Across the Great Divide: Chimeras and Species Boundaries

by

Katherine Anne Bourzac

B.A. Biology and Comparative Literature
University of Southern California, 2003

SUBMITTED TO THE PROGRAM IN WRITING AND HUMANISTIC STUDIES IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE IN SCIENCE WRITING
AT THE
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

SEPTEMBER 2004

Signature of Author: _____
Program in Writing and Humanistic Studies
June 10, 2004

Certified By: _____ 6/10/04
BD Colen
Lecturer, Program in Writing and Humanistic Studies
Thesis Advisor

Accepted By: _____ 6/22/04
Robert Kanigel
Director, Graduate Program in Science Writing
Professor of Science Writing

Across the Great Divide: Chimeras and Species Boundaries

by

Katherine Anne Bourzac

Submitted to the Program in Writing and Humanistic Studies
on June 10, 2004 in Partial Fulfilment of the Requirements for
the Degree of Masters of Science in Science Writing

ABSTRACT

We have always been fascinated by borderline creatures. Chimeras, hybrids of multiple animals—and sometimes humans—appear repeatedly in mythology across cultures from ancient times to the present. Since the early 1980s, scientists have been creating cross-species chimeras, first combining mouse species that could not interbreed naturally, then moving on to create chimeras from even more distantly related animals such as sheep and goats. Scientists use chimeras to study fundamental processes of life such as pregnancy, fetal development, and the progress of disease. Chimeras allow scientists to perform experiments that would otherwise be impossible.

Ancient chimera myths played on our anxieties about the boundary between man and animal. Interspecies chimeras strike the same chords of disgust and fear in some people as these ancient mythical chimeras did. This paper examines the science of chimeras and biological borderlines and the social implications of creatures that challenge accepted and comfortable ideas about the divisibility of the animal and human worlds.

Can human-animal chimeras be made? Activists Stuart Newman and Jeremy Rifkin have filed a patent application for human-animal chimeras, such as the humanzee, to protest patents on all life forms. Newman and Rifkin believe chimeras are emblematic of abuses of biotechnology and are on a slippery slope to human cloning and elimination of the distinction between natural and manufactured things. They are not alone in believing scientists should be more concerned about the ethical implications of their work. However, a majority of scientists, bioethicists, and scholars find Newman and Rifkin's viewpoint extreme.

The creation of chimeras between species—groups of animals that by definition cannot interbreed—may seem to challenge the historically-shaky biological species concept. Goat and sheep cells can work together in a single healthy organism. Does this undermine the taxonomical boundaries between them? While existing in a confusing zone between species, chimeras do not challenge the biological species concept as directly as may seem. When these chimeras are viable, they demonstrate shared common ancestry through evolution. Because chimeras cannot breed and generate more chimeras, they do not challenge the species concept.

Thesis Advisor: BD Colen
Title: Lecturer, Department of Writing and Humanistic Studies

Across the Great Divide: Chimeras and Species Boundaries

The wild-eyed creature wandered his lonely labyrinthine prison, wrathful and hungry. Minotaur, a man-eating giant, had a human body and a bull's head. His mother, the Queen of Crete, had him imprisoned in the Labyrinth, and his father Neptune—who had impregnated the Queen in the form of a bull—showed Minotaur no godly mercy. The hero Theseus slayed him. More than two thousand years ago, the ancient Greeks conjured up this story of a horrendous, half-human monster.

Creatures similar to Minotaur, called chimeras—hybrids of multiple animals and sometimes humans as well—figure repeatedly in mythology across cultures. Many of the gods of ancient Egypt and many Hindu gods are part human, part animal. However, in Western mythology and literature, the most frightening monsters are chimeras. Dante, for example, populated his *Inferno* with chimeras. On his journey through Hell, the poem's narrator encounters first the Minotaur, then a pack of Centaurs, who were horses with human torsos, then the Harpies—flesh-eating, screeching bird-women—and finally Geryon, whose honest human face belied his reptilian hide, hairy paws, and serpentine tail.

Chimera, who gave her name to this class of monsters, had three horrible heads. In depictions of Chimera on Greek pottery and in Etruscan sculpture, the lion head in front snarls, rearing back; the goat head below the shoulder blades lolls, spewing fire; and hissing from the tip of its serpentine tail is the head of a snake. Chimera's ribs jut out, suggesting the terrible hunger which drove her to ravage the countryside until she was killed by the hero Bellerophon on orders from the gods.

Jorge Luis Borges, the Argentine modernist writer fascinated by labyrinths, libraries, and tigers, described Chimera and other such creatures in his encyclopedia of monsters, *The Book of Imaginary Beings*. He called Chimera "an ephemeral or accidental monster" and claimed that people were bored with it even by Roman times; writing in 1957, he noted that her image had faded and that the word, which had come to mean "a vain or foolish fancy," was all that remained of her raging fire.

But rather than fade into the ancient past, chimeras have taken on real form.

Over the past two decades, chimeras have lept from the dark realms of mythology into biology labs. Scientists have been creating cross-species chimeras since the early

eighties, first combining mouse species that could not interbreed naturally, then moving on to create chimeras from even more distantly related animals such as sheep and goats. Today there are even chick-mouse chimeras and mice with human organs. Borges wrote of the creatures in his encyclopedia, "Our monsters would be still-born, thank God." Modern biology has brought these creatures to term.

But these lab-made chimeras are no three-headed man-eating monsters: most resemble the ordinary four-footed furry creatures they comprise. The scientists who create them do so to study such fundamental processes of life as pregnancy, fetal development, and the workings of the immune system. These chimeras allow scientists to perform experiments that would otherwise be impossible.

Yet cross-species chimeras strike the same chords of disgust and primal fear in some people that the mythical Chimera and Minotaur struck in the ancient Greeks. The ancient myths played on man's insecurities about the natural order, suggesting as they did the breaking down of boundaries between animal species, particularly between man and beast. The modern creation of chimeras raises some of the same questions, given its potential to at least in some sense erase species boundaries, including the boundary we cling to with the most insistence: that between humans and other animals. This border country is occupied by the great apes, chimpanzees in particular. Experiments that inevitably suggest that the boundaries between species may not be as firm as man has always believed them to be seem to evoke the fundamental, to some disquieting question: what does it mean to be human?

Developmental biologist Stuart Newman of New York Medical College has dreamt up a chimera which raises this very question. Newman has filed an application with the U.S. Patent Office describing a creature he calls the humanzee, a chimera part human, part chimpanzee. Imagine such a creature. Would it walk on two feet like us, or amble on all fours? Would it look like a hairy man with a flat nose, or a bare chimpanzee with stunted limbs? Would it be human, have rights, vote at age eighteen, take the bus, and even, like Dr. Frankenstein's monster, read Milton?

