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Buddy's Last Gift

A Dog Dying of Prostate Cancer Gives Researchers Clues That Someday May Better Treat Canine Cancer, For Both Dogs and Humans

Buddy was dying and there was nothing that could be done to save him. Prostate cancer is particularly aggressive in dogs. By the time there were enough symptoms to trigger a canine cancer checkup, his tumor had spread too widely for any chance of a cure.

Buddy, who had provided his family years of friendship and play, had one more gift to give. Though his situation was terminal, he was perfectly placed to be the first dog to try a new and non-invasive method of delivering a new cancer-imaging agent directly to the tumor. Though it couldn't save his life, a successful test would provide valuable research data, and provide hope to future Buddys and their owners.

Dogs, Man, and Prostate Cancer

There are only two animals in all of nature that regularly get prostate cancer, dogs and humans. The canine and human prostate gland and its diseases are very similar. Prostate tissues from both species undergo many of the same transformations believed to be important in this metastatic disease.

Among American men, prostate cancer is the most common form of cancer and the second leading cause of cancer death. At the time that it is diagnosed, this disease may be confined to the prostate gland, or it may have spread to other organs in the body such as the skeleton. When caught early, prostate cancer can be treated effectively with surgery or radiation therapy.

However, if the cancer has spread to other organs, hormone therapy or chemotherapy become the best treatment options. Unfortunately, most patients with advanced prostate cancer become resistant to such long-term intervention, meaning there is no effective cure for the disease at this stage.

The problem of prostate cancer is getting worse. The National Cancer Institute reports that human prostate cancer rates have increased 4.4 percent a year between 1973 and 1992, or more than a doubling of risk in a generation. Since 1992 the incidence has declined, but it is still 2.5 times the rate in 1973. Prostate cancer killed an estimated 31,900 men in the year 2000 alone.

One in every 150 male dogs more than eight years of age develops prostate cancer. Like the human condition, the canine disease is aggressive and spreads rapidly to lymph nodes, lungs, and bone. As symptoms are late to show themselves, most dogs are diagnosed with prostate cancer in its advanced stages.

Buddy's Case

Buddy showed up as a hungry and flea-infested stray on the Missouri farm of Megan Baebler's grandparents in 1992. Megan was 11 then, and she and her grandmother spent the day feeding Buddy and picking ticks off him. That lead to the inevitable question to mom and dad: "Can we keep him?"

Buddy, a Lhasa Apso mix, joined the home of the Baebler family in St. Louis County. He was a companion of Megan and her brother through the rest of grade school, junior high, and high school. In 1996, when Megan was 16, Buddy ruptured a disc in his spine that left his rear legs paralyzed. After surgery, Megan and her mom spent days waiting for Buddy to move his hind legs. One day, while Buddy was sleeping, they saw a twitch and knew that he was going to be okay.

That experience helped Megan decide to become a veterinarian. The next year, she began working for the family veterinarian, Dr. Stanley Feldman, MU DVM '74. In the fall of 2003, Megan began her studies at the University of Missouri College of Veterinary Medicine as one of the Class of 2007.

It was in September 2004 that Buddy began showing the first signs of prostate cancer. Everyone knew something was wrong when the ravenous Buddy began losing his appetite. Buddy's diagnosis was grim. The cancer had spread throughout his body with several organs involved. Typically, the last hope for treatment is radiation therapy delivered by a linear accelerator, such as at the MU Veterinary Medical Teaching Hospital, one of the few devices devoted to companion animal care. While the device focuses cancer-killing radiation on the tumor, it also can irradiate adjacent healthy tissue such as the bladder and colon.

If the cancer is caught early enough, the accelerator can deliver enough radiation to kill the tumor yet not harm the other organs. Buddy's cancer would require such a large radiation dose that it might also affect adjacent organs, risking the quality of his last days. The same problem faces physician oncologists treating human patients. The best course was to keep him comfortable and pain free.

Through her studies, Megan knew of research being done by the veterinary medical teaching hospital's oncology group. While Buddy's cancer was too far advanced for hope, she and her family thought he could make a contribution to one of these canine cancer studies.

Searching for an "Antibody Pre-Target"

Michael Lewis is a PhD chemist and biologist who serves as an assistant professor of veterinary medicine and surgery at MU with a joint appointment at the nearby Veterans Administration Hospital. His research specialty is finding ways to use radiopharmaceuticals to specifically target, image, and destroy prostate cancer with radiation but cause minimal effects in healthy tissue.

