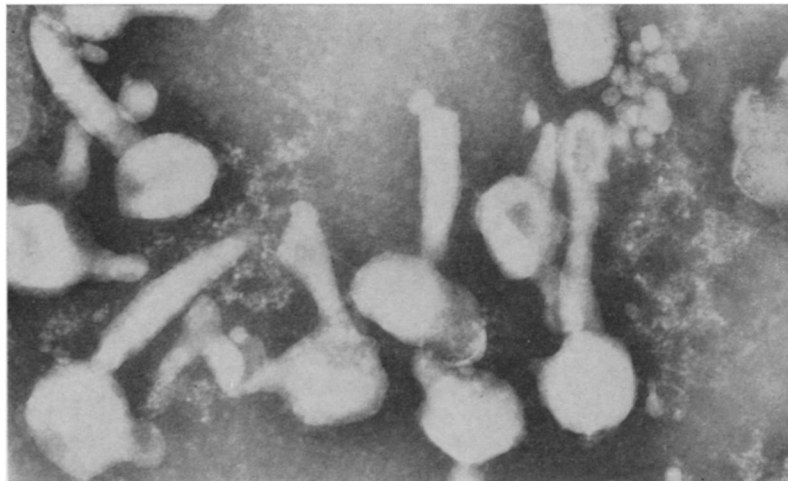


Teminism on the go

With speed unusual even in the fast-paced world of molecular biology, scientists pursue new cancer clues



St. Louis Univ.

Reversing dogma, a mouse RNA virus codes for DNA.

Howard Temin is a molecular biologist who was generally dismissed by his peers as a mild eccentric. Explaining the behavior of cancer-causing RNA viruses by a hypothesis that ran counter to the central dogma of his science, he tried to lead his colleagues down a new road, but none would follow. His ideas were too contrary, his evidence to defend them too slim to purchase much support.

Three months ago all that changed. Armed with better evidence, the University of Wisconsin researcher presented data that were too good to be ignored and catalyzed a flurry of activity within the scientific community. The foremost investigators rushed to their labs and succeeded in confirming his hypothesis, now referred to simply as Teminism (SN: 7/25, p. 54). Already a spate of papers confirming his preliminary results and elaborating on them has been published—the Sept. 5 NATURE alone carried four—and more are in press.

The effect on basic scientists involved in cancer research has been astounding

and exhilarating. Says Dr. Maurice Green of the St. Louis University Medical School, among the first to confirm the Temin hypothesis, "I haven't slept in three months. Within the next six months we should know with certainty whether this RNA-virus theory accounts merely for an interesting situation or is the major development some of us think it is."

Teminism illuminates the process by which tumor-causing RNA viruses are incorporated into host cells. Though it is far too early to assess the ultimate importance of this new knowledge, it is clear that it has provided investigators with a series of ideas and tools with which they can approach several problems in cancer research, ranging from therapy to the still-unresolved issue of whether viruses cause human cancer in the first place.

A virus can be either a core of DNA or of RNA enveloped in a protein coat. Specific viruses of both types are known to cause tumors in animals, though the mechanism by which either works remains a mystery. Nonetheless,

scientists have been able to make the logical assumption that once a DNA virus invades a cell, it is incorporated into the DNA, or genes, of its host.

But RNA cannot be incorporated into DNA and no such assumption could be made about these viruses, which were presumed to be quite unlike their DNA counterparts. And yet it was known that RNA tumor viruses persist through many cell generations, being passed on like any other type of genetic information. Indeed, Drs. Robert Huebner and George Todaro of the National Cancer Institute had gone so far as to theorize that all animal cancers, including those in man, are related to RNA viruses and that these viruses are present, but turned off, in most individuals (SN: 10/4, p. 308).

To account for the enigma of RNA tumor viruses, Dr. Temin suggested that these agents possess a special enzyme, or enzyme system, by which their RNA core is used as a template or blueprint for making DNA. In other words, when an RNA virus is incorporated into the DNA of its host cell, it has itself been translated into DNA with the same information for inducing cancer as was present in its natural state.

Dr. Temin met opposition on two grounds. First, many scientists were not prepared to believe that a simple RNA virus contained the postulated enzyme. Second, his proposition that RNA could code for DNA contradicted the central dogma of molecular biology, as put forward by Nobel laureates James Watson and Sir Francis Crick. That dogma states that genetic information travels a one-way street, from DNA to RNA to protein, and not the reverse. Though the near-heresy that it can also go the other way, initiating with RNA, was not original with Dr. Temin, he was the first to link it to theories of carcinogenesis. While hardly undermining the central dogma, Teminism surely makes it less dogmatic. At the same time, Teminism is consistent with the pre-



Columbia Univ.

Dr. Spiegelman: Seeking new therapy.



Todd Studios

Dr. Green: A major development.

sumption of DNA as the primary genetic material, and indeed many of the ideas developed in the last three months do fit existing theories.