Newman and Jeremy Rifkin, an activist variously called a gadfly, professional anti-scientist, and prophet, filed the patent application for the humanzee and other human-animal chimeras in 1997. They are still battling with the Patent Office, which

initially rejected their application. All the chimeric monsters of myth were ultimately slain by righteous—or self-styled—heroes. And while many scientists see Newman and Rifkin as a Don Quixote and Sancho Panza, out of touch with reality and tilting at windmills, they see themselves as modern-day Bellerophons riding forth to slay the monsters of modern biology. The pair want to see patents on any and all life forms outlawed; they have filed their chimera application as a form of sophisticated shock art to push legislation against such patents. For Newman and Rifkin, chimeras are emblematic of a host of ethical and moral difficulties raised by biotechnology.

To most scientists, biological chimeras aren't menacing; they are fascinating and exciting. "Not only is [the human-mouse chimera] *a* model, it's probably the *best* model you can get," said Paul Davis, a PhD student at Washington University, of the chimeras his lab uses to study to course of human diseases. Gary Anderson, chair of the Department of Animal Sciences at the University of California, Davis, feels a similar enthusiasm for the goat-sheep chimeras he used to study interspecies pregnancy in the 1980's, a period he recalls as "a very exciting time."

There are several kinds of biological chimeras, most of which are naturally occurring. In normal animals, all cells have an identical set of genes. A chimera is simply an animal with some genetically different cells. A person who has had a blood transfusion may technically be considered a chimera if some of the donor cells persist in the circulatory system. Mutations in a single cell during the development of the embryo can lead to genetically different patches of tissue in the adult. Joseph Merrick, the so-called Elephant Man, had a condition called Proteus Syndrome, a disease caused by a such a mutation in patches of tissue that causes them to grow abnormally. Chimerism is the suspected cause of Proteus Syndrome.

Another kind of naturally occurring chimera results from the fusion of fraternal twins in the womb. These chimeras are rare, but have been found in cows and recently in humans. Only about thirty human chimeras have been identified to date. We often hear that genes determine our intelligence, our tastes, our personality—in short, who we are. But most human chimeras with two genetically distinct kinds of cells have no more identity problems than everyone else; most will never know they are chimeras, especially if the embryos that fused to create them were of the same sex. Chimeras resulting from

the fusion of male and female embryos are often hermaphrodites, but not always: in a 1998 article in the *New England Journal of Medicine*, Lisa Strain and David Bonthron wrote that human chimeras range from anatomically normal, fertile men and women through male and female hermaphrodites.

Some lab-made chimeras are more dramatic in appearance. But whether lab-made chimeras look scary or not depends more on the viewer's preconceptions than anything else. As molecular anthropologist Jonathan Marks of the University of North Carolina noted, "Where you're coming from may define how you think about things." In 1987, *Newsweek* ran an article about goat-sheep chimeras that described them in terms suggesting monstrosity: the chimeras "have eyes that can stare back at you in a most unsettling way," according to the author. But examination of a few photos of these creations reveals normal-looking animals with coats that look a little patchy. They exhibit not a Medusa-like stare but the same large eyes that can be found on other, nonchimeric animals. One might just as easily project onto these eyes the same innocence and placidity we tend to read into the gazes of ordinary lambs. The goat-sheep chimera, according to *Newsweek*, "hardly cuts an impressive figure"—but then what domesticated ruminant does? It is unsettling to look at an animal and be unable to say what it is, even if you know what kinds of cells it's made of. However, if you were walking down the stalls at the 4-H fair and saw a goat-sheep chimera without knowing what it was, you might think it was a cute new goat breed.

All animals start out life as a single cell with a unique genome resulting from the fusion of sperm and egg. This cell duplicates itself again and again into billions of cells which will specialize in the embryo, becoming liver or heart or skin cells that will eventually form these parts of the body. If the chimeric monsters of myth are collages of body parts, biological chimeras are mosaics of cells. The term biological chimera usually refers to animals made of cells with different genomes: scientists make them out of cells from embryos that have already started developing from a unique sperm and a unique egg. Cells from the two embryos must be blended before they have begun to specialize; this way, the cells grow and develop together into one complete animal whose every organ has cells from both animals.

This blending of two genetically distinct kinds of cells creates an animal that is said to have two cell lines. These cells accept each other as self—even though they can be from animals as unrelated as different species—and continue developing like a normal embryo. A chimera "isn't a monster, it's an organism with more than one cell line," said Anderson, who has made goat-sheep chimeras. These unique cell lines can, amazingly enough, work together as one organism. Once the chimeric embryo is old enough, scientists implant it in an adult female to complete development. If all goes well with the pregnancy, the chimera will be born and continue normal growth.

Chimeras made in this way develop into patchy creatures, like a checkered quilt made of two colors of cloth. Goat-sheep chimeras have patches of both goat hair and patches of sheep wool all over their body; these spots correspond to areas of skin made of goat and sheep cells. But such chimeras are mixed through and through: every organ and tissue is a mosaic of cells from both embryos. The ratio of one kind of cells to the other may vary, but both kinds are mixed throughout the body. Looking at the animal's fur is a good way to estimate the overall cell ratio, Anderson said. "If you have a white animal with a black spot on its forehead," the rest of the animal will also have very few cells from the line with the black pigment. If you're looking at a chimera whose fur is a "50/50 mix" of black and white patches, "you're going to have a good mix in the rest of the body."

In 1980, Janet Rossant, then of Brock University in Ontario, and W.I. Frels of the Jackson Laboratory in Bar Harbor, Maine made the first interspecies chimeras to live to adulthood. Their animals were *Mus musculus–Mus caroli*, or lab mouse–field mouse chimeras. Frels and Rossant used embryos about four days old. At four days, a mouse embryo is a hollow little ball of cells with a clump of cells inside, called the inner cell mass. The cells forming the outside of the ball will become the placenta and do not become part of the adult mouse. Those from the inner cell mass are the real goods, eventually becoming the fetus. Frels and Rossant injected inner cell masses from lab mice into the hollow in the field mouse embryos, where the two inner cell masses mingled into one. After completing development inside mouse mothers, the chimeras were born. The results were sleek scurrying little things, like any other mice, who had patches of albino and agouti (banded) hairs in their coats.

Combining mouse cells to create chimeric mice that look normal does not seem very exciting. But *Mus musculus* and *Mus caroli* cannot interbreed in the wild. They are different species. And as such, centuries or perhaps millennia of conventional wisdom, scientific and otherwise, tell us that their flesh is not supposed to mingle. The very definition of species in biology is just that—species are groups of animals that can interbreed with one another to produce fertile offspring. This reproductive definition of species is called the biological species concept. The biological species concept tells us that no matter how similar two animals look, if they cannot interbreed or if their offspring are infertile, they are members of separate species. Horses and donkeys can interbreed, but because their offspring—mules—are infertile, they are different species.

