

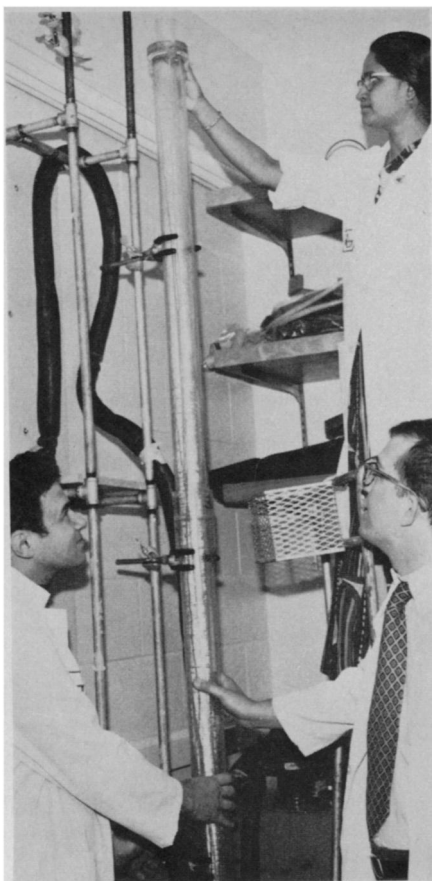
Bumblin cancer cells

Human cancer cells appear to make more genetic mistakes than do normal cells. A cancer virus may be at fault.

Researchers the world over are gradually stripping cancer of its secrets. The prevalent theory is that a virus incorporates its genetic information into the genes of a host cell, and such incorporation is what makes the cell become cancerous, go haywire. The genetic change must also be something that the cell can pass on to daughter cells, so that lots of haywire cells can make a tumor. How much of this theory is conjecture and how much a fact?

Some animal DNA cancer viruses—that is, those that have a molecule of DNA for their genetic information—are actually known to incorporate their information into the DNA (genetic material) of the animal host cell. How the DNA viruses pass their information, however, is a secret. Animal RNA cancer viruses—those with a molecule of RNA for genetic information—appear, when introduced into animal cells, to make DNA. The DNA is then presumably incorporated into the host-cell DNA. The biggest proof so far that this really happens came a few months ago when two groups of French researchers infected animal cells with an RNA cancer virus. The virus made DNA in the cells. When this DNA was harvested and put in other animal cells, it made them cancerous.

As for human cancer, viral causes are more tenuous. Some possible cancer-causing viruses, both of the DNA and



Inst. for Cancer Research

Loeb, Springgate and Gita Seal:
Does a cancer enzyme also goof?

The first two articles in this issue report new evidence from two completely different kinds of studies that cancers in humans may be caused by a virus. But the researchers advise caution in making interpretations.

RNA types, have been taken from different kinds of human cancer tissues. In recent months particles that resemble RNA cancer viruses have also been reported in human leukemia cells (SN: 12/2/72, p. 347) and in human breast cancer tissue. The best proof that cancer viruses might incorporate their genetic information into human cancer cells came in December. Sol Spiegelman of Columbia University reported that DNA made by a probable RNA cancer virus enzyme taken from human leukemia cells crossed—showed a genetic affinity for—DNA in human leukemia cells. The DNA made by the viral enzyme showed much less fondness for DNA in normal human cells (SN: 1/27/73, p. 56).

Now another plateau in the effort to convict viruses of causing human cancers has been reached. Two researchers with the Institute for Cancer Research at the Fox Chase Cancer Center in Philadelphia have found that human cancer cells appear to make more genetic mistakes than do normal human cells. This is the first time that evidence

for genetic goofs have been found in human cancer cells. A cancer virus may well be the villain.

Clark Springgate and Lawrence Loeb report the evidence in the January PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

They took crude extracts of human leukemia cells, which contained the usual cell enzymes that help make DNA. They threw a specified amount of DNA (genetic information) from the freezer in with the extracts. They anticipated that the foreign DNA would be replicated in copies precisely like the original molecules. But this wasn't what happened. The DNA copies that were made had a lot more mistakes than did DNA copies made from foreign DNA put with normal human cells.

These results can be interpreted several ways. "They may be a lot of nonsense," says Robert Gallo of the National Cancer Institute, and one of the scientists who reported RNA cancer virus particles in human leukemia cells. Loeb agrees. It is possible, for example, that the errors do not reflect DNA enzyme activity at all, but rather defective repair of DNA in leukemia cells. A more promising possibility, however, is that a mutation in one of the enzymes in the cancer cells might prevent the enzyme from copying DNA properly. An enzyme mutation would constitute a genetically induced event within the cancer cell.

The most exciting possibility is that there might be a new enzyme present in the cancer cells that fouls up normal DNA replication. This enzyme could be none other than the infamous reverse transcriptase—the enzyme that is known to help RNA cancer viruses replicate their genetic information. The enzyme is one of the particles Gallo and his colleagues found in human leukemia cells. If it turns out that there is a virus reverse transcriptase enzyme present in the human leukemia cells that induces mistakes in DNA replication, this would probably constitute the strongest evidence yet that RNA cancer viruses can cause a kind of human cancer. Of course, even if a cancer virus messes up the genes in a host cell, this does not necessarily prove that the virus is introducing its own genes into the genes of the host cell.

The challenge now facing Springgate and Loeb is to see whether cancer virus reverse transcriptase enzymes make more mistakes in DNA replication than do normal cell DNA-replicating enzymes. Loeb says they are now doing such experiments. They must also identify and purify a reverse transcriptase enzyme from the human cancer cells that experience errors in DNA replication. If they can do these things, attests Gallo, "It would be a monumental contribution." □