are ongoing habitat loss and degradation, and illegal hunting.

Alongside work by Paignton Zoo researchers and Kenyan authorities on the population in Arabuko-Sokoke, a Darwin Initiative project is under assessment in Zanzibar, to try to ensure the long-term survival of these animals on the island. The initiative requires surveys in Zanzibar to obtain reliable population numbers and the degree of fragmentation of the remaining animals along with research on the duiker's feeding ecology and social behaviour.

A Darwin initiative preliminary visit to Zanzibar was made in December 2005 and a base established within a forest reserve that allowed first-hand monitoring of Ader's duiker in its restricted remaining natural habitat. Data on food plants and their relative abundance were also gathered and dung samples were collected to investigate the potential for the use of DNA for establishing the identity of individuals. A satellite collar was also tested for its effectiveness for potentially tracking animals under forest cover.

Informal meetings were also held with village chiefs, forest rangers and local hunters to explain the project and assess the potential for community conservation and participatory monitoring.

There's little doubt that hunting remains a major threat to remaining populations of this antelope. Although hunting in Zanzibar is controlled through community management schemes, it is often difficult to implement these efficiently because of cultural sensitivities, along with the pressures of poverty, population growth and demand for natural resources.

Elusive: Scientists from Paignton zoo in the UK have produced what is thought to be the first photograph of the endangered Ader's duiker antelope in its native environment in Kenya. (Photo: Paignton Zoo Environmental Park.)

Q & A

Stephen J. O'Brien

Stephen J. O'Brien trained in Drosophila *genetics at Cornell under the mentorship of Bruce Wallace and Ross MacIntyre. He joined the National Cancer Institute as a post-doc in 1971 and is now chief of the NCI's Laboratory of Genomic Diversity, which he founded in the late 1980s. His is known for documenting the remarkable genetic uniformity of African cheetahs, resolving the taxonomic riddle of the giant panda's evolutionary origins and describing heretofore unrecognized species of orangutans, African forest elephants and Bornean clouded leopards. He is credited with the discovery of* CCR5-D32, *the first of twenty human AIDS restriction genes, as well as leading the Feline Genome Project, a major player in comparative genomics across the mammalian radiations. His recent books include:* Tears of the Cheetah and Other Tales from the Genetic Frontier *(St. Martin's Press, 2003),* Atlas of Mammalian Chromosomes *(Wiley, 2006), and* Genetic Maps - Locus Maps of Complex Genomes *(Cold Spring Harbor Press, 1988-1993). The Laboratory of Genomic Diversity has assembled over 62,000 animal and 424,000 human tissue/DNA specimens, facilitating wide-ranging studies of disease gene associations, species adaptation and natural history by O'Brien's many colleagues.*

How did you get into biology?
Science was my third career choice, after professional baseball and the Broadway stage. Lacking the required talent for these two dream careers, I dabbled with pre-vet and pre-med courses until an inspirational undergraduate teacher, James Edwards, lit a fire in my belly with tales of the ground-breaking discoveries by the visionary molecular biologists Avery, MacCleod, McCarty, Lederberg, Kornberg, Watson, Crick, Nirenberg, Jacob and

Monod. Genetic reasoning and study designs fascinated me, and I was pretty good at it. A graduate fellowship to study genetics at Cornell was to me a deliverance from salaried servitude.

Drosophila was the organism of choice for genetic research in the 1960s, and I was struck by the amazing inferences made in the early 20th century by intellectual giants such as Morgan, Bridges, Dobzhansky, Lewontin, Wright, Haldane and many others. Back then, population genetics was a sleepy academic discipline that molecular biologists disdained; yet I began to appreciate that population inference would shed a bold new light on the bigger questions of genic and species adaptation.

Looking back, I now believe the seeds of population genetics, however unappreciated then, formed the platform upon which three exciting new fields that I have been privileged to be part of – conservation genetics, DNA forensics and disease gene discovery using population genetic association – would emerge and flourish. My postdoctoral fellowship at NCI demanded a whole new learning curve – taking in cancer, oncogenes, retroviruses, immunology, tumor suppressors and AIDS – but one for which my early training in genetics was complementary.