However, cells from different species often work well together in chimeras. In this respect, they seem to test the meaning of the species concept.

Gary Anderson of the University of California at Davis did some of the most widely-publicized chimera experiments. Driving from the freeway along the edge of the UC Davis campus to the building housing Anderson's office, a visitor passes an open barn full of cows and a row of enormous glass greenhouses. It is hard to determine where the farmland ends and the laboratory begins. The Davis campus is a continuation of the green fields and pastures surrounding it and is set off from them by clumps of parking lots and large modern buildings. Much of the research done at Davis supports agriculture, the largest industry in California's San Joaquin Valley—if the valley were a state, it would rank behind only California, Florida, and Texas in the number of people involved in farming, forestry, and fishing.

Anderson, who made the goat-sheep chimeras described in the *Newsweek* article, feels strongly that his goat-sheep were "perfectly normal interspecies chimeras." Calling interspecies chimeras "normal" may seem like an unlikely use of the word. But at an institution like UC Davis, whose research websites frequently state that they are using biology to "improve" animals for human use and consumption, chimeras are almost run of the mill.

For many people, chimeras' potential to push the meaning of species boundaries is unsettling. Anderson saw this potential as an opportunity to study the nature of

reproductive boundaries between species. He wanted to know what causes interspecies pregnancies to fail. By asking this question, Anderson hoped to learn something about the nature of normal pregnancies. There was a practical side, too: in the eighties, interspecies pregnancy seemed a promising solution for species facing extinction.

By definition, species cannot interbreed. For the most part, they also cannot carry each other's pregnancies—for example, a sheep cannot carry a goat fetus to term—except occasionally, and then only with a lot of intervention from scientists. Zoos have long been interested in preserving their endangered collections using this interspecies pregnancy. Ideally, scientists would implant a fetus from the endangered species into a female of another, common species to carry the pregnancy. Normal pregnancy puts endangered animals at risk: both the pregnant mother and the fetus might die, resulting in one fewer endangered animal instead of one more and bringing the species closer to extinction. And as theologian Ted Peters writes in an essay called "DNA and Dignity," "it is a mark of cosmic shame for a species to become extinct through human actions." In theory, it would be less of a loss if, for example, a cow or a goat died while carrying an endangered Arabian oryx made by in vitro fertilization. In reality, for the oryx and most other endangered animals, there exists no common species so closely related that it is capable of carrying their pregnancies.

"Our approach was to try to define the underlying mechanism or at least learn something about why interspecies fail, because that might give some clues about how to prolong the pregnancies or how to select compatible species for carrying the pregnancies," said Anderson.

Before Anderson's work, it had long been assumed that the primary barrier to interspecies pregnancy was the immune system. Cells are covered in proteins and other molecules that act as a sort of nametag explaining to the immune system that they belong in the body. Foreign cells, viruses, and other particles, on the other hand, are wearing what the cells of the immune system see as a sort of molecular target. These molecular targets, which signal the immune system to attack, are called antigens. This is why organ transplantation is tricky: the recipient must take drugs to suppress the immune system so that his body does not turn on and kill the foreign organ.

Interspecies pregnancies were thought to fail because the mother's immune system would detect species-specific antigens from the fetus, then attack and reject it. Chimeras allowed Anderson "to do an experiment we couldn't possibly have done otherwise—that is, establish an interspecies pregnancy that the mother wouldn't recognize as foreign." If immune rejection is the primary reason interspecies pregnancies fail, then goat-sheep chimeras, whose immune systems tolerate both species, should be able to carry both goat and sheep pregnancies. Anderson found that they couldn't.

The first set of Anderson's experiments eliminated species-specific antigens as the cause of the failure of goat-sheep interspecies pregnancy. For these experiments, Anderson made what he called "overt" chimeras. These he made by mixing cells from early goat and sheep embryos. These chimeras, which had sheep and goat cells mixed throughout their bodies, carried sheep pregnancies but never carried a goat to term. "They would get pregnant [with goats] but lose them by about sixty days or so, which is when a goat loses a sheep pregnancy."

As Anderson pointed out, these first experiments create a similar scenario—at least immunologically—to normal pregnancies. All pregnancies, even normal ones which do not cross the species boundary, require the mother to harbor foreign tissue. Because individuals within a species are genetically different, the fetus is teeming with antigens: the mother's immune system reacts to anything that is not self. But immune attack on the fetus is suppressed to a large degree in all pregnancies. Keeping this in mind, Anderson realized there must be something else at work in the failure of interspecies pregnancies.

Anderson's second set of experiments showed that though the immune system may be a factor in the failure of goat-sheep interspecies pregnancies, there are other very important, as yet undetermined, reasons these pregnancies fail. Rather than mixing cells from early-stage embryos to make overt chimeras—which are very different from the biologically normal animals used in interspecies pregnancy attempts—they made goats with a steady supply of sheep cells in their blood. "Scientifically these were very interesting," Anderson said, "but they weren't very interesting to look at" because they just looked like goats.

To create these chimeras, Anderson gave the goats a transplant of the sheep stem cells which give rise to the blood. These sheep cells created sheep immune systems in the goat. But the sheep and goat immune systems were not at odds with one another. Rather, the goat and sheep cells acted together as one immune system that tolerated both goat and sheep antigens. When making chimeras in the lab, scientists combine the cells, as Anderson said, "prior to the time when the fetus determined what's self and what's foreign." This generates a chimeric immune system that, Anderson explained, thinks, "I'm sheep, I'm goat, I'm perfectly happy with both."

When these goats reached maturity, they were impregnated with sheep fetuses genetically identical to the sheep cells in their blood. This completely eliminated the immune system as a factor in the failure of the pregnancies. If immune rejection were the primary barrier to interspecies pregnancy, the goats in these second experiments would have been able to carry the sheep pregnancies. The goats should have been tolerant of sheep antigens. They also should have been tolerant of the individual sheep fetuses' unique molecular signatures. But the pregnancies still failed.

Given that cells from the two species can work together so closely to form one coherent, functioning, healthy self, it seems strange that goats and sheep cannot interbreed or carry each other's fetuses to term. But pregnancy involves complex chains of causality that must be performed with a certain degree of reciprocity, in which one misstep may lead to a chain of events terminating the pregnancy. The pregnancy could fail because a chemical signal "isn't there on the right day," said Anderson.