When Dr. Temin presented preliminary evidence that this postulated enzyme did in fact exist and that RNA was being used as a template for DNA, his announcement was like a bugle call to his colleagues. Dr. Green and his colleagues in St. Louis, Dr. David Baltimore at the Massachusetts Institute of Technology and Dr. Sol Spiegelman of Columbia University are among those who have demonstrated Teminism. They report the presence of an enzyme, RNA-dependent DNA polymerase, which participates in the synthesis of a strand of DNA from the RNA template. There follows a series of events in which an RNA-DNA hybrid is formed, and then a DNA-DNA duplex which can be inserted into the natural DNA of the host.

Not one but three specific enzymes are involved in this process, according to Dr. Spiegelman, "All three," he says, "are vital to the final conversion of a normal cell to a cancerous one." In studies thus far, only those RNA viruses known to cause tumors have been found to possess these enzymes, though Dr. Spiegelman speculates that other RNA viruses, closely related to tumor viruses but not themselves carcinogenic, may contain them.

In any case, the unproved presumption of the moment is that none of these enzymes function in normal cells. Therefore, in theory, it may be possible to devise drugs which will selectively block the cancer-causing process without damaging cells. Already, the Columbia University group is pursuing this idea with actinomycin-D, itself too potent for human use but experimentally useful, and with certain of the rifampicins (SN: 1/17, p. 70) a relatively recently studied class of antibacterial-antiviral agents.

While therapeutic prospects are being tentatively explored, scientists are also using the fruits of this research to search for RNA viral information in human tumors. Here two routes are open. First, known tumor-causing viruses can be induced to synthesize DNA in the laboratory and then, in culture, this can be exposed to bits of human tissue to determine whether any DNA-RNA hybrids are formed, indicating the presence of complementary RNA in the tumor. Second, investigators can assay human tumor tissue for presence of RNA-dependent DNA polymerase, easily identifiable by laboratory methods. With both these approaches in mind, mass screening programs are contemplated. Dr. Todaro, who recently identified the first virus to be found in human breast tissue (SN: 6/27, p. 611), is eager to put it to this test to determine if it really is a cancer-causer. □

BLUE-COLLAR WORKERS

In group of the '70's



UAW

Blue-collar workers: Progress has been substantial, prejudice is low.

The strength of the Wallace vote in the 1968 Presidential campaign has focused considerable political attention on the blue-collar worker. The Democrats have been shaken by the voting disaffection, and the Republicans are teased by a potential new voting bloc.

The perturbation in the political process is bringing subsequent changes in Government and social science research interest. Jerome Rosow, the Assistant Secretary for Policy, Evaluation and Research in the Department of Labor, in April issued a memorandum titled "The Problem of the Blue-Collar Worker." Rosow focused on the purported economic strains of blue-collar families and the social problems that white blue-collar workers were facing from nonwhites in areas of housing, education and jobs.

The Ford Foundation has helped spur research in the area with a grant to the Center for Manpower Policy Studies at George Washington University in Washington, D.C. The center's studies on blue-collar workers are now being completed. The preliminary results indicate that although blue-collar workers may be expressing economic stress due to general economic conditions, their rise in earnings in the past decade has been about the same as other major occupational groups'. Other parts of the study suggest that race relations among blue-collar workers, at least outside of the South, are better than had been believed.

A major concern of representatives of blue-collar interests has been that blue-collar earnings are not advancing as much as other occupational groups'. Dr. George Miller of the Census Bureau compared median earnings of various occupation groups between 1959 and 1968 and found that white blue-

collar earnings rose from \$5,877 to \$7,452, an increase of 27 percent during the decade. White professional and managerial workers earnings rose from \$8,246 to \$10,175, a 23 percent increase. Black blue-collar workers rose in income from \$4,003 to \$5,756, a 44 percent increase. "In spite of talk of blue-collar workers falling behind in earnings, they have kept up. All occupational groups have moved up the same," says Dr. Miller. The blue-collar workers, however, would point out that in actual dollar gains, they have not kept pace.

In investigating blue-collar attitudes toward blacks, Dr. Richard Hamilton of McGill University in Montreal queried white populations regarding the rights of blacks. He finds that in non-South regions of the country, there are no differences in response between blue-collar and white-collar workers. In general, the attitudes are positive. However, Dr. Hamilton reports that in the South blue-collar workers are less tolerant than white-collar workers. "Working class authoritarianism is only to be found in the South," he says. "The level of tolerance in the American population is a lot more advanced than most people think. The silent majority is extremely tolerant." Dr. Hamilton attributes the tolerance in part to the presence of blacks on television as well as increased personal contact between blacks and whites in shopping centers and neighborhoods.

Dr. Jules Cohn, a management consultant, finds similar results after assessing orientation programs in some 250 companies nationwide. He interviewed more than 600 foremen and workers and finds that blue-collar workers are generally more curious and apprehensive than antagonistic toward new em-