Extending Pet Longevity: Our Companions in Sickness and in Health

By Rick Docksai

Pet owners everywhere would like for their companion animals to live longer, and veterinary medicine is finally making that possible. Emerging developments in gene therapy, cancer treatments, surgery, and nutrition have the potential to give our four-legged friends many more years of life.

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Human life spans have expanded dramatically in the last hundred years and could expand even more in the next hundred, thanks to progress in medicine. Yet, our dogs, cats, and other domestic animals are living only marginally longer than their ancestors. This might not be so for too much longer, however.

Veterinary medicine is evolving. Injuries or illnesses that would have consigned a dog or cat to euthanasia just a few years ago are now very treatable. And more progress is yet to come, thanks to promising recent breakthroughs in genetics, along with continuing improvements in nutrition, surgery, and disease treatment. A dog today can enjoy 12 to 15 years of life, on average. Don't be surprised, however, if it becomes normal late in this century for a dog to still be alive and tail-wagging at age 20 or 25—or even 30!

Domestic dogs have been in our homes and lives for the past 10,000 years, according to anthropologists. But Labrador retrievers, Chihuahuas, whippets, and the thousands of other breeds we know today only came into being over the last few centuries. Dogs of 8000 BCE looked much more like wolves, their feral cousins.

We all know how those ancient domestic dogs became today's dogs: breeding.

Humans still selectively breed dogs, and other animals, as well. But one crucial difference sets today's breeding apart: This is the "genetic age." After J. Craig Venter and colleagues successfully sequenced the human genome circa 2000, other research groups went on to sequence the genomes of chimpanzees, dogs, pigs, horses, cats, chickens, and alpacas.

Knowing an animal's genome is a key to knowing the genes that compose it—and that, in turn, is the key to learning how to modify those genes as desired. The end result: the same animal breeds we know and love, sans the ailments that make their lives all too short.

The University of California–Davis School of Veterinary Medicine is a hub of noteworthy work in this area. Its geneticists made key contributions to the mapping of horse, dog, and cat genomes, and they're now figuring out how to apply this knowledge toward preventing and treating diseases. They have already discovered a genetic mutation for polycystic kidney disease in Persian cats, for example, and have created a diagnostic test that screens for the gene in kittens as young as eight weeks old. The school's cardiologists, meanwhile, have found the gene mutation responsible for hypertrophic cardiomyopathy, the most common cause of feline heart disease.

Another research group at UC–Davis identified a gene mutation that causes Dalmatians to suffer bladder stones and excessive uric acid levels, and they developed a diagnostic tool for breeders to screen it out of their litters. Still other UC–Davis researchers are getting to the bottom of the genetic factors for the canine ailments hyperuricosuria, brachycephaly, Alaskan Husky encephalopathy, spinal dysraphism in Weimaraners, and autoimmune hypoadrenocorticism in Nova Scotia Duck Tolling Retrievers.

It's the same process that breeders have been engaged in since the first domestic dogs. But whereas breeders through the ages have had only blind trial-and-error to guide them and have only been able to see the outcome of a mating after the puppies have been born, genetics can now let us control the outcomes from the moment of cell conception. What might have taken traditional breeders many generations of pups being born, maturing, and mating may now be done in one laboratory experiment.

"It was humans who created all those breeds of dogs over thousands of years. Now we can do it more quickly with genes," says José Luis Cordeiro, futurist and technologist who founded the World Future Society's Venezuela chapter. Cordeiro has written and spoken extensively on genetics, among many other cutting-edge areas of technological innovation.

The University of Pennsylvania hosted a remarkable test case in the new technology in 2013, in an experiment that gave sight to three puppies that had been blind from birth. The researchers identified a gene that codes for certain vital proteins in the eye—the puppies had a mutated gene that left this protein coding out. Next, the researchers synthesized a new version of the gene that did code for the protein. Then they planted it inside viruses and injected the virus into the puppies' eyes. The virus "infected" the dogs' eyes with the gene, and a month later, the puppies could see.

Using viruses to implant new genes is actually an increasingly common practice, according to Emily Anthes, a science writer who described several such experiments in her book on animal bioengineering, *Frankenstein's Cat: Cuddling Up to Biotech's Brave New Beasts* (Farrar, Straus and Giroux, 2013). The viruses don't make their hosts sick, but they do infiltrate the host's cells and, in so doing, introduce the new gene into the host's system.

