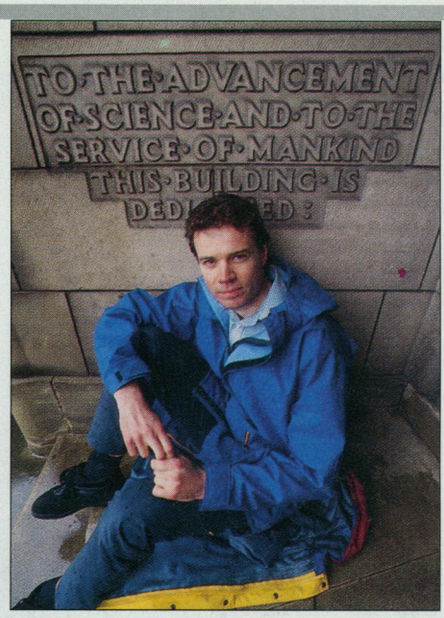
Unlikely Recruit: Andrew Leigh Brown



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AIDS is such a complex, multifaceted process that it has drawn researchers from many fields of research. There are virologists and immunologists, molecular biologists and epidemiologists, pharmacologists, oncologists, primatologists, experts in drug use, sexual behavior, hemophilia, and pregnancy. But even in that list a researcher trained to study *Drosophila* genetics stands out. And, indeed, Andrew Leigh Brown of the University of Edinburgh sees the differences between his original field and his current one. "AIDS is a lot harder work, and the problems are much bigger."

Actually, as Leigh Brown's promising start in AIDS research shows, it makes good scientific sense that the field should attract a population geneticist with a firm understanding of *Drosophila melanogaster*. In 1990, Leigh Brown, a 40-year-old Anglo-Scot, became a familiar name to AIDS researchers when he showed how his brand of molecular genetics could track the spread of HIV from a single infected batch of clotting Factor VIII through an entire cohort of hemophiliacs. A large study like this had never been done, and it opened up a window on the history of the epidemic that had seemed to be shut tight.

Accomplishments like those have attracted the notice of some well-known investigators. Leigh Brown is "bright and young and he'll continue to become a researcher who is at the forefront," says Gerald Myers, a Los Alamos National Laboratory researcher who tracks the spread of HIV through the world. "His potential is considerable."

That potential appeared at a tender age. At 24, possessor of a brand new Ph.D. from England's University of Leicester, Leigh Brown had already had his first publication in *Nature*, a single-author report on enzyme polymorphism in field mice. From there he moved on to *Drosophila* work, first at London's Imperial Cancer Research Fund, later at the University of Sussex, studying the evolution of "transposable elements" in flies. These genetic sequences, also known as "endogenous" retroviruses, can move from place to place in a host cell's genome, causing mutations as they go.

Leigh Brown moved to the University of Edinburgh in 1984, and 2 years later he experienced a pivotal career moment while reading a paper that analyzed changes in HIV over time in a single patient. The paper "posed a number of questions that were unresolvable, but the nature of the questions made me realize there was a role for a population geneticist in AIDS," he says.

After studying the published genetic sequences of HIV, Leigh Brown began wondering what forces influenced the changes in viral genetic sequences in any given infected person. That's when he began investigating a cohort of hemophiliacs. He observed how the swarm of HIV strains in each person changed, and, using genetic analysis, he traced the infections in each member of the cohort back to a single lot of the blood clotting protein known as Factor VIII. When he presented that data at the 1990 international AIDS conference in San Francisco, it put him on the AIDS research map. "People were surprised that this kind of analysis could be used with HIV," Leigh Brown says.

What was initially surprising, however, has since become a key part of the field. Leigh Brown has gone on to examine in detail the selective forces that act on HIV as it spread through a heterosexual cohort in Edinburgh and plans to begin similar analyses on samples from Uganda. In addition, he heads the newly opened Centre for HIV Research on the Edinburgh campus.

Leigh Brown's current research involves going beyond epidemiologically linked cohorts to find out what type of HIV is initially transmitted among the population at large. His work shows that even though people who have been infected for some time harbor many forms of HIV, among newly infected the various isolates show remarkable genetic similarities.

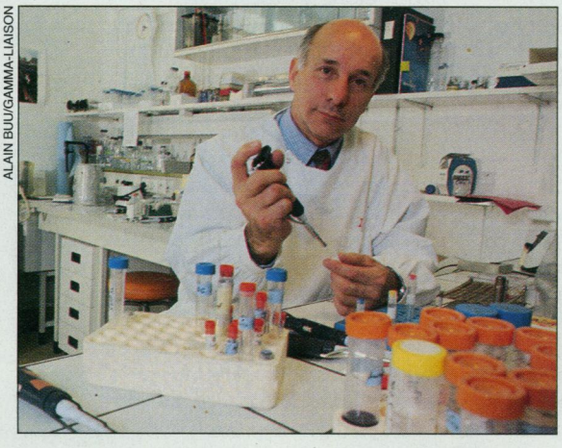
Leigh Brown is currently trying to find out whether one type of virus is preferentially transmitted and, if so, why that happens. The answers could significantly influence AIDS vaccine development. Sounds like a job cut out for a population geneticist.

–J.C.

Laughing Last: Marc Girard

Marc Girard remembers skiing in Keystone, Colorado, in the winter of 1989 and being ribbed by several top immunologists. They had come to Keystone for the annual AIDS conference held there and Girard was a target because he was one of the few researchers attempting to protect chimpanzees with HIV vaccines, something that, at the time, had never been reported. "They were laughing at me, saying, 'Marc, you can go back and try for years and it will never work.'"

By the fall of 1989, there was a new punch line and the joke was on Girard's colleagues, because he and his collaborator, Patricia Fultz of the University of Alabama, had protected a chimpanzee with an HIV vaccine. "I was very comforted by the observation that it worked," says Girard, a deputy director of the Pasteur Institute in Paris. He was also relieved, since the joke might well have continued to be on him: "I thought [success] was easier than could have been anticipated."



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Following that success, Girard, 56, is viewed as one of the world's leading authorities on AIDS vaccines and chimpanzees. "Marc is a major force in AIDS vaccine development," says Duke University's Dani Bolognesi, himself an influential AIDS vaccine researcher. Girard heads a French government-sponsored AIDS vaccine task force and organizes the annual Cent Gardes meeting, a much-praised AIDS conference.

In many ways it seems fate steered Girard to his current work. "I do believe in serendipity," says Girard. "The word doesn't exist in French, and it's the best English word I know." For starters, his father was a veterinarian who developed a foot-and-mouth disease vaccine for livestock.