by ecologist P. Dee Boersma of the University of Washington (UW), Seattle, pored over 136 recovery plans, FWS's blueprints for endangered species under its jurisdiction, addressing some 2600 questions for each plan.

The fruit of this labor—"a huge and onerous spreadsheet," as one of the foot soldiers calls it—was not a total slam against the agency. The study lauds FWS for steadily improving its use of science, for instance, by adopting better defined measures of a species' status.

But several practices came under fire. Over the last decade, FWS has relied increasingly on recovery plans designed to preserve many species facing common threats in the same habitat. The analysis revealed that species in such plans are more likely to be in decline than are those in plans custom-built for their own survival, even after adjusting for when the plan was written. Probing further, the study found that FWS's multispecies plans tend to be lighter on biology than the single-species plans. That's "a very disturbing and unsettling trend," says UW's Alan Clark, who led this part of the analysis. He cautions that the study is not an indictment of multispecies plans in general. These may well work, he says, as long as they don't give short shrift to individual species.

Nevertheless, conservation biologists are chagrined that multispecies plans, so good in theory, are struggling in the field. The finding "caught me by surprise," says biologist David Wilcove of Princeton University. FWS, he notes, began drafting such plans in response to criticisms that the agency moved too slowly, and in a piecemeal fashion, in getting recovery efforts under way. "They are now vulnerable to the charge that they are providing inadequate analysis," Wilcove says. "For the FWS, it's a can't-win situation."

More disappointment comes from the study's critique of critical habitat, a designation that the Endangered Species Act provides to extend protection to a beleaguered species' home range. Lawsuits forced FWS to accelerate designations last year, bleeding time and money from the listing of new species and for little if any gain: The study concludes that critical habitat designation does not correlate with better data on the habitat or improved measures to preserve it.

FWS puts a positive spin on the analysis. The findings do not depict an agency failing in its mission, insists Martin Miller, recovery chief in FWS's endangered species division. He welcomes the criticisms and plans to incorporate them into new recovery guidelines now being prepared. And he pledges to build on FWS's newfound links with academia. "We see that as one of the most important benefits" of this exercise.

Jamie Clark, FWS director from 1997 to 2001, says the "thoughtful and incisive" study should help the agency shape its efforts, which she thinks should continue to feature multispecies planning and critical habitat designation. Devising sound plans is a struggle for an agency in perpetual crisis, she acknowledges. The key to success, she says, will be to "slow down the fire hose of everything else that's happening at FWS long enough to focus on science." **–BEN SHOUSE**

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DEVELOPMENT

Mutations Reveal Genes in Zebrafish

To piece together an organism's blueprint, developmental biologists have to work backward. By deliberately disabling genes and watching what happens, researchers can discover the roles the genes play in development, gradually piecing together a building plan for an embryo. Even for a relatively simple fish, the task is daunting.

No stripes. A normal zebrafish (top) and a mutant fish with irregular coloring.

In a significant step toward a blueprint for vertebrates, a team of developmental geneticists has just published new results from a large-scale screen of zebrafish mutations. In a 13 May online publication by *Nature Genetics*, Nancy Hopkins, Adam Amsterdam, Gregory Golling, and their colleagues at the Massachusetts Institute of Technology describe 75 mutants and—unlike previous screens—the genes responsible for the deformities. The work is "a technological tour de force" that will speed the efforts of other researchers in the field, says developmental biologist Len Zon of Harvard Medical School in Boston.

Zebrafish are ideal models: They are easy to care for, they reproduce quickly, and their see-through embryos enable researchers to easily spot missteps in development. Essentially, scientists simply need to create genetic mutations, usually with a chemical, and then examine the embryonic wreckage. When they find an especially interesting phenotype —one eye instead of two, for example—the researchers then try to find the mutation that caused the abnormality. Such work began in earnest in the 1990s, and in 1996 groups in Tübingen, Germany, and Boston published dozens of papers describing a zoo of deformed fish (*Science*, 6 December 1996, p. 1608). But pinpointing a single mutated gene requires breeding hundreds of fish and can easily take more than a year. As a result, researchers have so far cloned genes responsible for only about 70 of the thousands of mutants the project created.

To speed the gene-tracking process, Hopkins and her colleagues used a genetically engineered retrovirus to create mutations. The virus enters the reproductive cells of parent fish and inserts itself into the genome—sometimes disrupting a gene. If the disrupted gene is crucial to development, the resulting offspring show the effects. Although the virus is not as efficient as chemicals in causing mutations, it has a key advantage: The affected genes are relatively easy to track down. The researchers use reverse polymerase chain reaction to locate the viral genes in the genome of the deformed embryo and then sequence the regions on either side of the inserted DNA looking for traces of the disrupted gene. About half the time, Hopkins says, the first attempt yields a likely gene at fault. The team has found some genes in as little as 2 weeks.

Consistent with earlier screens, two-thirds of the mutants had either an unusually small head and eyes or general central nervous system degeneration. Researchers usually ignore such nonspecific mutations, focusing their resources on abnormalities that affect a single process or organ system. But the Hopkins team gave all its mutants equal treatment. Many of the culprits behind the general deformities are so-called housekeeping genes that control basic cellular functions such as DNA repair and protein manufacture, as researchers had suspected. But this is the first time anyone has shown in such detail the developmental roles of those basic genes, Amsterdam says.

When the project is finished in 2 to 3 years, Hopkins says, the team will have identified roughly one-fifth of the genes required to make a 5-day-old larva, when the fish is "quite a significant little vertebrate animal," able to swim and search for food.

"The advantage of this screen is that it is comprehensive. It allows you to envision getting a phenotype for every gene expressed and functioning during embryogenesis," notes Marnie E. Halpern, a developmental biologist at the Carnegie Institution of Washington in Baltimore.

The project, partly funded by Amgen, will likely help human geneticists as well: All 75 genes described in the paper have human counterparts. **–GRETCHEN VOGEL**

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