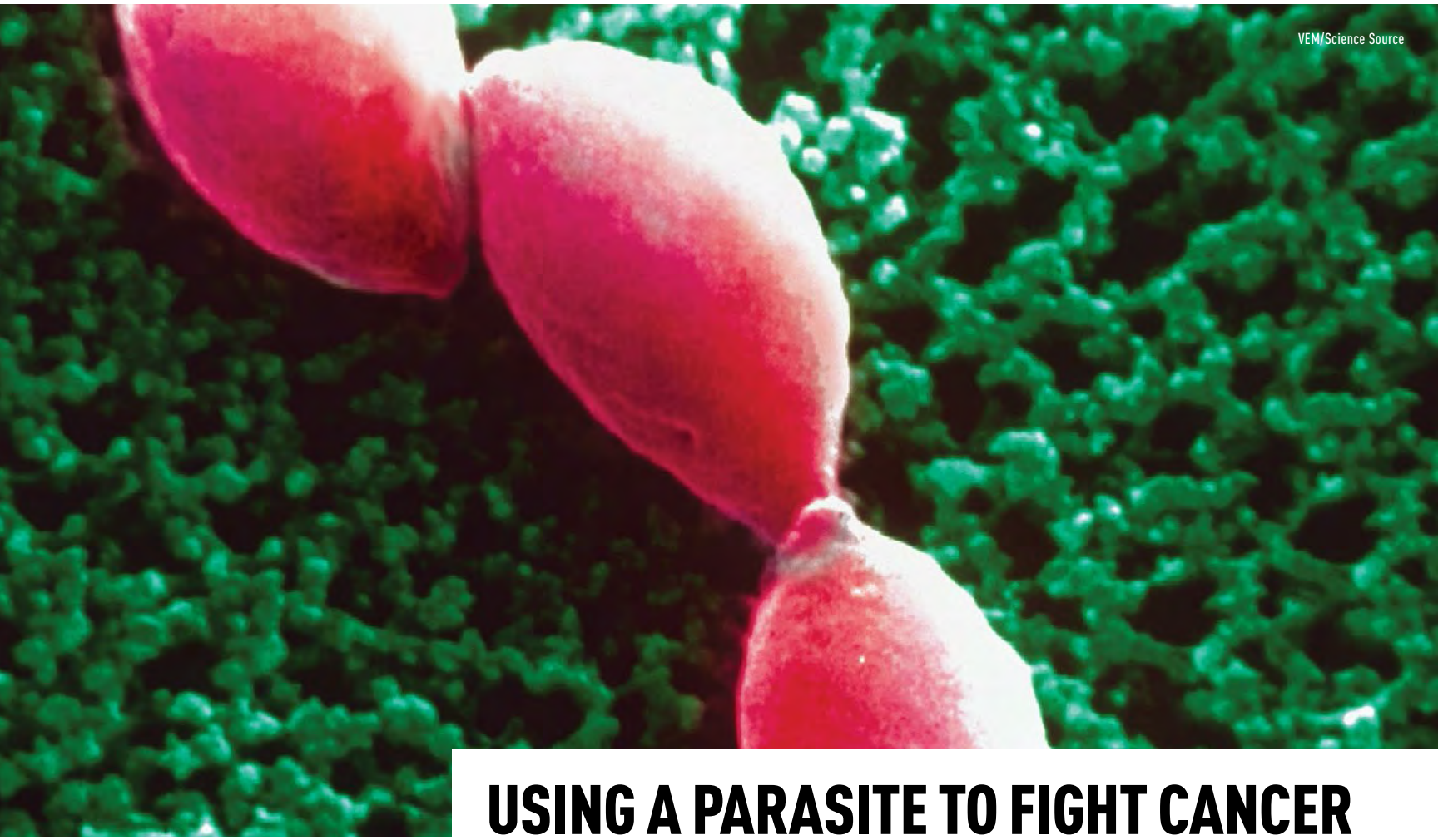

VEM/Science Source

Toxoplasma Gondii, the parasite that causes toxoplasmosis, is being used by Geisel researchers as a possible way to stimulate the immune system against tumors.