The failure of the chimera pregnancies suggests that mothers react to fetuses of different species in some other way than immune rejection. Anderson's experiments do not mean the immune system is not involved in the rejection of interspecies pregnancies, but that there are other important factors. "It's some other problem like failure to form a functional placenta or improper signaling between the mother and the embryo," he said.

This suggests there is a limit to the cooperation that is possible between goats and sheep. Still, the degree to which their cells cooperate in chimeras seems barely possible. Cells in a goat-sheep chimera go far beyond simple tolerance. Not only do they not attack one another, they work together in incredibly intricate processes. The processes of life on the cellular level are mind-boggling, the result of intricate tangles of chemical

cause and effect in which small-scale changes can be magnified into larger ones and back again. One would expect that, on this level and especially within tissues and organs, sheep and goat cells might somehow antagonize or miscommunicate with each other.

In general this was not the case, even in the very mixed, overt chimeras. By all measures, Anderson said, the goat-sheep chimeras were as healthy as any nonchimeric animals. "Long after these experiments were done, they had no use but we kept them around and they became aged animals. They died of natural causes. Generally they were fully healthy."

Anderson and his team even had a chimera that produced both goat and sheep sperm, and viable sperm at that—he fathered both sheep and goats. "The cellular changes that have to take place in a two month period from a round cell to this highly specialized cell," the sperm, are complex. Several different kinds of cells are involved; all must perform specific functions in a specific order. One miscommunication or misstep could lead to faulty sperm or no sperm. "It's a highly coordinated process and yet it shows that the two species could work together," said Anderson.

When informed of Anderson's research, Samuel Stanley, who does chimera research at Washington University, was also amazed that an animal could produce both goat and sheep sperm. "Whoa-ho-ho!" he exclaimed. "That's really interesting."

The fact that such a chimera is possible almost seems a challenge to the biological species concept. However, as noted earlier, biologists draw species lines based on reproduction. Goat-sheep chimeras are, in a sense, sterile. Male chimeras can produce goat and sheep sperm; female chimeras goat and sheep eggs. There are no "geep" gametes. Neither the goat sheep not any other chimera is a novel species. "Geep" was the name given Anderson's goat-sheep chimeras by the media. Anderson chafes at the mention of the word, presumably because it suggests that the animals were a new species. "Scientifically they were goat-sheep chimeras," he said, visibly annoyed.

Does the degree of cooperation between sheep and goat cells in a chimera suggest that the animals are more closely related than previously thought? Anderson doesn't think so. Sheep and goats "diverged a long long long time ago and they're really quite distinct." To many people, says Anderson, the animals look very similar. People think that "sheep are goats with wool or goats are sheep with hair. I raise sheep at home and

when people are walking by they say, 'Oh look at the goats!' and I say 'They're not *goats*!' "

Asked several times what the real differences are between goats and sheep—given how similar they are in appearance—he repeatedly responded that goats and sheep are two entire taxonomic categories apart (the level above species, genus. "Just the fact that they're not only a different species but they're a different *genus*." Goats are in the genus *Capra*, sheep in genus *Ovis*. At the same time, however, he acknowledges the somewhat arbitrary nature of taxonomy. "Humans sat down sometime and said, 'Let's classify critters into different species.'"

The biological species concept is already beleaguered enough without challenges from interspecies chimeras. It certainly does not fit plants and even has a hard time categorizing mammals. Bacteria reproduce asexually; while they exchange genes with one another, these exchanges are not part of their reproductive process. Scientists cannot use the same methods to classify extinct animals now represented only by fossils as they can to classify living organisms. Relying as it does on reproductive behavior and success, the biological species concept cannot be applied to the dinosaurs, early mammals, and many other long-gone creatures. This is no small matter: ninety-nine percent of all species that have ever lived on Earth are now extinct. Scientists classify these animals and plants based on physical characteristics such as bone structure or the lines a of leaf imprint in shale.

Molecular anthropologist Jonathan Marks challenged the very idea of the species concept, saying that "it can't really be a biological species concept because it doesn't work with plants—plants are notoriously promiscuous." Plants easily interbreed across the species barrier. Marks noted that through the 1960's, a scientist named Reginald Rugglesgates "was a holdout for the position that blacks and whites were actually different species of people as opposed to different populations. When pressed on this patently ridiculous argument, it turns out this guy was trained in botany." Because interbreeding communities aren't species in plants, "the business of an interbreeding community defining species didn't even bother him."

Nor are species designations in class mammalia clear-cut. The notion that "there's a species barrier to reproduction is not true because obviously there would be no

mules," said Harriet Ritvo, a historian specializing in the history of animal classification at the Massachusetts Institute of Technology. Marks noted that while dogs and cats don't interbreed, dogs back-cross with wolves. *Vos indicus* and *Vos taurus* are different cattle species that interbreed and have fertile offspring. There are countless such examples.

Classification of the animal world has always been problematic, and the boundaries between animals have been shifting since the inception of taxonomy. Thinkers since Aristotle have attempted to classify organisms but the process was haphazard until the 18th century. Swedish doctor Carolus Linnaeus decided to bring the same order to biology as Newton had brought to physics. As he saw it, his method of assigning each organism a binomial (such as *Homo sapiens*) was the equivalent of Newton's mathematical formulae. His *Systema naturae* was "an authoritative guide to the arrangement of plants, animals, and minerals as ordained by God and discerned by the author," Marks summarized ironically in his book *What it Means to Be 98% Chimpanzee.*

But *Systema naturae*—Latin for *Nature's System*—was no revealed word of God, set and needing no revision. No matter how formulaic the taxonomic categories, classification is an act of interpretation. Theologians dispute the meaning of religious texts and literary critics attempt to unravel Kafka; biologists' text is the natural world. Linnaeus came out with twelve editions of his work and biologists are constantly revising it.

Rather than presenting a new and radical challenge to the biological species concept, chimeras like Anderson's show us that what he called "fundamental biological processes, which include complex cellular interactions" are shared across species—even, in the case of the goat-sheep chimera, across genera. Given what is already known about shared common ancestry through evolution, this is unsurprising.

Humans and mice are much more distantly related than goats and sheep, but chimeras between the two work surprisingly well. "It surprises me that it's so viable," graduate student Paul Davis said of the chimera model he uses to study disease pathways at Washington University in St. Louis. He and his advisor Samuel Stanley, a professor of medicine and microbiology at the university, repeatedly used words like "surprising" and "unexpected" to describe their chimeras.

Goats and sheep are in different genera. Humans and mice are in the same kingdom (animals), phylum (back-boned animals), and class (mammals). We diverge before goats and sheep, at the order level—they scurry off with the other rodents, we with our big brains and opposable thumbs join the primates. But enough has been preserved throughout the course of evolution that tissues and cells from humans and mice can form chimeras.