What is the best advice you have been given? This gem was given to me by my graduate advisor Ross MacIntyre, who once told me that the most important lesson he could teach his students was *not* how to know a discipline well, *not* how to design a great experiment and *not* how to compose a cogent research grant proposal or manuscript. The most critical skill a scientist can nurture is the ability to recognize an important scientific observation when you see it and then to pursue the evidence so aggressively that the skeptics are silenced. To miss the first part is reminiscent of comments I encounter not so uncommonly after a Nobel award is announced. Have you ever heard colleagues then quip "Oh, I had similar data long before they did. It's in my files and I never published it!"? Translation: "I didn't recognize the significance of my own data"; or worse, "I was too inflexible to pursue this nattering and surprising result. Instead, I followed conventional wisdom in a steady predictable research tact." A day doesn't go by when I don't learn new things, but I have never forgotten the advice I received long ago about considering the implications of one's own inexplicable findings.

Did any single favorite paper or author exert extraordinary influence on your science perspective? Actually, no! There were scores, if not hundreds of advances, papers and discoveries that have invigorated my curiosity and enthusiasm. Human culture benefits from monogamy, which lends stability to family tradition and child rearing. Scientific advances are just the opposite. New discoveries invariably come from multiple fresh perspectives, new eyes, and innovative ideas. I have benefited enormously from my impressions of Ernst Mayr, Theodosius Dobzhansky, Victor McKusick, Howard Temin, Bob Gallo, Eric Lander and Craig Venter. Indeed, in managing my laboratory, I have consciously avoided a narrow focus by facilitating diversity across science disciplines. Place a fledgling field ecologist specializing in bird migratory behavior adjacent to a molecular virologist dissecting regulatory signals in HIV long terminal repeats (LTRs), and at first they see nothing in common. But more often than I can count, apparently disparate disciplines inform and influence each other more profoundly than a lab full of like-minded specialists in any field. Science is learning, so what better than disciplinary integration, competition, and cooperating *in situ* of a fast moving molecular biology/genomics laboratory?

Do you have a scientific hero? I answer this question with some trepidation. There are many heroes of science whom I admire and wish to emulate for their insight, prescience, innovation and leadership. But one unheralded group whom I really do appreciate is that of the communicators of science to the lay public, the prolific speakers, popular writers and television science commentators who inform the public of the excitement of real science with unusual clarity. They portray an image of science that is far richer than memories of Dr. Frankenstein, of "Back to the Future" mad scientists or of befuddled mathematics professors. We need more like Carl Sagan, David Suzuki, Marlin Perkins, even Mr Wizard. An engaging and knowledgeable science spokesman stands before a TV camera and exudes confidence and enthusiasm for the mysteries of life, of our universe, of science.

Yet many of my scientific colleagues disparage such popular efforts to simplify and explain complex subjects to the public; and the more visible the spokesperson becomes, the louder the cumulative hectoring from "serious scientists". Is the outcry a true defense of the precisely accurate? Do we realize that the tendency to produce cumbersome, caveat-burdened sentence fragments in pursuit of exact correctness is a recipe for an extended public yawn? The curious public, who pay for and are eager for science, benefit greatly from clear, articulate, approachable spokesmen and spokeswomen of scientific enquiry.

Science discovery can be every bit as exciting as the Indiana Jones chronicles. Features about searches for cures, vaccines or elusive lost species on science shows, such as those on the Discovery Channel, Nova or PBS, are crucial to shoring up public support and funding; even lawmakers watch TV. Today's grant review study sections exert endless energy to carving up smaller and smaller pies of available resources, sinking their colleagues in hope of local benefit. My remedy is better public communication, better

visibility, and better accountability to reluctant donors to encourage vastly greater resources. For these reasons, I admire the art of science communication, and try my best to capture the energy when a TV crew arrives to feature our own research discoveries.

