on the work. For many clinicians, “the idea of scientifically testing your methods is still foreign,” Montgomery says. “They think it’s a waste of time and money they could be using to help their patients.” But objectively assessing methods is “the best way to improve them.” The first application of science at RCT is to test which approaches are most effective for which kinds of patients.

Some studies focus on torture’s physiological legacy. One effort is to probe changes from falanga, the beating of the soles of the feet. Victims cannot walk far without excruciating pain, even if their feet appear undamaged. Using magnetic resonance imaging, RCT specialists have uncovered a thickening of a tendon in the foot in falanga victims. The finding should help document abuse and may lead to better treatments. Having such forensic tools “can be crucial in some cases,” says David Rhys Jones, a human rights lawyer at the Medical Foundation for the Care of Victims of Torture in London.

The center’s research is not limited to the lucky few who make it to Copenhagen. Several epidemiological studies are under way, including one to track children of torture victims to assess mental health consequences across generations. Another study focuses on prisons in Nigeria, examining the relationship between guard training and prisoner abuse. (On 28 June, AAAS, publisher of Science, will host a forum on scientific and legal issues surrounding torture and prisoner treatment.)

RCT staff members say they are frustrated at how slowly the awareness of how to diagnose and treat torture has filtered out to the wider medical community. Since the Vietnam War, an immense amount of work has been done on posttraumatic stress disorder, a complex of psychological problems that persists after witnessing traumatic events. Yet “almost no data is out there on torture, which causes worse symptoms,” says Labrosse. Hospitals still tend to overlook or misdiagnose torture victims, adds Prip, so “we’re trying to get torture rehabilitation into the standard medical curricula.” Just providing it as an optional course would be “extremely useful,” says Duncan Forrest, a physician at the Medical Foundation, “because there is widespread ignorance among doctors.”

One of the most important lessons is that the mental scars never completely heal. Labrosse is worried about Massoud, who canceled an appointment last month. She says that some images of torture in Abu Ghraib are strikingly similar to Massoud’s drawings of his own experiences, and the evocation of his torment has triggered a relapse of anxiety attacks. RCT may be able to piece victims back together, but they remain fragile.

–JOHN BOHANNON

John Bohannon is a writer based in Berlin.

Healers. Edith Montgomery and Belinda Labrosse in the RCT research library, the largest collection of torture-related documents in the world.

Evolutionary Biology

Changing a Fish’s Bony Armor In the Wink of a Gene

Genetic researchers have become fascinated by the threespine stickleback, a fish that has evolved rapidly along similar lines in distant lakes

A sassy little fish—a mere 6 centimeters long—that can turn a threatening red, builds nests, and feuds with competitors is now becoming a star in research on genetics and evolution. Long a favorite of behavioral scientists, the threespine stickleback is garnering attention for what it can reveal about genes, morphology, and the speed at which a species can adapt. Half a dozen recent papers on sticklebacks show “all kinds of interesting things about the genetic and molecular basis of how organisms evolve,” says David Kingsley, a vertebrate geneticist at Stanford University.

First class. Colorful enough for a Swiss stamp, sticklebacks have captivated a growing number of biologists.

This new research adds weight to a provocative idea that a little DNA—perhaps just a single gene—can control many traits that affect an organism’s ability to thrive; in this case, the gene may have enabled sticklebacks to evolve out of tight situations. Not only have sticklebacks adapted quickly to past and current environmental change, but several researchers have documented that they still retain a remarkable adaptive flexibility.

Since the 1930s, the prevailing view has been that evolution moves in a slow shuffle, advancing in small increments, propelled by numerous, minor genetic changes. But some have challenged this dogma, notably H. Allen Orr, an evolutionary biologist at the University of Rochester in New York. In 1992, he and his colleagues argued that just a few genes, perhaps even one, could power long-term change. Such change could rev up speciation. Lately, the Orr camp seems to be gaining ground, in part because of studies of sticklebacks, says R. Craig Albertson, an evolutionary biologist at the Forsyth Institute in Boston. He and others are finding that “simple genetic changes can have profound effects.”

