



*“I’m the  
cancer queen!”*

BRITTA BENINGFIELD  
SURVIVOR

*Photography: Jeremy Peplow*

# A TUMOR'S UNDOING

## *From Within*

### TIL THERAPY RESEARCH AT MOFFITT CANCER CENTER

By Ann Miller Baker

#### WHAT IF THE ULTIMATE CANCER-FIGHTING WEAPON COULD BE FOUND WITHIN A PATIENT'S TUMOR?

Instead of chemotherapy drugs and their collateral damage to healthy cells, this weapon would seek out the tumor where it lives, evade its protective mechanisms and deliver a cancer-killing payload.

Moffitt researchers are leaders in advancing this concept, called TIL therapy, through clinical trials of these personalized cancer killers produced in its own Cell Therapies facility.

Patients like Britta Beningfield are living proof of TIL's potential power.

"I'm the cancer queen!" she laughs. Six years after her initial melanoma diagnosis and treatment at Moffitt, her cancer made an unexpected return in 2012. She was weak, with abdominal pain that was originally attributed to a gallbladder attack. By the time she returned to Moffitt, she required emergency surgery to stop internal bleeding from the metastasized melanoma tumor that had eroded through her stomach and into her pancreas.

Beningfield had also been through radiation therapy at Moffitt

to tame an unrelated cancer in her tonsils in those intervening years. When first told of the melanoma's recurrence, she had plenty of will to fight – but drew the line when it came to more chemotherapy.

"I needed to plan out the rest of my life, and asked – how long do I have? They said - think months, not years," she remembers.

That's when she decided to learn more about a clinical trial mentioned by her Moffitt surgeon, Amod Sarnaik, M.D.

"My only choices were to die or try this new treatment called TIL," she says. "And thank goodness I did it, because I'm still here."

#### MOFFITT HAS HISTORY WITH TIL

Dr. Sarnaik, a surgical oncologist in Moffitt's Department of Cutaneous Oncology, has been the principal investigator on five Moffitt TIL therapy clinical trials. Co-investigator Shari Pilon-Thomas, Ph.D., is an associate member in Moffitt's Immunology Program. Both spent time at the National Cancer Institute (NCI) to learn firsthand about TIL therapy. It was in NCI's Surgery Branch in the 1980's where the concept's use was first explored

for patients with advanced melanoma by Steven Rosenberg, M.D., Ph.D., along with James Mulé, Ph.D., now Moffitt's associate center director for Translational Science.

"Many patients with cancer have immune cells that infiltrate their tumor," explains Dr. Pilon-Thomas. The problem is that cancer finds ways to disarm our immune system - in this case, small white blood cells called lymphocytes that include our T-cell defenders. It's possible to recharge them for the fight by giving potent drugs, but not without serious side effects.

"Instead," notes Dr. Sarnaik, "we can actually reprogram the tumor infiltrating lymphocytes (TIL) outside of the body with drugs, wash all the drugs away and infuse only those TIL cells back into the patient."



Immunologist Shari Pilon-Thomas, Ph.D., and cutaneous surgical oncologist Amod Sarnaik, M.D., are co-investigators for TIL therapy clinical trials at Moffitt.



Photography: Jeremy Peplow

Obtaining the cells begins with surgery to remove some of the patient's tumor. In the lab, tumor tissue is divided into small bits. Each sample is bathed in a mixture complete with high-dose IL-2 (interleukin-2), a naturally-occurring protein that encourages immune cells to grow. As a result, the tumor in each sample dies off, leaving only T cells. A few surviving T cells from each sample are tested to see which react most strongly to the tumor. The best cancer killers are multiplied to be infused back into the patient in massive numbers – “80-billion superheroes,” Beningfield calls them. “I visualized them attacking my cancer.”

There are only five cancer centers nationwide that can generate a patient's own TIL cells. Moffitt is one of them, with a multimillion-dollar Cell Therapies Core on the Moffitt McKinley Outpatient Center campus, made possible in part through generous support from the Dr. Miriam & Sheldon G. Adelson Medical Research Foundation, Donald A. Adam and the Donald A. Adam Family Foundation and Swim Across America.

#### MAKING SPACE FOR SUPERHERO CELLS

While Moffitt was growing Beningfield's “superheroes” in the Cell Therapies lab, she was going through her own preparatory regimen for infusion in early 2013. More chemo – first outpatient, then inpatient. “Not to shrink the tumor,” explains Dr. Sarnaik. “It's in fact to reduce the patient's own immune system temporarily, so that the TIL cells have space to expand when we infuse them.” After infusion, patients are also given the same IL-2 that had been used to encourage immune cell growth in the lab – though at a much lower dose because of its potential side effects in the body.

Beningfield is no stranger to chemo, and knew this treatment would be aggressive. Beyond that, it was hard for Dr. Sarnaik to explain exactly what she might anticipate after the TILs were infused. “One of the challenges of this treatment is that it's highly personalized. So, cells from one patient will biologically behave differently from another.”

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“Some patients will just sail through the treatment without too much in the way of problems. Most patients develop fever. And while their white count is so low, we have to give them powerful antibiotics as a precaution against infection.”

