Montagnier Pursues the Mycoplasma-AIDS Link

In the face of stubborn skepticism from the AIDS research community, Luc Montagnier presents new results

Paris—LAST YEAR LUC MONTAGNIER, co-discoverer of the AIDS virus, created quite a stir when he proposed that the virus may not work alone in causing AIDS. Mycoplasmas—single-celled organisms resembling bacteria but lacking a cell wall—could also be playing a key role, he said. The reaction to Montagnier's proposal was sharply divided. Almost all researchers working on AIDS said Montagnier was out on a limb. But experts in mycoplasmas didn't find the idea so farfetched. Both groups agreed on one point, however: Montagnier needed more data.

Now he's come up with some. In a paper published in December in the proceedings of the French Academy of Sciences,* Montagnier's group at the Pasteur Institute in Paris, working with collaborators at the Centre National de la Recherche Scientifique in Marseilles, reports that antibodies against mycoplasmal peptides can block HIV replication in the test tube, suggesting that the bacteria-like microorganism may cooperate with the virus in producing the symptoms of AIDS.

But the new findings have not overcome the division between those working on HIV and mycoplasmologists. AIDS experts contacted by *Science* made it clear that they don't think a single cofactor is required in all cases of AIDS and that Montagnier's new data are too sketchy to be conclusive. But mycoplasmologists who have heard about Montagnier's results are—perhaps predictably—more enthusiastic.

What Montagnier's group has now done is to make antibodies by immunizing rabbits with a specific peptide from a sequence common to at least two species of mycoplasma. The antibodies inhibited replication of the AIDS virus in fresh lymphocytes from HIV-negative donors as well as in a cell line enriched in CD4—the receptor that HIV binds to in entering its target cells.

The effect seems to be highly specific: The peptide used for the immunization is thought to be involved in the binding of the mycoplasma to the cells it infects, and antibodies raised against another part of the same mycoplasmal protein had no effect. Nor did serum from rabbits that had not been immunized with the peptides.

These results, if confirmed, could provide support for the notion that mycoplasmas and HIV work together to attack the T-cells of AIDS patients. They suggest, Montagnier says, that if the mycoplasma is prevented from binding to the cell, HIV replication is inhibited in some fashion.

Montagnier stresses that his new report represents only preliminary research. He notes that he can't rule out the possibility that the antibody recognizes a structure on the cell or on the virus, rather than on the mycoplasma—although when his group looked for viral proteins recognized by the antibody, they didn't find any.

So far, specialists in HIV infection haven't been carried away. "I'm not sure we really need major cofactors to explain HIV pathology," says David Klatzmann, an immunologist who was a key figure in the early French work that determined that HIV preferentially infects T4 cells.

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Thomas Folks, chief of the Retrovirus Diseases Branch of the Centers for Disease Control in Atlanta, agrees. "I still haven't seen anything here which tells me that mycoplasma is playing a major role as a cofactor. But I think Montagnier is looking at some very interesting associations. It does look like there are mycoplasma gene products that. . . may be enhancing the replication of HIV."

"The critical issue here is whether mycoplasma plays a role in HIV infections of people," says Malcolm Martin of the National Institute of Allergy and Infectious Diseases. "Given the absence of epidemiological evidence that there's an association between the two, then all of this work, while perhaps valid in the laboratory, might be totally irrelevant."

Montagnier says he has isolated and cultured mycoplasmas from the blood of HIV-positive subjects, both symptomatic and asymptomatic. He also finds evidence of mycoplasmal DNA in HIV-negative subjects, although the organism is apparently not present in concentrations high enough to be cultured. (Similar results have been reported by Shyh-Ching Lo of the Armed Forces Institute of Pathology—see *Science*, 11 May 1990.) But Montagnier has had difficulty getting his new work published. One paper, for example, was rejected last year by *Nature*.

"I have high resistance from the virologists, and high enthusiasm from the mycoplasmologists," Montagnier says. In recent months he has been collaborating with a "task force" of mycoplasmologists in France, England, and the United States to study the mycoplasma-AIDS connection more closely.

"I think there has to be a union between those people who have experience with mycoplasma and those who have experience with HIV to try to understand this interaction," says Joseph Tully of NIAID, a leading U.S. mycoplasmologist who has kept in close touch with Montagnier. "We know that mycoplasmas can do a lot of things to lymphocytes, monocytes, and other types of blood cells. It's conceivable that they are doing something to the blood cells that makes them more susceptible to the attachment of the virus."

Montagnier has developed a model in which an originally benign mycoplasmal infection serves as a "general activator" of the immune system during HIV infection and particularly of those cells in which the virus grows. And is mycoplasma the only cofactor needed in AIDS? "Maybe I am wrong in saying that it is the only one," Montagnier says. "But mycoplasma is a better candidate, because it is present everywhere."

For the moment the situation is a scientific standoff. Montagnier keeps working, although he isn't gaining immediate acceptance. Mainstream AIDS researchers, on their side, are struggling to keep an open mind—particularly in view of Montagnier's role in the discovery of HIV. "I think that whenever a scientist with the status and track record of Luc Montagnier finds something," says Folks of the CDC, "the scientific community owes it to them to investigate and see exactly what they're talking about." ■ MICHAEL BALTER

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*L. Montagnier, *et al.*, *Comptes rendus de l'Academie des sciences*, 311: 425 (1990).