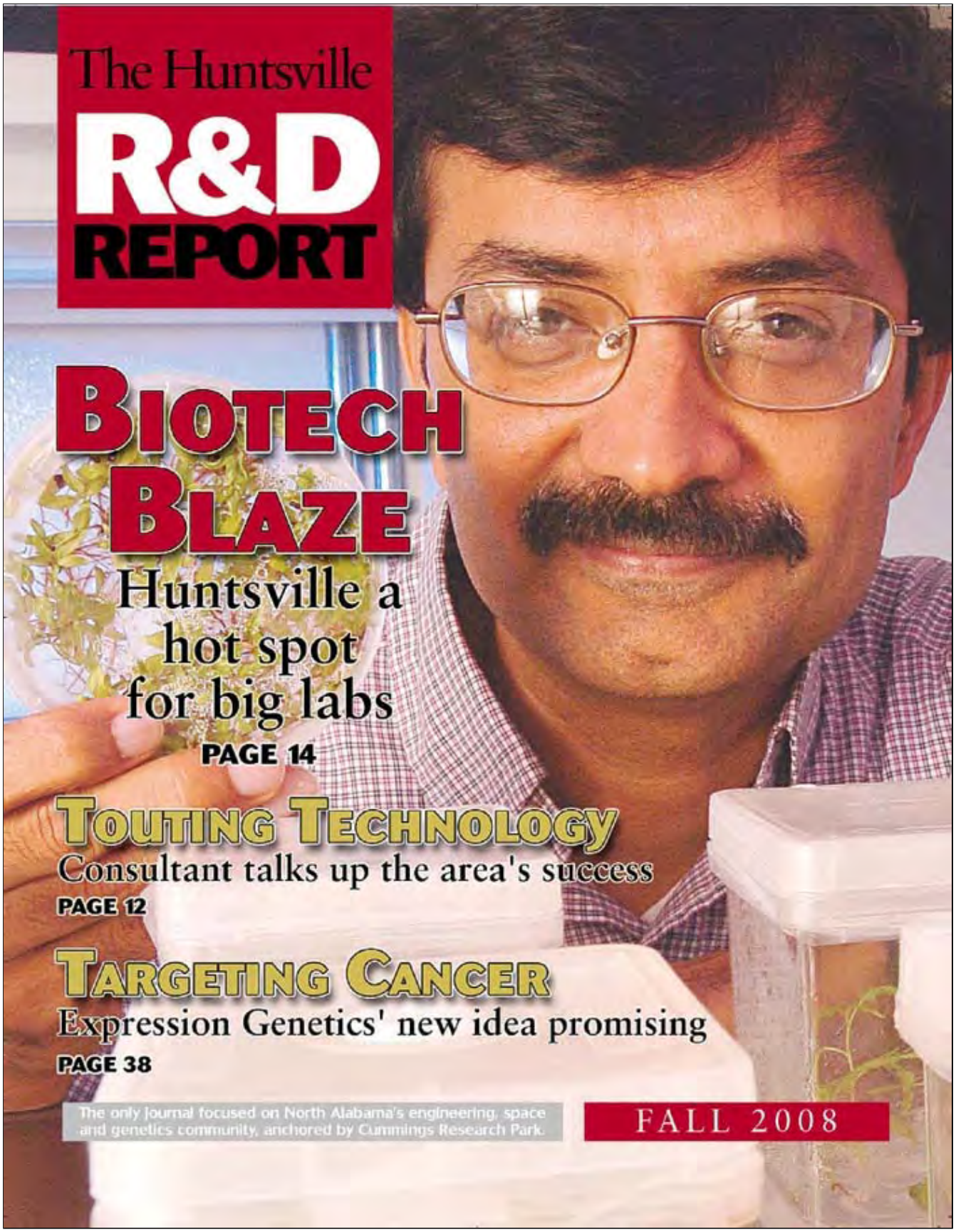
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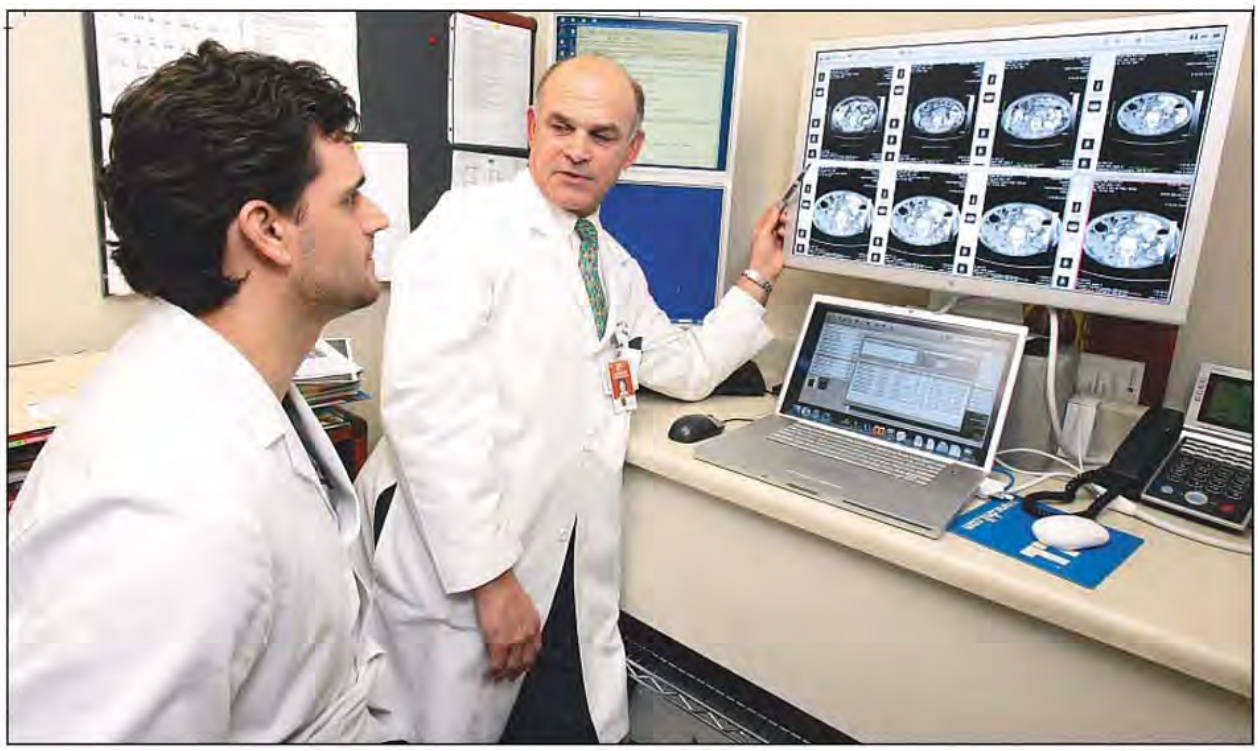

