

Whole virus from a human tumor

Scientists working in two laboratories have identified a virus associated with a human breast cancer

Though the evidence linking viruses and animal cancers is conclusive, that implicating viruses in human tumors remains circumstantial. Using the electron microscope, scientists have photographed what look like virus particles in human tumors. One cancer-virus theory suggests, in fact, that tumor-causing viruses in man are defective viruses, elusive bits of whole viruses (SN: 10/4, p. 308).

Whole viruses of a kind called Epstein-Barr have been recovered from individuals with a form of cancer known as Burkitt's lymphoma and from persons with mononucleosis (SN: 4/12/69, p. 350), suggesting a tie between those two diseases. But EB viruses have been isolated with relative ease from large numbers of normal volunteers as well; no direct cause-and-effect relationship between the virus and cancer has been demonstrated.

The probability of a connection between a virus and a human cancer persists nevertheless. Many scientists are quite willing to concede that unequivocal proof that viruses cause human cancer may never be developed, at least not by the standard technique of injecting a suspect virus or viral particle into a human subject to see what happens. Circumstantial evidence will have to do.

Strong new evidence of that kind has been developed by a team of scientists at the National Institutes of Health in Bethesda, Md., and is supported by the work of an investigator in New Jersey. In the June 13 *NATURE*, Dr. George Todaro, with Drs. Victor Zeve and Stuart A. Aaronson, reports isolation of a whole virus from human breast cancer tissue. Morphologically, the virus Dr. Todaro and his colleagues found is like the Bittner virus, an agent isolated

in 1934, which clearly causes mammary tumors in mice.

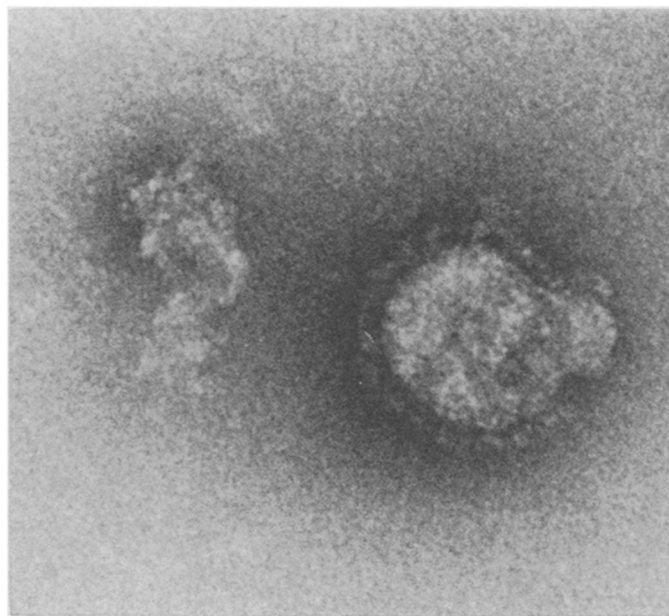
Assessing the significance of the virus isolation, Dr. Todaro says: "It increases the probability of virus involvement in human breast tumors. We're very excited about this achievement.

"However," he stresses, "it does not constitute proof that this virus causes cancer." Some cause-and-effect evidence would be obtained by injecting primates with the virus, but it could take 10 years or more for signs of a tumor to appear—a long and costly experiment.

Identification of the breast tumor virus was made in two ways. First, it was confirmed by electron microscopy. Second, and more importantly, it was confirmed by radioactive labeling techniques. Dr. Todaro credits this second method with the fact that the virus could be isolated at all.

