

MALLINCKRODT FELLOWSHIP WINNER TO STUDY DOG XENOGRAFTS

Developing a dog model for human cancers could help researchers overstep the limitations of studying tumors in nude mice.

THE SOCIETY OF NUCLEAR Medicine has chosen cancer researcher Gregory A. Wiseman, MD, to receive this year's Mallinckrodt Fellowship Award. Having succeeded in transplanting human tumors into immunosuppressed dogs, Dr. Wiseman proposes to study the uptake of antibodies targeting these xenografts. The sponsors of the annual funding for promising research in nuclear medicine, Mallinckrodt Medical, Inc., will present a \$30,000 check to Dr. Wiseman at SNM's Annual Meeting in Cincinnati, Ohio.

Dr. Wiseman is the first to succeed in growing human tumors in dogs, according to advisor and colleague Dr. Wil B. Nelp, professor of medicine and radiology and head of nuclear medicine at the University of Washington Medical Center in Seattle. The senior resident/fellow in nuclear medicine and oncology at the University of Washington Medical Center injected cultured human melanoma cells beneath the skin of mature dogs and the xenografts grew into vascularized, golfball-sized tumors.

Dog Models

Developing a dog model for human cancers could help researchers overstep the problems intrinsic to studying tumors grown in nude mice and other immunodeficient rodents. Mice are too small for growing multiple tumors for serial studies, and the small transplanted tumors grown in mice are difficult to image and yield limited results in radiolabeled antibody distribution, toxicity, and dosimetry studies. Dogs are closer to humans in size, which makes them better models of human physiology. As

in all animals, however, the dog immune system tends to reject transplanted human cells.

Immunologists warned Dr. Wiseman that human tumor growth in dogs might not be possible, but he accomplished the transplants with the first cell line he had available, human melanoma cell line A375. "We were just more persistent," Dr. Wiseman says, "and luckier in choosing a cell line."

Details of the Study

In his preliminary study, Dr. Wiseman suppressed the immune systems of the dogs with oral cyclosporine, the cyclic peptide given to human organ transplant recipients, and injected the cultured cancer cells subcutaneously. Tumors grew successfully in 43 out of 44 implantation sites among four dogs, and after 90 days reached volumes of up to 20 cubic centimeters. The xenografts appeared under microscopy as viable malignant cells laced with blood vessels, and the excised tumors showed specific binding to radiolabeled anti-melanoma monoclonal antibodies. "I was surprised that I really should be able to do xenografts like these in a fully functioning immune system," says Dr. Wiseman.

"The awards committee was impressed with the potential of this methodology particularly in its relationship to the study and application of radiolabeled monoclonal antibodies for diagnosis and treatment of various types of cancer," says William J. MacIntyre, PhD, chairman of SNM's awards committee and staff nuclear physicist, department of nuclear medicine, Cleveland Clinic Foundation, Ohio. In a letter of



Gregory A. Wiseman, MD

support for Dr. Wiseman's proposal to the awards committee, Fred Appelbaum, MD, an associate professor at the University of Washington School of Medicine and member of the Fred Hutchinson Cancer Research Center, both in Seattle, said he was "particularly impressed" with the initial reproducibility of the melanoma results. "I am excited to see to what extent other human malignant tumors can be grown, and at what sites in the body," he wrote. Dr. Appelbaum is Dr. Wiseman's advisor at the Fred Hutchinson Center.

Radioimmunotherapy

In his fellowship proposal, Dr. Wiseman outlines plans to try to grow other human malignancies such as lung, colon, prostate, lymphoma, and ovary malignant cell lines in dogs.

(continued on page 27N)

Commentary

(continued from page 24N)

ing costs of health benefits for employees, large corporations have negotiated managed care plans with HMOs and contracted with consultant firms to monitor quality in those plans.