Stanley's lab implants human fetal tissues into adult mice to model human diseases. Davis explained how they create the chimeras. "We have a collaboration with the birth defects center at Washington University and they send us fetal tissue at 90-92 days old. We take those fetal intestines and implant a small, centimeters-long tissue section into the back of the mouse. You slice the mouse open on the dorsal side [the back] and you implant the tissue and just close up the mouse." The tissue grows "and you've got a human intestine" living in an easily accessible spot on the mouse's back.

Stanley and Davis use a strain of mice, called severe combined immune deficient (SCID), bred for deficiencies in their immune system. SCID mice don't have an important class of immune cells—those which, among other functions, cause transplant rejection. "We know we're getting around tissue rejection because we're using mice with no immune system, so they can't really reject the [human] tissue." These mice do not incorporate the human tissues to the extent that goat and sheep became integrated in Anderson's overt chimeras. "You're really using the mouse as a vessel to be the carrier for human tissue," said Stanley.

Davis got involved with this work "because it was absolutely cool." The "first corollary" of microbiology, he said, "can be summed up like this: if you don't have a model, you're screwed. That's the end-all, be-all....If there's not a model in which to study your organism, don't study it." And SCID-human chimeras are "the best model you could ever have...for virtually any pathogen. Not only is it *a* model, it's probably the *best* model you can get because it's actual human tissue, not a mouse or ape but actual human tissue."

"You can actually mimic a number of things that would be happening in the human in the mouse," Stanley said. SCID-human chimeras have been used to model a number of processes in the human body. "To look at organogenesis—how an organ

develops—it's turned out to be a nice system. The other thing that's been nice is the idea of studying human-specific pathogens," agents of disease like bacteria. Scientists have used the chimeras to test early anti-HIV drugs and model diseases from cystic fibrosis to rheumatoid arthritis to cancer. Stanley and Davis study *Entamoeba histolytica*, an amoeba that causes dysentery (horrible diarrhea) and liver abscesses among other symptoms.

Davis said they hadn't anticipated how well these SCID mouse-human chimeras would work. "It was kind of a grand experiment with no hypothesis—hey, let's see if this would work." They knew the SCID mice would not reject the tissue. "But I think it was to our surprise that it would *accept* the tissue....we were surprised that it wasn't ignored by the mice," Davis recounted. In other words, the mice go beyond not attacking the human tissue. When you make a new addition to your house that has a sink or a toilet, you add on to the plumbing. The mice do the same thing when the human tissue is added, growing new veins and arteries to provide a blood supply for the human intestine or liver or skin.

Also, in Stanley's words, "pretty unexpected" was the way the mice responded to signals from the human immune system. He and Davis are studying the role the immune system might play in causing the symptoms of dysentery after infection with *Entamoeba*. In the SCID mouse-human chimeras, there was communication between human immune cells and mouse cells. Immune cells interact with one another by way of signals called chemokines, molecular messages which often read something like "attack!" Stanley said, "It turns out the mouse cells can actually respond to a number of the human chemokines," even some that have no equivalent in mice. "That is pretty exciting, and it's what makes the model work."

For microbiologists like Davis and Stanley, the SCID-human models make possible a range of experiments that would be impossible in humans and other organisms. In order to understand the progression of diseases, Stanley and Davis want to learn what cells and molecules are where in the body during different times after infection. To determine this, they can kill and dissect the chimeric mice at any point during the experiment. "There are a number of techniques, all of which you can do in real time, all

of which you could never do on a human being without opening up the gut and killing them," Davis said.

Davis explained that nonchimeric mice and even apes like chimpanzees are not adequate models for studying many human diseases: many bacteria, amoebas, and other agents of human disease behave differently in these animals than in humans. *Entamoeba* causes liver abscesses in mice but not dysentery. "That's why we have to use a chimera."

In spite of his confidence that there is much to be learned about human health by studying disease in chimera models, Davis does not like to be too specific when explaining his research to friends and family. "I really don't get into detail about where exactly the tissue comes from." He prefers to let people assume the lab uses tissue left over from colon surgeries performed on adults. "I think the [use of fetal tissue] makes people the most uncomfortable. I generally say I stick human gut into a mouse."

The very idea of chimeras is disturbing to many people, in part because of the monsters people associate with the name. "A lot of these kinds of experiments, people don't understand the scientific point and they think it's kind of 'let's do science fiction,'" said a cell biologist at MIT's Whitehead Institute who, because of the controversial nature of chimera research, spoke on condition of anonymity. MIT historian Harriet Ritvo agreed. "I think the word 'chimera' is actually unfortunate, because it has those two overtones: one is monster, the other is imaginary. When we say something is chimerical, it does make it sound as though the scientists are off there in never-never land."

People may also be influenced by the myth of the mad scientist who plays god. Such characters are commonplace in our popular culture—especially movies—and their roots may be traced to Mary Shelley's *Frankenstein*, whose monster is a chimera. Shelley provides a portrait of science gone horribly, irresponsibly wrong. Dr. Frankenstein, blinded by scientific hubris, sets out to expose "the deepest mysteries of creation" but ends up unleashing a violent creature whose capacity for human feelings fills him with angst, making him all the more volatile. While such warnings from the realms of literature and the popular culture are important, especially as scientists' capabilities to manipulate life grow almost daily, the myth that a good number of

professional scientists have succumbed to a sort of "Frankenstein syndrome" has seized the popular imagination with unduly strong force.

Anderson, who has been accused of playing god like Dr. Frankenstein, does not look the part. Anderson sees no problems with his chimera research because they treated the animals well. The goat-sheep chimeras died of natural causes long after experiments were over—they kept them because Anderson's graduate students had become attached. "Some of the students did anything but kiss them on the lips." Anderson did not consent to a behavioralist's proposal to study the chimeras—whose brain tissue was chimeric, just like the rest of their bodies—because it would have involved what he felt would be a traumatic separation from their mothers.

David Smith, a bioethicist currently in residence at the Yale Bioethics Project, does not believe the creation of interspecies chimeras like Anderson's raises any special ethical questions. Smith, a practicing Episcopalian, said, "I don't see why there's something sacrosanct about the exact species divisions we've got. That doesn't strike me as a serious problem." However he believes the SCID mouse-human chimeras raise more difficult questions. When you put "this bit of fetal intestine" in a mouse, "there may be some issues as to the source of the fetus." But he classes these models as "research on human tissue using a mouse host." Smith concluded, "Unless or until we're creating something that is in some significant way human or humanoid, I don't have a serious problem, and I don't think anybody should."

