New Test Spots Cancer Cells in Blood

Tumors often fail to announce their presence until very late, making them difficult, if not impossible, to cure. By the time a tumor produces symptoms or grows large enough to be noticed, it may already contain more than a billion cells.

An experimental technique to detect rare cancer cells shed into the blood by a fledgling tumor has raised the hope that physicians will one day spot cancers at much earlier stages. The method, which can spot a single tumor cell in a milliliter of blood, may also help physicians choose among cancer therapies and monitor how patients respond to those treatments.

The idea that tumor cells slip into the bloodstream is not new—that's apparently how cancers spread—but the ability to find those few cells among many millions of blood cells is a relatively recent development.

Some investigators have employed a technique called PCR to screen blood samples for cells with cancer-causing mutations. Others have laboriously used microscopes and stains that highlight tumor cells to look for such cells in blood samples. These efforts have generally been sensitive enough only to spot a single cancer cell among 100,000 to 1 million blood cells.

In the latest research, a group led by Jonathan W. Uhr of the University of Texas Southwestern Medical Center in Dallas developed a technique that enables them to identify one tumor cell among 10 million to 100 million blood cells.

Their method starts with microscopic iron particles attached to antibodies. The antibodies bind to surface proteins present on epithelial cells—from which most cancers originate—but not on blood cells. The scientists use a magnet to separate epithelial cells from other cells in the blood.

Uhr and his colleagues then add to the remaining cells an antibody that binds to another surface protein on epithelial cells. The antibody is fused to a molecule that fluoresces, letting the investigators use a laser to isolate the marked cells. The laser also helps them examine properties of cells such as size. This information and data from additional tests suggest that the detected epithelial cells indeed come from tumors.

When tested on 30 people with breast cancer, 3 with prostate cancer, and 13 with no cancer, this technique revealed that people with cancer had significantly more epithelial cells—presumably shed by tumors—in their blood. Moreover, those with the most widespread cancer had the highest number of epithelial cells, Uhr's group reports in the April 14 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

"The number of tumor cells in the blood correlated quite well with the clinical status of the patients," says Uhr.

The investigators also followed eight breast cancer patients for up to 10 months, relating changes in epithelial cell numbers directly to responses to therapies. Epithelial cells disappeared from one patient's blood when she responded to chemotherapy but rose when she stopped treatment and suffered a relapse. When another round of chemotherapy put the disease into remission, the epithelial cells again vanished.

"This is a sign that the test is working," notes Ronald A. Ghossein of Memorial Sloan-Kettering Cancer Center in New York, who has also led efforts to detect shed tumor cells in blood.

Ghossein, Uhr, and other researchers caution that many more patients need to be examined before physicians can reliably use any information about the number of epithelial cells in blood.

Uhr plans to examine whether noncancerous diseases also cause epithelial cells to be shed into blood. It's also vital to determine how many of these cells can show up in the blood of a healthy person, he says, so physicians won't mistakenly diagnose disease.

"I think a word of caution, until more is known about the clinical significance [of finding epithelial cells in blood], is appropriate," agrees John G. Sharp of the University of Nebraska Medical Center in Omaha. —*J. Travis*

Starting up quick quantum searches

Searching a telephone directory's alphabetical listings to match a given number with a name can be an onerous task. If you were unlucky, you might end up having to check every entry.

Using a conventional computer would speed up such a massive search considerably, but the task would probably still take a huge number of steps. A computer based on quantum mechanical principles, however, offers the theoretical possibility of performing certain computations and searches in significantly fewer steps (SN: 1/14/95, p. 30).

Now, researchers have for the first time demonstrated experimentally the operation of a simple quantum computer that can perform an efficient search, going all the way from a given initial state to the final answer in one step.

Isaac L. Chuang of the IBM Almaden Research Center in San Jose, Calif., Mark Kubinec of the University of California, Berkeley, and Neil A. Gershenfeld of the Massachusetts Institute of Technology describe their feat in the April 13 PHYSICAL REVIEW LETTERS.

In a conventional computer, information can be stored and processed as strings of bits, each of which has one of two values, 0 or 1. Quantum computers deal with qubits—the quantum analogs of ordinary bits. Unlike bits, qubits are not confined to two states but can exist in a combination, or superposition, of states. That makes it possible to perform several logic operations simultaneously.

Mathematicians and computer scientists have proved that a quantum computer would require fewer steps than a conventional computer to perform certain mathematical operations, such as factoring whole numbers (SN: 5/14/94, p. 308). In 1996, Lov K. Grover of Bell Laboratories at Lucent Technologies in Murray Hill, N.J., demonstrated theoretically how a quantum computer could speed up database searches (SN: 8/31/96, p. 143).

Chuang and his colleagues used a solution of chloroform molecules as a quantum computer and employed nuclear magnetic resonance techniques to establish and detect states (SN: 1/18/97, p. 37), allowing them to perform Grover's quantum search algorithm on a list of four items. Their experiment represented the four possibilities by means of a pair of two-state quantum systems corresponding to the two possible spins of the carbon and hydrogen nuclei making up chloroform molecules. The search picked out the required state.

"Their results show that it is possible to locate the desired item in one step, as predicted, and that it is possible to determine that there is indeed only one item to be found," Jonathan A. Jones of Oxford University in England comments in the April 10 SCIENCE. Jones and his colleagues have recently performed a similar quantum search using hydrogen nuclei in cytosine molecules.

This demonstration is an important milestone, Grover says. Researchers can start to think seriously in terms of implementing quantum algorithms instead of just devising quantum on-off switches. —*I. Peterson*