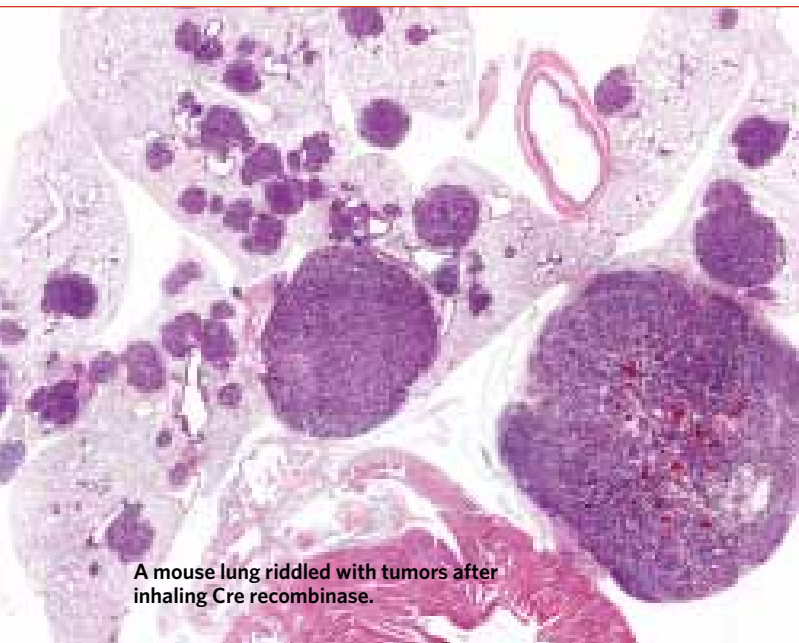


Brookes University in England who has been interviewing the collectors, says that the number captured recently could be as high as 4,000 a year.

It's not yet clear what, if any, impact Patarroyo's unconventional methods are having on local populations. (Owl monkeys aren't endangered or even threatened.) Although the monkeys receive a dose of artemisin to rid them of malaria before they are released, some Colombian scientists have expressed concern that they may be spreading diseases. Maldonado is worried that the liberated monkeys might be dying off. Eduardo Fernandez-Duque, a behavioral ecologist at the University of Pennsylvania who studies owl monkeys in Argentina, says that the animals are highly territorial. "If I were to release an owl monkey from the lab into a forest filled



A mouse lung riddled with tumors after inhaling Cre recombinase.

with owl monkeys," he says, "I would be very concerned that other monkeys may just beat the animal to death."

Camilo Pirajoín, the vet who oversees Patarroyo's lab in Leticia, says that doesn't happen. But his evidence is largely anecdotal. The monkeys that participate in Patarroyo's experiments receive small tattoos. "We know that those animals can live in the jungle," Pirajoín says, "because the collectors have recaptured them." —Cassandra Willyard

Next top model

David Dankort was 4 years into his postdoc at the University of California, San Francisco, without a single paper to show for his work since his PhD. His first two major projects had failed, and if his third experiment didn't pan out, he was ready to kiss his academic career goodbye. In a last-ditch effort, Dankort had constructed transgenic mice that could be induced to form cancer by activating a particular enzyme. In early 2005, as part of the final test of the experiment, he sedated his mice, placed a solution containing a virus expressing the enzyme under their noses, and waited a couple of weeks. "I'm waiting, I'm waiting, and I start to think: 'Am I imagining or are these mice ill?'" Dankort recalls. He

weighed the mice, and found that they had lost a few grams. Dankort then dissected the mice and found that their lungs were riddled with tumors. "I was floored," he says. His experiment worked. It met his goal of creating a model that mimicked the natural progression of cancer in humans more closely than any other, and landed him two high-impact papers.

Dankort, now an assistant professor at McGill University in Montreal, started working on his model in 2003 in the hopes of recapitulating the most common cause of lethal human skin cancer: malignant melanoma. Dankort didn't want to build any old mouse model, though. He wanted to ensure that his transgenic mice were hit with cancer-causing mutations in the same way as people in the real world. "When you're trying to model human cancers in mice

you should at least stack the deck so that things are set up as closely as possible to the human condition," Dankort says.

