Notes From the Field: How a Molecular Geneticist Got Wet

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When I was growing up in Southern California, I wanted to be many things, including a doctor, a lawyer, a veterinarian, and the first woman president. But the thing I loved the most was the ocean, and I spent as much time as possible at the beach, swimming in the waves, combing for shells, and exploring the tide pools. So I have always had this lurking desire to become a marine biologist, live on a boat, and follow dolphins around. But when I went to college, I had decided that I was going to be an orthopedic surgeon and duly embarked on my pre-med courses and ended up with a major in Molecular and Cellular Biology with an emphasis on Genetics. But those lurking desires to be a marine biologist kept popping up and I spent the summer after my junior year at the Duke Marine Lab in Beaufort, North Carolina. This was my first real exposure to science and scientists and I loved it. Any ideas about orthopedic surgery were gone, and I wanted to be a scientist. I particularly loved living at the marine lab, where I got to spend all day doing molecular biology and all my free time swimming and exploring in the ocean. But when it came time to apply to PhD programs that fall, I decided that although I loved marine biology, molecular biology and genetics were the tools that I needed to study biological problems. I thought that someday I could use those tools to explore marine biology. So I never did submit my application to the University of Hawaii and instead went to Princeton University. There, I joined Tom Vogt’s lab and received excellent training in mouse developmental genetics. But sometimes during those long days in the lab when nothing was working and it seemed like grad school would never end, I would think about how I really wanted to be a field biologist, where I could be outside working with “real” organisms.

However, when I finished my PhD, I somehow forgot about that lurking desire to do fieldwork and marine biology. I decided to stay within the world of developmental genetics, but fortunately was accepted as a post-doc in David Kingsley’s lab at Stanford University. David is also a mouse geneticist, but it was clear that he had broad interests in evolution, particularly in the amazing diversity of skeletal morphologies present in vertebrates. So David and I started to ask the question: “What kinds of genetic and molecular changes actually contribute to morphological variation in natural populations?”. In order to address this question, we wanted to find a vertebrate organism that had lots of phenotypic variation (particularly skeletal), but we needed to be able to cross these variable populations in order to take a genetic approach to identify the genes underlying this variation. To find our ideal organism, we spent one of the most fun summers of my career in science: we went to the library and read about all sorts of crazy systems that I never knew existed and talked with many different people in diverse fields. Because we were interested in vertebrate evolution, fish were an obvious candidate group, given the dazzling array of phenotypic diversity and the relative ease of raising large numbers of fish in the lab. It was as I was walking across the Stanford campus with an armful of books on fish that I realized that my lurking desire was actually being fulfilled: I was going to use molecular biology and genetics to study marine biology!

When David came across a chapter by Mike Bell about threespine sticklebacks in a book called The Evolutionary Genetics of Fish, he immediately gave it to me to read. We both knew we had found our ideal organism (Fig. 1). The threespine stickleback has evolved a huge diversity of morphologies and behaviors in the last 10,000 years since the glaciers melted. However, there was some work to suggest that you

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could still cross these diverse populations in the lab and that differences in some traits appeared to be controlled by a relatively small number of genes. Furthermore, sticklebacks have been incredibly well studied. Initially, most work in sticklebacks focused on behavior, as pioneered by the 1973 Nobel laureate Niko Tinbergen in founding the field of ethology. However, sticklebacks have also been used for studies of evolution, ecology, physiology, toxicology, and parasitology. Although no molecular and genetic tools existed in sticklebacks, we decided that we could build the resources needed to identify genes that control morphological variation in sticklebacks. However, we could never invent the wonderful and rich biology of the threespine stickleback.

We contacted Dolph Schluter, a leader in the field of ecology and evolution who uses sticklebacks to investigate the mechanisms that have contributed to speciation of sympatric populations of sticklebacks in lakes in British Columbia. Dolph was incredibly excited about the possibility of bringing genetics and genomics to sticklebacks and immediately set about establishing crosses and providing some samples so we could start building libraries, isolating markers, and developing a genetic linkage map of the stickleback. Much of the early work required bringing the same type of approaches to the fish that David and I had already seen work so well for mapping and cloning of classical skeletal traits in mice. Within a year of starting I had isolated enough markers to build an initial genetic map, just in time for the 1999 International Stickleback meeting held in Vancouver. We subsequently used this map to study the inheritance of a variety of interesting evolutionary differences between stickleback species (Peichel et al., 2001). Since then, molecular tools have really begun to snowball for the fish (Kingsley et al., 2004), culminating in a recent decision by the NIH to sequence the stickleback genome.