Salty past

Kingsley is a convert to stickleback research. Five years ago he and his postdoctoral fellow Katie Peichel turned to it when they were looking for a way to add a touch of reality to their studies of the genetics of bone development. Neither lab mice, the subject of their previous work, nor lab-bred zebrafish offered much insight into the causes of natural variation in a natural setting. So Kingsley and his students searched for a species with a rich natural history literature and a lifestyle that would enable both field and lab studies. “The stickleback had everything we wanted,” he recalls. About the same time, zebrafish expert John Postlethwait of the University of Oregon, Eugene, was on a similar hunt, casting about for a fish with a well-known biology and an interesting evolutionary background in which he

CREDITS: (TOP TO BOTTOM) THEO C. M. BAKKER/UNIVERSITY OF BONN; J. BOHANNON could apply molecular techniques he had developed. He, too, landed the stickleback.

Both researchers were attracted by a huge body of knowledge on sticklebacks—at least 2000 scientific papers and seven textbooks—dating back to the 19th century. The fish's fame increased in 1973 when Nikolaas Tinbergen won a Nobel Prize based in part on his studies of stickleback behavior, which is now the focus of perhaps 100 labs, according to Kingsley.

Another draw was the stickleback's evolutionary history, which includes a major transition. Sticklebacks were once a solely saltwater species that migrated from the sea to streams and lakes to breed; as the glaciers retreated up to 22,000 years ago, some settled in lakes. Although they evolved to look very different from their ancestors, they often came to resemble their counterparts who were evolving in a similar way in lakes that are geographically distant (*Science*, 14 January 2000, p. 207). These lakes now are natural laboratories for evolutionary studies, says Susan Foster, an evolutionary biologist at Clark University in Worcester, Massachusetts: "These remarkably divergent populations have created a unique resource," in part because freshwater and saltwater populations can interbreed. Recently, molecular genetic studies have been added to stickleback science. Says Kingsley: "We are beginning to collect real data on the number and location of the chromosomal regions that control substantial evolutionary modification." Those regions can control multiple characteristics.

One fish, two fish ... At Stanford a technician feeds the hundreds of sticklebacks needed for gene searches.

Armor is optional

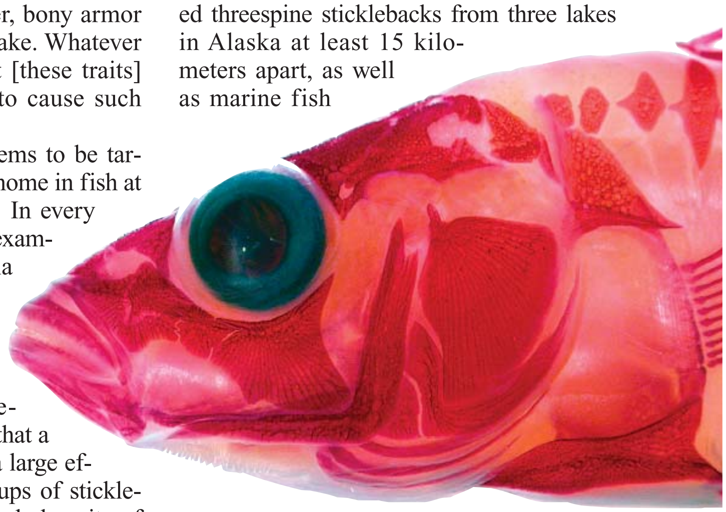
Genetic studies took off several years ago when the Kingsley and Postlethwait groups independently began to breed threespine sticklebacks from lakes with marine counterparts. The research teams have examined many thousands of offspring since then and have started to home in on genes underlying physical differences. They focused first on genes underlying the size, number, and locations of plates located along the sides of the fish, then included analyses of the fish equivalent of a pelvis and hind limbs, or pelvic spines on their undersides.

Oceangoing sticklebacks are built for battle. Prominent spines stick out behind their lower fins, and their bodies are covered with as many as 35 plates—presumably to fend off predators. But spines and plates are reduced or missing in most of their freshwater cousins, probably an adaptation to the new habitat. It pays to lose the bulky armor, says Michael Bell, an evolutionary biologist at the State University of New York, Stony Brook: Lakes may favor lightness because they typically have places to hide, if fish can dart into them fast enough. Because fresh water lacks the rich calcium reserves of salt water, bony armor could also be too costly to make. Whatever the cause, "selection against [these traits] must be incredibly strong" to cause such rapid evolution, says Foster.

