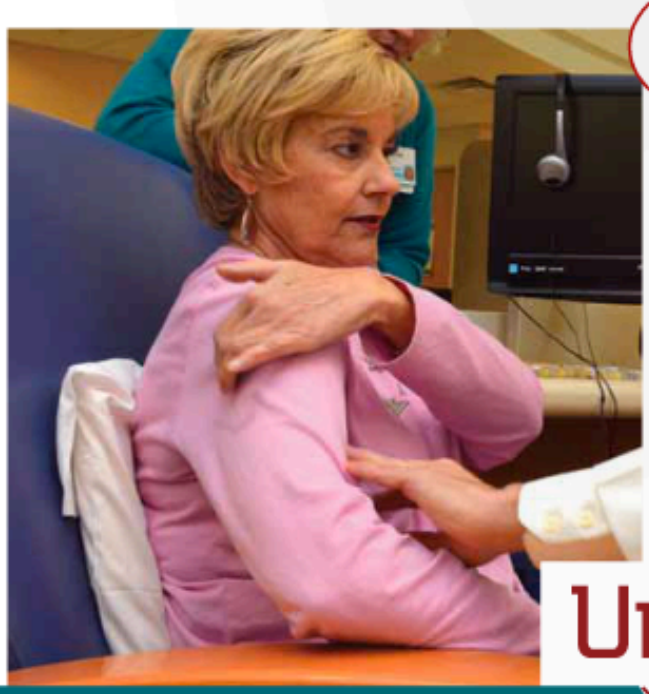
Taking a Shot at Cancer

CLINICAL TRIALS ENSURE CUTTING-EDGE TREATMENT



JOYCE CHAVIS GRU Clinical Trials Patient

After Joyce Chavis of Aiken, S.C., underwent surgery and chemotherapy for stage IV colon cancer in 2009, her treatment went well—so well, she says, that there were no signs that the cancer would ever come back.

Until it did.

BY DANIELLE WONG MOORES

Last December, her doctor found that her cancer had metastasized to her liver. Because Chavis was on blood thinners, she was no longer a candidate for a standard therapy combining chemotherapy and Avastin. Instead, her oncologist referred her to the Georgia Regents University Cancer Center's new Phase I clinic.

Homegrown Invention

At about the same time that Khleif was doing his initial studies into cancer vaccines, Dr. David Munn, a pediatric oncologist and Associate Director of the university's Cancer Immunotherapy Program, together with Dr. Andrew Mellor, Director of the Immunotherapy Center, was making a significant finding of his own.

Certain enzymes send signals to the immune system that foreign objects—food, for example—are safe. Tumors, however, can evolve and mimic these signals to prevent the immune system from doing its job. "You don't have to worry about the dumb tumors. The immune system takes care of those," said Munn. "The tumors that come to clinical attention are the ones that have figured out some way to activate those enzymes and elude the immune system."

For example, an enzyme called IDO keeps the immune system from seeing a growing fetus as a foreign object. Munn hypothesized and confirmed that certain tumors use this same pathway to suppress immune response. About 14 years ago, he and Mellor discovered a new drug in their GRU lab—called one-methyl-tryptophan, or 1-MT—that would reactivate the immune system so that it would recognize and attack cancerous tumors.

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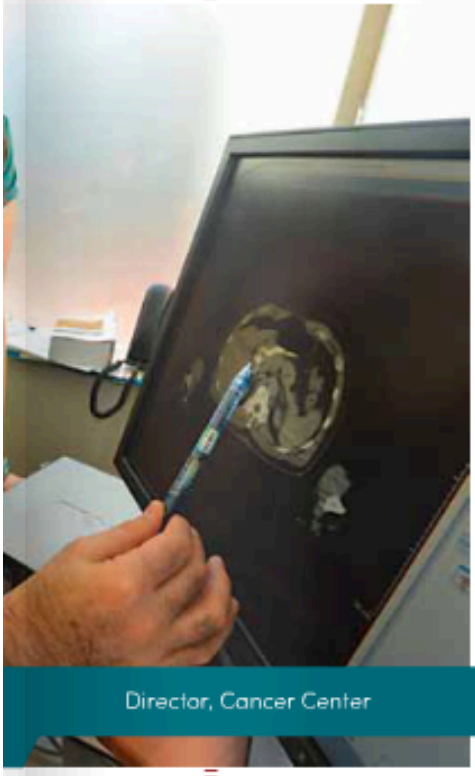