But Smith also pointed out that as far as our reactions to chimeras go, "it's all pretty intuitive." Something about chimeras just feels unnatural, eliciting a "yuck!" from many people. At the same time, we seem to have always been fascinated by chimeras and hybrids. There may be something primeval, instinctual in this. A 15,000 year-old Paleolithic cave painting in Dordogne, France, dubbed "man as ox" by anthropologists, shows a stooped human body with the long-horned head of an ox. A hairy man with an ape head and cat-like ears runs across a 5,000 year-old Neolithic rock painting in Saharan Africa, toting an axe.

In the *Book of Imaginary Beings*, Borges wrote, "Human forms with bull heads figured, to judge by wall paintings, in the demonology of Crete," the island where

Minotaur was said to dwell. "Most likely the Greek fable of the Minotaur is a late and clumsy version of far older myths, the shadow of other dreams still more full of horror."

The shadows of these ancient dreams are long, stretching across centuries of high and low culture and into the present day. The Manticore, a beast the Greeks derived from a Persian creature whose name meant "man-eater," made a come-back as a symbol of horror and violence in literature in the nineteenth century. Manticore was a red lion with a man's face, three rows of sharp teeth, a scorpion-like tail ending in a stinger, and a taste for human flesh. Gustave Flaubert gave him a voice in *The Temptation of St. Anthony* (1874): "Through my nostrils I exhale the horror of the lonely places of the earth....I consume armies when they venture into the desert." W. B. Yeats immortalized the Manticore in his poem "The Second Coming"(1921):

...somewhere in the sands of the desert
A shape with lion body and the head of a man,
A gaze blank and pitiless as the sun,
Is moving its slow thighs, while all about it
Reel shadows of the indignant desert birds...
And what rough beast, its hour come round at last,
Slouches towards Bethlehem to be born?

The chimeras which figure in the movies to this day are also shadows of ancient dreams. Pliny wrote about werewolves in his first century AD encyclopedia; a sixth century AD Nordic helmet depicts the transformation of warriors into wolves during combat. A Mexican mask of jade and shells dating sometime between the second centuries BC and AD depicts an anthropomorphic bat deity. And what are vampires but human-bat chimeras?

Given this age-old fascination with chimeras and hybrids, Stuart Newman and Jeremy Rifkin are sowing what some call their anti-patent propaganda on fertile ground. Newman explained his path to the humanzee patent in terms of each decade of his career. As a graduate student in the sixties with a background in the physical sciences, he recounted, "I was kind of influenced by the people who invented the atom bomb and then turned against it." Newman suggested that physicists waited until they were working on the atom bomb to address ethical issues. When biologists began exploring the

explanatory power of genes in the seventies, Newman began to worry. "There was a real centering on the gene as being able to describe and account for every biological feature," which Newman calls the "ideology of genes." In the late 1970s, Newman co-founded the Council for Responsible Genetics, to address "possible abuses of genetic technologies."

In the eighties the US Patent and Trademark Office began approving patents on life forms. The first to be patented was a bacterium genetically engineered to clean up oil spills. This case went all the way to the Supreme Court in 1980, where the justices ruled that "anything under the sun that is made by man" is patentable. This has since been interpreted by the patent office to mean that animals that have some how been modified in the lab—by the addition of a gene, for example—are patentable. "There are even some judges that said that bacteria are more like chemicals than living things." Newman saw this as the beginning of "the erasure of [the boundary between] the technological and the natural by the ideology of genes."

"In the early nineties, Jeremy Rifkin, who I had known through political work, came to me and said, 'Is there anything that could be patented, medically beneficial, feasible, and also very disturbing, raising all these points about how just because something is useful and can make money and so on, it's not necessarily desirable?'" summarized Newman. He remembered having read about the creation of goat-sheep chimeras like Anderson's and came up with the human-animal chimera patent.

Rifkin denied an interview request through his secretary.

Their application, which Newman is no longer giving to the press on the advice of his lawyers, is still stalled at the patent office. (The office began publishing pending patent applications online in 2001; this policy does not apply retroactively to patents filed before 2001 that are still pending.) Newman says the application covers human-animal chimeras created using the techniques Anderson used to make goat-sheep chimeras, that is, combining early embryo cells. "We claimed not only the chimeric embryos but the animals that would result from chimeric embryos." If they are granted the patent, they will have a monopoly on human-animal chimera technology for 20 years and would be able to legally block its use. They hope their application is rejected after a revamping of patent law and will continue to challenge any rejection of the application up to the

Supreme Court—unless Congress legislates against the patenting of organisms in the meantime.

Newman and Rifkin believe the only way to keep humans unpatentable is to make all life forms unpatentable. They believe a policy that allows patents on some organisms will lead down a slippery slope to patents on humans. David Weldon, a republican in the House of Representatives, introduced legislation to ban patents on human embryos. Newman said of the bill, "I think that's a good step but if it has fifteen mouse cells and one human cell, is it a human embryo or not?" Because it would be difficult to establish what percentage human cells a chimera would need to have to be a human, Newman believes "the only consistent position...is to be against the patenting of any organisms.

Newman described the kind of legislation he would like to see. "My own recommendation would be to ban patents on all organisms and to ban research that modifies human embryos." In addition to stopping human-animal chimera research, such a ban would prevent scientists from "transplanting nuclei and mitochondria [cell components] and doing germ-line genetic engineering," modifications to the genome that will be passed on to an animal's progeny. Newman believes such modifications "will lead to genetically engineered people."

Newman and Rifkin believe that commercial incentives in our society are so strong that if the creation of chimeras is not stopped by law or court decision, we could one day see human-ape chimeras and other modified semi-humans produced for cheap labor, military service, and other forms of exploitation. "The people with the economic power will be in a position to consume everybody and everything else," said Newman. "Given the kind of economic system we live in, everything gets turned into products and consumables."

"I have no doubt that we can make things that are quasi-human or part-human and this will undermine our sense of ourselves," said Newman. He believes chimeras like the *Mus musculus – Mus caroli* and goat-sheep are the first step towards blurring boundaries on a slippery slope that will lead to those around us. "People start thinking about their children as being subject to manufacturing, prenatally... when you start being able to manufacture, making multiple attempts at seeing if you can improve the clone, then you start thinking about people as being very different from 'everybody has the same value.'"

Thomas Murray, president of the Hastings Center, a bioethics think tank in New York, believes Rifkin and Newman's concern about commercialization "is a quite important one, and it will come up often." Murray said that "when one has strong motives and means, the economic power to make things happen, to press certain ends, [then] irrespective of the moral merits, the legal niceties, or the social implications, things get driven." However, Murray thinks Newman, whom he described as a friend, "takes an idea that has considerable merit...and he pushes it, he makes an absolute out of it."