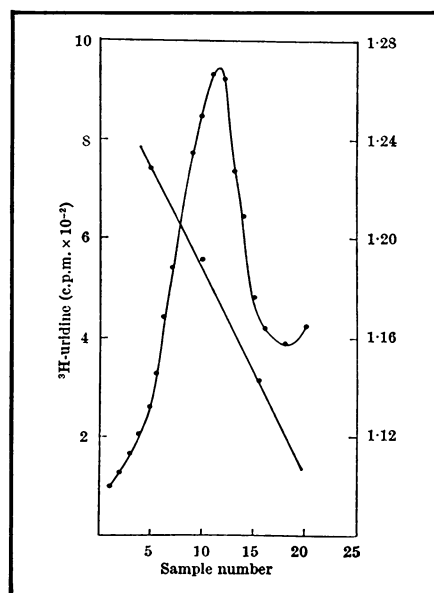
To a large extent, scientists have looked for viruses by examining cells. A dead cell, for example, can be taken as evidence of a virulent virus at work. But tumor viruses generally do not kill cells. They usurp their genetic machinery and persist in using it to make new viruses. Says Dr. Todaro: "We began looking for a virus in tumor tissue by trying to determine whether new viruses were being made, not by their property of killing cells."

If cells in culture are producing a virus, the team reasoned, radioactively labeled uridine should be incorporated into detectable viruses present in the medium. Indeed, this proved to be the case. The virus Dr. Todaro isolated is an RNA virus—a protein coat enveloping a strand of ribonucleic acid. Uridine is one of the bases from which RNA is made. Therefore, if cells were making new viruses, they would have to use



Zeve

Human breast tumor virus, magnified 400,000 times.



NATURE

Uridine uptake signals tumor virus.

available stores of uridine, radioactively labeled so that they could be detected. Cell strains from normal individuals showed no signs of uridine uptake, thus ruling out the possibility that they were making viruses. Cells from tumor tissue, however, did include the radioactive uridine.

This work alone, while remarkable, might not have been so significant. But it is underscored by a coincidental development: Working independently of the NIH scientists, Dr. Dan H. Moore of the Institute for Cancer Research in Camden, N. J., isolated and photographed the same virus in the milk of only six of 90 women with no history of breast cancer, while they found it in four of nine women with such a history.

While the identification of the virus in the tumor tissue and the milk does

not prove it causes breast cancer, it does provide scientists with needed insights and support for ideas.

The isolation technique itself may be one of the most valuable aspects of Dr. Todaro's work. Many virus-screening methods rely on biological and immunological tests geared to the search for a particular virus. The method Dr. Todaro applied may have more general use.

"It seems," he says, "to have general applicability in searching for occult, nonlethal viruses." Far less expensive and less time-consuming than electron microscopy, it also offers a potential advantage over that technique, at least for initial virus searches. Once a virus candidate is uncovered, its identity could then be confirmed subsequently by electron microscopy.

In addition, the striking likeness between the human breast tumor virus and the Bittner virus suggests that viruses associated with human cancers are as specific as those that cause animal tumors. The Bittner virus produces mammary tumors in some mice, presumably those hormonally or genetically susceptible to its effects. And it causes only breast tumors.

The discovery also has clinical implications. Experience with the Bittner mouse virus, which has been well studied and characterized, indicates that the presence of a virus may be a warning that breast tumors may develop.

A simple antibody-antigen screening technique for the presence of the virus could be an outgrowth of its isolation, Dr. Todaro suggests. An antibody to the virus or antigen would be developed in laboratory procedures. Subsequently, human sera would be mixed with those antibodies. Presence of the virus would manifest itself if a reaction occurred.

It also raises some concern about the safety of women whose milk contains this virus nursing their babies. Mouse experiments show that the virus can be transmitted from mother to young, ultimately leading to tumors in the offspring. Says Dr. Moore, "There is as yet no real reason for women not to nurse their babies, but a similar mechanism of transmission in man is a distinct possibility."

It is likely that additional virus-search projects will be launched in the wake of the breast tumor virus isolation. Both Dr. Todaro and his colleagues and Dr. Moore are participants in the Special Virus Cancer Program, a top priority \$30-million-a-year activity at the National Cancer Institute. It constitutes something of a crash program in the virus-cancer area and is specifically designed to coordinate and pass on leads from one investigator to another. □

ON THE PROWL

Ph.D.'s in high schools

In most European countries teachers in secondary schools usually have doctoral degrees in their academic specialties. In the United States this has not been the case; in fact in some quarters there is even some prejudice against having people with too many degrees teaching in high school.

