Public release date: 18-Feb-2007

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Cancer cells more likely to genetically mutate

When cells become cancerous, they also become 100 times more likely to genetically mutate than regular cells, researchers have found. The findings may explain why cells in a tumor have so many genetic mutations, but could also be bad news for cancer treatments that target a particular gene controlling cancer malignancy.

The research was led by Dr. Lawrence Loeb, professor of pathology and biochemistry at the University of Washington School of Medicine in Seattle. Loeb will present his research Feb. 18 at the meeting of the American Association for the Advancement of Science in San Francisco.

Most types of cancer are believed to begin with a random genetic mutation that makes a normal cell go horribly awry. This is followed by mutations, which endow the cancer cells with properties allowing them to grow without normal controls to become a tumor. These mutated genes would be targets for chemotherapy.

But Loeb had another idea that he originally hatched many years ago ‧what if the cancer cells changed somehow, and became much more likely to mutate? These "mutator" cells would develop dangerous genetic mutations at a much faster rate than normal cells, which might account for the high number of mutations seen in tumor cells.

Since the technology of cancer genetics has dramatically improved, Loeb and his colleagues have only recently been able to test this hypothesis. They found that tumor tissue had random mutation rates up to 100 times higher than normal tissue from the same patient. The "mutator" hypothesis seems to be correct.

Now for the bad news: if cancer cells do indeed become "mutator" cells, traditional chemotherapy and other drugs may never be very effective against advanced tumors.

"This is very bad news, because it means that cancer cells in a tumor will have mutations that protect them from therapeutics," Loeb explained.

A chemotherapy drug may target a particular oncogene, which is a gene that affects the malignancy of a particular cell. But if cancer cells are mutator cells, a single tumor may have cells with many different types of oncogenes and drug-resistant genes. That chemotherapy drug may kill off some of the cancerous cells, but millions of other cells in the tumor will live on. To be effective, a chemotherapy treatment may have to target more than one oncogene ， so-called combination chemotherapy.

Not all of the news is bad, though. Loeb believes this research may eventually help physicians determine the stage and malignancy of a tumor by testing the number of its mutations. The more mutations, the further along the tumor may be in its development to malignancy or metastasis.

Loeb's work may also lead to a discovery of why cancer cells are becoming mutator cells. If scientists understand what happens in a cancer cell that makes it become a mutator, they might be able to prevent that from happening in other cells, or slow down the mutation rate.

"The idea is that if you might normally get exposed to something in the environment at 20 years old that would give you cancer by age 55, then if we cut the mutation rate in half, you might not get cancer until age 90, and you may even die of something else before that," Loeb explained.

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NOTE: Dr. Lawrence Loeb will discuss his research at a AAAS news briefing, held at 2 p.m. Pacific Time, Sunday, Feb. 18. His symposium will be held later that afternoon at 3:30 p.m.