GLENN BEAEKE

Dr. Philip McGee, left, and Dr. Marshall Schreeder look at CT scans of a patient on a clinical trial.

Targeting cancer

Rocket City thought process leads to a promising new cancer therapy delivery system

By KIMBERLY BALLARD

An aggressive, untamed error in DNA is at the root of cancer, causing cells to continually divide and grow unrestrained in the human body until the rogue cells succeed in replacing good DNA with damaged cells.

Traditional treatments involve chemotherapy and radiation, both proven to kill cancerous cells. But instead of killing the cancer, what if biomedical research could empower the body to fight cancer from the point of the first cellular error? What if the body could correct the division of the rogue cells before they take root and begin ravaging the body with more damaged DNA?

This approach is known as gene or molecular therapy, or nuclear therapeutic medicine. For over 30 years, research has suggested certain genes can trigger a cancer-fighting protein known as cytokine. Researchers theorize that if the genes that stimulate the cytokine were applied to the cancerous area, the body could be reinvigorated to reawaken the immune system and fight the damaged DNA on its own. As part of the research, a long-suspected cancer-fighting gene known as Interleukin-12 (IL-12) has been isolated.

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SPECIAL DELIVERY

"The devil has been in finding the vector, or the carrier molecule, that will deliver the payload to the patient's target cells," says Dr. F. Joseph Kelly, board certified gynecologic oncologist at Huntsville's new Clearview Cancer Institute. "It appears Expression Genetics has developed a product that rises to the challenge."

Huntsville's Expression Genetics Inc. has utilized innovative polymer delivery technology to develop a line of highly versatile TheraPlas-branded immunotherapy products. If they continue to show positive testing results, these products may be an important breakthrough in cancer treatment.

