PROFILE: OLIVERA FINN

Directing a Life in Science

After forgoing theater ambitions, and despite early marriage and motherhood, Olivera Finn has risen through immunology's ranks thanks to her work on cancer vaccines

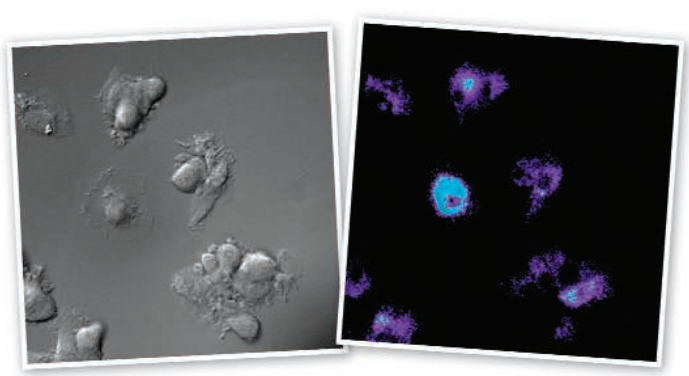
Take a look at Olivera "Olja" Finn's life, and you can tick off the actions women are supposed to avoid if they want to advance in science. Get married fresh out of high school. Check. Interrupt your education for your husband's sake. Check. Allow his career to take precedence over yours. Check. Have children before you have a job and give birth at what seem like inopportune times, such as shortly before you start graduate school. Check.

Yet Finn has, with great success, pursued career and family goals simultaneously. She celebrated her 40th wedding anniversary last month, has raised a daughter and a son, and, at the age of 59, already has grandchildren. Professionally, Finn has prospered. Nearly 20 years ago, she discovered the first cancer antigen, a tumor molecule that elicits a reaction from immune cells. And despite spending her youth in Communist-run Yugoslavia, Finn has climbed the academic ladder in the United States—she is chair of immunology at the University of Pittsburgh in Pennsylvania and has served as president of the American Association of Immunologists. She argues that interweaving career and family is essential. "I don't think we live long enough to do things sequentially."

Colleagues laud her work in cancer immunotherapy, the goal of which is to enlist the immune system to combat tumors. In an extension of her tumor antigen discovery, Finn's group is gearing up to test a vaccine to prevent benign colon growths from spawning deadly cancers. Her effort is rare in that most cancer "vaccines" are not preventive; they're designed to treat serious tumors. The few preventive cancer vaccines approved for use target tumor-causing pathogens such as the hepatitis B and human papilloma viruses rather than growths themselves, as Finn's vaccine does.

"The field has advanced faster because of her," says Martin Cheever, a medical oncologist at the Fred Hutchinson Cancer Research Center in Seattle, Washington. Finn deserves credit not only for her scientific insights, he adds, but also for her devotion to nurturing other scientists' research and fostering cross-disciplinary collaborations. Without such prompting, "cancer biologists and immunologists [usually] sit on their own sides of the fence," notes immunologist Ralph Steinman of Rockefeller University in New York City.

The courage, tenacity, and independent-mindedness Finn needed to start anew in a strange country also characterize her science, says Paola Castagnoli, scientific director of the Singapore Immunology Network and Finn's friend since the late 1970s. Finn is currently exploring the provocative idea that infections throughout life, including chickenpox and other childhood diseases, prime our defenses against cancer. "She is a very good scientist because scientists should not be conformists," says Castagnoli.



Ready to rumble. Activated dendritic cells light up after exposure to the cancer antigen MUC1.

CREDITS (TOP TO BOTTOM): RON FONTANA; OLJA FINN

The accidental scientist

Growing up in what was then Yugoslavia, Finn aspired to direct plays. But she strayed from the script once she met Seth Finn, an American college student on a foreign exchange program. Over her parents' objections, the couple married and moved to the United States. She'd been studying English since age 7, so language wasn't a barrier. What shocked her, she says, was Americans' ignorance of foreign affairs, obsession with money, and willingness to make long-haul commutes.

After briefly attending college in California and Indiana, she ended up in Puerto Rico, where her husband was serving in the Coast Guard. At the urging of her father, a theater manager with geology and biology degrees, Finn had followed the technical track at her Yugoslavian high school. In Puerto Rico, her scientific ambition blossomed. For an undergraduate project at the Interamerican University in San Juan, where she completed her bachelor's degree in biology, Finn figured out missing steps in the life cycle of a hookworm that circulates among humans, birds, rats, and cockroaches. The work involved poking around seedy areas of downtown San Juan and picking up roaches as big as a tablespoon, but she loved it. "The life of research—getting data and making hypotheses—consumed me," she says.

After finishing a Ph.D. and a postdoc at Stanford University in Palo Alto, California, Finn set up her own lab at Duke University in Durham, North Carolina. She chose Duke because Seth, who

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by that point had earned a Ph.D. in communications from Stanford, had landed a position at the nearby University of North Carolina, Chapel Hill. When she arrived at Duke in 1982, it was a hotbed of transplant immunology research, and she focused on identifying what triggers the rejection of donated organs. Her group reared T cells extracted from patients who'd received kidney transplants and nailed down which of the donor's antigens, or molecular markers, provoked the cells to attack. Although hundreds of molecules could potentially prompt a rejection response, typically only one or two antigens did, her team discovered.

That success spurred Finn to ask whether the same techniques might shed light on cancer–immune system interactions. Scientists had known since the 1950s that cancer cells can rouse the immune system. In fact, a debate has raged since then about whether the immune system thwarts many incipient cancers, or whether the immune response is too feeble to curb most abnormal growths. However, in the early days of this debate, scientists didn't even know what antigens on tumors trigger an alarm.