Others, according to Dr. Sarnaik, will develop low blood pressure which can require intensive care. It's one of the reasons these patients are cared for by specially trained nurses and also followed through Moffitt's ICE-T service (see page 7), for immune cell therapy protocols. Beningfield mostly just wanted to sleep throughout the therapy and recovery, but remembers her care team talking about a transfer to ICU. “I just thought about my boyfriend to raise that blood pressure so I didn't have to go,” she says with a chuckle.

The good news, says Dr. Sarnaik, is that most of these side effects are temporary and reversible. But for Beningfield, the best news showed up in abdominal scans. Within three months, these scans showed the cancerous mass on her pancreas was shrinking. One year after TIL therapy, Dr. Sarnaik says, there

was no evidence of disease in Beningfield's body. That's still the case, though she gets scans every six months to be sure.

For now, that means more time for the painting she loves and the garden full of flowers that she tends outside her St. Petersburg home. She credits her Buddhist philosophy of "being happy no matter what" along with the support of her surgeon brother and sister-in-law ("my advocates - much more adept at medical issues") for getting her this far in her cancer journey. She's grateful for Dr. Sarnaik, her nurses and everyone at Moffitt - "my one-stop cancer shop," she says. "If everyone could have access to a facility of Moffitt's caliber, there would be a lot more cancer survivors still walking around in this world."

"There is just no way she would still be here if it hadn't been for TIL therapy," says Dr. Sarnaik. "I just wish it worked that way for everybody. That's my wish."

### EXPANDING TILS USE

Making that wish come true will take more research, more patients like Beningfield willing to enroll in clinical trials, and the funding to conduct them.

While Beningfield's clinical trial of TIL combined with a checkpoint inhibitor drug was funded through an NCI grant called SPORE (Specialized Programs of Research Excellence), other Moffitt TIL trials rely on grants from non-profits including the American Cancer Society and Swim Across America, as well as partnerships with biotech companies like Lion Biotechnologies which is committed to pursuing FDA approval of TIL therapy for wider use (see sidebar).

Dr. Sarnaik calls it the "it takes a village" approach to funding. "You need all these different elements in order to gain access to the resources that are required for something that's incredibly complicated and costly but highly effective." He says Moffitt's experience with TIL for incurable metastatic melanoma shows some degree of tumor shrinkage in half the patients on trials. One in five of all trial patients will maintain that response a year or more.

"We have patients originally deemed incurable who are now seven years post-TIL therapy - some of whom have been rendered free of disease," he says with pride. "We think those patients are, in fact, cured. So now, our efforts are focused on making the process available to more people, making it more effective, and applying it to other cancers - not just melanoma." Moffitt researchers have initiated, published or are in the process of publishing studies of TIL therapy for sarcoma, bladder, cervical, pancreatic and lung cancers.

"I think we've learned enough now from our experience with melanoma that we should be able to translate it into other cancer subtypes," he says with hope. "I like to think that, right now, we've hit a double and we're really looking for a home run."

Many more patients like Britta Beningfield are counting on it.

## ALLYING with BUSINESS For Better Therapies

### *Moffitt And Lion Biotechnologies*

While many of Moffitt's TIL therapy clinical trials are investigator-initiated and government grant/philanthropy-funded, alliances with business leaders in biotech and pharma are an essential element in getting such new therapies to patients.

"There's a track record in this country where academics develop an idea," explains Amod Sarnaik, M.D., surgical oncologist and principal investigator for several Moffitt TIL clinical trials. "But in order to commercialize these emerging therapies, to get FDA approval that makes them available to patients nationwide, you need to have a pharmaceutical or biotech company involved." Moffitt's Office of Innovation and Industry Alliances facilitates these mutually beneficial arrangements.

Among Moffitt's growing list of corporate alliances, Lion Biotechnologies has been instrumental in advancing TIL therapy. The California-based biotech company set up an office in the University of South Florida Research Park to facilitate this relationship. In December 2016, Moffitt's Innovation Office finalized a new three-year Sponsored Research Agreement between Shari Pilon-Thomas, Ph.D., an associate member in Moffitt's Immunology Program, and Lion, as well as a Clinical Grant Agreement that supports ongoing Moffitt trials of TIL therapy in combination with the checkpoint inhibitor nivolumab for patients with metastatic melanoma. Dr. Sarnaik serves as the principal investigator on Lion-sponsored clinical trials.

"We are very pleased to continue our research collaboration with Moffitt," said Maria Fardis, Ph.D., MBA, Lion Biotechnologies' president and chief executive officer, in announcing the agreements to the press. "This is the third study combining TIL plus a checkpoint inhibitor that Lion will have supported."

"This partnership with Lion Biotechnologies will further Moffitt's efforts to lead the way in providing cutting-edge immunotherapies to cancer patients in Florida and beyond," added Moffitt Associate Center Director for Translational Science James Mulé, Ph.D.

"The study's basic goal is to validate the safety, feasibility and effectiveness of a centralized growth strategy for TIL that will allow patients to be treated all over the United States, in areas that don't have access to a state-of-the-art cell therapy facility like we're blessed to have here at Moffitt," said Dr. Sarnaik.