ROSAT Data Hint at a Closed Universe

Using an X-ray satellite to detect that a vast cloud of hot gas envelops a small group of galaxies, astronomers have calculated that the group must contain an extraordinarily high proportion of dark matter — material that doesn't emit light, yet exerts a gravitational force.

If the distribution of dark matter within this group is typical of that in the myriad other small groups of galaxies elsewhere in the cosmos, the universe might have enough mass to halt its expansion and eventually collapse in on itself, says Richard F. Mushotzky of NASA's Goddard Space Flight Center in Greenbelt, Md.

He and his colleagues, David S. Davis of Goddard, John S. Mulchaey of the Space Telescope Science Institute in Baltimore, and David Burstein of Arizona State University in Tempe, reported their findings this week at an American Astronomical Society meeting in Phoenix.

When Mushotzky and his team asked that the X-ray observatory ROSAT cast its eye on a trio of galaxies known as NGC 2300, the astronomers merely wanted to find out why one of the galaxies appeared distorted, as if it had slammed into a massive object. Their observation had such low priority on ROSAT's work list that they weren't certain the satellite had ever carried it out until a data tape arrived at Goddard last June.

As they expected, ROSAT detected a hot gas cloud that emits X-rays but not visible light. A collision with hot gas could account for the distorted shape of the spiral galaxy in NGC 2300. But surprisingly, the researchers found that the gas cloud was both huge and hot, with a diameter of 1.3 million light-years and an average temperature of 10 million kelvins. To keep such a hot, energetic cloud from flying off into space, the team calculated, NGC 2300 must contain 10 to 30 times as much mass as the total visible mass of its three galaxies.

That range ranks among the highest proportions of dark matter yet inferred for any galaxy system, Mushotzky notes. Until recently, he adds, most researchers searching for dark matter have used visible-light studies, focusing on individual galaxies or clusters of 100 or so galaxies. These researchers have calculated that dark matter exceeds visible matter by a factor of three to five, he adds.

But roughly half of all galaxies, including our Milky Way, are members of small groups. So if NGC 2300, which lies 150 million light-years from Earth, isn't some oddball group — and that's a big if, Mushotzky admits — then the dark-matter estimate could mean that the expanding universe has enough mass to eventually collapse back on itself. The single ROSAT measurement, Mushotzky adds, makes it impossible to predict whether the universe is in fact absolutely closed or is poised between expanding forever and undergoing collapse.

NASA

Visible-light image of three galaxies that make up the group NGC 2300, combined with false-color X-ray image of a gas cloud (pink) that envelops the group.

Calling the new study "exciting and important," Douglas O. Richstone of the University of Michigan in Ann Arbor cites other studies that support it. Earlier ROSAT findings that many galaxies have collided or merged relatively recently suggest that the universe has a high density, Richstone argues. Only a high-density universe would have enough mass to produce large mergers and collisions billions of years after the universe began expanding, he notes.

Nonetheless, cautions Burstein, "One massive group does not a closed universe make." He and his colleagues hope to refine their temperature measurement of the gas cloud using an X-ray detector aboard Astro-D, a Japanese satellite scheduled for launch next month. The team also plans to observe other small galaxy groupings with ROSAT. — *R. Cowen*

AIDS codiscoverer censured for misconduct

The U.S. Department of Health and Human Services released a report last week concluding that government AIDS researcher Robert C. Gallo committed scientific misconduct in connection with his codiscovery with French scientists in 1984 of the virus that causes AIDS. The report found that Gallo misrepresented his laboratory's ability to grow the virus from a sample donated by the French, a move that had the potential to obscure the significance of the French contribution to the discovery of the cause of AIDS.

The report — produced by HHS's Office of Research Integrity (ORI) — adds fuel to an eight-year-old international controversy over the lucrative patent rights to blood tests for AIDS that use pieces of the AIDS-causing virus to detect antiviral antibodies in infected individuals. It also prompts questions about Gallo's future as director of the National Cancer Institute's Laboratory of Tumor Cell Biology, one of the largest federal biomedical laboratories.