Commenting on the Rifkin-Newman worldview, bioethicist Smith finds it "hard to be such a complete prophet of doom....It's so clear to me that the vast majority of people" don't look at children as property to be manufactured, "and are unlikely to look at it that way...As soon as people's attention is called to the extent to which that property metaphor is being used out of its appropriate context, they see right away what's going on and they don't like it."

"I think that is excessively cynical," Smith said of Newman and Rifkin's ideas about the power of the profit motive in our society. "We've lived with nuclear weapons now almost fifty years and never used them again. Humankind *can* do all kinds of things that it *doesn't* do. I don't think it's absolutely cast in stone that we will do all those bad things."

Linda Guidice, whose extensive credentials in reproductive health include the directorship of Stanford Medical School's Division of Reproductive Endocrinology and Infertility, said that designer babies are not all that appealing to most people, at least for the time being. Guidice discussed these and other biotechnology issues as part of a panel of scientists and ethicists during a session called "Creating a World We Don't Want to Inhabit?" at the 2004 annual meeting of the American Association for the Advancement of Science, in Seattle. Reproductive technologies have not yet changed the way parents look at baby-making, Guidice said. "Most couples want happy healthy children but the definition of happy and healthy I think may eventually change. We can certainly carry this down the slippery slope. But currently there's not really a demand for designer babies."

The way Newman and Rifkin see things, creating chimeras is one of the first steps towards the creation of legions of unnatural animals. If we keep creating more and more unnatural things, they argue, we will eventually forget the distinctions between those products and natural things. "There is a fundamental difference between things that evolved and arose outside of human fabrication, and things that are made by humans. That distinction permeates all cultures, it's very deep, and a lot of ethical things are based on it," Newman said.

Given that many scholars argue that the natural/unnatural boundary is culturally-determined, it is not one most scientists take into account. "Science, in particular biology, came out of natural philosophy," said Newman. "Now it's come to the point where almost the only word you're not allowed to say as a scientist is the word 'natural.' In other words 'natural' has this kind of old-fashioned, unscientific tone about it."

Anderson clearly does not value or define "natural" things in the same way as Newman. Some of Anderson's current research includes genetic manipulation of pig stem cells—"doing things you can't do with cross-breeding"—"for the benefit of pigdom." Asked what he meant by this phrase, he replied, "Our first grant was from the National Pork Producers." For many scientists, improving animals means making them better-suited to human needs.

Scientists such as Anderson argue that humans have been altering plants and animals for millennia through domestication and breeding, and many place the creation of chimeras and genetically modified foods along this continuum. The development of agriculture is generally held to have been necessary (if not sufficient) for the development of civilization. Domestication of plants, which made agriculture possible, began around 8000 BC with crops including peas and wheat. Animals were domesticated even earlier, beginning with dogs around 10,000 BC and sheep, goats, and pigs in 8000 BC. Our relationship with these animals is a long one relative to human history.

Molecular anthropologist Marks provided a description of the usual narrative applied to domestication: domestication was a deliberate act on the part of man to bend the natural world to our needs and desires. "As far as creating life-forms that have never been seen before—of course we've been doing that ever since we domesticated grains

and animals. Corn can't even breed in the wild, so that took a *lot*—thousands of years—of human intervention to make," he said.

Gil Whittemore, a Boston-based lawyer with a PhD from Harvard in the history of science, framed the difference between modern biological modification and ancient domestication as one of time-scales. "We're gaining the capacity to change things very rapidly....One side will say, 'you're changing nature so dramatically that you may end up releasing organisms that are harmful,' and others say, 'well, this sort of genetic manipulation has gone on for a long time.'"

Marks is in the latter group. "The question is, given that people have always been manipulating nature and constructing new natural forms, is [biological manipulation] something totally unprecedented? As far as I can tell, it's not. It's experimental manipulation towards a particular goal but I think so is the original domestication of horses and wheat."

In this view, the creation of chimeras—whatever moral valence one assigns the act—is on a continuum with earlier manipulation of nature. The ability to create chimeras is the result of a rapid acceleration in biological knowledge and laboratory techniques, but it is still part of this history.

Newman sees the creation of chimeras and a whole range of other techniques of biological manipulation as a radical departure from our history. In order to make these kinds of claims, Newman—who as both a scientist and a person engaged in a legal battle is very concerned with consistency—has to argue that domestication was a "natural" process, rather than one directed by humans.

"This idea that domestication was people ben[ding] animals to their needs is really losing credibility." Dogs "latched onto people," he said, "it was animals turning humans to their needs even more so." People took advantage of, but did not cause, changes in corn, which were "a natural fluke." Ritvo, whose field of research largely centers around relationships between humans and animals (as in Victorian zoos) has a somewhat more moderate point of view. "Of all the animals in the world only a few have been domesticated," so the animals that were must have been "in a sense preadapted to domestication." That is, many already had characteristics that made them suitable to our

needs and activities. Many now-domestic animals, for example, had a herd structure that allowed people to "kind of filter in at the top" and become boss.

The distinction between natural and unnatural is, for Newman, an integral and valuable part of all human cultures. "The kinds of changes genetic technology induces are very different from the changes that either led to domestication or led to evolutionary change. The companies that produce these genetically-engineered [organisms] say, 'oh you know it's no different from what humans have been doing by domestication.' I think that's really deceptive." He believes the loss of the natural/unnatural distinction will lead to a devaluation of life. "I think it's a danger to the culture to see this kind of human, commercially-motivated manufacturing technology as being no different in their words from what goes on in evolution or domestication."

Interspecies chimeras like goat-sheep and SCID-human mice cross what to Newman and Rifkin is a natural species boundary. "I think people do have this big stake in being able to tell the natural from the unnatural but it's always a problematical stake," said Ritvo. She posits that the distinction between natural and unnatural "may be important and nonexistent at the same time."

Many of Rifkin and Newman's critics agree that there should be limits to biotechnology, that it can and sometimes does go too far. But people find their all-or-nothing approach—drawing hard species barriers and saying we shouldn't cross them, drawing hard and fast distinctions between natural and unnatural—very hard to swallow. Many use the word "excessive." "To rule out potentially therapeutic interventions because it's a further intrusion of technology is much too sweeping, much too general, and too greatly minimizes human resilience and human imagination and human community," said Smith.

In an email correspondence, Donna Haraway, professor of the History of Consciousness at UC Santa Cruz, expressed a similar view. "I do not think a ban on patents on any and all life forms makes sense," Haraway wrote. She suggested that Rifkin and Newman's approach oversimplifies things. "Respect for life forms...is the criterion, and it has to be struggled over, not solved by the 'one true position.' The 'ban all X' approach smacks of the absolutism of too much animal rights discourse for my taste."