But David and I wanted to get wet, too! From our reading, we knew that interesting populations had been described from across the distribution of sticklebacks in the Northern hemisphere. We wanted to collect from different populations to establish crosses to map differences in morphological, physiological, and behavioral traits. So we set off with our waders,
nets, and minnow traps to become real field biologists. Our first few trips were not so successful because we were looking in the fall, when sticklebacks are not as abundant. But the following spring, when the fish are breeding near the shore, we learned that we could collect hundreds of fish just by leaving our traps overnight.

Collectively, we have now been to some beautiful and remote places, from Vancouver Island and the Queen Charlotte Islands in British Columbia (Fig. 2), the Olympic Peninsula in Washington, the Outer Hebrides in Scotland (Fig. 3), the Northwest Territories in Canada (Fig. 4), Hokkaido Island in Japan, and Iceland! On all these trips, as I was happily tromping around in the mud with my rubber boots or waders, I could not believe that I was actually working! Collecting sticklebacks is not particularly difficult field work...you drop traps in the afternoon, go eat a good meal and drink a beer, and come back in the morning to get your traps full of fish (Fig. 2). However, we have had some challenges, many of which involve the boggy muddy habitats preferred by sticklebacks. More than once I have sunk to my waist in mud! On our trip to the Outer Hebrides in Scotland (Fig. 3), David and I were walking across the peat bogs when I took a step and the next minute was literally up to my armpits in a bog. Luckily, it was me who fell in as David was able to pull me out. If it were the other way around, I am not sure I would have been able to pull David out of the bog. David was also nice enough not to take my picture while I was still stuck in the bog and even let me go back to the hotel to change my clothes (after collecting our fish, of course).

It's not just people who get stuck in the mud. On our trip to Wood Buffalo National Park in the Northwest Territories (Fig. 4), we took our rental car (the only one in hundreds of miles and NOT a four-wheel drive) on a seasonal dirt road and got it stuck in the mud. After digging in the mud for about an hour, we gave up and walked (with the mosquito netting covering our faces) a few miles to the nearest house, which luckily had a big truck and a very nice man who...
was able to pull us out of the mud. He then informed us that there was now a paved road leading to the lake we were trying to visit! So we got our fish after all. On this trip, we had also been warned that we should have a ranger accompany us with a rifle to some of our sites because of the local black bear populations. However, there was also an anthrax outbreak affecting the buffalo population during our visit, so all of the rangers were busy. On that particular trip we never saw any of the local black bears. The following year I returned with Pam Colosimo, one of the grad students in David’s lab, and not only did we have the same rental car, we saw at least nine different bears up close. We were just waiting for one to attack us while we were holding a trap full of tasty sticklebacks!

I seem to be followed by disease outbreaks on my collecting trips. I collected some sticklebacks from a pond in Olmsted Park in Boston, which I thought would be a relatively safe place. However, I also sunk to my waist in mud in this pond. The next day we heard that a bird with West Nile virus had been found dead next to the pond there that day! Despite these minor inconveniences, most of our trips have been successful scientifically and a great way to see incredibly beautiful and remote places that I probably never would have visited otherwise.

Not only has the stickleback project been a fun way for us to travel around, but work in our lab as well as other labs has really begun to yield exciting insights into the molecular nature of skeletal evolution and parallel evolution of traits in independent populations (Cole et al., 2003; Colosimo et al., 2004; Cresko et al., 2004; Shapiro et al., 2004). Our work is also extending beyond just morphological differences into physiological differences, behavioral differences that lead to reproductive isolation, and the evolution of sex determination. The further development of genetic and genomic tools for sticklebacks, including a full genome sequence, means that stickleback research will be increasingly powerful for integrating the fields of genetics, evolution, ecology, develop-
ment, and behavior. And I get to play in the water and call it a job!

LITERATURE CITED


FIG. 4. Katie Peichel setting traps at the Salt River in the Northwest Territories, Canada.