MedicalXpress

Molecular detectors may refine cancer treatment

July 19 2007

University of Florida researchers have successfully used molecular probes to detect subtle differences in leukemia cells from patient samples, an achievement that could lead to more effective ways to diagnose and treat cancer.

The strategy, described in a recent issue of Clinical Chemistry, involves engineering short, single strands of DNA or RNA called aptamers to seek out and bind with specific proteins in body fluids.

UF scientists designed the aptamers to bind to cells and molecules associated with leukemia, a cancer of the blood and bone marrow that annually claims about 21,000 lives in the United States, according to the National Cancer Institute.

Researchers also found the first evidence that slight molecular differences can exist even within the same samples from patients with adult T-cell leukemia, a cancer that strikes the immune system's own protective cells.

"Our selective aptamers clearly confirm there are several subcategories of adult T-cell leukemia," said Weihong Tan, Ph.D., a UF Research Foundation professor of chemistry at the College of Liberal Arts & Sciences and a member of the UF Shands Cancer Center. "At present, doctors have had only their experience to rely upon to determine the best treatment for these patients. Our findings will give doctors an effective tool to more precisely make a diagnosis and to tailor treatments."

UF researchers built designer probes using cancer cells as a template, capitalizing on the ability of aptamers to fold into well-defined, three-dimensional structures that bind to targets. The process relies on the fact that different types of cells exhibit unique surface features, so aptamers can recognize and bind with these target cells — and only these cells — even in the presence of other, closely related cells.

The scientists found that three of six aptamers they selected for study adhered to all types of cancerous cells but ignored normal blood and bone marrow cells. In combination, the six aptamers produced distinct patterns that characterize different cancer cells, suggesting that the technique could be useful to detect the molecular fingerprints of cancer in people.

The next step toward developing a clinical diagnostic tool involves matching patient data with these molecular profiles. The research team — working with W. Stratford May, M.D., Ph.D., director of the UF Shands Cancer Center, and Ying Li, M.D., Ph.D., a clinical assistant professor of pathology, immunology and laboratory medicine in the College of Medicine — has analyzed additional patient samples to build a database that may one day help doctors select the best treatment strategies.

“We are linking the medical histories of patients to specific aptamer binding patterns,” said Tan, who is also affiliated with the UF Genetics Institute. “We should soon be able to say patients who belong to this specific molecular binding pattern should have ‘such-and-such’ treatment. Different molecular patterns of cancer patients will point to different treatments.”

Current tests to diagnose leukemia use antibodies, proteins that have the ability to identify harmful substances. But such methods do not capture subtle variances in the molecular signature of cancer cells.

Once an aptamer probe has proved its utility, it can be inexpensively reproduced in a DNA synthesizer.

“Physical scientists mostly use cultured cellular models to demonstrate a principal, and then we leave the findings behind for the biological scientists to use — if they want,” Tan said. “But through collaboration we have pushed the demonstration through to an almost clinical application.”

Source: University of Florida