The report's findings center on a key sentence in one of the 1984 scientific papers in which Gallo describes his team's discovery of an AIDS-causing virus and cites evidence suggesting that the virus differs from the one called LAV, which was isolated by Luc Montagnier and colleagues at the Pasteur Institute in Paris. In that paper, Gallo wrote that the apparent difference between LAV and his group's virus may result from "insufficient characterization of LAV because the virus has not been transmitted to a permanently growing cell line for true isolation and therefore has been difficult to obtain in quantity."

By examining earlier drafts of the paper and records from Gallo's laboratory, the authors of the ORI report obtained evidence that Gallo and his colleagues had in fact transferred LAV to a permanent cell line — a crucial step in producing sufficient viral proteins for the development of an AIDS test. ORI concludes that while the misrepresentation "did not invalidate the basic findings of [Gallo's] research . . . [it] had the potential to impede the rapid advancement of research efforts with LAV" by dissuading other researchers from working with the virus.

Gallo terms the entire investigation "endless and incompetent" and contends that the disputed sentence pertained only to the French team's inability to grow significant quantities of LAV, not to the work of his own laboratory. "After reviewing everything I and my colleagues have ever published on the discovery of the AIDS virus and the development of the AIDS blood test, ORI could only take issue with a few trivial mistakes and a single sentence written by me," he says.

The ORI asserts that by "falsely reporting" his laboratory's work with LAV, Gallo committed scientific misconduct — a finding that reverses the conclusion reached in 1991 by a National Institutes of Health investigative office that examined the matter. The ORI confirms the NIH finding

that a scientist who had worked in Gallo's laboratory, Mikulas Popovic, committed four "relatively minor" instances of misconduct by recording apparently false data from several AIDS experiments outlined in the 1984 papers.

Based on the findings, the ORI proposes that NIH – and any other federally funded institution that may subsequently employ Gallo or Popovic – monitor the scientists' "recording and reporting" of data for a period of three years. The ORI also recommends that NIH "consider whether any other actions are appropriate in relation to Dr. Gallo or the management of [his laboratory]."

Gallo and his attorney, Joseph Onek of the Washington, D.C., law firm Crowell & Moring, say they will appeal the ORI recommendations to the only remaining recourse, a judicial board within HHS.

But the Pasteur Institute's attorney, Michael A. Epstein of the New York City law firm Weil, Gotshal & Manges, claims the ORI report "is a significant event" in the renewed dispute over AIDS blood test royalties. Epstein has petitioned HHS to reopen the 1987 settlement that splits the royalties among Gallo, Montagnier, their institutions, and a foundation to fund AIDS research in developing countries (SN: 7/18/92, p.46). "This shows that the statements Gallo and the U.S. government made in 1986 to get the settlement were all lies," he asserts.

An NIH spokeswoman says the agency will await the outcome of Gallo's appeal before deciding upon taking any additional action against him. – *C. Ezzell*

Preventing AIDS pneumonia

(As the result of a production error, this article was difficult to read in the 1/2/93 issue. We regret any inconvenience this might have caused.)

Daily doses of the sulfa drug trimethoprim-sulfamethoxazole (TMP/SMX) help AIDS patients fend off recurrences of a life-threatening form of pneumonia more effectively than do monthly treatments with aerosolized pentamidine, according to a pair of studies comparing the two widely used preventive medications.

However, the authors of the studies conclude that because it produces fewer side effects than TMP/SMX, aerosolized pentamidine may still prove preferable for protecting some AIDS patients from *Pneumocystis carinii* pneumonia.

This form of pneumonia strikes many people with AIDS and kills a large number of them. In the mid-1980s, physicians began prescribing pentamidine or TMP/SMX – both of which are also used to treat established cases of *Pneumocystis carinii* pneumonia – for AIDS patients as a preventive measure. Without such therapy, 65 percent of patients taking the anti-AIDS drug zidovudine (AZT) who survive an initial episode of the pneumonia suffer further bouts.

In the first study, researchers led by Robert S. Holzman of New York University School of Medicine in New York City and W. David Hardy of the University of California, Los Angeles, found that 150 AIDS patients who inhaled an aerosol form of pentamidine once a month ran more than three times the risk of developing a recurrence of *Pneumocystis carinii* pneumonia as the same number of patients taking daily TMP/SMX. However, the researchers report in the Dec. 24 NEW ENGLAND JOURNAL OF MEDICINE, roughly one-fourth of the TMP/SMX patients had to stop taking the drug because it caused severe weakness or abdominal pain.

