aggressively solicit "more input from younger researchers in the trenches who have the ideas." But it was a symbolic moment as well. The meeting reflected a changing of the guard in AIDS research, as young researchers establish themselves as leaders in the field (see main text) and the center of gravity in U.S. AIDS research shifts away from NIH. That shift became evident to the outside world earlier this year when NIH's Office of AIDS Research (OAR)—a body shaped in large part by young researchers—completed a massive review of NIH's $1.4 billion AIDS portfolio. Its main recommendation: Extramural researchers should have more control.

Indeed, the recent history of OAR itself speaks of the growing political power of the new guard. The young researchers played an instrumental role in convincing Congress to pass legislation in 1993 that gave the then-obscure OAR the power to oversee the NIH's entire AIDS research portfolio. Not only did several prominent younger researchers like Ho lobby for the change, but they worked with AIDS activists who masterminded the OAR overhaul, which included replacing Fauci as its head with immunologist William Paul.

Mark Harrington, 36, a member of the Treatment Action Group, co-author of a critical review of the NIH's AIDS research program in 1992 that served as a reform manifesto, says activists like himself and younger researchers bonded as the clinical-trials network took shape in the 1980s. "It's there where we first met," says Harrington. "We came up against the same powers-that-be that they mentored with and had to gain their independence from." He says the younger researchers were more willing to have activists involved in designing trials: "They were closer to us. There were no barriers."

The 1993 legislation also directed OAR to conduct a top-to-bottom review of NIH's AIDS research; again, younger researchers played a leading role. The same ones who met with Fauci at Cent Gardes were among the 114 members of the six subpanels that conducted the OAR review. And they were not the only representatives of their generation. "Take all the panels together, they're largely this generation [of younger researchers]," says Ho. The review, which OAR plans to release in full by next week, calls for sweeping changes (*Science*, 15 March, p. 1491).

Whether Congress will give OAR the muscle the new guard is seeking is a big question right now, as a House bill passed last week removed the office's ability to control the AIDS budget (*Science*, 21 June, p. 1733). Virologist Joseph Sodroski of the Dana-Farber Cancer Institute in Boston, a participant at the Cent Gardes meeting with Fauci, is confident that the OAR review will lead to important changes. "It looks to me like there's a sincere effort with people at the NIH to be more critical," Sodroski says. Another participant of the Cent Gardes gathering, who asked not to be named, is more circumspect. "The old guard has maintained its position and has not really responded to the change and has protected their own turf," this scientist says. ADARC biochemist John Moore, who also attended the Cent Gardes powwow, has deep misgivings as well: "I came out of the meeting very optimistic, and that optimism has completely disappeared."

Paul, OAR's director, says he understands the young guard's concerns: "They've been good citizens, and they want to make sure that they don't get caught in that old saying, No good deed goes unpunished." But he notes that even if the House language makes it into law, it gives OAR the power to move 3% of an institute's funds to any other program, without limiting the recipient. The report, promises Paul, won't be a paper tiger. –J.C.

F. GAY WATSON

Topping the charts. Alabama's team has some of the most cited AIDS papers.

allowed them to grow at a blinding speed.

The UAB AIDS program started in 1985, when the school recruited Hahn and her husband Shaw. At the time, Hahn and Shaw were postdocs with Gallo, who was then embroiled in a vicious dispute with the Pasteur's Luc Montagnier over who discovered HIV. Shaw's Ph.D. adviser, Albert LoBuglio, had joined UAB (he is now head of its cancer center) and made an offer to lure Shaw to Birmingham—a move some UAB researchers argued against. "The last thing they wanted was to touch people out of Gallo's lab," recalls Hahn. But the offer was made and accepted, and UAB scored a double recruitment.

Hahn and Shaw soon began to publish their work in high-profile journals. "The science worked," says Hahn. "We were able to be very productive outside of the sheltered structure of a big lab." They also began to attract a cadre of other researchers. One important convert to AIDS research was Hunter, who previously worked on Mason-Pfizer monkey virus. "There's an enthusiasm here that by working together we can actually have an impact on AIDS research and on the disease itself," says Hunter, who has headed the NIH-funded Center for AIDS Research at UAB since its inception in 1988. Other converts were Casey Morrow, who switched from polio research to AIDS vaccine work; mucosal immunologist Jiri Mestecky; and pediatrician Richard Whitley. In addition, the group recruited many younger scientists who were just starting their independent careers, including Michael Saag, 40, who did a postdoc in the Hahn-Shaw lab and is now a top AIDS clinical researcher.

Today, UAB's AIDS program has a $25 million budget and a large faculty. Its 55 principal investigators, who are spread across several different departments, include such notable recruits as primatologist Patricia Fultz, drug-resistance specialist Victoria Johnson, epidemiologists Sten Vermund and Richard Kaslow, pediatrician Grace Aldrovandi, and behavioral scientists Ralph DiClemente

and Laura Leviton. "One reason it is working here is that there's no sense that 'This is my area, this my work, you stay out of it,' " says Fultz.

ADARC's $6.7 million budget means it has a considerably smaller program than UAB. And because many of the researchers do work in overlapping areas, the internal competition can get intense—separate papers on chemokine receptors just came out in the 20 June issue of *Nature*, for example, from different ADARC teams. Another difference with UAB is that ADARC, based in New York City, houses its diverse array of AIDS researchers under one roof—which begs a comparison to the Manhattan Project. "Well, we are in Manhattan, aren't we?" quips biochemist John Moore, 39, one of 11 staff investigators at the center.

