Cancer-killing invention also harvests stem cells

January 4 2007

Associate Professor Michael King of the University of Rochester Biomedical Engineering Department has invented a device that filters the blood for cancer and stem cells. When he captures cancer cells, he kills them. When he captures stem cells, he harvests them for later use in tissue engineering, bone marrow transplants, and other applications that treat human disease and improve health.

With Nichola Charles, Jared Kanofsky, and Jane L. Liesveld of the University of Rochester, King wrote about his discoveries in "Using Protein-Functionalized Microchannels for Stem Cell Separation," Paper No. ICNMM2006-96228, Proceedings of the ASME, June 2006. King's team includes scientists at StemCapture, Inc., a Rochester company that bought the University patent for King's technique in November 2005 to build the cancer-killing and stem cell-harvesting devices. The technique can be used in vivo, meaning a device is inserted in the body, or in vitro, in which case the device resides outside of the body – either way, the device kills cancer cells and captures stem cells, which grow into blood cells, bone, cartilage, and fat.

When King was working at the University of Pennsylvania from 1999 to 2001, one of his labmates discovered that bone marrow stem cells stick to adhesive proteins called selectins more strongly than other cells -- including blood cells -- stick to selectins. When King came to the University of Rochester in early 2002, he started studying the adhesion of blood cells to the vascular wall, the inner lining of the blood vessels. During inflammation, the vascular wall presents surface selectins that

adhere specifically to white blood cells. These selectins cause the white blood cells to roll slowly along the vascular wall, seeking signals that tell them to crawl out of the bloodstream. This is how white blood cells migrate to bacterial infections and tissue injuries. King set out to find a way to duplicate this natural process.

First, he noted that the selectins form bonds with the white blood cells within fractions of a second, then immediately release the cells back into the bloodstream. He also realized that selectin is the adhesive mechanism by which bone marrow stem cells leave the bloodstream and find their way back into bone marrow. This is how bone marrow transplantation works. Finally, he learned that when a cancer cell breaks free of a primary tumor and enters circulation, it flow through the bloodstream to a remote organ, then leaves the bloodstream and forms a secondary tumor. This is how cancer spreads. He put these facts together with one more, very important fact: the selectins grab onto a specific carbohydrate on the surfaces of white blood cells, stem cells, and cancer cells. Associate Professor King decided to capture stem and cancer cells before the selectins release them.

Harvesting Stem Cells

Because bone marrow stem cells stick to selectin surfaces more strongly than other cells, King's group coated a slender plastic tube with selectin. They then did a series of lab experiments, both in vitro and in vivo using rats, with this selectin-coated tube to filter the bloodstream for stem cells. It worked, and the King Lab discovered that they could attract a large number of cells to the wall of their selectin-coated device, and that 38% of these captured cells were stem cells. King envisioned a system by which doctors could remove stem cells from the bloodstream by flowing the cells through a device, and make a more concentrated mixture containing, say, 20-40 percent stem cells. These stem cells could then be used for tissue engineering or bone marrow transplantation.

This is a non-controversial way of obtaining stem cells that can be differentiated into other, useful cells.

King's team can capture significant amounts of cells of the lymphatic and circulatory systems, and potentially mesenchymal stem cells, which are unspecialized cells that form tissue, bone, and cartilage. Current procedures enable the specific capture of hematopoietic stem cells, which grow (or differentiate) over time into all of the different blood cells, and the specific capture of stem cells that differentiate into bone marrow cells. The device itself uses a combination of microfluidics, or fluid flow properties, and specialized selectin coatings.

Killing Cancer Cells

Another exciting application of King's invention is filtering the blood for cancer cells and triggering their death, an innovative, new method to prevent the spread of cancer. When someone has a primary cancer tumor, a small number of cancer cells circulates through the bloodstream. In a process called metastasis, these cells are transmitted from the primary tumor to other locations in the body, where they form secondary, cancerous growths.

As a cancer cell flows along the implanted surface, King's device captures it and delivers an apoptosis signal, a biochemical way of telling the cancer cell to kill itself. Within two days, that cancer cell is dead. Normal cells are left totally unharmed because the device selectively targets cancer cells.

The apoptosis signal is delivered by a molecule called TRAIL that coats the cancer-killing device. Cancer cells have five types of proteins that recognize and bind to TRAIL, but only two trigger cell death. The other three are called decoy receptors. Healthy cells contain a lot of decoy receptors, giving them a natural protection against TRAIL, whereas

cancer cells mainly express the two receptors that signal cell death.

During the death of the cancer cells, TRAIL is not depleted or used up in any way, and in fact, it stays active for many weeks or months. The same TRAIL molecules can kill enormous numbers of cancer cells.

A possible way to use the cancer-killing invention is to implant the device in the body before primary tumor surgery or chemotherapy. When doctors remove a primary tumor, the procedure itself can release cancer cells into the bloodstream. King's device would grab those cancer cells and kill them, greatly reducing the possibility of metastasis.

Associate Professor King envisions that the device would use a shunt similar to the type used in hospitals today. This shunt would reside on the exterior of the arm or be implanted beneath the skin. Some of the blood flow would bypass the capillary bed and instead go into the shunt, which could remain implanted for many weeks, continually removing and killing cancer cells. King's first targets are colorectal cancer and blood malignancies such as leukemia.

Source: School of Engineering and Applied Sciences University of Rochester