Dr. Lewis' studies are designed to be the next step from the most advanced treatment option now available - the surgical implantation of radioactive "seeds" inside the prostate gland. This is designed to deliver enough radiation to kill the tumor, but not endanger adjacent organs.

With his collaborators, Dr. Lewis envisioned something that would make seeds seem crude by comparison. He foresaw delivering cancer-fighting radioactivity exclusively to the tumors through the bloodstream. Tumors require a large supply of blood – such a "vector" of delivery seemed promising.

The plan was to introduce radioactive molecules into the blood that would accumulate only in tumor tissue with the surplus radioactivity staying in suspension until it can be eliminated. An early problem emerged – no suitable delivery vector would do this effectively.

The team then began to look at a two-part plan. Part one would be to find a substance that would exclusively stick to tumors. Part two was to find a radioactive material that would stick to the first substance. This concept lead to the breakthrough of "antibody pre-targeting."

To pre-target the tumor, the researchers chose an antibody, CC49, known to "stick" to cancer cells when a streptavidin molecule is attached. With this antibody covering the tumor, biotin (one of the B vitamins) was introduced. It exclusively and quickly sticks to streptavidin. Attached to the biotin are the radioactive atoms.

The concept promised a fast way to attach radioactivity to the tumor while the unused radioactivity flushes out of the body through the urine.

Preliminary laboratory testing showed great promise. Now was the time for its first use on a cancer patient. Within the MU Veterinary Medical Teaching Hospital was a candidate.

Buddy's Contribution to Cancer Research

“The focus of our procedure with Buddy was to deliver radioactivity to develop a very detailed image of the cancer,” said Jeffrey Bryan, a board-certified DVM oncologist and research assistant professor in the College of Veterinary Medicine oncology group.

Dr. Bryan is a co-investigator with Dr. Lewis on the Antibody Pre-Targeting project. “With this phase tested, our future goal will be to deliver a lethal radioactive payload via the same method.”

On an otherwise ordinary morning at the MU Veterinary Medical Teaching Hospital, Buddy received his first quick injection. Drs. Lewis and Bryan, and the rest of the oncology and radiology teams, monitored the accumulation of radioactivity in the tumor and other organs and tissues on the screen of a gamma camera, a device that can track each radioactive molecule.

As hoped, the blood-borne radioactivity rapidly attached to the tumor – the camera showing it like a black and white picture. The camera also watched the radioactivity as it made its way out of Buddy's body.

Unexpectedly, the team saw something exciting – the targeted radioactivity was finding and sticking to other previously unknown tumors that had not been detected with conventional imaging. "The first challenge of treating a cancer patient is always finding all of the tumors," explained Dr. Bryan. “This was an unexpected bonus.”

The process took only three intravenous injections. The total amount of radioactivity introduced to the body was a fraction of a therapy dose, causing no harm or pain to Buddy.

The research team was delighted. The first procedure was everything that they were looking for in an imaging agent, plus the discovery of previously unsuspected tumors. While it was only a first step, nothing indicates that the method can’t be tried as a future therapy with a different form of radioactivity – possibly someday becoming one of the least invasive ways to treat cancer in dogs and humans.

Though Buddy's procedure was a success from a research point of view, his cancer had spread too far for any hope of a cure. Nonetheless, he was a pioneer in the truest sense of the word, giving gifts to humans and dogs that have yet to be fully realized.

A Collaborative MU Effort That Has Been Successful Before

As one of a few universities with a school of medicine, college of veterinary medicine, research reactor, and other research-oriented colleges on the same campus, the University of Missouri-Columbia has already produced three successful radio-pharmaceutical products.

Working collaboratively, using research expertise from each college, MU has developed Quadramet for relieving the pain of bone cancer, TheraSphere for treating liver cancer, and Ceretec for improved imaging of stroke or brain injury victims. The effort to produce a radio-pharmaceutical for prostate cancer was funded by the Department of Defense Prostate Cancer Research Program, University of Missouri Research Board, and the MU College of Veterinary Medicine Committee on Research.

Resources also came from the MU School of Medicine, Harry S. Truman Memorial Veterans' Hospital, and MU Department of Chemistry.

Visit the Morris Animal Foundation (MAF), which launched the CCC's effort to cure canine cancer.