USING A PARASITE TO FIGHT CANCER

THE IDEA OF USING THE BODY'S IMMUNE SYSTEM TO FIGHT CANCER is not a new one, but researchers are just now beginning to see the fruits of this idea in the lab—and hopefully soon in the clinic. "As tumor immunologists, we recognize that there is a revolution underway," says Steven Fiering, an immunologist at Geisel. "Historically, there have been three main approaches to treating cancer: radiation, surgery, and chemotherapy. Immunotherapy is becoming the fourth leg."

In a recent study published in the *Journal of Immunology*, Fiering and his colleagues used a weakened strain of *Toxoplasma gondii*, a parasitic protozoan responsible for the disease toxoplasmosis, as an adjuvant to increase the effectiveness of a melanoma tumor vaccine made from the patient's own tumor. The strain of *Toxoplasma gondii* used was developed by David Bzik, a Geisel immunologist. Like normal *Toxoplasma gondii*, this strain entered human cells and stimulated a strong immune response, but it was unable to replicate once inside the human body and, after about a week, the individual cysts either died on their own or were eliminated by the immune system.

Toxoplasma gondii is a particularly effective adjuvant because it stimulates a cell-mediated cytotoxic immune response that targets only infected cells. "It's the very type of response you want to get against tumor cells," says Fiering. It triggers the release of interferon gamma from the cells around it, which then make a cytokine called IL-12 at very high levels. Those two immune system cytokines are the key signature of the anti-tumor immune response, says Fiering. "That's the idea; we're going to stimulate the right type of immune response, and since it's already in the tumor, the response also happens to the tumor itself."

Fiering says it's possible the approach they used in the lab could be used directly in the clinic for melanoma. If a tumor recurs after it has been removed surgically it can be very

OVERHEARD

"I'm in awe of this community."

—MARK ISRAEL, MD, DIRECTOR OF THE NORRIS COTTON CANCER CENTER, QUOTED IN THE *VALLEY NEWS* AFTER THE 2013 PROUTY, WHICH THIS YEAR RAISED $2.6 MILLION FOR CANCER RESEARCH

difficult to eradicate. "Our idea would be, instead of surgically removing the tumor, to inject an immunostimulatory set of agents, one of which could be the *Toxoplasma gondii* strain, thus stimulating the immune system to attack the tumor," Fiering says.

The team also published a study using a similar approach with *Toxoplasma gondii* in ovarian cancer. But Fiering says they're a little further away from taking that to the clinic, because the current treatment for ovarian cancer is to surgically debulk the tumor, removing as much as possible, and then using chemotherapy. This usually results in a remission for one to two years, at which point the tumor often recurs but is much more difficult to treat with chemotherapy. Fiering and his colleagues are working on approaches that could perhaps take the tumor at the time of surgery and make it into a tumor vaccine, adding the *Toxoplasma gondii* to help

"IT'S THE VERY TYPE OF RESPONSE YOU WANT TO GET AGAINST TUMOR CELLS."

stimulate the immune system to attack the tumor when it shows up again. This is a very personalized approach, because it uses each individual's tumor cells, and thus it is less convenient than a drug that can be used off the shelf. However, says Fiering, it's a promising possibility because it can work very powerfully against tumors.

"Everything in the immune system is in a balance," says Fiering. "If we can upset the balance in the tumor that is immunosuppressive and make it immunostimulatory—once that release has happened, system-wide immunity can develop. We get a response in the lymph nodes and throughout the system."

LAUREN ARCURI WARE

Barbara Kinney/Clinton Foundation

REBUILDING IN RWANDA

In August, Bill Clinton and Chelsea Clinton visited Rwanda to see the progress made by the Human Resources for Health (HRH) program in Rwanda. Geisel is one of eight medical schools involved in the HRH program, which is helping to improve health and health care in Rwanda by training physicians and rebuilding the nation's medical education system. Above, Chelsea Clinton and Agnes Binagwaho (Rwanda's minister of health and a Geisel faculty member) visit with a young patient at a hospital in Kigali.

OVERHEARD

There are a lot of American men. Some are grumpy. Some are tired. Some may not even be interested in sex at the moment. And all of them are aging. This is the intended audience for the Low T campaign. Whether the campaign is motivated by a sincere desire to help men or simply by greed, we should recognize it for what it is: a mass, uncontrolled experiment that invites men to expose themselves to the harms of a treatment unlikely to fix problems that may be wholly unrelated to testosterone levels.

—LISA SCHWARTZ, MD, AND STEVEN WOLOSHIN, MD, WRITING IN *JAMA*