ADARC was the brainchild of author and biologist Lewis Thomas, who encouraged Irene Diamond to invest money from the foundation that was set up with real estate profits made by her late husband Aaron into a basic research AIDS center. In 1989, the nascent center contacted Ho, who, after studying at Harvard University with virologist Martin Hirsch, had moved on to the University of California, Los Angeles. "I was actually a little surprised," says Ho. "I was 36 at the time, and to head up something like this, I just thought they were going to pick a more senior figure."

HANK MORGAN

ADARC horse. This team came from nowhere to the front of the pack.

Ho got the job, and with $11 million from the foundation and another $3.3 million from New York City, the center officially took over the seventh floor of the city's Bureau of Laboratories building in April 1991. (ADARC was then affiliated with New York University, but last month was transferred to Rockefeller University.) "The place has developed more or less along the lines we had planned," says Ho. "We have people with a lot of different backgrounds converging, and so we can do things extremely quickly." ADARC's accomplishments can also be measured by its steady growth: In September, the center will nearly double in size when it completes the refurbishing of yet another floor of labs, and in short order plans to grow from 70 employees to 120.

As with the UAB researchers, the ADARC scientists depend heavily on each other for everything from reagents to know-how—and they are encouraged to work with outside groups, too. "That's the spirit of this place," says Ruth Connor, 33, who concentrates on pathogenesis questions. Eric Delwart, 37, who studies the genetic diversity of HIV, says his generation has learned from the battles that marred the field for so many years: "We don't want to repeat it."

Angling for results, not prizes

The success of younger investigators at leading AIDS research institutions such as ADARC and UAB helps to explain the cultural shift that is taking place throughout the field. But larger forces are also contributing to these changes. For one thing, the science of HIV and AIDS has become vastly more complex. Although dramatic progress has recently been made in drug therapy, few scientists still entertain fantasies of finding *the* cure. Vaccine developers have also been humbled over the years. "In the beginning, people had more of the feeling that they'd be an overnight hero who would solve the problem and get great rewards," says Salk's Trono. "This concept has changed because of the difficulty in solving the problem. Each of us can contribute somehow, but none of us on our own can do it." UAB's Vermund, 42, adds: "There is this older culture that was very much tied up in Nobel Prize angling, and this got in the way of what the true mysteries were in the field."

The scientific challenge, in effect, has matured the culture. "Back in the early years, every day counted," says Joseph Sodroski, 41, of the Dana-Farber Cancer Institute in Boston, a virologist who did his postdoc with William Haseltine, who helped identify many of HIV's genes. "As the field matures and you get into structural biology, the development of vaccines or effective therapy, [you realize] those long-term questions are likely to be around for a number of years. It encourages people to feel cooperative." Molecular biologist Mario Stevenson of the University of Massachusetts agrees. "Previously, when there were camps and big names taking chunks of the field, the research was not as inclined to look at very specific and fundamental issues," says Stevenson, 39. "The field is more sophisticated now. There isn't this camp sense or mentality anymore, and people are more willing to interact."

To David Baltimore, a Nobel Prize–winning retrovirologist who shifted into AIDS research relatively recently, the culture is becoming more civil because the questions being asked today have less immediate medical relevance. "I've learned that the more medically relevant the question, the worse the social behavior," says Baltimore. "When something is really hot and has direct medical relevance, people's behavior is atrocious. If you're working on something like *Drosophila*, people are much more collaborative and better behaved."

Michael Emmerman, 37, a molecular biologist at the Fred Hutchinson Cancer Research Center of Washington in Seattle who did a postdoc in Montagnier's lab, says: "There are more people trained in this kind of biology and more people watching every step you make." And many of these people, he notes, grew up together: "We're at the same time in our careers and we knew each other as postdocs and now know each other as assistant and associate professors."

With the passing of time, the bitterness of the early disputes between the Gallo and Montagnier labs—which even ensnarled the leaders of their countries—has faded. The old battles live on in memory, and "it was an unfortunate period," concedes Anthony Fauci, head of the U.S. National Institute of Allergy and Infectious Diseases. "Not taking any sides about who's right or who's wrong, it lent a flavor to the field of 'Gee, what a strange, bizarre field this was.'" Now, says Fauci, some young researchers have never heard word one about it: "I have young people coming into the field who don't even know what we're talking about. It's an era that passed them by."

Although the hallmarks of the early AIDS research culture—vicious credit spats and backbiting—are less common today than they were a decade ago, the field is still highly competitive. And this means that the threat of divisiveness is ever present. Many of the younger researchers now leading the field remain on guard against an outbreak of the old ways. "It's not like the younger generation is immune," says UAB's Vermund. Some have even witnessed backsliding lately. "In the past few years, I've attended conferences where I've seen clique, allegiance stuff popping up," says the University of Washington's Mullins. "I've actually talked to people about it to help them remember history. We don't want to get back to that."

But researchers of both the old and new generations seem to recognize that the main thing they must contend with is not the research culture, or peer competition, but their own ignorance. Despite recent progress in deciphering how HIV is structured and how it functions, the virus still has the upper hand, leaving plenty of unanswered scientific questions up for grabs.

–Jon Cohen