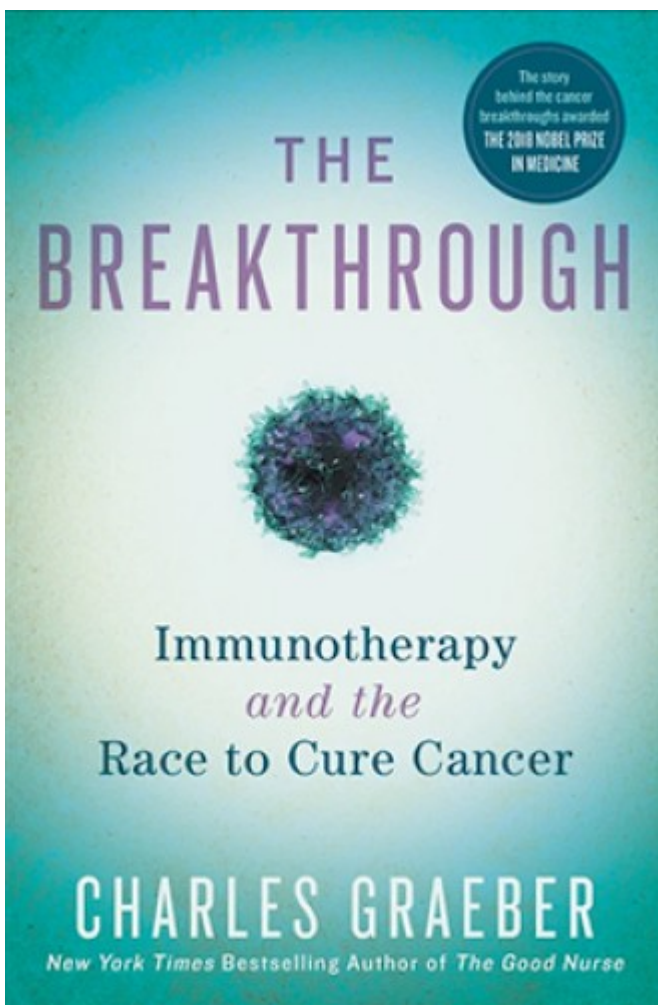


Immunotherapy's believers and skeptics

Some scientists couldn't quite explain what they were seeing. Others literally couldn't believe it.

by [Kristel Clayville](#) in the [April 24, 2019](#) issue

In Review



The Breakthrough

Immunotherapy and the Race to Cure Cancer

By Charles Graeber

Twelve

Climate science is not the only science where *believe* has become an important verb in public debates about the data. As a chaplain for a transplant team, I often heard medical professionals utter the phrase “believe in transplant,” as if the science of replacing human organs required belief in order to work. The funny thing is, belief just might be required—not to make the science work but to get the research off the ground.

Charles Graeber picks up on this observation in his book on the history of immunotherapy. As he describes the interwoven drama of patients, cancer researchers, immunologists, pharmaceutical companies, and the Food and Drug Administration, he finds that belief is the dominant reason immunotherapy treatments for cancer have begun to hit the market. But any well-told story of belief contains its opposite as well, and Graeber also shows how much of the struggle to bring immunotherapy to cancer treatment has been due to disbelief that gained the authority of scientific fact.

Graeber’s story of belief in medical research begins with one of the orienting questions of cancer research: Why doesn’t the immune system fight cancer? To give this question context, Graeber gives us a brief history of the research on the immune system. The attempt to understand the immune system was organized around what can only be called a philosophical inquiry: Where do we end and where does the cancer begin? Rather than looking for specific physical borders between “cancer” and “us,” the question is more about recognition. One theory is that the immune system doesn’t fight cancer because it can’t distinguish it from the rest of us. We and our cancers are too similar to trigger an immune system response.

But of course, the immune system can learn. That is the theory (now proven) behind vaccinations. The immune system can learn to recognize viruses and can then fight them off. But can the immune system learn to recognize cancer cells as “not us”? The believers whose stories form the through line of Graeber’s narrative think it can. The naysayers think it can’t.

The naysayers have evidence on their side, and it was peer reviewed. An influential 1975 article on immunotherapy and cancer showed that in mice the immune system did not recognize cancer.

The believers had evidence too, but it was in the form of anecdotes, and mostly with human patients. These anecdotes included patients getting better and fighting off cancer once their immune systems were trained to recognize it. Such stories included tumors melting away, a decrease in tumors in an area, and what seemed like spontaneous remissions. Stories aren't data, but they can create data.

The believers could not explain exactly why their patients were getting better, but they believed what their eyes had seen. In that way, the patients' stories did create data: those scientists and medical professionals who believed what they saw continued to seek out evidence that would meet the standards of the naysayers.

One of the most compelling moments of the book comes when physician and researcher Bob Schreiber describes a lab meeting at which he presented evidence from an experiment that he had finished. The findings: animals with suppressed immune systems developed more tumors more rapidly than animals with normal immune systems. His colleagues responded that "cancer cells are too close to normal cells to be recognized as non-self," arguing that cancer cells "are not subject to immune notice." In short, they responded with their previous beliefs about how the immune system works; they did not think Schreiber's data challenged their previously held beliefs. It was as if he had no data. His colleagues simply didn't believe that the immune system could recognize the tumor, and no amount of data could change their minds.

The believers, like Schreiber, redoubled their efforts, sought out more data, ran more experiments, and developed a more nuanced picture of how the immune system works. This nuanced picture was enough to get their first drug into clinical trials.

However, those trials were designed to capture short-term results. The cancer immunotherapy drug worked on a different time scale and with different evidence of success. Previous cancer drugs had to show improvement in tumor size on medical imaging, while the immunotherapy approach relied on patient feedback in the short term. Patients reported feeling better and being able to do more, though their initial imaging looked worse. In order to demonstrate the power of immunotherapy for cancer, the FDA would have to design a new kind of clinical trial, one that took into account patients' reports early in treatment and their alignment with imaging much later in the treatment.

The history of cancer immunotherapy is still unfolding. Graeber notes that immunotherapy is a “science built on stories.” He tells these stories in a way that honors the complexity of the roles of belief and evidence in medical and scientific research. His narrative encourages us to imagine what we could achieve if we were willing to believe more patient stories and incorporate the messiness of human life into the research process.