Researchers led by Margriet M.E. Schneider of the University Hospital Utrecht in the Netherlands report similar results in another study in the same journal. Schneider's team found that none of 142 AIDS patients taking daily TMP/SMX developed *Pneumocystis carinii* pneumonia, while six of 71 AIDS patients receiving pentamidine treatments monthly fell ill. – *C. Ezzell*

Cyclosporin-protein complex controls genes

Three research reports reveal new details of the molecular mechanism underlying cyclosporin's ability to prevent the rejection of transplanted organs and to slow fungal infections.

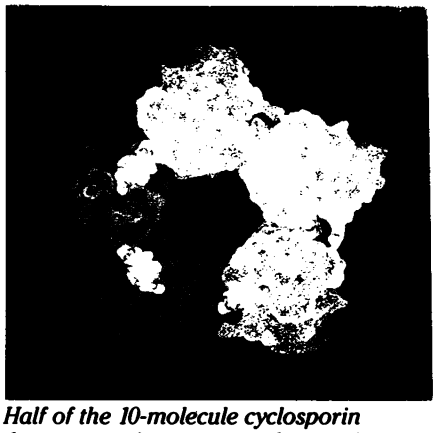
Cyclosporin works by first attaching to a protein called cyclophilin. This molecular duo then suppresses the responses of the immune system, most likely by interacting with an enzyme called calcineurin.

By pushing the limits of both nuclear magnetic resonance (NMR) spectroscopy and X-ray crystallography, two research groups have visualized this duo. Their separate reports appear in the Jan. 7 NATURE.

Earlier computer models had shown multiple connections between the two kinds of molecules. But some of these connections, called hydrogen bonds, were different in the real complex, says Stephen W. Fesik of Abbott Laboratories in Abbott Park, Ill.

Fesik and his colleagues used sophisticated NMR techniques to determine the structure of cyclosporin-cyclophilin pairs in solution. "The structures [obtained by the two groups] are remarkably similar," he says.

Unlike many other proteins, which twist or bend to make a tight fit with their partner molecules, cyclophilin maintains its shape when it binds to cyclosporin, adds Malcolm D. Walkinshaw, a crystallographer with Sandoz Pharma Ltd. in Basel, Switzerland.



Half of the 10-molecule cyclosporin (lightest blue)-cyclophilin (colored) complex.

Walkinshaw and his colleagues made crystals of this duo. But determining the exact positions of the atoms proved quite difficult. As they crystallize, these molecules congeal to form layered rosettes containing 10 to 12 pairs, he says. Thus, he could not study lone pairs, as did Fesik's group. However, while probably not the biologically active form, the rosette provides key information about each pair's structure, he adds.

In the crystals obtained by the Sandoz team, each of five cyclophilin molecules attaches to one side of each of five cyclosporin molecules. The shape of cyclophilin seems to promote the formation of a five-molecule unit, Walkinshaw explains.

To avoid contact with water, the five cyclosporin molecules then proceed to seek out five other cyclosporin molecules and to snuggle up against them. Thus, 10 cyclophilins wind up facing outward, with 10 cyclosporins sandwiched between them.

Each cyclosporin molecule arranges its amino acids into a ring with various chemical side groups sticking out. The crystal structure reveals that one hydroxyl side group in cyclosporin actually forms a hydrogen bond with its amino-acid backbone and not with cyclophilin.

This link helps maintain the shape of the cyclosporin molecule as it attaches to cyclophilin, says Walkinshaw. Researchers can now consider these details when they use computers to design new, possibly more effective surrogates for cyclosporin.

Using genetic engineering techniques, Thomas G. Larson and Donald J. Nuss of the Roche Institute of Molecular Biology in Nutley, N.J., have confirmed that this complex exerts its effects by altering the rate of gene expression. Cyclosporin ceases to work in chestnut blight fungus mutants lacking cyclophilin (SN: 8/8/92, p.84), they report in the Jan. 1 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. – *E. Pennisi*