The beginning of a change in the American custom may be under way thanks to the current slowdown in employment for scientists, with physicists in the vanguard. Concerned because many newly graduated Ph.D.'s were having trouble finding positions, two physics professors at the University of Texas in Austin, Drs. Robert Beck Clark and F. W. de Wette, decided to see what could be done about placing physics Ph.D.'s as high school teachers.

They discovered that Texas was a good place to begin, because certification is easier to obtain there than in many other places. In Texas a school supervisor can get a temporary emergency certificate for a person who does not have the required education courses by stating that an emergency exists.

When such people come to get permanent teaching certificates, a law that Dr. Clark describes as a "very progressive piece of legislation" allows them to go before a board of three university professors and have a training course designed to meet their needs. Many of the requirements can be satisfied by examination.

Drs. Clark and de Wette circularized school administrators in Texas to see how they would respond to the idea of having Ph.D. physicists in their classrooms. Some were willing to try, but, says Dr. Clark, "a lot of other people were very frightened."

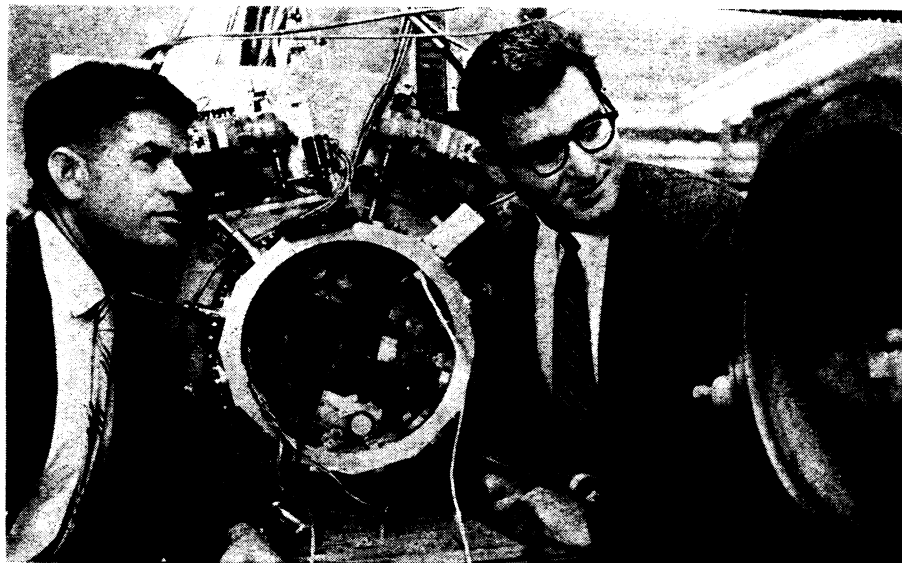
Armed with some definite openings, Drs. Clark and de Wette then went looking for physicists to fill them. They got many more applicants than jobs.

One difficulty in keeping Ph.D.'s happy as high school teachers is that high schools give no opportunity for research. Drs. Clark and de Wette propose that this can be solved by offering teachers adjunct positions in university or industrial research groups. They know of laboratories, they say, where research groups have wanted to have someone working with them, but did not have the money for additional faculty or staff salaries. In such cases, says Dr. Clark, the lab could offer adjunct appointments without salary to Ph.D. high school teachers.

So far no Ph.D. physicists have been hired by Texas high schools, but Dr. Clark points out that the schools customarily do not make their final hiring decisions until late in the summer. Dr. Clark hopes that if a few physicists can be hired this year, and if they perform well, they may convert the skeptics, and the program will really roll in future years.

He does not envision a flood of Ph.D.'s swamping the high schools. "There are not many with the right personality for secondary teaching," he says, and he estimates that a few hundred high school positions in the country may eventually be filled by Ph.D.'s.

Drs. Clark and de Wette hope that the idea will spread. So far they have had inquiries about what they are doing from physicists in Colorado, Utah, California and Ohio. "If we have made a contribution," says Dr. Clark, "it is that we have softened the system, and people are now thinking." □



Frank Armstrong
De Wette and Clark: Finding jobs for Ph.D. physicists in Texas high schools.