“We are all modified fish,” says Dr. Karen Crow, who heads a marine biology/evolutionary genetics lab at San Francisco State University. Crow studies specific genes that direct the growth and development of appendages in tiny, translucent fish embryos. One of the species she works on is the leafy sea dragon—an otherworldly creature similar to a seahorse but with fluttering, leafy, branch-like body ornaments that Crow calls “dermal appendages.” These elongated, skin-covered structures look like fins. They can arise from various parts of the body, however, and rather than propelling the sea dragon, they help camouflage it as it hides amidst undulating seaweeds.
Crow’s research focuses on the evolution of novelty that can lead to diversity if the new features are beneficial...

A fascinating connection starts to emerge between the seemingly different worlds of fish and people when one considers that human developmental anomalies often occur in appendages. Humans and bony fishes share many developmental genes and indeed, both evolved from an ancient common ancestor. Crow now stands at this evolutionary crossroads, trying to read the genetic map that will help her explain how novel structures such as dermal appendages arise in sea dragons and other fishes. The genetic mechanisms she hopes to unveil could also help explain how new body structures such as limbs arose from fins during vertebrate evolution. And it may shed light on the way certain gene mutations can produce limb malformations in human embryos.

One of the important genetic mechanisms Crow studies is genome duplication. All vertebrates, humans and fish alike, have experienced ancestral genome duplications—the creation of a second copy of the entire genetic code—at several key points in their evolutionary history. The duplication of genes or whole genomes, says Crow, may contribute to the evolution of novel structures such as leafy-looking appendages in sea dragons. “The idea is that if you have an extra copy of a gene,” she says, “you can maintain one copy to perform the ancestral function, and then you have an additional copy for evolution to tinker with.”

Stated formally, Crow’s research focuses on the evolution of novelty that can lead to diversity if the new features are beneficial to the organism developing them. Because of the vital role genes play, Crow explains, most of them are “constrained.” They cannot acquire significant mutations or they will be selected against: Individuals with severe mutations will likely die out, their lineage will come to an end, and the mutation will not be passed on to future generations. This genetic extinction, Crow says, is a defense mechanism naturally embedded in the evolution of life. However, in lineages that have undergone a genome duplication, one set of genes can
carry out vital gene functions and “the extra copies can acquire changes and explore the empty canvas of evolutionary space to see if it confers a selective advantage.”

In her research at SF State, Crow is using the tools, techniques, and ideas of a relatively new field of study—Evolutionary Developmental Biology, or Evo-Devo for short. Evo-Devo has gained momentum in the last 15 years after researchers invented techniques that made it easier to sequence DNA. Crow describes “a marriage between the old discipline of embryology and development and the new emerging technology of molecular biology and molecular evolution.” This union, she says, sparked Evo-Devo, the discipline that explores the evolution of diversity and novelty. Around the same time that researchers began sequencing genes with some facility, they started comparing human and animal genomes and unearthing the many genes they share. These findings radically changed the idea that humans are uniquely specialized and at the same time, ignited the Evo-Devo field.

For several years, Evo-Devo researchers compared “model taxa.” These, Crow explains, are groups of model organisms such as fruit flies, humans, mice, zebrafish, frogs, and chickens. “They were the first organisms researchers all around the world investigated from a variety of viewpoints,” she says, “and for which they sequenced the whole genome.” Crow’s approach to Evo-Devo is unique in that she studies non-model taxa still lacking a reference genome at this point. That is, she chooses unusual organisms such as sea dragons and paddlefish and applies to them principles already understood in widely investigated species such as zebrafish. She hopes these studies on genetically unmapped species will help her and other researchers gain more insights into the evolutionary mechanisms responsible for the astonishing diversity of life.

Crow’s passion for nature has its own evolutionary history. It started when, as a little girl, she dreamed that one day she would become a forest ranger. Years passed and, during a summer job as a ranger at Channel Islands National Park in California, Crow was so awestruck by the beauty of this rugged natural environment that she decided to become a marine biologist. She enrolled at Moss Landing Marine Laboratories, an affiliate of SF State. She pursued her Master’s degree at SF State and her PhD in ecology and evolution at UC Santa Cruz. She went on to postdoctoral research at Yale University, and began job hunting at various institutions that were looking for an evolutionary biologist. When her graduate advisor from SF State, Ralph Larson, retired, he notified her about the available position; the Department of Biology hired Crow in 2007. Since then, she has divided her time between conducting research in her laboratory and teaching the Biology of Fishes and graduate seminars in evolutionary developmental biology.

From her first day as a SF State professor, she knew she could
work here happily. “We have core facilities including a Cell and Molecular Imaging Center for microscopy, and a Conservation Genetics lab for molecular biology. And then my lab has all the equipment my students and I need to do the majority of our research.”

The College of Science and Engineering also focuses on research, and provides necessary support in the form of reasonable teaching loads, says Crow. Even though the UC system is notoriously more research-oriented than the CSU system, Crow proudly notes that within CSU, “San Francisco State has distinguished itself as a research campus. And now I’m thrilled to walk into the footsteps of Ralph Larson who was a great ichthyologist, mentor, and teacher.”

