'A Community of Scholars'

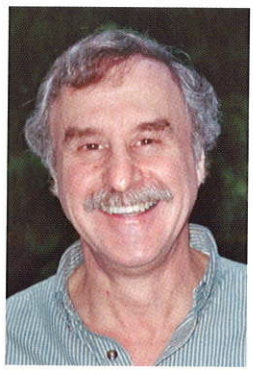
Steven Henikoff has been a member of the Fred Hutchinson Cancer Research Center for nearly 30 years. When it comes to trainees, his lab is as much a study in independence as it is in nucleosome dynamics. *By Meredith W. Salisbury*

If Steven Henikoff has thought seriously about leaving the Fred Hutchinson Cancer Research Center since he started working there in 1981, there's no sign of it today. "I found the Hutch right from the start to be the ideal place to do what I want to do," he says. "There's never been an incentive to change." He's serious: Henikoff, who has a joint appointment at the University of Washington, has never so much as taken a sabbatical since he joined.

But why should he? Henikoff has made a stellar reputation for his lab — as much for the science performed there as for the credit he gives to the people who join him as grad students or postdocs and the opportunities that open up to them as Henikoff alums.

The lab's focus includes epigenomics — including histone variants and DNA methylation — and centromeric chromatin. His lab has also been the birthplace of tools essential to the community, such as TILLING (or targeting induced local lesions in genomes), a large-scale approach to reverse genetics that relies on mutagenizing whole populations and then screening them for mutations. The approach was invented in Henikoff's lab years ago, and while it's no longer part of his research, his team still supports it "as a service for various organisms."

In a recent project, Henikoff's team helped tease apart the mystery of the centromere, such as how it's maintained "despite the fact that sequence doesn't seem to matter," he says. In work just published in *Cell*, Henikoff and postdoc Takehito Furuyama discovered that, while all nucleosomes wrap DNA in the same direction, the nucleosomes in centromeres actually wrap it in reverse. "It has some really profound implications," Henikoff says. "All the interaction surfaces that are holding together that nucleosome are facing away from each other." The idea that comes out of this finding is that it's the wrapping pattern that's causing the centromere to be so different from the rest of the chromosome.



STEVEN HENIKOFF

Independent minds

Henikoff says it was the practice of his PhD advisor, Matt Meselson at Harvard, that showed him how important it was to let students carve out their own paths. "He gave us a lot of independence," Henikoff says of his days studying *Drosophila* RNA in the late '70s. "I felt that that was great training to be self-reliant."

In his own lab, Henikoff makes clear the benefits of interacting with colleagues while emphasizing the need to establish one's own projects. "I try to make the lab more a community of independent scholars," he says. "I don't encourage at all team research." Genomics as a field lends itself to the concept of team research, he says, but he believes a better approach is to encourage collaborations while ensuring that each scientist is responsible for and invested in his or her own projects. "I think that's the best training," he says. "After you leave your postdoc, you're going to be out there on your own" and he wants to make sure his trainees leave the lab equipped to stand on their own feet. To that end, Henikoff avoids any impulse to micromanage. "I'm not going to look over anyone's shoulder," he says.

Another element of the Henikoff philosophy is to empower researchers by reminding them not to rely on the tools at hand. Over the years, the lab has released a number of tools that became commonly used by the community, and the reason for that is Henikoff's refusal to be constrained by what's available. If a scientist in his lab wants to do an experiment but the tools don't exist to perform it, Henikoff likes to see that person delve into building the necessary tools rather than abandon the research path in favor of something that's more in line with existing technologies.

>NAMING NAMES

Just since 2000, the Henikoff lab has been home to some 25 trainees. Here are just a few of the students and postdocs who have earned their stripes there.

TAKEHITO FURUYAMA

A current postdoc with Henikoff, Furuyama recently published a paper in *Cell* demonstrating a finding that the PI calls "the most exciting thing we've ever done" — that is, evidence that nucleosomes in the centromere wrap DNA in the opposite way that all other nucleosomes do. "We basically think that it's the wrapping of the DNA that is responsible for all the differences that we see" in how centromeres behave and function, Henikoff says.

HARMIT MALIK

Now the PI of his own lab at the Hutch, Malik did his postdoc with Henikoff from 1999 to 2003. His focus has been studying evolutionary signatures of genetic conflict, Henikoff says, adding, "I learned more from him than he learned from me, that's for sure." Malik was awarded a Presidential Early Career Award for Scientists and Engineers by President Barack Obama this year.

CLAIRE MCCALLUM

McCallum was the brain behind TILLING, the tool that has become synonymous with Henikoff's lab in the time since her graduate work there from 1996 to 2002. Her quest for the mutation of a known gene helped launch the method of mutagenizing all genes and screening them; it also led to a company she launched, which is now part of Arcadia Biosciences. The original TILLING work "led to a very nice study, a nice story, a nice publication," Henikoff says.

PAULINE NG

During her years as a graduate student in Henikoff's lab, Ng came up with the idea that deleterious nonsynonymous changes in protein sequence could be predicted based on evolutionary information. That work led to an algorithm called SIFT. After leaving the lab, Ng worked at Illumina and is now a senior scientist in genomic medicine at the J. Craig Venter Institute.

BAS VAN STEENSEL

Van Steensel, a postdoc with Henikoff from 1998 to 2000, helped get the lab into genome-wide profiling, Henikoff says. After his time at the Hutch, van Steensel went on to the Netherlands Cancer Institute, where he heads up his own lab.