These actions are designed to contain cost without sacrificing quality. Recent studies published in the *Journal of the American Medical Association* indicate that quality of care generally has not declined after seven years of DRGs, the government initiated pre-payment care plan for hospitalized medicare patients. Despite these cost-containment measures, however, health care costs to government continue to rise, in large part because of increasing volumes of medical services. To discourage physicians from increasing volumes of services, the Health Care Financing Administration (HCFA) is implementing formulae that reimburse specialties less for volumes of services exceeding the prior year's volumes.

These trends reflect what we all know: To maintain income, we're all working harder, delivering more services, and having less time for everything else. We seem to have less time for SNM work during this critical period when SNM's need for our talents and attention have increased.

To respond effectively to these demands, SNM needs structural reorganization. We need medical and scientific leaders who can dedicate the additional time necessary to meet the challenges of today. A president alone, or with a handful of others, all of whom have the demands of other full-time jobs, won't be as effective in the 1990s as such a cohort might have been ten years ago. In addition to our officers, we need professional leadership dedicated to SNM, and capable of representing nuclear medicine before the government, other medical specialty groups, and the scientific community.

Naomi P. Alazraki, MD

President, The Society of Nuclear Medicine

Guidelines

(continued from page 16N)

the radiologist and president of SNM's Brain Imaging Council says. "We want to be able to hand people percentile numbers—this pattern gives you an 80% chance of Alzheimer's disease, this gives you a 60% chance of multi-infarct dementia." The findings of the dementia consensus panel will be published in a number of journals, according to one of the panel's co-writers, Ronald S. Tikofsky, PhD, research associate professor and director of brain imaging research, department of radiology, Med-

ical College of Wisconsin, Milwaukee.

Regardless of the procedures used to establish practice policy guidelines, Dr. Alazraki and others say that nuclear medicine specialists should work together with radiologists who carry out nuclear medicine procedures. The American College of Radiology approved several sets of clinical practice guidelines late last year that touch upon nuclear medicine. "We have to work with all of the other specialties," says Dr. Fletcher. As important, says Dr. Dillehay, "is to write these guidelines so they reflect the way we want nuclear medicine to be

practiced." Gathering sufficient data to determine how nuclear medicine should be practiced, and hammering out a consensus with radiologists and other specialists—that is the delicate task ahead.

J. Rojas-Burke

References

1. Kelly, JT, Kellie, SE, Appropriateness of medical care. *Arch Pathol Lab Med* 1990; 114:1119-1121.
2. Liability premiums reduced for anesthesiologists. *QA Review* 1989; 1-6.
3. Kellie, SE, Kelly, JT, Medicare peer review organization preprocedure review criteria. *JAMA* 1991; 265:1265-1270.

Xenografts

(continued from page 17N)

"It is possible that not all tumors will grow in the immunosuppressed dog, but the melanomas Dr. Wiseman tried grew very well," says Dr. Nelp. "This is real ingenious work and should provide a model that has certain advantages for work on solid tumors." Solid tumors of the liver, lung, ovaries, and other organs have proven more formidable in resistance to treatment with radioactive antibodies than radiosensitive tumors such as lymphomas (see *Newsline*, December

1990, p. 15A). Among the problems blocking the advancement of radioimmunotherapy is the low rate of incorporation of antibody into tumor. Dr. Wiseman is comparing tumor blood flow to tumor size, and specific antibody binding of tumor to tumor blood flow, looking for relationships. He suspects this might lead to a way to increase the rate of uptake of radioactive antibodies into malignant tumors for improved detection and treatment of cancers.

Dr. Wiseman is completing the second

year of his special three year combined fellowship at the University of Washington Medical Center and conducting his research at the Fred Hutchinson Cancer Research Center. Dr. Wiseman graduated from the University of Wyoming, Laramie in 1978. Awarded his medical degree from the University of Utah Medical Center, Salt Lake City, in 1983, he worked at the Mayo Clinic in Rochester, Minnesota until 1989.

J. Rojas-Burke