"Whatever the functional version of the gene is, they'll place it in a virus and they inject it into the relative system in a dog, and the virus does what it does best: infects the dog's body and implants the functional gene to replace the version of the gene that's gone haywire," says Anthes.

If we can engineer blindness out of dogs, then we could surely engineer many more disorders from them, too—including those that kill them, such as diabetes, dementia, and cancer. The National Institutes of Health did something like this for mice in 2013. Toren Finkel of the National Heart, Lung, and Blood Institute led some colleagues in engineering mice so that their bodies would produce just a quarter of the usual levels of mTOR, a protein that regulates cell growth, metabolism, and energy balance. The engineered mice grew up smaller than average but lived 20% longer: median life span of 28 months among the males and 31.5 months among the females, as opposed to 22.9 and 26.5 months for average male and female mice.

Genetic engineering won't work for every condition, however. Many human and animal disorders have multiple genes behind them, and many individual genes code for many traits and functions. Deleting multiple genes in a dog's genome would be very risky—change one gene, and we might negate the dog's stomach cancer risk but inadvertently set the dog up for heart failure and brain death. Anthes looks forward to gene alterations becoming more common for a specific range of conditions—i.e., those in which the disorder is attributable to one solitary gene.

Making Old Cells Young Again

More mouse life extension took place in 2012 at the University of Pittsburgh's School of Medicine. A research team headed by Johnny Huard, professor of orthopedic surgery, microbiology, and molecular genetics, and Laura Niedernhofer, associate professor of microbiology and molecular genetics, obtained stem-cell-like progenitor cells from several young mice and injected them into older mice that had been specially bred to age too quickly and were consequently showing advanced age-related physical decline, including major muscle loss. After the injections, the mice regained their muscle mass and lived two to three times longer than expected: They were supposed to live 21 to 28 days, but some lived 66 days or even longer.

According to Niedernhofer, as a human or animal's body ages, many of its tissues come down with "stem cell dysfunction"—i.e., the cells don't replicate and reproduce like they used to, so the tissue can't repair itself or replace dying cells. So, halt the stem cell dysfunction, and you'll slow age-related body damage.

Cordeiro has an additional suggestion: Let's look more closely at the cells that don't age. He distinguishes somatic cells, the ones that constitute most of our and animals' bodies' tissues, from germinal cells, which include stem cells and many single-celled microbes, such as bacteria. Somatic cells grow old and die; the germinal cells do not. A bacterium can live indefinitely, as long as it has stable food sources and isn't eaten by a larger microbe.

"Bacteria are basically immortal," he says. "Life originated to live, not to die, and that is why bacteria basically do not age. It was with multicellular organisms and sex that the aging process began, since some cells specialized in reproduction and continuing life—the germinal cells—and other cells just supporting them—the somatic cells."

There are other cells that seem to live forever or close to it. Plant cells are among these, hence the forests whose trees are centuries old. Unfortunately for us and our four-legged pals, cancer cells are also germinal—they are deadly specifically because they live on and keep replicating when the body needs for them to die.

If we study all of these cells further and discern what keeps them going, we may find ways to keep healthy cells living longer, too. Cordeiro notes one such clue in telomerase, an intracellular compound that sustains cells' genomes. All cells have it, but they lose it gradually throughout their lives. Once it is gone, the cells can no longer replicate. Cancerous cells, however, somehow regenerate their telomerase supplies and keep going. Researchers in both human and veterinary medicine have been studying telomerase over the past 15 years to look for ways to use it constructively to give new life to aging healthy cells.

There's a huge difference between a bacterium and a dog. But both have DNA, and both run at the cellular level with many of the same enzymes and molecular processes. Further studies of bacteria could thus offer us some clues for keeping dogs and other pets alive.

We also have some multicellular life forms that can teach us secrets to living longer. Cordeiro notes that lobsters can live a hundred to two hundred years before being killed and served up as dinner entrées, and that they show no signs of aging throughout. Certain water-dwelling organisms, including hydra, planarian flatworms, tardigrades, and Turritopsis jellyfish, also pass the hundred-year mark with ease.

"Longevity research is just beginning, and we do not know where it will lead us to, but we can certainly see that somatic cells in multicellular organisms can copy longevity characteristics from germinal cells, and also from stem cells," Cordeiro says.