This selective pressure seems to be targeting the same part of the genome in fish at various geographic locations. In every population researchers have examined, from Japan to California to Iceland, they are finding the same thing: A gene or set of nearby genes is causing the loss of certain parts of the fish's armor. "It's remarkable," says Postlethwait, that a single gene could exert such a large effect in so many different groups of sticklebacks. Along with armor, "a whole suite of bony characters is changing," he says, including jaw shape and bones associated with protecting the gills. This is not what researchers had expected to find. But when they tried a breeding experiment, the same pattern emerged: Small DNA segments affected vast areas of bone and armor.

In one study, Kingsley and Stanford graduate student Pamela Colosimo crossed well-armored marine fish with fish from Paxton Lake in British Columbia. The lake fish had only the front plates—the first ones to form during development. Colosimo measured the pattern, number, and size of the plates in the progeny, then by genetic analysis pinpointed the stretches of DNA involved in plate formation. One area had the greatest sway, accounting for 75% of the number and distribution of the plates, she, Kingsley, and their colleagues reported in the 30 March online journal *PLoS Biology*. Changes in this stretch of DNA sequence caused a fivefold reduction in the number of plates, whereas three other stretches had a slight effect. The same small stretch of DNA proved equally influential when they studied freshwater fish from a California lake 1300 kilometers distant. Their geographic distribution virtually guarantees that the fish lost their plates independently, says Kingsley.

Similar findings have appeared in work by Bell and William Cresko, Postlethwait, and their colleagues at the University of Oregon. Using a different strategy, they narrowed the cause of a change in some of the body armor to a single gene. Cresko collected threespine sticklebacks from three lakes in Alaska at least 15 kilometers apart, as well as marine fish



Tough guy. Saltwater sticklebacks carry armor of bony plates and spines.

CREDITS (TOP TO BOTTOM) COURTESY DAVID KINGSLEY/STANFORD UNIVERSITY; W. A. CRESKO *ET AL., PNAS* **101**, 6050 (2004) from two sites. After confirming that there were large, consistent differences between lake fish and sea fish, they performed breeding studies. In one experiment, they crossed marine and freshwater fish and found that the resulting offspring all had a complete set of armor and a fully formed pelvis—suggesting that the DNA, or allele, belonging to the marine fish overrode the effects of the allele of the freshwater cousins. In the second generation, the researchers saw that three out of four had a full set of this armor, confirming a dominant allele, they reported in the 20 April issue of the *Proceedings of the National Academy of Sciences*.

Next, the Oregon researchers tested to see if the altered pelvis and lateral plates of the lake fish were controlled by the same genes in each population. They expected the opposite: that the gene involved in armor loss would be different in the three groups because each had evolved that trait independently. But their surprising finding was that the alterations were always in the same gene. Dolph Schluter, an evolutionary biologist at the University of British Columbia in Vancouver, Canada, reached the same conclusion, this time with marine and freshwater fish from British Columbia and Japan. Although the DNA sequence has not been identified, "it could well be the same gene everywhere," says Schluter, who is reporting these results in an upcoming issue of *The American Naturalist*.

Bell has found that, from an evolutionary perspective, this gene may change at lightning speeds. In the most recent issue of *Evolution*, he and his colleagues report on a case in Alaska where plates disappeared in most fish within a decade. The findings come from Loberg Lake near the Cook Inlet in southern Alaska, where in 1982, the Alaska Department of Fish and Game had prepared the water for restocking with salmon and trout by poisoning all the fish in it. Eight years later, Bell and his colleagues found that the sticklebacks were back, this time with plates, suggesting that they had come upstream from a saltwater inlet.

As Bell's team sampled the lake for the next 10 years, taking note of the stickleback's plate makeup, the number of armored fish declined. In 1990, 96% of the sticklebacks had the full suite of plates; in 1993, only 39% did. His crew spotted the beginning of this transition in 1991, noting that some individuals had just the front plates. By 2001, that variety represented 75% of the sticklebacks sampled. The number of plates also declined—from 33 to 32 in the fish with all their plates and from seven to six and a half in those with just the anterior ones. "It was obvious that things were changing very fast," says Bell.

The results suggested that natural selection had taken its toll on the armored fish in just a few years. "That wouldn't happen if you had to wait for new mutations to occur," notes Postlethwait. Instead, he thinks the allele responsible for the loss of plates was present all along. But its effects were muted because it was recessive and rare in the population. "When you get into fresh water, [the situation] would change rapidly," he explains. Fish that still carried the allele for plates didn't thrive.

