specific, light-initiated hydrolysis of cyclic GMP (see box on page 501), it has proved very difficult to demonstrate a reduction of the cyclic nucleotide at physiological light conditions.

One clear possibility here is that, of the quite large mass of cyclic GMP in rods, only a very small amount is free and available for binding with the channels. Changes in this component might not be detectable by current methods. Another aspect of this is that, as Nelson Goldberg of the University of Minnesota illustrated quite forcefully, light stimulation also induces increased guanyl cyclase activity, which resynthesizes the cyclic GMP. The result is a light-initiated increase in turnover.

For some biochemists, the idea of a change in cyclic GMP flux as a gate controller is attractive, presumably via an energy-linked process. For others, the accelerated machinery provides a neat mechanism for inducing a spike increase in cyclic GMP activity, specifically if hydrolysis is turned on just slightly before synthesis. The fact that, as has been demonstrated with the patch experiments, direct application of cyclic GMP to the channels can turn them on in the apparent absence of much of the rest of the cell's biochemical machinery tends to support the change in activity rather than change in flux idea.

However, some biochemists, including Bownds, wonder whether cyclic GMP is indeed the whole story. They wonder whether there are yet more components to be discovered, parallel pathways to be uncovered. For instance, one candidate recently considered as a potential messenger in photoreceptors is inositol triphosphate. Results with this compound so far are tantalizing, if somewhat conflicting.

Meanwhile, calcium appears to be in search of a job. Fortunately there is one readily at hand. One repeated observation is that reduced levels of calcium decrease the light sensitivity of rods. Combine this with the possibility that one effect of light is to reduce intracellular calcium, and with the demonstration that reduction of calcium modulates the metabolic machinery for the turnover of cyclic GMP, and the potential emerges that calcium might be the mediator of light adaptation. Whether calcium modulation of cyclic GMP turnover can account for the range of physiological light sensitivity remains to be seen.

The Dahlem meeting certainly produced a surprise for most participants: it is not often that a research field turns around quite so dramatically.

—ROGER LEWIN

AIDS Virus Genomes

The molecular characterization of the virus that causes AIDS (acquired immune deficiency syndrome) continues to move at a rapid clip. Four groups have now determined the complete nucleotide sequences of the genetic material of viruses that have been linked to the disease.

Paul Luciw of Chiron Research Laboratories in Emeryville, California, Jay Levy of the University of California, School of Medicine, in San Francisco, and their colleagues report the sequence for the virus they have christened "AIDS-associated retrovirus" (ARV) in this issue of *Science* (p. 484). A second group, including Lee Ratner, Flossie Wong-Staal, and Robert Gallo of the National Cancer Institute, Mark Pearson of E. I. du Pont de Nemours and Company in Wilmington, and William Haseltine of Harvard's Dana-Farber Cancer Institute, report sequences for two isolates of the virus designated "human T-cell lymphotropic virus-III" (HTLV-III) in the 24 January issue of *Nature*. A group from Genentech, Inc., in San Francisco, is also publishing AIDS virus sequences in an upcoming *Nature* issue. And the fourth group, from Luc Montagnier's laboratory at the Pasteur Institute in Paris, published the sequence for the virus they have called "lymphadenopathy-associated virus" (LAV) in the January issue of *Cell*. Despite the different names given these viruses, there is now general agreement that they are variants of the same virus.

One question that the sequence data can help answer concerns how closely the AIDS virus resembles other retroviruses, especially HTLV-I and -II. All four groups find that there are substantial differences between the genome of HTLV-III and the HTLV-I and -II genomes, although some short segments show resemblances. "ARV is no more closely related to HTLV-I and -II than to other retroviruses," Luciw concludes. Simon Wain-Hobson of the Pasteur Institute presented similar findings for LAV at the recent "HTLV Symposium," which was sponsored by the NCI and held in Bethesda, Maryland, on 6 and 7 December. However, Gallo notes that there are other points of similarity between HTLV-III and the other two HTLV's that would favor including them in the same viral category.

Another important question, one that bears upon the possible mode of action of the AIDS virus as well as its relation to HTLV-I and -II, concerns whether its genome contains a "long-open reading frame" (LOR region) near its right-hand end similar to those in the HTLV-I and -II genomes. The products of the HTLV-I and -II LOR regions increase viral and possibly cellular gene expression, according to Haseltine, and this activity may be what causes the malignant transformation of infected cells. Haseltine, Wong-Staal, and their colleagues also have evidence that HTLV-III produces an analogous factor.

The organization of the ARV genome does not show a LOR region comparable to that of HTLV-I and -II, Luciw says, although it does have a protein-coding sequence about half the size of LOR in an analogous location. He notes that the organization of the ARV genome is very similar to what Wain-Hobson proposes for LAV. The Gallo group has a different interpretation of the coding sequence arrangement in the right-hand region of the HTLV-III genome. Although they do not see a separate LOR region there, their results indicate that the long *env* gene has a dual function. Depending on how the messenger RNA product of the gene is spliced, it can produce either the protein that forms the viral envelope or a protein of size comparable to the HTLV-I and -II LOR products.

Finally, restriction mapping of the genomes of various AIDS virus isolates has already shown that these may vary in structure, a result that is being confirmed by the sequence analyses. For example, the sequence of the long terminal repeat of HTLV-III, which was determined by the Gallo–Wong-Staal group and also appears in this issue (p. 538), differs in about 5 percent of its nucleotides from the long terminal repeat of ARV. Sequence analysis may help to identify viral gene segments that are highly conserved, and thus important for viral activities. Moreover, the corresponding peptides might eventually prove useful for producing reagents to detect infection by the virus or a vaccine to protect against AIDS.—JEAN L. MARX