Making Surgery Less Invasive

Whether the patient is a human or an animal, surgery always carries risks of complications and long-term aftereffects. Good veterinarians make surgery a last resort and, when they must use it, look for the lowest-impact surgical procedure that will get the job done. As such, the search for "minimally invasive" procedures is a key R&D area.

North Carolina State University's veterinary researchers have devised a very promising new tool for minimally invasive cancer treatment called the Varian Novalis Linear Accelerator, which zaps cancerous tumors with concentrated beams of radiation instead of scalpels or, worse, chemotherapy regimens. Using radiation to kill cancerous cells has been a treatment choice for both animal and human patients for a long while, although the radiation's tendency to damage healthy cells near the tumors has made physicians and veterinarians alike reluctant to use it in many cases.

North Carolina State's device softens the treatment's adverse impacts considerably, however, by utilizing two new technologies: Image-Modulated Radiation Therapy (IMRT) and Image-Guided Radiation Therapy (IGRT). IMRT shapes the radiation beam to precisely match the contours of the tumor, so that the healthy tissue and vital organs surrounding the site will be left well enough alone.

The IGRT function, meanwhile, uses on-board imaging and CT scanner tools to identify exactly where any single tumor is each day of treatment. The veterinary team can photograph the cancerous sites daily and pinpoint any changes in tumor size or position. Then they can adjust the radiation beams accordingly.

The Novalis system's IMRT and IGRT functions make it a much more attractive treatment for many more cases. Veterinarians in the past have had to write some cancer-stricken pets off as untreatable because the tumors were too close to vital organs

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for surgeons to remove them without risking severe organ damage. The Novalis system's smart radiation beam negates this risk. Veterinarians can use it to excise many new cancerous sites that had up until now been beyond their reach. Moreover, treatment time could be much shorter and pose far fewer side effects—which could greatly up the chances that a pet owner will decide that more cancer treatments for his or her pet will be worth it.

"The Varian Novalis will be able to treat some types of tumors and cancers that could not be treated with previous machines and technology," says Mike Nolan, NC State assistant professor of radiation oncology and biology.

UC–Davis is making similar strides forward in minimally invasive surgery. The campus's One Health Institute, which fosters integrated research into human health, animal health, and ecology, is pioneering a new technique to deliver chemotherapy drugs directly into any tumors deep within a dog's skull. Neurologists at the institute have used the procedure on several dogs, and the results have been so encouraging that they are now adapting it to use as a treatment for people.

As surgical options such as these improve, veterinarians will gain more and more capability to treat animal cancers that they would previously have written off as untreatable. That's important, since more than 50% of dogs and 33% of cats will develop some form of cancer during their lifetimes, according to NC State data.

Improved Pet Nutrition

Ask any historian why we humans are living longer today than we were in the 1700s, and chances are one of the reasons given is: "We're eating better." Most of us have far more proteins, vitamins, and minerals in our diet than people 250 years ago did, and certainly, the nutrients in our diet strongly affect our chances for living long and healthy lives.

The same holds true for our pets. UC–Davis studies have determined that cats, like people, need daily doses of chloride and vitamins A, B, D, and K; pregnant female cats that get enough daily zinc will be less likely to give birth to kittens with cleft palates.

The supplement L-Carnitine isn't just for humans. Studies find that dogs need it, also, for their circulatory systems and muscles, and that canine heart disease is much less common and less acute in dogs that have enough L-Carnitine in their diets. The pet food industry has caught on to this and now has been selling L-Carnitine supplements and L-Carnitine-enriched dog food for the past decade.

How effective are they? Just ask Matthew Bryce Deutsch, a Maryland resident who has raised two shih tzus. One of them came down with heart palpitations. At the suggestion of Bill Faloon, a colleague and director of the Life Extension Foundation, he began feeding her daily L-Carnitine supplements. The heart palpitations subsided considerably.

It doesn't surprise Deutsch much that the same nutrients that boost human longevity can help other mammals live longer, too. Our anatomy and theirs are a lot more similar than surface-level appearances would suggest, he notes: Ignore their fur, tails, snouts, and claws, and you find the same basic muscles and organ tissues in us and them, albeit in different sizes and shapes.