Kingsley's group ran similar breeding studies, showing that pelvic spines recapitulated this evolutionary path. And when they hunted for the DNA that was affecting these changes, they homed in on a candidate region already identified last year by Nicholas Cole, Cheryll Tickle, and their colleagues at the University of Dundee, U.K. (*Current Biology*, 16 December 2003). Cole's team noticed that the spineless fish didn't even have the beginnings of a limb; this led them to test genes in other vertebrates, including one called *Pitx1*, known to initiate limb formation. It was a good choice: The Pitx1 protein was missing in the freshwater stickleback and present in the marine one. Adding further support, they noted that mice with no *Pitx1* activity have smaller than normal hind limbs and are asymmetrical, just like the freshwater sticklebacks.

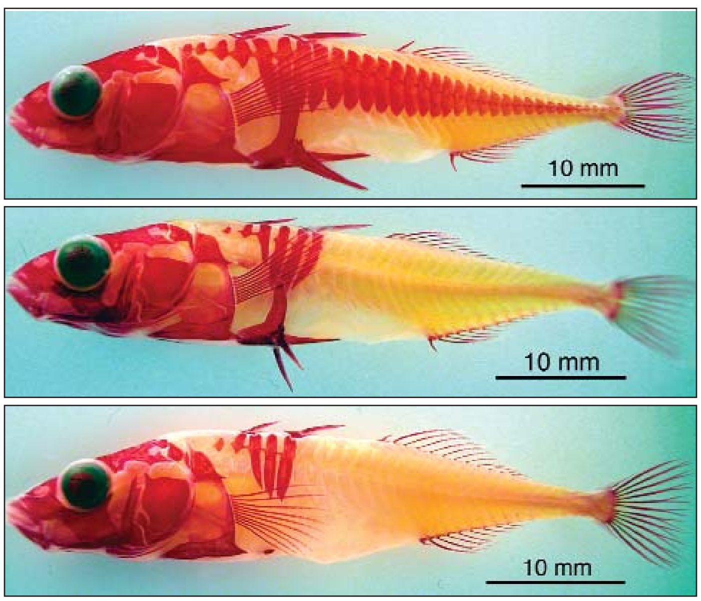
Together with postdoctoral fellows Mike Shapiro and Melissa Marks, Kingsley's breeding studies showed that this gene in sticklebacks was located in the region in which his analysis had shown the gene affecting spines should be. But when he analyzed genes from both types of fish, he found that the sequences were the same. This did not explain why the intact gene was inactive in freshwater sticklebacks. The solution, he and his colleagues concluded in the 15 April issue of *Nature*, is that a change in the gene's regulation—and not in the gene itself—caused the lake sticklebacks to lose their spines. Simply changing the way a gene is regulated in one part of the anatomy or at one point in development "is one of the ways to make a [change in a] very powerful development control gene without having detrimental effects," says Kingsley.

Researchers have found that other organisms such as birds seem to exhibit the same or similar new traits because of changes in the activity of the same genes, even when the species are unrelated (*Science*, 19 March, p. 1870). No one knows exactly why. It could be that certain genes or bits of regulatory DNA are particularly prone to mutation. Or perhaps rapid evolutionary responses are channeled into genes that don't affect development on a broad scale, so as not to short-circuit an organism's ability to survive. As a result, "you find the same gene involved more often than you would initially expect," says Schluter. He and other stickleback experts are trying to solve this puzzle.

Help may be on the way. Kingsley, who teaches a course on stickleback biology, is finding that biologists who work on other organisms are turning toward this fish to answer their research questions. Already they have a genetic map and a partial genomic library of the stickleback. By the year's end, with support from the National Human Genome Research Institute, they should have a draft of the entire 6.75-million-base genome sequence.

Bell hopes that these studies will lure even more developmental, evolutionary, and genetic biologists to the study of these fish. Evolution occurs at many levels, involving modifications of DNA sequence, alterations in development, shifts in behavior, changes in community structure, and, ultimately, survival. It's important to see how these various levels interact during natural selection. Adding molecular genetics studies to stickleback science, he predicts, "will allow us to tie up everything in one neat package."

–ELIZABETH PENNISI



Going, going, gone. Sticklebacks in fresh water undergo genetic changes causing them to lose bony body plates (*middle*) and pelvic spines (*bottom*).

CREDIT: W. A. CRESKO *ET AL.*, *PNAS* **101**, 6050 (2004)