identify and quantify CTLs that recognize specific microbial peptides. The method, called tetramer staining, uses genetically engineered complexes consisting of four HLA-peptide subunits—each of which contains the specific peptide of interest—to detect CTLs taken directly from patients. The complexes bind so tightly to the CTLs' receptors that even small numbers of cells are readily detectable.

Using this technique, a team led by McMichael, including Oxford researchers Graham Ogg, Rowland-Jones, and Nowak, along with Nixon and David Ho at Aaron Diamond, published in *Science* earlier this year the first clear evidence that higher levels of HIV-specific CTLs are correlated with lower concentrations of HIV in the blood of infected patients (*Science*, 27 March, p. 2103)—a finding consistent with the view that CTLs play a major role in controlling the virus. "This technology has had a tremendous impact on our understanding of the relationship between CTLs and [viral burden]," says Walker. As for how important immune escape will turn out to be in the development of AIDS, Walker says, "I am sure Andrew will be the one to sort this out."

**–Michael Balter**

FRANCE

# Duo Brings Hope of Immune Restoration

**PARIS**—When Brigitte Autran and Christine Katlama attended medical school in Paris together in the 1970s, they had much in common: Both were specializing in infectious diseases, a field long dominated by men; both were avid and competitive skiers; and a few years later, as newly graduated doctors, they were among the first French physicians to take care of AIDS patients. Yet their paths diverged soon afterward. While Katlama continued caring for patients, Autran left clinical medicine for a career in basic immunological research.

But in the early 1990s, the pair teamed up again, to lead one of France's most successful AIDS research collaborations. Over the past year, Autran and Katlama—who now both work at the Pitié-Salpêtrière Hospital in Paris—have published a series of encouraging reports showing that the battered immune systems of HIV-infected patients may recover, at least partially, if powerful combinations of drugs are used to reduce their viral burdens. Although AIDS researchers are still debating how much recovery actually takes place, most agree that the French team's findings have helped open the door to this important possibility. "[This] research has had a significant impact on the understanding of the immunopathogenesis of HIV disease," says Mario Roederer, an immunologist at Stanford University.

Immunologist Quentin Sattentau, of the Center for Immunology in Marseilles, says that Autran and Katlama have gained a place among France's leading AIDS researchers because "they are tough when they need to be and are not worried about stating their opinions in a forceful way." The two began laying the groundwork for their recent discoveries more than a decade ago, while they were still working independently. After leaving the clinic for the laboratory, Autran began working with Pitié-Salpêtrière immunologist Patrice Debré to elucidate the role of the immune cells known as T lymphocytes in fighting HIV infection. In 1987, Autran and Debré, along with other French co-workers, published a landmark paper in *Nature* demonstrating that HIV-infected patients produce large numbers of killer cells, called cytotoxic T lymphocytes (CTLs), directed specifically against the virus. This key finding, simultaneously reported by Bruce Walker and his colleagues at Massachusetts General Hospital in Boston, effectively countered the views of some researchers at the time that CTLs were of little importance in the immune system's response to HIV.

Meanwhile, Katlama was making her own mark on HIV research. As one of the small number of French physicians willing to devote themselves to studying the disease in the 1980s, she quickly developed a reputation as an expert on the opportunistic diseases, such as cytomegalovirus (CMV) infection, that ravage AIDS patients. And in 1985, Katlama's insistence that a patient from the Cape Verde islands off the west coast of Africa had AIDS—a diagnosis many of her colleagues doubted—led to the discovery of HIV-2, a West African variant of the virus that usually causes a milder form of the disease. Later, Katlama would emerge as an international leader in clinical trials of anti-HIV therapies. For example, her team was the first to demonstrate the efficacy of the anti-HIV drug 3TC and among the first to show that combining drugs could lead to better control of the virus.

FREDERIC REGLAIN/GAMMA LIAISON

**Reunited.** Brigitte Autran *(left)* and Christine Katlama believe the immune system can recover if viral load is reduced.

Thus when Autran and Katlama reunited several years ago, their experiences in basic and clinical research meant they were well placed to study how the immune systems of HIV-infected patients were responding to combination therapy. Their biggest breakthrough came in 1997, when, in collaboration with other French colleagues including Debré and immunologist Jacques Leibowitch at Raymond Poincaré Hospital outside Paris, the pair reported in *Science* that patients in advanced stages of HIV infection who were treated with combination therapy could recover some of their ability to mount immune responses against CMV and the tuberculosis bacterium—two of the most important opportunistic infections afflicting AIDS patients (*Science*, 4 July 1997, p. 112).

In addition, after a year or so of therapy, these patients apparently begin regenerating so-called "naive" T lymphocytes, immune cells that have not yet been exposed to foreign antigens—a key criterion for immune system reconstitution. And more recently, Autran and Katlama, along with Guy Gorochov of Pitié-Salpêtrière, have demonstrated that antiviral treatments can help the crippled immune systems of HIV-infected patients, which are able to respond to fewer and fewer invaders as the disease progresses, to partially recover their capacity to respond to a wider range of invading organisms—another crucial indicator of immune system health.

Autran cautions that she and Katlama have yet to demonstrate that the immune system of HIV-infected patients can be completely restored to normal, although she adds that there may be "no major limitations" to this restoration if the virus can be adequately controlled over the long term. But many researchers credit Autran and Katlama with providing new hope that this welcome possibility might become a reality. The pair's work, says Roederer, "demonstrates that there may be a slow, sustained reconstitution of the immune system ... [which is] the ultimate goal of AIDS therapy."

**–Michael Balter**