

Cutter



TO: Jan Peterson

DATE: May 17, 1984

FROM: Milt Mozen

COPIES TO: G. Mitra
J. Levy

SUBJECT: Synopsis of Jay Levy study on
retrovirus inactivation in Koate®

On May 9, 1984, a press release was issued by the University of California San Francisco relating to the finding of a retrovirus, lymphadenopathy-associated virus (LAV)*, having a major role in AIDS, and to the fate of a mouse retrovirus exposed to our process for the manufacture of Koate®.

These studies were under the direction of Jay Levy, M.D., UCSF Associate Professor of Medicine, and an investigator in the Cancer Research Institute. Dr. Levy reported these results in Toronto at a joint meeting of the American Society of Clinical Oncology and the American Association for Cancer Research. The studies with Koate were carried out in collaboration with researchers at Cutter namely, Dr. George Mitra, Mel Wong, and Dr. Milt Mozen and were designed to determine whether the retrovirus could survive the conditions used for preparing Koate®. The experiments were carried out by spiking human plasma with a mouse xenotropic type C retrovirus resembling LAV and then fractionating the plasma to Koate® and determining where the retrovirus migrated during fractionation and how much survived at each purification step. Additionally, the retrovirus was added at the final step of Koate® purification and its inactivation determined at various time points during Cutter's heating process of 68°C for 72 hours.

The results of these studies showed that fractionation without the heat treatment step caused only a small amount of retrovirus activity loss. This finding differs from the widely held opinion that a retrovirus could not survive such a process. However, when Koate® containing retrovirus particles was subjected to Cutter's heating process, no retrovirus were detected after 72 hours. However, retrovirus were still measurable at 48 hours.

We believe these findings are very significant. First, because they show that a retrovirus similar to LAV is more hearty than previously thought. Second, that the heat regimen adopted by Cutter is effective in totally inactivating this retrovirus. It is important to note that in this study only Cutter's heating conditions were tested, and it cannot be assumed that the heating conditions of all manufacturers would be similarly effective in eliminating retroviruses. Dr. Levy will soon be publishing these results.

*LAV is believed by some investigators to be identical to the recently described HTLV-III.

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7:00 AM (PDT), WEDNESDAY, MAY 9
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UC-SAN FRANCISCO STUDIES CONFIRM FRENCH FINDING OF RETROVIRUS IN AIDS
AND DEMONSTRATE A RETROVIRUS COULD BE PASSED THROUGH BLOOD CLOTTING FACTOR

TORONTO -- A UC-San Francisco virologist today reported results of two studies that add further support to the theory that a retrovirus plays a major role in acquired immune deficiency syndrome.

A study by Jay Levy, MD, UCSF associate professor of medicine and an investigator in the Cancer Research Institute, confirms findings by French scientists that a retrovirus -- lymphadenopathy associated virus (LAV) -- could be the primary cause of AIDS. So far, Levy has found evidence of LAV or a LAV-like agent in blood cells of 28 of 50 AIDS patients in San Francisco. In three of the 28, Levy's laboratory has direct proof of the similarity to LAV.

The study was reported here today at a joint meeting of the American Society of Clinical Oncology and the American Association for Cancer Research.

Last year, researchers (F. Barre-Sinoussi, L. Montagnier, J.C. Chermann) at the Pasteur Institute in Paris discovered LAV in blood of AIDS and pre-AIDS patients in France. The suspected virus grows preferentially in certain lymphocytes (white blood cells), which become damaged or diminished in AIDS patients. The loss of these cells appears to be responsible for their inability to fight off opportunistic infections and cancer. Levy's research group found retroviral enzymes and proteins in white blood cells, as well as antibodies to LAV, which indicate infection, in over 50 percent of the patients studied. Evidence of the virus was not detected in any of 21 healthy controls. For the study, Levy used reagents supplied by the Pasteur Institute researchers to compare his isolates with theirs. Electron micrographs also have confirmed the similarities, Levy reported.

The relationship of the UCSF LAV-like agent and LAV to the HTLV-III retrovirus, recently described by Robert Gallo of the National Cancer Institute, is not yet known, says Levy. Recent reports, however, indicate strong

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UCSF Studies on Retrovirus in AIDS -- Page 2

similarities between LAV and HTLV-III. Although they are major steps in AIDS research, Levy cautioned that these new findings do not yet establish absolute proof that either virus or a similar one is the cause of AIDS. He is conducting experiments, infecting animals with the UCSF isolates, in an attempt to determine whether or not they are responsible for AIDS.