In the mid-1980s, Finn decided to track down these telltale tags. Looking back, the decision to shift to tumor immunology was naïve, Finn says. The lab's skill in identifying rejection antigens "gave us a confidence that was exaggerated." Finding cancer antigens turned out to be much tougher. For one thing, whereas a transplanted organ riles the immune system, tumor cells elicit a much weaker response.

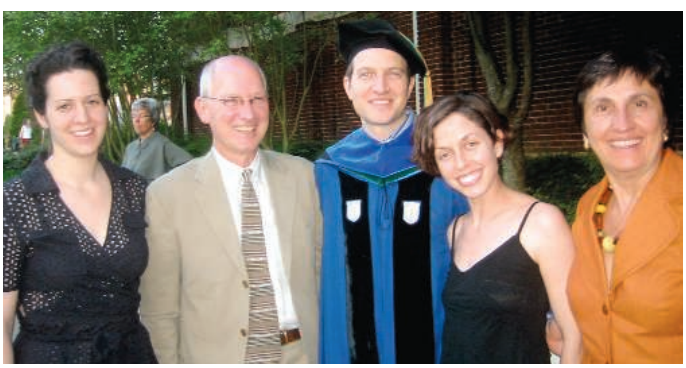
Weak, yes, but not undetectable, and by 1989 Finn's lab had nabbed the first cancer antigen, a protein called MUC1 that protrudes from pancreatic and breast tumor cells. Human T cells keyed on this antigen, her team reported.

MUC1 also decorates normal cells in several organs, so why don't T cells pounce on those tissues? The answer came in work Finn continued after moving to the University of Pittsburgh in 1991. Normal MUC1 is festooned with carbohydrate chains, which are nearly absent from the protein fashioned by cancer cells. The pattern is clear, Finn says. Tumor antigens usually differ from their normal counterparts in some way, such as structure, quantity, or cellular location. For cyclin B1, which helps propel cells through mitosis, quantity explains why it can act as a tumor antigen. In normal cells, the amount of cyclin B1 remains low except for a spike at the beginning of mitosis. Yet cancer cells churn out the protein nonstop. MUC1, cyclin B1, and the like are not "self" antigens but "abnormal self" antigens, Finn says.

Family time

As Finn talks about her life, you don't hear any regrets—she clearly doesn't regard her early marriage and motherhood as youthful indiscretions. Finn, who started graduate school at Stanford with a 7-month-old son to tend, encourages women at the same stage of their careers to have children. If you think you'll have more time for parenting later in life, you are wrong, she says.

Carrie Miceli, who was Finn's first graduate student and is now an immunologist at the University of California, Los Angeles, says she followed Finn's example, although she waited until starting her own lab to have a child. "It was great to see a woman with kids and a family who was not talking about what a compromise it was," says Miceli.



The next generation. Finn with her daughter Sonja (*left*), husband, Seth, son Sasha, and daughter-in-law Carey Storan.

Finn and her husband took turns going for advancement. After Seth's job led them to North Carolina, the choice to move to Pittsburgh was hers. For 4 years, Seth commuted every week between Pennsylvania and North Carolina before being hired by Robert Morris University in Pittsburgh.

The cancer shot

For more than a decade, Finn has worked to package the tumor antigen she discovered into a vaccine that would prevent cancer. Her group conducted initial safety trials of a MUC1-containing vaccine, using patients with advanced pancreatic cancer. In 2005, for instance, the researchers reported that the vaccine produced no obvious side effects—and also seemed to promote an immune response to MUC1 in some recipients. Yet the U.S. Food and Drug Administration (FDA) balked at her proposal to test the vaccine in healthy people, she says, partly because of the fear that it would trigger autoimmunity, an immune assault on normal tissue.

Now she's finally getting a chance. This summer, her group will launch a 5-year trial to determine whether injections containing abnormal MUC1 can prevent recurrence of intestinal adenomas. Surgeons usually remove these benign growths because they can morph into colon tumors. However, adenomas often sprout again after the operation. The study's control group will be historical: past patients who were operated on by the same doctors. Finn concedes that even this trial isn't ideal. The researchers are testing the vaccine's ability to prevent adenoma regrowth, not its ability to fend off cancer in healthy people. Moreover, the patients will be elderly, and the response to vaccines dwindles with age.

Age's affect on immunity also figures into an idea that has captured Finn's interest. Work by her group and other labs suggests that many of us receive "natural" vaccinations against cancer from an unexpected source: pathogens. A variety of body invaders, including those that cause childhood diseases, spur the production of the same abnormal self antigens as cancer cells. The chickenpox virus, for instance, sparks an explosion in cyclin B1. The mumps virus prompts cells to display denuded MUC1. Getting sick in our youth, when our immune systems are primed to make the memory cells that can confer lifelong immunity, might spare us from cancer later on, Finn proposes.

To test the idea, Finn teamed up with epidemiologist Daniel Cramer of Brigham and Women's Hospital in Boston and colleagues. They found that women who'd undergone events that can lead to infections or inflammation—including intrauterine device use, pelvic surgery, and broken bones—were more likely to carry antibodies to MUC1, a sign of an immune response. These women also had a lower risk of developing ovarian cancer, the researchers reported in 2005.

In a life full of challenging career moves, Finn is pondering her next and last. She says she would like to work at FDA to help pave the way for preventive cancer vaccines. "People used to say it would take 10 years to evaluate [these] vaccines, but it's been 10 years and we are still discussing how it will take 10 years." As in her family life, Finn is not inclined to wait.

–MITCH LESLIE

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