

► community during that debate, although some think that he may move to the political centre as minister of science.

In a written statement provided to *Nature*, Rebelo dismissed concerns about his position on global warming. “The debate about climate change exists independent of my opinion,” he said. More broadly, Rebelo said that his duty as minister of science is to listen to — and fight for — the academic and scientific community in Brazil.

He has limited power to influence climate policy, although the ministry does oversee some national assessments and some climate reports to the United Nations. One area that will receive considerable attention is the ministry’s funding for science, which has been squeezed by competing demands in recent years.

But Rebelo is not the only appointment to raise eyebrows. Rousseff named Kátia Abreu, who fought environmentalists as a senator and agricultural lobbyist, to head Brazil’s agriculture ministry. And both appointments come at a sensitive time: although the rate of Amazon deforestation has dropped by 82% since 2004, the pace of land clearing spiked sharply in 2013 — and it seems to be on the rise once again.

Rousseff has never had a good relationship with environmentalists, who say that she is hiding behind Brazil’s relative success in reducing deforestation while pushing for major dams and ports that will only increase pressure on forests. Now, after a bruising election, she is looking to rebuild support in Congress in the middle of corruption scandals that have tainted her party.

The Communist party, of which Rebelo is a member, has been a “small but loyal” member of the governing coalition led by Rousseff’s Workers’ Party, and it is also friendly with the agricultural caucus, says Steve Schwartzman, an anthropologist with the Environmental Defense Fund in Washington DC, who has worked in Brazil for decades.

One key to Brazil’s success in curbing deforestation and carbon emissions over the past decade was the involvement of multiple agencies, but that kind of coordinated approach could be more difficult today, Schwartzman says. “These ministerial appointments cast a lot of doubt on what we can expect from this government.”

Helena Nader, president of the Brazilian Society for the Advancement of Science, takes a more conciliatory approach: she says that scientists should give Rebelo some time at the ministry before judging him. More broadly, Nader says that she isn’t expecting a major backslide on environmental issues by the new Rousseff government.

“Nevertheless,” she says, “only time will show.” ■



The cat genome is out of the bag, and has already helped to pinpoint a gene involved in kidney disease.

GENOMICS

‘I can haz genomes, too’

Cats sparked an Internet meme complete with its own grammar, but dogs have dominated genetics labs — until now.

BY EWEN CALLAWAY

Cats may have beaten dogs on the Internet but felines have been a rare breed in genetics labs compared with their canine counterparts. Now, at last, cats are clawing their way into genomics.

At a meeting this week in San Diego, California, a close-knit group of geneticists unveiled the first results from an effort to sequence the genomes of 99 domestic cats. The work will benefit both humans and felines, the researchers say, by mapping the mutations underlying conditions that afflict the two species, such as kidney disease.

“It’s a great time to be in cat genomics,” says William Murphy, a geneticist at Texas A&M University in College Station who is involved in the effort. Plummeting costs for DNA sequencing now make it possible to do genomics cheaply — and cat genomics, long under-funded compared with similar efforts in dogs, is benefiting, he says. “We’re finally at the point where we can do all sorts of things we wanted to do 5 or 10 years ago.”

The first cat genome sequence¹ — from an

Abyssinian named Cinnamon — was reported in 2007. But the sequence contained significant gaps and errors, which slowed efforts to map genes. A high-quality version of Cinnamon’s genome was not published² until late 2014. Domestic dogs, meanwhile, have become a darling of geneticists: their full genome³ was reported in 2005, and the sequence has been continually improved. Hundreds of genes underlying canine diseases and traits are estimated to have been discovered, compared with as few as a dozen for cats.

The discrepancy can be traced back to the early 2000s. After the completion of the human, mouse and rat genomes, the US National Institutes of Health organized a commission to decide on their next target; the dog genome was selected for high-quality sequencing, whereas cats were put on hold.

That got some cat geneticists’ backs up. “The truth is there were more powerful people interested in dogs,” says Stephen O’Brien, director of the Theodosius Dobzhansky Center for Genome Bioinformatics in St Petersburg, Russia, who led the initial cat-sequencing efforts. But canine researchers were able to make a

compelling case. Pet dogs suffer from many of the same conditions as humans, from narcolepsy to arthritis. And the intensely inbred nature of dog breeds made it relatively easy to identify disease-causing genes: because there is little genetic variation within any particular breed, the genes that cause disease in affected individuals stand out.

Dogs had other advantages, too. The existence of kennel clubs, which maintain 'breed standards' and are full of enthusiastic pet owners and veterinary surgeons, helped dog geneticists to recruit subjects for study. "Given the resources they had, they were discovering new genetic diseases in breeds almost daily," says Niels Pedersen, a veterinary scientist at the University of California, Davis.

