Delivering a one-two punch against cancer

Chemotherapy has been a powerful weapon in the fight against cancer. But too often, it is a shotgun blast against deadly tumors, taking down not only cancer cells, but the patient's healthy cells as well.

However, Dr. Trent Spencer, of the Aflac Cancer Center and Blood Disorders Service of Children's Healthcare of Atlanta, is developing a novel approach to fighting some of the worst childhood cancers – by making immune cells that naturally fight cancer also drug-resistant – and allowing them to survive – and continue to work – even under a chemotherapy assault. Spencer is also an assistant professor of pediatrics at Emory University's School of Medicine.

Spencer's new treatment, which he termed DRI or "drug resistant immunotherapy," could arm medicine with a new and powerful one-two punch against cancer – and already it has shown remarkable results.

"There are so many things that look promising in the pipeline (against cancer), "said Spencer. "This is just one more. I'm not sure we're there yet in terms using the word, 'cure', but there's definitely promise."

Unlike gene therapy, Spencer's method does not genetically alter cells to change the course of cancer development. Instead, he and his team genetically engineer 'immunocomponent cells' to not only attack the cancer, but resist the damage that chemotherapy typically causes.

Chemotherapy often has serious side effects – especially for children. From poor growth to learning disorders to infertility to secondary cancers, the current drugs can have serious consequences. But "if we can bring down the toxicity," Spencer says – by reducing the amount of damage done to healthy cells, "the side effects will also ease."

And most importantly, a two-pronged approach would allow physicians to use chemotherapy, but also have immune cells to fight the cancer as well, said Spencer.

Already in the lab, Spencer found stunning success in live subjects with this new treatment. Using live subjects that have cell lines that mimic an aggressive cancer, he discovered that if the team first used chemotherapy to destroy the growth of the cancer and then use immunotherapy, many of the cancer cells still survived and the live subjects died.

But when Spencer and his team took the approach of concurrent chemotherapy and DRI, the cancer appears to be unable to endure the assault of both the chemotherapy and the strengthened immune cells which target any remaining cancer cells for destruction.

The process was fairly straight-forward. First, the team would grow tumors in mice "relative to a small child's fist" in a human. They would then conduct DRI - and within a week, they were able to see several cases where the tumors shrunk. Within two weeks, the tumors had been reduced to "nothing."

"Consistently, the live subjects have an extended life span," Spencer said. "We don't know if they're 'cured' yet. But we do know it's far more beneficial to do dual treatment."

Spencer hopes to see human clinical trials using DRI in the near future.

Spencer and his team has picked two immune cells to alter and evaluate for study - T-cells and NK92, which have been shown to successfully kill malignant cancer cells and can be bioengineered to be resistant against conventional chemotherapy drugs. "This could be a much more effective treatment of cancer," he said.

But does genetically altering immune cells run the risk of creating hyper-vigilant immune systems? Spencer said early studies say, 'no.'

"We're not trying to rev up the immune system," he said, pointing out that the cells are altered outside of the patient and then re-injected and directed toward the tumor.

The ramifications of such a discovery are encouraging in a field where patients often face poor prognoses against aggressive cancers, such as neuroblastoma, one of the most common cancers among infants, and glioblastoma, the most common brain tumor.

Both of these cancers are known to be difficult to treat, "as reflected in poor survival rates in patients," who have progressed to late stages of the disease, according to Spencer, who's research is funded by CURE Childhood Cancer.

And if DRI proves to be consistently effective, it could work in conjunction with the emerging techniques of gene therapy. "One treatment could be layered with another."

"We're not running on the roof tops shouting that we've cured cancer," Spencer said. "But a lot of people are eagerly working with novel therapies – and it's gratifying to be a part of that."