Dankort focused on a single base-pair substitution in codon 15 of the then-understudied oncogene *BRAF*. He built an inducible mutant that maintained *BRAF*'s normal sequence in early life, but could adopt an alternate, mutated form later in life, which in turn altered the *BRAF* protein. (Dankort swapped the normal and mutant versions by activating an enzyme called Cre-recombinase, which catalyzed site-specific recombination of DNA.) Although his primary interest was melanoma, as a first test, Dankort tried inducing lung cancer in his mice. "I needed to see if they worked," he says.

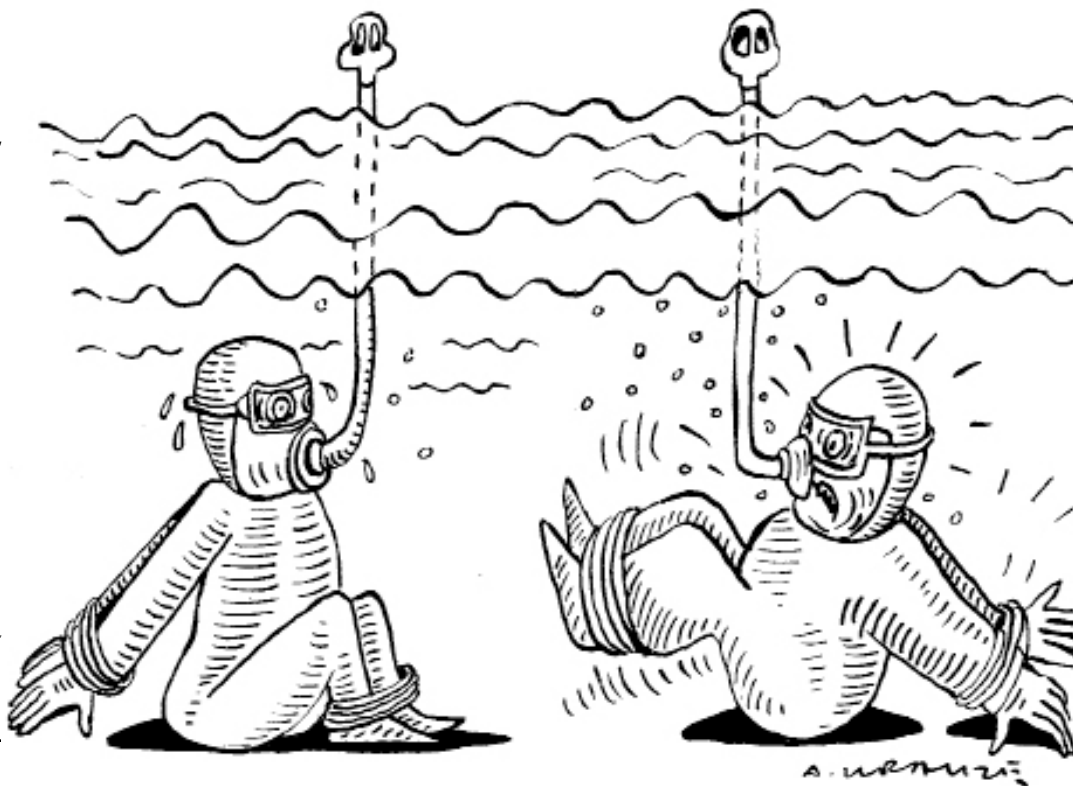
The *BRAF*-deficient mice all produced white, lumpy lesions on their lungs, yet intriguingly, these tumors were all benign (*Genes Dev*, 21:379–84, 2007). When Dankort knocked out either of two tumor suppressor genes, however, the mice developed "massive and quick" lung cancers, he says, indicating that *BRAF* mutations alone were insufficient to cause full-blown cancer.

Dankort then turned his attention to melanoma. He modified his mice so that he could activate the Cre-recombinase in melanocytes simply by painting the mice's skin with a particular chemical. Again, the mice produced benign lesions—little, black moles—that only progressed to melanoma when combined with tumor suppressor gene silencing (*Nat Genet*, 41:544–52, 2009).