In fact, both cats and dogs offer insights into human disease, including those associated with old age. In 2004, a team led by geneticist Leslie Lyons of the University of Missouri in Columbia (and owner of two female cats, Withers and Figaro) discovered that mutations that cause polycystic kidney disease — a major cause of renal failure in older individuals — occur in the same gene in humans and cats¹. Cat versions of type 2 diabetes, asthma, retinal atrophy and numerous other conditions have close similarities to human disease. Cats can also become infected with a virus that is closely related to HIV and experience symptoms similar to those of people with AIDS.

In the hopes of speeding up the discovery

of genes related to these conditions last year, Lyons launched the 99 Lives cat genome sequencing initiative, playfully hosted on a site called Lyons' Den. She discussed the effort on 11 January at the Plant & Animal Genome conference in San Diego.

Lyons' team is cobbling together funding from anywhere it can find it. The researchers are asking private owners, breeders and

"I would love to eradicate all genetic disease in cat breeds before we're done."

Any owner can participate," she says. All the data will be made public after the results are published.

With the money raised so far, the team has sequenced the genomes of 56 cats, including fancy breeds such as Burmese; cats with specific diseases; and a kitten named Dragon and his parents Ares and Marcus — the hope is to use the feline trio to narrow down the genetic basis for traits they share, such as their silver, curly coats.

Even Robert Wayne, a canine geneticist at the University of California, Los Angeles, agrees that Lyons' effort is important. "I hope she raises money for it," he says.

Insights from cat genomics extend beyond

even pet-food companies to donate the US\$7,500 needed to sequence the genome of a single cat, which could be one of a donor's choice. "Any cat can participate.

disease. Razib Khan, an evolutionary geneticist at the University of California, Davis, wants to use genome sequences to chart the domestication and spread of cats throughout the world, and to determine how different domestic and wild cats are genetically. "There's always the question — are they domesticated at all?" he says. The 2014 publication that included Cinnamon's genome already identified differences between domestic and wild cats, including genes expressed in the brain that are possibly linked to the docility of (some) house cats. "Wild cats will hand you your behind if you get next to them and domestic cats will sit on your lap," O'Brien notes.

Lyons is also keen to see genomics help felines. "I would love to eradicate all genetic disease in cat breeds before we're done," she says. Her team's discovery of the cause of polycystic kidney disease has reduced its prevalence among Persians, by removing cats with the mutation from the breeding pool. Her lab is now developing drugs that could treat the terminal condition in cats — and perhaps in humans. But human health, Pedersen says, is not the only goal. "I'm in it, and Leslie's in it, for the good of cats." ■

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HEALTH

First biosimilar drug set to enter US market

But such cheaper, generic versions of biological drugs face scientific, regulatory and patent hurdles.

BY HEIDI LEDFORD

After years of debate, the US Food and Drug Administration (FDA) is poised to allow the sale of biosimilars, cheaper versions of complex and expensive biological drugs used to treat conditions such as cancer and autoimmune diseases. On 7 January, an FDA advisory panel decided unanimously that a drug made by Sandoz, the generics arm of Swiss pharmaceutical giant Novartis, should be accepted as a replacement for filgrastim (Neupogen), an immune-boosting drug for people undergoing cancer treatment made by Amgen of Thousand Oaks, California.

Such knock-offs are called biosimilars

because the drugs that they mimic, dubbed biologics, consist of complicated molecules that are made in living cells and are impossible to copy exactly. Even copying them inexactly is immensely challenging — despite the expected approval of the Sandoz drug, the difficulties involved in creating and evaluating biosimilars may limit their infiltration of the marketplace. The field is also littered with patent issues, especially with regard to how the drug is manufactured. In the case of filgrastim, Sandoz is challenging some of the legal requirements for approval.

"We're starting from scratch," says Jordan Paradise, a specialist in technology law at Seton Hall University in Newark, New Jersey. "A lot of

the scientific uncertainty is still there."

Unlike typical drugs, which are relatively small molecules made through biochemical processes, biologics are large protein molecules produced by genetically engineered organisms. Living cells may chemically modify the proteins they make by adding complex sugars and other compounds at certain positions. The exact conditions under which cells are grown can alter the pattern of these modifications, and thus the molecule's structure and behaviour. The result is a drug so complex that it is difficult — if not impossible — to fully characterize.

Because biosimilars are inexact copies, they are required to undergo more testing than an ordinary generic drug. The European Union has been evaluating and approving biosimilars for the past decade, but the United States did not have a way to do so until regulatory legislation was passed in 2010. Biotechnology companies have been waiting to find out how the FDA would evaluate the drugs.

Patient advocates hope that biosimilars can reduce drug costs by increasing competition. Biologics are expensive: researchers have calculated that treatment of metastatic colorectal cancer with bevacizumab (Avastin) costs about US\$75,000 per year of life gained (V. Shankaran *et al. Oncologist* **19**, 892–899; 2014). A report last year by the RAND ▶