



The revolutionary work of an HSC pathologist is contributing to the development of a futuristic laboratory that could vastly improve the early detection of diseases.

Pathology, the study of the nature of diseases, is a pure research function of medicine that has relied on labor-intensive methods to isolate and analyze disease. But the costly and painstaking work involved in pathology—and attendant human errors—could some day give way to a revolutionary new “laboratory of the future” developed by an OU Health Sciences Center pathologist.

Dr. David J. Brigati, director of the new Automated Molecular Pathology Diagnostics Center, has developed automated diagnostic tests that could dramatically improve the early detection of some diseases.

Brigati is the inventor, designer and developer of the world’s first automated instrumentation for tissue gene and antigen detection. Using a computer-assisted robot, Brigati has developed rapid, cost-effective gene

probe tests for detecting infectious, genetic and malignant diseases in anatomic specimens. He is known as the “father of automated molecular pathology” for his invention of solid phase capillary action technology. Besides developing the new technology for use at HSC, Brigati has helped automate more than 250 immunopathology and molecular diagnostics laboratories throughout the country.

In Brigati’s laboratory the automated robot processes body tissues one step at a time, shaving small sections from the tissues, staining them and analyzing their microscope-magnified images.

The process uses antibodies and DNA probes made in the laboratory to trace diseased cells in the body. Antibodies, immunological molecules the body uses to defend against organisms, sometimes are injected into the tissues to help trace the presence of diseased cells. DNA probes,

nucleic acids that bind to similar chemicals in tissue sections, also can be injected to determine whether the abnormal genes of a virus are within cells of the tissue.

Central to Brigati's new process is his invention of a special microscope glass slide with a 150-Micron gap that takes liquids into the material being studied and removes them by capillary action.

"We're trying to use these methods to diagnose diseases quicker," Brigati says. The new technique is being used to test for such diseases as Down's Syndrome, Papilloma virus (cervical cancer), Cytomegalovirus (infections in chemotherapy patients), Epstein-Barr virus (tumors in the lymph nodes) and other forms of cancer.

"We also detect and separate cancers into different types arising from the lymph glands, skin, organs and other cells," he adds. "Many times tumors look almost identical and can be identified only from chemical markers. This prevents a lot of misdiagnoses. The whole test takes about an hour."

Among his goals for the new technology, Brigati wants to make the system work for detecting genetic diseases. "We want to see a single mutation—cystic fibrosis, for instance—under a light microscope," he said. "We think we can do that within the next few months."

Brigati also is interested in developing "prognostic indicators" to determine how badly a specific type of cancer will behave in the body. "We look for markers in the cancer cell that mark rapid growth or slow growth," he says. "We'd like to use that information to tailor the way a cancer is treated."

Formerly chief fellow in the department of pathology at Memorial Sloan-Kettering Cancer Center in New York City, Brigati holds an M.D. degree from State University of New York and a B.S. degree in biology and pre-medicine from Fordham University. He served his residency at Yale-New Haven Hospital in New Haven, Connecticut.

Brigati taught for seven years at Penn State College of Medicine, where the David J. Brigati Distin-

Brigati's tests stand ready to assist in tailoring cancer treatment. Eventually his work at OU could allow pathologists to uncover latent cancer in the cell of origin long before the disease develops and spreads.

guished Professor Award was endowed by the college. He was an assistant professor of pathology there when he resigned to establish OU's pathology diagnostic center. He also is director of immunopathology and adjunct associate professor of orthopedic surgery at OU. In April he received the Aesculapian Award from the medical student class of 1993 for excellence in teaching basic sciences. Brigati's wife Doreen assists him as a full-time volunteer at the pathology diagnostic center.

Brigati's research has led to technology that readily transferred to economic development. He and a colleague, David C. Ward, developed non-radioactive probe technology. They were the first to visualize human and viral genetic information in formalin fixed paraffin embedded tissue sections. In 1982, Brigati developed the first colorimetric southern blot technique sensitive to one gene copy per cell in the same laboratory. These two signal technologies helped create the first biotechnology company, Enzo Biochem Inc., New York, to market non-radioactive DNA probe technology. Non-radioactive probes are now sold worldwide by Enzo, Digene Inc., DuPont, Molecular Biosystems Inc., and Boehringer-Mannheim.

Brigati has developed other technology, including the first automated methods for immunocytochemistry and in situ DNA hybridization, that have found quick acceptance in commercial applications. He holds seven U.S. patents for his technology, and three additional patents are pending.

Currently, Brigati is developing a new line of immunocytochemical reagents for fungus testing with Immuno-Mycologics Inc., a Norman company. He plans to start his own DNA company in Oklahoma next year.

Brigati believes his work at OU could someday allow pathologists to

uncover latent cancer in the cell of origin long before the disease develops and spreads.

The new automated laboratory is funded by the Oklahoma Center for the Advancement of Science and Technology, the Presbyterian Health Foundation and several private sources.

Brigati has published many papers on research leading to development of the new diagnostic system. His laboratory technology currently is being studied by the international medical community for its potential of accomplishing precise and cost-efficient diagnostic information.

International fellows participating in the research include Dr. Jin-Han Kang, assistant professor of pediatrics at Catholic University Medical College, Seoul, Korea, and Dr. Chang-Soo Park, assistant professor of pathology at Chonnam University Medical School, both funded by the Republic of Korea. Park recently returned to Korea to implement the new diagnostic technology.

Two other M.D.s, both from Yale University, also are participating as research fellows at the pathology diagnostic center lab. Dr. Julia Iezzoni is researching breast cancer markers, and Dr. Jon Reed is working on infectious disease agents.

In just two years, Brigati and his colleagues have introduced 59 new one-hour automated immunochemistry tests to the Oklahoma Memorial Hospital at the Health Sciences Center. He has a personal motivation for his contributions to the field of pathology.

"I'm a 10-year survivor of Hodgkin's Disease," he says. "That's what got me started."

"I came along when the disease was curable."

— RANDALL TURK
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