

Irving Weissman

Irving Weissman is not afraid to wade into the murky waters of stem cell politics. Whether he's in the lab or knee-deep in the Missouri river, he has always had a knack for hooking the big one.

Irving Weissman may be most famous for his pioneering research and advocacy on stem cells. But among friends, 'Irv', as he is affectionately called, is considered a 'renaissance woodsman' and his weakness for fishing is the stuff of legend.

"One time we were at a black-tie dinner in New York City, which ended at about 11 p.m.," recalls Frederick Alt, a cancer geneticist at Harvard University and Weissman's friend. "We rented a car, drove all night to Boston, slept ten minutes when we arrived, and then went fishing right away," Alt says. Later, Weissman gave a talk, met other researchers, then went fishing again that night.

Weissman has had considerable luck reeling in scientific discoveries. In 1987, he isolated the first bone marrow-derived stem cells from mice and, soon after, identified human hematopoietic stem cells. "He had to have tremendous confidence and energy to tackle a problem of that magnitude," says former student Owen Witte, who is now a professor of microbiology and molecular genetics at the University of California in Los Angeles. "Everyone knew that hematopoietic stem cells existed, but no one knew how to find them," Witte says. "Only Irv had the confidence, persistence and thoughtfulness to do it."

Weissman runs one large research laboratory at Stanford University, another at Hopkins Marine Station, and has founded three companies. His research and advocacy often take him away from home, but when he is in California, he makes sure he reads Harry Potter every night to his 10-year-old daughter. How does he find the time to juggle all his responsibilities? "I prioritize ... and I don't always deal with all this," he says, pointing to the piles of manuscripts, paperwork and journals stacked from floor to ceiling in his office—so much so that it is hard to close the door.

With such a busy mentor, people in Weissman's lab have to be independent, notes former student Sean Morrison, who is now an assistant professor in cell and developmental biology at the University of Michigan. Still, the spirit in Weissman's lab is "fun," without the highly competitive atmosphere of most high-powered groups, students say. "Irv is very generous to the people in his lab, he'll bend over backward for them," Morrison says.

Growing up in Montana, Weissman had an early start at both fishing and science. At age 16, inspired by Paul de Kruif's *Microbe Hunters*, he joined the laboratory of a local pathologist. He spent the next few summers helping with experiments in transplantation immunology. By the time he was 18, he had coauthored two papers. "I was engrossed in the subject," Weissman says. "I never thought I'd be a hard worker, but science was interesting and fun—by that point, my path had become clear."

Within the scientific community, Weissman is known for his resolute stance against stem cell plasticity—the idea that stem cell lineages are not rigidly defined and the cells can de- and transdifferentiate into many different tissues (*Nat. Med.* 10, 445–446; 2004). The concept has been used by opponents of embryonic stem cell research to make the case that adult stem cells are sufficient for research and therapeutic purposes.

"We were excited when we heard it reported that hematopoietic stem cells could transdifferentiate into heart, brain and muscle," Weissman says. But despite many attempts, he says, his lab has not been able to reproduce those results.

There are alternative explanations for many of these observations, Weissman adds, and he cautions against the movement to test these approaches in the clinic (*Cell* 116, 639–648; 2004). "It's very easy for biologists to come up with a phenomenon that looks exciting, but you can't believe it until it is repeated," he says.

Some in the field say Weissman has campaigned adamantly against stem cell plasticity because it contradicts his model of stem cell lineages. But others note that Weissman is a rigorous scientist and dedicates enormous resources to repeating experiments.

"Irv can be aggressive about trying to correct the scientific record," says Morrison. "In cases where people publish a high-profile paper that doesn't hold up, he takes it upon himself, as a leader in the field, to set the field straight ... he's also not shy about telling people that they're wrong."

Even outside the scientific community, Weissman is not afraid to court controversy. As director of Stanford's Cancer/Stem Cell Biology and Medicine Institute, he is helping raise the estimated \$120 million needed to complete the institute. But in January 2003, he created a stir when he announced that the institute's researchers would create new human embryonic stem cell lines through nuclear transfer (*Nat. Med.* 9, 156–157; 2003). The US government does not allow federal funds to be used for such experiments and the Senate is considering an outright ban of the procedure.

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Kris Novak

Weissman says much of the dispute over nuclear transfer—also called therapeutic cloning—stems from misunderstanding. "Once you clearly explain the research to people, they understand the potential," he says. "It's amazing how many people have never heard a clear explanation of the science." Weissman frequently travels to Washington, DC to educate politicians on stem cell research, but laments that most politicians give him only five minutes to make his case.

This is not the first time Weissman has challenged the government. In the 1960s, he placed advertisements in national newspapers and organized a protest against the role of physicians in the Vietnam war. "I was saying that, as MDs, we couldn't practice in the military and still be true to our oath to make any patient our first priority, ignoring politics, religion, etc.," he says. As a result, he says, the US National Institutes of Health denied him a position he had been previously offered. "I almost moved to Canada after I got my MD," he says.

These days, Weissman is championing a \$3 billion California state ballot initiative to fund stem cell research. In 2001, the Bush administration restricted federal funding for stem cell research to a small number of available cell lines. If the ballot initiative is successful, California would become the first state to fund stem cell research. "One thing you can say about Irv is that he's fearless," says Morrison. "If it's important, he wants to work on it."

Kris Novak, San Francisco