Director, Cancer Center

Innovative Clinical Trials

georgiahealth.edu/cancer/trials or 888-658-0422

To date, the GRU Cancer Center has 90 phase I, II or III clinical trials open, with 12 new trials set to launch soon, focused on cancers that affect Georgia and the Southeast. These new trials include:

A Pilot Study to Test the Feasibility and Immunologic Impact of Sipuleucel-T (Provenge™) Administered with or without anti-PD-1 mAb (CT-011) and Low Dose Cyclophosphamide in Men with Advanced Castrate-resistant Prostate Cancer

The trial is the first in the country to investigate prostate cancer treatment combining Provenge with two other cancer-fighting drugs, CT-011 and cyclophosphamide, and looks to improve survival rates.

A Pilot study to test the feasibility of the combination of Gemcitabine and anti-PD1 monoclonal antibody (CT-011) in the treatment of resected pancreatic cancer

The treatment combines a standard chemotherapy drug with a monoclonal antibody that may help the immune system fight pancreatic cancer.

A Phase 1 Dose Escalation Study of BMS-982470 (Recombinant Interleukin-21, rIL-21) in Combination with BMS-936558 (Anti-PD-1) in Subjects with Advanced or Metastatic Solid Tumors

This Phase I study investigates the combination and clinical benefits of two cancer drugs in patients with locally advanced or metastatic cancer.

Phase III Study of Rindopepimut/GM-CSF in Patients With Newly Diagnosed Glioblastoma (ACT IV)

This study will investigate the efficacy and safety of an experimental cancer vaccine combined with the current standard in patients with recently diagnosed glioblastoma, a type of brain cancer, who have tumors that express the EGFR protein.

After years of bench and animal studies, the drug founded in a GRU lab is going into clinical trials. While it still may be some years before the treatment could be approved in children (trials typically must first be conducted and proved in adult populations), one of Munn's goals as a pediatric oncologist is to speed this process so that children most in need of these new treatments can benefit.

"We want to be able to enroll more pediatric patients into these early-phase clinical trials," he said. "But what makes this more challenging is that no one center really has enough patients for early-phase clinical trials just in its own center. Our hope is to reach out to several large clinical programs and join our science with their enthusiasm for moving these trials into children."

It's the type of work that could take a lifetime, and said Munn with a smile, "It has. And what's nice too is to have a local university cancer center offering something not invented in New York or elsewhere that trickled to us, but something that we actually invented here."

That is the promise of clinical trials—that the research done today will benefit the patients of tomorrow. For her part, Chavis is optimistic—after all, she's already seen what clinical trials can do: During her initial treatment for colon cancer, Chavis took a drug, now FDA-approved, that Rixe worked on developing earlier in his career.

And for Khleif, who once gave presentations titled "Taking a Shot at Cancer," the exciting recent work in the vaccine field gives him hope that cancer treatments, one day soon, could be as simple as a shot. "I'm proud I stuck to it," said Khleif. "It's great to know now after this many years that this growing field is extremely important and one of the milestones in cancer treatment." ✣

Speedy Sequencing

The GRU Cancer Center is now the only cancer research center in the state that can sequence the entire human genome in 24 hours for about $6,000—thanks to an upgrade in technology that researchers believe will allow them to develop more targeted therapies for cancer. Until very recently, the cost was more than $20,000 to sequence an individual genome.

Cancer researchers used to have to analyze individual genes—often many thousands of them in a process spanning several years—for mutations, scouring certain regions of the genome implicated in specific tumor types, said Lesleyann Hawthorn, a geneticist and Director of Shared Resources at the GRU Cancer Center. But over the past decade, years have morphed to weeks, and now hours, as technology has improved through a push by the scientific community for faster and less-expensive gene sequencing.

"Nationally, since 2001, scientists have been working toward sequencing the human genome within 24 hours and for under $1,000, and we are now approaching that," said Hawthorn, noting that the first draft of the human genome took 13 years and $3 billion to sequence. "As a result, our researchers are now able to work more effectively in identifying specific mutations in hard-to-treat tumors, to help us develop treatments targeted to that particular person and tumor type."

Along with the genome-sequencing upgrade, the GRU Cancer Center can now sequence single exomes—the protein coding part of the genome—on a single run of a new instrument called the MiSeq. All upgrades and new instrumentation were supported through a $2 million grant from the Georgia Research Alliance. ◆