The graduate students that share Crow’s lab are well-acquainted with both her competence and her passion. “She is intensely interested in the work we are doing,” says Master’s candidate Jessica Maxfield. “I think the best part of working with her is [her] enthusiasm and we-can-do-it attitude. I can’t help but get excited about a new idea or process because she is so excited. And she loves a challenge.” In her cutting-edge field, Crow must be farsighted and innovative with her research approaches and she shares these with her students. She constantly sends papers to get her students involved, says Maxfield, and pushes them to read about new ideas and techniques.

Crow’s risk-taking, innovative attitude is balanced by her rigorous scientific approach, but is occasionally enlivened by humor, as well. Maxfield recounts a lively “algae fight” she and Crow had on a field trip to Half Moon Bay to catch fish. And she recalls the story of the smelly, decaying sturgeon someone found in the Bay last year and that Crow kept in the lab freezer for months, waiting for the right moment to dissect it with students. “It was fascinating and exciting,” says Maxfield. “Only Karen would have the foresight to think a dead, smelly fish would make an afternoon of fun.”

While a marine biologist’s work can be diverting, it is more often difficult and detailed—but nonetheless intellectually fulfilling. “Lab work such as sequencing genes is in itself very tedious,” says Crow. “But it’s pretty satisfying when you get some kind of analysis or an output, and you go ‘Oh, that’s interesting. That’s not what I expected!’” Like all good science, Crow’s work starts with a hypothesis. One such hypothesis is that leafy, branch-like body organs or “dermal appendages” arose independently in the sea dragons, a group within the same family as the seahorses and pipefish. Since sea dragons’ close relatives lack these very long structures, the appendages “are considered a novelty,” Crow says. She analyzes and compares the DNA from all seahorse family members, sea dragons included, to look for patterns of mutation that are different in species with dermal appendages. “There is a solid theoretical framework,” she explains, “that says that duplicate genes may play a role in the evolution of novel structures. Because these appendages are novel structures, I’d like to know if the particular genes I study—which are known to have been duplicated in ray-finned fishes—have played a role in the evolution of these structures.”

All ray-finned fishes—which basically include most of the organisms we think of as fish—have fins made up of a web of skin supported by “rays” or bony spines. Back in the mists of time, the ray-finned fishes diverged from the lobe-finned fishes and this latter group gave rise to the coelacanths, lungfishes, amphibians, reptiles, birds, and mammals (including humans). This kinship is what links humans and fish. It also explains the fact that both have shared developmental genes. Crow studies a particular class of
Crow’s research. “It definitely exhibits a modified body plan,” says Crow, “and it’s so conspicuous that it makes up about a third to a half of the fish’s total length.” Crow is hypothesizing that Hox genes are involved in the origin of distally elongated fields in both sea dragons and the American paddlefish.

Because the American paddlefish is closely related to the sturgeon, stores sell paddlefish eggs and call them caviar. Crow has a collaborator in Oklahoma who works at the Tishomingo National Fish Hatchery and breeds paddlefish to insure that natural stocks are maintained. During the breeding program, he sends paddlefish embryos and larvae to Crow at SF State. She then studies the organisms at various developmental stages “to see when our genes of interest are being expressed.”

She recently sequenced the paddlefish transcriptome (genes being actively transcribed) during early stages of rostrum development. To do this, she and student Julia Taylor dissected the rostrum from larvae just as that “cricket bat” had begun to elongate. After extracting all the RNA molecules representing the genes being expressed in the embryo’s rostrum, they were able to obtain partial sequences of all those genes. “With the help of my colleague and bioinformaticist, Dr. Chris Smith, we were able to search this database to determine if any of our genes of interest were expressed during rostrum development. And, we were delighted and surprised by what we found,” Crow says. “Neither duplicate of our top candidate was expressed at this stage, which was somewhat surprising. But several other Hox genes are, and to our knowledge, this is the first discovery of any Hox gene expression in the anterior region of a vertebrate—the region towards the nose where the paddlefish rostrum is situated.” Interestingly, she continues, “when we investigated additional pairs of duplicate genes, we found several in which only one gene copy is expressed in the rostrum. So this means that the duplicate genes are divergent enough to have unique expression patterns, in a novel feature that arose in this species.”

A very long time ago, when Hox genes diverged in ancient fish lineages via gene duplication and mutation, new structures arose and the underlying genetic changes were passed on. When Hox mutations appear in humans, the outcome can be severe malformations. This important correlation, Crow says, is one of many important reasons for studying the genetic changes that lead to novel structures. She would like to know how often variation occurs in those genes, how fast it occurs; and what factors are associated with it.

When Crow talks about the significance of her research, she lights up, exudes passion—and occasionally decries those duties that slow her down. “Bureaucracy swallows up a lot of the time that I would rather spend in the lab,” she says. The tiny translucent fish embryos growing in that lab, however, will hold on to their genetic secrets only until this tenacious SF State researcher finds the key to unlocking them. One suspects that eventually, she will explain the mechanisms that regulate the development of unusual body structures. This will contribute to our understanding of how diverse body structures arise in evolution, and could potentially contribute to breakthroughs in human health. We are, after all, just “modified fish,” that swam astray on the long evolutionary path from the past to the present. ☞