Getting the IL-12 gene into the target area has been tried in various forms in the past. In fact, it was one of the early setbacks to gene therapy, giving it an early reputation for failure. "Many of the early clinical tests were premature," says Danny Lewis, president and CEO of Expression Genetics. "There wasn't enough understanding of how genes work, and they had not yet established an effective gene when they began testing. As a result, they failed." Attempts to ingest the gene or

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CCI gynecologic oncologist Dr. Joe Kelly, left, and Expression Genetics CEO Danny Lewis discuss the new therapy delivery system.

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inject it with a hypodermic needle only made the recipient nauseous before the body discarded it as waste.

But now, the Expression Genetics EGEN-001 delivery system shows promise, and has been listed in the Top 100 Great Investigational Drugs by *R&D Directions* magazine. "EGEN-001 is composed of the well-known IL-12 gene expression plasmid and proprietary synthetic biocompatible delivery polymer, fully developed here in Huntsville," says Lewis. "Pre-clinical testing shows this product is best used

Lab manager Susan Eva with an Immunoassay instrument that identifies and measures cancer markers in a blood sample.

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in conjunction with chemotherapy in the fight against ovarian cancer."

PHASE 1 TESTING

Over the past few months, Dr. Kelly has been conducting a Phase I test of the new biopharmaceutical drug in the treatment of three ovarian cancer patients at Huntsville Hospital. A Phase I test is granted by the Food and Drug Administration's Center for Drug Evaluation and Research in a small number of volunteers as the first stage of human testing of a new drug under investigation. In it, the drug's effects, side-effects and dosage ranges are explored.

Ovarian cancer is the deadliest of gynecological malignancies in women. It has a prevalence of 167,000 women in the U.S and 55-75 percent of women diagnosed with ovarian cancer relapse within two years of treatment.

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Medical technologist Masha Mason does microscopic examination of blood slides.

"Ovarian cancer is long overdue for alternative treatment," Dr. Kelly says.

The study allows Dr. Kelly to utilize Expression's proprietary polymer delivery technology to carry the IL-12 gene directly to the cancerous areas. "The EGEN-001 polymer breaks through the cell wall, and upon delivery, the IL-12 gene hooks onto the cancerous cell," he says. Once inside the nucleus of the cell, the gene can release the cancer-fighting agent cytokine, which interferes with the body's reckless reproduction of damaged DNA. According to Dr. Kelly, test results show promise as a breakthrough in cancer treatment.

"Our key focus is on the safety of the patient," Dr. Kelly says. "Currently, these three ladies are participating in our testing under what we call informal consent. They are made aware of every aspect of the treatment and are under very strict observation at all times. We take extra steps and precautions to assure they are progressing without showing any signs of unexpected pain, side effects or unforeseen problems. In fact, they have doctors and nurses fawning over them day and night, to assure their comfort and monitor their reaction to the EGEN-001 product."

In a Rocket City kind of way, Lewis explains the way his product is engineered to work. "You have the payload, which is the IL-12 gene. The EGEN polymer is the vehicle – the Mars Rover or the space shuttle. It is propelled or administered into the nucleus of the cancerous cell using a catheter, which is the rocket, so to speak." Lewis says he and Kelly think there is another reason to be excited about the future of this technology. "Now that we have a delivery vehicle, we can change out the payloads to address different types of cancers or develop a cancer-fighting cocktail that uses chemo to kill the existing cancer and TheraPlas gene therapy to silence bad genes causing the uncontrollable growth of damaged DNA."

Dr. Kelly has been monitoring toxicity in all of his test patients, measuring the effects the drug has on the human body and the degree to which the patient may get sick. He determines doses, adjusts frequency and monitors the effects the drug has on the cancer. "So far, EGEN-001 shows no side effects like those found in many cancer treatments, such as excessive hair loss, nausea or discomfort," Dr. Kelly says. "We do see some elevation in fever, but that is considered a good sign because it shows the body's immune system recognizes the administration of the drug, and to some degree, it proves it is having an effect."

Expression Genetics has spearheaded the continued development of technology fundamentally researched

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by Dr. Khursheed Anwer, PhD, who is its vice president for research and development. The group studies being overseen and administered by Dr. Kelly are a point of pride and a visionary achievement for the company, according to Lewis. "It speaks volumes about the level of professionalism and out-of-the-box thinking in our area."

Since the basis of scientific research consists of repetition, Dr. Kelly looks forward to moving to the next level of testing, which will increase the number of patients as well as the level of treatment. "We have proven we can safely administer and deliver the drug. Now we just need to get it to do what we want it to do."

GLENN BAESKE

CCI medical technician Melinda Hilt uses a blood chemistry analyzer machine to test a sample.