Dankort wasn't the only one to model *BRAF*'s role in melanoma, however. Within a span of 6 weeks, two other groups published reports also modeling the exact same mutation. In one paper, researchers at Tufts Medical Center in Boston, Mass., reported a more traditional model, with the mutated *BRAF* gene behind a foreign promoter (*Oncogene*, 28:2289–98, 2009). The other study, led by Richard Marais of the University of London's Institute of Cancer Research, used Cre-recombinase in "more or less exactly the same" way as Dankort did, Marais says (*Cancer Cell*, 15:294–303, 2009). "This is the best way to build a model and I guess

we each independently came up with it.” But unlike Dankort’s mice, Marais’ *BRAF* mutants developed locally invasive melanomas even without the loss of tumor suppressor genes. Marais chalks up this difference to genetic background effects, whereas Dankort says that discrepancies in treatment regimes and knock-in constructs are also potential explanations.

Dankort and Marais’s models together provide “a huge advance in the field of melanoma preclinical science,” says David Tuveson of the Cancer Research UK Cambridge Research Institute. “However, there is much work to be done to clarify which model is going to be the most informative about melanoma or if they are both going to be useful for different reasons.” —Elie Dolgin



Military minds

With his hands tied behind his back and his feet bound together, Charles Alexander Morgan III splashed into the water of the Olympic-size pool at the Navy Diving and Salvage Training Center in Panama City, Fla. with no equipment—except, that is, a dive mask that hung uselessly by its strap from between his clenched teeth. As the water engulfed his body, air bubbles shot towards the surface and he sank quickly to the pool’s bottom. But he didn’t panic. Having spent much of his childhood in the water, Morgan, who studies the biology of stress and post-traumatic stress disorder (PTSD) at Yale University School of Medicine, was surprisingly calm about the particular predicament in which he currently found himself. And it’s a good thing too, as staying relaxed in this situation is really the only way to keep from blacking out.

Many of the military trainees who complete the same task during their 1-month training course are not so fortunate. Morgan had recently come to the training center to look for physiological correlates of stress, trying to identify those individuals better equipped to deal with stressful situations. Trainees are subjected to several dangerous underwater missions, including the one that Morgan

Why do some people panic in stressful simulations, while others stay calm?

otherwise they have failed the course and are asked to leave. Fifty percent of participants are cut by the end of their first week.

Morgan measured the levels of the steroid hormone dehydroepiandrosterone (DHEA)—implicated in how organisms cope with stress—in the trainees both before and immediately following their final underwater navigation exam: a nighttime underwater swim from 3 miles offshore in the ocean to a target on the beach, in which they cannot resurface until they reach the shore, where they are judged based on their time and distance from the target.

He found that high levels of both DHEA and DHEAS (the sulfated derivative of DHEA) predicted superior performance. Furthermore, trainees with higher DHEA levels following the test reported fewer symptoms of dissociation—a common response to trauma involving feelings of detachment from oneself and the world—which again translated into

tried out himself, during which many soldiers lose consciousness. Once revived, they are given 60 seconds to recover and jump back in the pool,

better performance in the underwater task (*Biol Psychiatry*, epub June 3, 2009). “It’s the first time I’ve seen a really solid behavioral correlation between DHEA in human beings,” says neuroscientist Joe Herbert of the University of Cambridge.

Morgan first noticed DHEA’s role in a military situation in 2000 when he was conducting experiments at the Army’s Fort Bragg survival school training program in North Carolina. There, in a simulated prisoner-of-war camp, soldiers are subjected to coercive interrogations employing sleep and food deprivation, among other techniques. Again, Morgan found that people with higher DHEA fared better (*Arch Gen Psychiatry*, 61:819–25, Aug. 2004).

Although the data are merely correlative, it does raise the possibility that DHEA is mitigating the neurotoxic effects of cortisol, the “stress hormone,” says psychiatrist Owen Wolkowitz of University of California, San Francisco. Cortisol levels rise in times of acute stress, causing a boost in energy, memory, immunity, and pain tolerance, all of which help the organism deal with the demands of the stressful situation. On the other hand, prolonged exposure to high levels of cortisol and other glucocorticoids (such as in a combat situation) can kill nerve cells in the brain. ▶