



## A Protozoan Pays Off

C. David Allis, Ph.D.

Joy and Jack Fishman Professor, Laboratory of Chromatin Biology, The Rockefeller University, New York, NY

I always thought I'd go to medical school. But then my professor at the University of Cincinnati, Steven Keller, suggested that I try working in a real lab. Michael Bharier at the University of Cincinnati Medical School took me under his wing. It was the right place, right time, and perhaps the right mix of personalities.

My assigned project required me to go into a cold room and do some real biochemistry on a purification project. I set up these chromatographic columns and fractionated an extract. I didn't expect it to work, but remarkably, it did in a big way. It seemed like something alive, with a personality, had come off the column, and that was my "lightbulb moment" when I decided to pursue a career in science.

I did my Ph.D. work with Anthony Mahowald at Indiana University and my postdoc with Martin Gorovsky at the University of Rochester. I studied development in *Drosophila* for my Ph.D. work and then, to some people's dismay, during my postdoc. I switched to an even simpler model, the single-celled organism *Tetrahymena*, a protozoan. There were a lot of people who said, don't waste your time—study an "important" cell. But the protozoan model was perfect for studying chromatin, which is what I continue to study today. *Tetrahymena* lent itself to finding answers better, more quickly, and more efficiently than other models, so it ended up being a smart choice. We probably couldn't have made some of the big discoveries that our lab is best known for with many other organisms. I've spent quite a chunk of my career studying chromatin. For more than 20 years, we made a very dedicated emotional, intellectual, and thankfully, a National Institutes of Health (NIH)-funded commitment to finding an enzyme that modified histones in a particular way. When a graduate student in my lab, Jim Brownell, came to me and said he really wanted to make that enzyme his thesis goal, I was nervous. I knew it could be a real dead end if he

didn't get it. It was one of those awful projects that didn't have a safety net. If you got it, you were famous, but if you didn't, it was kind of like "game over."

I'll never forget the moment when Jim bounced down the hallway with a piece of X-ray film that proved that we had the enzyme, a histone acetyltransferase (HAT). Jim was normally not a super-excitable kind of guy, at least on the outside, and here he was skipping and dancing. He had taken on this gutsy project and made it happen. It was a defining moment for our lab and a turning point for the field. This happened in 1996, and the field hasn't slowed down since.

The impact has been far bigger than I could have ever imagined. It turns out that this particular enzyme exists in every organism and acts as a master regulator for gene activity, and it's dysfunctional in many human cancers. People have now made drugs against these activities, and these drugs are being proven therapeutically useful in people now. I've always believed that if you study a really basic problem in biology, chances are that in some way, shape, or form it will connect with human health and human biology, and it's been satisfying to see that happen with our work.

The next big chapter will be to determine how you faithfully inherit chromatin modifications and the chromatin marks. Right now it's kind of a black box. All the indications are that there is something that you can inherit that's not tied to the DNA. We have some ideas as to what might be going on there, but there's a lot of work still to do.

At the end of the day, the best part of this job is the "people part." Scientists are a special breed, and I feel really lucky that I've had some really great ones come through my lab. They've made great things happen with their creativity, hard work, and dedication. The ultimate thrill is to watch your students and postdocs go out and start their own labs and maybe even pass you up. It's a wonderful thing.

-As told to Christie Aschwanden, a freelance writer based in Colorado.