

UCLA Scientists Transform HIV Into Cancer-seeking Missile

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Camouflaging an impotent AIDS virus in new clothes enables it to hunt down metastasized melanoma cells in living mice, reports a UCLA AIDS Institute study in the Feb. 13 online edition of Nature Medicine. The scientists added the protein that makes fireflies glow to the virus in order to track its journey from the bloodstream to new tumors in the animals' lungs.

"For the past 20 years, gene therapy has been hampered by the lack of a good carrier for therapeutic genes that can travel through the blood and aim itself at a precise location, thereby minimizing harmful side effects," explained Irvin S.Y. Chen, Ph.D., director of the UCLA AIDS Institute. "Our approach proves that it is possible to develop an effective carrier and reprogram it to target specific cells in the body."

The UCLA team employed a two-step approach to transform HIV into a cancer-seeking machine. First, the scientists used a version of HIV from which the viral pieces that cause AIDS had been removed. This allowed the virus to infect cells and spread throughout the body without provoking disease.

"The disarmed AIDS virus acts like a Trojan horse \sqrt transporting therapeutic agents to a targeted part of the body, such as the lungs, where tumors often spread," said Chen, a professor of medicine, microbiology, immunology and molecular genetics and a member of the Jonsson Comprehensive Cancer Center at the David Geffen School of Medicine at UCLA.

Second, the scientists stripped off HIV's viral coat and redressed it in the outer suit of the Sindbis virus, which normally infects insects and birds. By altering the Sindbis coat, they reprogrammed the AIDS virus, which ordinarily infects T-cells, to hunt down and attach to P-glycoproteins -- molecules located on the surface of many cancer cells. The UCLA team is the first to prove that modified HIV will target and bind with P-glycoproteins.

"P-glycoproteins cause big problems by making the cell resistant to chemotherapy," said Chen. "They act like soccer goalies and punt therapeutic drugs out of the cancer cell. This prevents the drug from taking effect and allows the tumor to continue growing unchecked."

In order to track the carrier's journey, the scientists added luciferase √ the protein that makes fireflies glow √ to the AIDS virus. They injected the camouflaged HIV into a vein in the mouse's tail and used a special optical camera to watch the carrier's movement.

"The virus traveled through the animal's bloodstream and homed straight to the cancer cells in the lungs, where the melanoma had migrated," said Chen.

When the researchers held the mouse under the camera, the luciferase illuminated the cancer cells, which glowed through the animal's bones, muscles and fur. The method is non-invasive and does not cause pain or harm to the animal.

Though excited at proving that HIV can be used to target cancer cells, Chen emphasizes that the carrier must be further enhanced for safety and specificity before it can be tested as a gene-therapy method in humans.

"Our next step will be to test whether we can direct therapeutic genes to

the precise location where cancer cells reside," Chen said. "This approach offers many potential applications for controlling cancer and other diseases."

"We may be able to boost immune-system surveillance at tumor sites, identify cancer cells' exact location and kill them before they cause damage," he added. "Beyond cancer, it may be possible to correct acquired and genetic diseases where the mutations exert their harmful effects on the body."

Melanoma is a serious form of skin cancer. According to the American Cancer Society, an estimated 59,580 Americans will be diagnosed with melanoma in 2005, and about 7,770 people will die of the disease.

Source: UCLA

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