Do you have a favorite scientific journal? Although I have several favorites which illuminate my life, I am particularly fond of *Cat News*, a quarterly newsletter edited by noted conservationist Peter Jackson of IUCN. *Cat News* publishes short essays about new developments relating to non-domestic wild cat species, from lynxes to tigers to lions and snow leopards. Felid observations, conservation anecdotes, sightings in remote corners of the world, even wildlife trade prosecutions are described. Without the encumbrance of peer review, the articles describe phenomena, happenings, occasional science and stories around a group of species about which, a generation back, I became scientifically curious. Without these intrepid (often amateur) naturalists' reports and muses, the genetic hypothesis that we inspect would not exist.

Why your unusual interest in cats? There are many answers to this question, some scientific, some cultural and some personal. Cats are fascinating in so many ways, not the least of which is their unrivaled pre-eminence atop the food chain in every place they occur. Evolution has created 37 magnificent predators that represent true winners in nature's struggle for existence. Mankind has been fascinated with big cats since the dawn of written history and cave art, deifying, fearing and depredating cats. It seems a shame that in the autumn of such a glorious majesty over the world's ecosystems, nearly all cat species are today considered threatened or endangered. Can science help reverse this trend? I believe it can; I hope we can.

Isn't it unusual for someone at the National Cancer Institute to work the genetics of wild animals? I realize that some feel that our work on charismatic icons of conservation might seem, at first glance, far from the NCI's mission, but years ago we realized there are unrecognized benefits in the wild. Our first goal, to help stabilize and recover dwindling populations of endangered species, was assisted by population and phylogenetic approaches which revealed cryptic genetic "footprints" of historic bottlenecks, migration and isolation. Conservation genetics, now an agenda item for many conservation management plans, was born.

The second benefit, and one I have softly articulated before (most recently in "*Tears of the Cheetah*", my 2003 popular book of genetic adventure stories) is that free-ranging species have evolved genetic solutions to deadly diseases analogous to incurable human maladies. Wild species endure cancer, AIDS, deadly infections like SARS and Ebola, arthritis, chronic wasting disease, and immunodeficiencies. Yet animals have only their intrinsic genomic variability and natural selection as a defense. Genetically resistant individuals survive the assault and pass their adaptive gene variants to their descendents. Hard-wired natural genetic solutions to models of deadly human diseases await discovery in natural populations of our mammal relatives. Comparative genomics, which line up homologous genes in diverse mammals, connects the dots from animal resistance to human applications, spurring novel therapies. The strategy is proven. What awaits is genomic mining of the ~5000 mammal species who have evolved genetics solutions to deadly diseases. I am anxious for the next generation of genome scientists to integrate fields of disease gene discovery in wild species with human medicine. When that occurs, our two goals will be nicely achieved: species conservation on one hand and cures to human maladies on the other. The future is ours to grasp!

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Quick guide

Nuclear envelope

Elisa Dultz and Jan Ellenberg

What is the nuclear envelope? By separating the genome from the cytoplasm, the nuclear envelope defines the hallmark of eukaryotic cells, the cell nucleus. The envelope is made up of inner and outer nuclear membranes, which enclose a lumen, the perinuclear space, which is continuous with the endoplasmic reticulum (ER) lumen. The inner and outer nuclear membranes are connected at the sites of nuclear pore complexes, large, aqueous protein channels that mediate all traffic through the nuclear envelope. Underneath the inner nuclear membrane of multicellular organisms lies the nuclear lamina, a peripheral meshwork of intermediate filament proteins called lamins and their associated proteins (Figure 1).

What is the function of the nuclear envelope? It is a barrier separating nuclear processes such as transcription from cytoplasmic processes such as translation. The selective transport of macromolecules between the two compartments of a eukaryotic cell via nuclear pore complexes makes it possible for gene expression to be regulated, for example at the levels of pre-mRNA splicing and mRNA degradation, not seen in simpler prokaryotic cells. It is increasingly evident, however, that the nuclear envelope is not simply a passive barrier: it also has a critical role in the organization of chromatin, gene expression, nuclear anchorage to the cytoskeleton and cell division.

So how do molecules get in and out of the nucleus? The nuclear pore complexes, made up of about thirty different proteins termed nucleoporins, serve as selective gates in the nuclear envelope. The hydrophobic interior of the channel excludes macromolecules depending on their size and hydrophilicity. While