In a separate presentation at the ASCO and AACR meetings, Levy today reported results showing retroviruses can survive procedures previously used to produce the clotting factor (Factor VIII) used by hemophiliacs. Levy, working with researchers from Cutter Laboratories in Berkeley (Milton M. Mozen, PhD, and George Mitra, PhD), tested the stability of a mouse retrovirus, resembling LAV, through the clotting factor production process. The process did not substantially inactivate the retrovirus, Levy reported.

This is counter to previous beliefs that a retrovirus could not survive such a process, and the study possibly explains why some 30 hemophiliacs in the United States have developed AIDS. The factor, used by hemophiliacs to prevent uncontrollable bleeding, is usually prepared from blood contributed by thousands of donors. The study by Levy and his coworkers did indicate that the heating procedure used now by Cutter eliminates the retrovirus effectively.

The process is now being used by manufacturers of Factor VIII to further minimize the chances of hemophiliacs contracting AIDS, says Levy.

Taken together, Levy's studies -- indicating presence of LAV or a LAV-like agent in the blood of AIDS patients in San Francisco and demonstration that a retrovirus can be transmitted in blood clotting factors -- lend further support to the theory that a retrovirus is involved in AIDS.

Levy's research is supported by grants from the state of California and the National Institutes of Health. His UCSF research team includes Susan Kramer, PhD, Lyndon Cshiro, PhD, Anthony Hoffman, Jill Landis and Joni Shimabukoro.

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Wed., May 9, 1984 ** S.F. EXAMINER B7

UCSF scientists identify AIDS virus

By Richard F. Harris
Examiner science writer

For the first time, scientists at the University of California at San Francisco have identified among local AIDS patients a virus suspected of causing the disease.

The virus is identical to one called LAV, first isolated at the Pasteur Institute in Paris, and probably the same virus identified by scientists at the National Cancer Institute, said Dr. Jay A. Levy, whose virology lab made the discovery.

In a separate study, Levy also found that a similar "retrovirus" survived an old process that had been used to produce from human blood a clotting factor for hemophiliacs, but is killed by recently adopted heat treatment. These findings are good news to hemophiliacs concerned about the clotting factor they now receive, while

explaining why batches produced earlier caused AIDS in a few cases.

Levy is to make both announcements today at a joint meeting of the American Society of Clinical Oncology and the American Association for Cancer Research in Toronto.

In an interview before his talk, Levy said the findings add further evidence to the theory that acquired immune deficiency syndrome is triggered by a retrovirus that cripples the immune system and can be transmitted in blood.

Levy sampled 80 AIDS patients in San Francisco and found evidence of the virus in 28. He said one reason the virus was not found in 100 percent of the samples may be because the disease killed all the infected blood cells before samples were taken.

"The other explanation is this is not a universal virus found in AIDS pa-

tients," Levy said, but another "opportunistic infection." Despite optimistic reports from the National Cancer Institute, there is no definitive evidence that the AIDS virus has been positively identified, he said.

The virus Levy isolated is identical to the French virus, called LAV. Although photographs of the organism under the electron microscope reveal no differences between the French agent and HTLV-III — the U.S. cancer institute's prime suspect — the two organisms have yet to be compared directly, Levy said.

In his second study, Levy isolated a mouse retrovirus that is similar to but distinct from the AIDS suspect and subjected it to acid baths, crystallization and other patented techniques used in processing blood to produce the clotting factor for hemophiliacs.

The results showed that a retrovi-

rus could survive these rigors, but that the virus was killed by a heat-treatment process now used by Cutter Laboratories, which mass-produces clotting factor.

Clotting factor, which is used to prevent uncontrolled bleeding in hemophiliacs, has been singled out as responsible for about 30 AIDS cases among hemophiliacs.

More than 4,100 cases of AIDS have been reported in the United States, primarily among sexually active gay men. As of May 4, 515 cases have been identified in San Francisco, including 188 deaths.

Isolation of the suspected AIDS virus, if confirmed, could lead to a widely available diagnostic test for the ailment in six months, and a vaccine for the disease in two or three years, federal scientists predict.

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