"They're basically us. It's just that their organs are disproportionate. All mammals are basically the same except for their shapes and organ proportions," says Deutsch. "Even rats have all the same organs that we do and muscles that we do. They just have their organs in different proportions."

That said, our pets also have some unique nutritional needs of their own. Researchers are finding these, too, and advising pet food companies accordingly. For example, UC–Davis researchers discovered the mitigating effect that the nutrient taurine has on feline dilated cardiomyopathy, a heart disorder that kills large numbers of cats. Many lines of cat chow are now taurine-enriched, and the cats have less heart disease to show for it.

New Pathways to Pet Health

Human medical care has seen massive growth of specialized fields of care over the last 30 years. Veterinary care has, too. New fields of urology, neurology, and orthopedics have cropped up within veterinary hospitals, thanks to each discipline having more tools at its disposal and more training required to properly use them all.

Boaz Arzi, assistant professor of veterinary dentistry and oral surgery at UC–Davis, sees it firsthand in new integrations taking place between veterinarians and researchers in other fields, such as bioengineering. He also sees it in the proliferation of new specialized-training programs over the last few years. A resident-in-training at the UC–Davis veterinary school can now attend any of a wide array of three-year specialized programs, on top of the general-practice fundamentals that the basic veterinary accreditation covers. Arzi himself benefited from this specialized-training option and attests to the many more career opportunities that it makes possible.

"The training in veterinary dentistry and oral surgery in combination with training in biomedical engineering did wonderful things for my career and opened many doors," he says.

Good medical care isn't cheap, unfortunately. We can expect veterinary care to become pricier and pricier, just like human medical care. And some of the cost drivers will be the same: higher-cost procedures to keep older patients—in this case, animal patients—living longer. But it's a price that the human pet owners will, by and large, be willing to pay.

Some soften the financial burden via insurance. The pet-insurance market is small but growing and could become a significantly sized industry in years to come.

"I think certainly history has shown that pet owners will not spare any expense in taking care of their pets," says Anthes. "There has been a growth in end-of-life care and intervention for animals, and there will be a demand for these technologies."

Healthier Humans, Too

You don't have to be a pet owner to benefit from all these advances in veterinary health. Thanks to the similarities of these animals' bodies to ours, a treatment that saves an animal's life often turns out to work well in people, as well. Modern medicine teems with medical treatments that first went into use in veterinary clinics. Many more are sure to follow, especially as new treatments under development at UC–Davis, NC State, and other institutions described above gain traction.

"Both animals and humans may serve as a 'disease model' for each other and, when applicable, we integrate treatment approaches accordingly," says Arzi.

An example is the mTOR mouse-engineering experiments. Finkel is hopeful that human Alzheimer's patients could gain more years and undo some of the disease's damage if they undergo protein modifications like that which he and his colleagues achieved in the mice. The researchers intend to nail down exactly how aging in mice and human cells occurs at the molecular level.

"Aging mechanisms seem to follow similar patterns in multicellular organisms, and once we discover some of these patterns in one species, we will be able to use them for other species," says Cordeiro.

Cancer research for humans is also moving forward more quickly, thanks to veterinary R&D. IMRT and IGRT therapies are now in use in human cancer surgery and are already saving human lives just as they are pets' lives.

When his first shih tzu died, Deutsch took a step that some might call extraordinary: He had her cryogenically frozen, in anticipation of tissue-regeneration or cloning technologies one day becoming sophisticated enough to bring her back.

"These dogs were like siblings to me. And 15 years of life just isn't enough. It's not fair that I get to live so long a life and they couldn't," says Deutsch.

Many more pet owners besides Deutsch have frozen their pets, and for the same reason. Their sentiment is understandable. And the science is, in fact, quite sound—research into methods for regenerating and replicating cells is going places and could very well "resurrect" dead animals within our lifetimes.

But what if we don't have to wait until a future time to bring our dying pets back? Suppose that we can heal their bodies here and now and not have to freeze them in the first place. That, too, is a hope that dog owners—and cat owners, horse owners, and owners of just about any other pet or farm animal besides—can cling to, thanks to the real-life breakthroughs that researchers at UC–Davis, North Carolina State University, and other institutions are bringing forth. ❑

About the Author

Rick Docksai is senior editor of THE FUTURIST. E-mail rdocksai@wfs.org.