

CHANCE FAVORS THE PREPARED MIND

A conversation with Dr. Peter Forsyth about treating brain cancer patients, advances in virotherapy and an old cash register

Neuroscience, molecular genetics, bioinformatics and epidemiology. Words like these would make most people feel a little intimidated about sitting down with Moffitt Cancer Center's Neuro-Oncology Department Chair who collaborates with some of the brightest minds in the world to understand how and why tumors develop in the central nervous system, as well as what causes their growth and resistance to therapy. But anyone who spends a little time with Dr. Peter Forsyth can easily see that his scientific side is more than matched by his deep sense of compassion. Especially for cancer patients. And so, the intricate words were dismantled pretty easily as he began with a simple story about a woman and her restaurant.

"I went into this because I was interested in diseases, and I thought the brain was cool, because it's so complicated. And then I met a patient whose restaurant was losing money because she worked the cash register. It was a small, family-owned restaurant, and her husband noticed at the end of the day that they were taking in twenty bucks, or thirty bucks or something." He explains how this woman had a tumor in one side of her brain that was making her ignore the left side of the world. Because of this, she wasn't ringing in the dollars on the receipts – she was only ringing in the cents. "It's true. I just thought it was fascinating. That this was a cancer that affected people's lives in such a profound way." The tone was set. While we would certainly be discussing some high-level subject matter, we would really be talking about human beings. And how their everyday lives are affected by a disease that Dr. Forsyth is fighting with a healthy dose of big words and old-fashioned creativity.

Enter virotherapy – treatment that involves attacking tumors with live viruses. Not a new approach, but one that continues to evolve from its earliest days and reveal more possibilities on the horizon. Dr. Forsyth's first experience with viruses and cancer cells came in 1997 when he teamed up with another scientist and conducted an experiment with a naturally occurring virus in an artificial environment. A month later, his partner called with the results: the virus had infected and killed cancer cells while leaving normal cells alone. They then tested it on animals, injecting 30 mice that had brain tumors. In about three weeks, most of the mice were cured and most of the tumors were gone. "They shrank and went away, so it was amazing," Dr. Forsyth recalled. As he described their next experiment he sketched rapidly on a piece of paper, like a student in class whose mind is racing. "The other experiment we did is we took brain tumors. We put one here and we put one over here (pointing to his drawing) and only injected this side, but then the tumor on the other side shrank and went away from a viral infection. So it was really cool because it had a huge effect, it happened very rapidly and it would infect and kill remote cancer cells." This is very important when it comes to brain tumors and their removal with surgery. Because it's not just the tumor you're dealing with, but also all the little tumor cells that spread to other parts of the brain. According to Dr. Forsyth, some viruses can actually go out and infect and kill those remote invasive cells, which are the

ones you can't get to with radiation or chemotherapy. This brings promise, driving further exploration and testing with viruses in the fight against cancer.

Currently Dr. Forsyth and his team are working with the myxoma virus, a relative of poxvirus that was proven to only infect European rabbits. In the 1950s, myxoma was used in Australia as a solution to overpopulation. But to establish that it would only kill the rabbits, it first had to be tested on every other species. And to alleviate public anxiety, the lead investigators actually injected themselves with myxoma to confirm that it was also safe for humans – a move which today would only take place in a Hollywood blockbuster. Hollywood, however, couldn't have scripted Dr. Forsyth's story any better. That's because he's not only working with the world's expert on myxoma, but also because this expert is his good friend and fellow Canadian, Dr. Grant McFadden, who happens to be just up Interstate 75 in Gainesville. Along with Dr. McFadden, Dr. Forsyth is working on different ways to modify the myxoma virus. Because this virus has been mostly sequenced, it has a skeleton that you can add to and subtract from. This makes it possible to attack cancer cells with many different forms of it. But in order to have success, Dr. Forsyth says you have to be collaborating with others who think about things from different angles. "It's a teamwork thing. You need to be in a place where you're part of a team and ready to make discoveries. And to do something. Chance favors the prepared mind."

It's hard not to get excited hearing Dr. Forsyth talk about his work with virotherapy as well as advances others are making. But as we shifted gears from mice to humans, it became clear that the excitement around use of viruses in treating cancer must be matched with the right levels of responsibility, patience and humility. "The challenge for us is, it's easy to make discoveries in the lab and easy to make discoveries in animals. But it takes a while to get through the regulatory protections to make sure the kinds of things you want to do are safe." According to Dr. Forsyth, having passionate people working too quickly and doing things unsafely can hurt everybody – not the least of which is patients. When it comes to being passionate, his work clearly speaks for itself. And as for describing his concern for patients, mere words simply fall flat. During this interview, the photographer struck up a conversation with Dr. Forsyth – nothing intended but to lighten the mood and create a relaxing atmosphere for nice pictures. "Brain cancer," responded Dr. Forsyth when asked what he specifically treats. That's when the photographer revealed he has a family member recovering from brain tumor surgery. And that's when the rest of Dr. Forsyth's world disappeared. Suddenly there were no pictures being taken, no crew walking around with equipment, no tape recorders, no schedule to keep and no story. All that was left was two men. One describing someone's battle with cancer and the other hanging on every word.

While one of Dr. Forsyth's patients who was treated with a virus in 2003 is still alive and well today, many others have not experienced this success. Yet he doesn't view this as some people might. Because to him it's not just about numbers. "If you're treating fifteen patients and the tumor shrinks in three people, and you think like a statistician, what does that matter? Nothing. But if you think like a person or a scientist, it's different. Hold on, these people are

still living five and seven years later. Like this one (referring to his patient). He's telling me something, right? So we need to listen to him. What is it? Why did it work for him and not someone else? And focus on that. Medicine is not statistical, you know? It's personal. Everybody matters." When it comes to cancer itself, however, Dr. Forsyth has a little less compassion. He views the normalcy of the disease almost as an epidemic itself, and wants to change that. "We've accepted cancer as a society, because we're not surprised by it anymore. We need to start saying no." Then, in the same manner as when he began the interview, he shared a personal story.

"When I was a medical student in Canada I was walking to one of my classes. And there were all these huge, old buildings. There was a thousand-bed rehab center just empty and decaying, so it was obviously from the turn of the previous century. I met my mentor and asked him about it. I told him it was really creepy and looked like a Stephen King set or something. And he said, 'Oh, it's a TB sanatorium.' And I was like, 'Really? Well, what's TB?' He said, 'You don't know what TB is?'" Dr. Forsyth paused for a moment, his passion settling into quiet confidence and reflection. "We have to make cancer like TB, so that our kids don't know what it is."