The legal aspects of the Rifkin-Newman patent baffle Gil Whittemore, who is active in the American Bar Association's section of Science and Technology Law. "I think the intellectual property system as a whole is under a lot of challenges. We're simply in a period where there is an extensive debate on the patent system as a means of encouraging research versus other systems." However, he points out, "the whole idea of patents is to encourage people to use new things, not to prevent them." Patents exist "to get the technology applied. [Newman and Rifkin are] using patent law for the opposite purpose."

Whittemore pointed to some possible ways the nature of the patent system could cause their patent plan could backfire. If they get the patent, "they will have battled hard to establish the opposite precedent of what they wanted." If their patent is denied, they might still generate enough interest in Congress to create legislation. "The question is which way the Congress would go in terms of changing the statute." Congress "could say, 'let's change it so everybody can get these patents.'... Government control does not always equal wisdom."

Newman and Rifkin have not applied for international patent rights. Even if their best case scenario comes true, Whittemore notes, scientists could move overseas to do the research. Having written his doctoral thesis on the history of radiation protection standards, Whittemore brought up comparisons to nuclear technologies. "In order to do the uranium separation at Oak Ridge, they built the world's largest factory....But the physical size and expense of one of these [biological] labs is very small on the world scale. It's not that much effort for somebody to move their lab to South Korea or some other country."

For their application to be approved, Newman and Rifkin must demonstrate that human-animal chimeras like the humanzee are viable. Of all their human-animal chimeras, the humanzee is most likely to work because of our close relationship to the great apes in general and chimpanzees in particular. Newman and Rifkin often cite the creation of goat-sheep chimeras like Anderson's as evidence that the humanzee is biologically possible. If the boundary between goats and sheep can be broken down, they argue, the boundary between chimpanzees and humans might be even weaker because we share a more recent common ancestry with chimps than do goats and sheep.

Years since divergence is one measure of species' relatedness to one another, but not a very good one. By this particular measure, we are a little "closer" to chimpanzees than goats and sheep are to each other: humans and chimpanzees diverged around six million years ago, compared with sheep and goats' seven million years.. "The number of years since divergence doesn't necessarily mean much," cautioned Anderson. "It's more important where they ended up rather than how many years ago they split." Goats and sheep ended up with very similar characteristics where it matters for the creation of chimeras: "Sheep and goats have enough compatibility even though they're different genera—same gestation period, same size."

Anderson, who does not know nearly as much about the primate reproductive system as he does about ruminants', does not believe a humanzee pregnancy would work. However, Marks, a molecular anthropologist who knows less about reproduction but whose research has centered on questions of how closely related we are to the great apes and what it means to us, said he does not think there would be any significant reproductive incompatibilities that would prevent the humanzee from being carried to term.

"If you had a humanzee gestating in a chimp, you'd have a much bigger head than the chimpanzee mother is expecting, so you'd want to deliver that by c-section I should think. Or have a human mother carry the humanzee," Marks mused.

By any measure—years since divergence, percentage genetic similarity, simple observation—humans and chimpanzees are very closely related, just like sheep and goats. The numbers for our percentage genetic similarity to chimpanzees range from 95 to 98% but this is "just genetics being able to slap a number on it, which it's hard to do anatomically...the important thing is, it's a really big number," said Marks. "We've known for 300 years that we're similar to chimpanzees."

Ever since we've known that, it has bothered us.

And some would argue Rifkin and Newman's plan to use these emotions to get attention for a cause is exploitative. Haraway, author of *Primate Visions*, a wide-ranging critique of 20th century primatology that delves into taxidermy, eugenics, and apes in the space program, pointed to some of the ways this plan exploits human emotions and

anxieties about apes. "Truly, I think Rifkin dreams up things to be afraid of sometimes," she wrote in an email correspondence. "Yes, I think Rifkin is being exploitative to use the mythical human-ape chimera with the most cache, but it's great theatre and he's a dynamite propagandist." She wrote that chimeras should not get her attention as much as the mistreatment of animals such as chimpanzees does, but that she is "as vulnerable to the frisson of illicit mucking around with Nature as any other white child of colonial culture."

Newman and Rifkin's humanzee taps into ancient anxieties about the boundary between humans and the rest of the natural world; in a sense, the humanzee is a modern version of myths exploring this boundary. "If you look at myths worldwide, you get half-man, half-beasts as a very common motif. Of course their status is that they're not quite human," said Marks.

In the 16th century, Europeans were confronted with apes for the first time when they traveled to Africa and Asia. "The farther away explorers got from Europe, the more different the people were, the more different the animals were, and the more different the behaviors and languages of the people were," said Marks. The people seemed not quite human and the apes seemed not quite animal. Marks noted that the "motif of monstrous peoples is an old scene in European travel literature." Many of these stories—Scythians with one eye in the middle of their foreheads, African Blemia without heads, Indian Monocoli with one giant leg they used as a sunshade—were lifted from Pliny's *Historia Naturalis*, a first century Roman natural history. "Obviously these people are mythological but they are on the borderline between human and not-human, they are represented as being 'human comma *but*.' "

Apes have long been seen as creatures treading the boundary between humans and the rest of the animals. "I think the first chimpanzee to be displayed in Europe was in the 1730's...it's obviously not a human, it's obviously more similar to humans than anything else," said Marks. "They're training it to walk upright, they're training it to sip tea and make its bed and all this. You get Rousseau arguing that these are just a different kind of people—people but not people."

Linnaeus could not read English, so when was classifying humans in the 18th century, he did not have access to contemporary, scientific information about primates.

He based his classification of apes on their descriptions in Latin literature. Linnaeus derived his division of the apes into more and less human-like, or anthropomorphic, directly from Pliny. Marks explained, "The less anthropomorphic descriptions [Linnaeus] makes the first species of the genus *Simia*, that becomes *Simia satyrus*," after the prurient forest-dwelling Satyrs of Greek myth, who were half-human, half-goat. "The more anthropomorphic descriptions of the apes he calls *Homo troglodytes nocturnus*, cave-dwelling man of the night." In the contemporary version of primate taxonomy, humans are the only living species in genus *Homo*. Linnaeus put some of the apes in our genus. "The question of 'are [apes] human, are they not' was essentially answered both ways by Linnaeus," said Marks.

When Europeans first encountered apes, "One question that inevitably lept into the minds of these people is could they mate with humans?" Ritvo said. "The answer seems to be no but especially when perceptions were a little blurred so that people were not distinguishing clearly...between those apes and humans who lived in those particular areas, there were lots of stories about apes stealing women and mating with them." While other ideas about possible human-animal combinations have faded away with the rise of modern biology, "the one thing that's lurked around as a possibility is a human-ape hybrid," Ritvo said. After all, as Marks noted, we now know that "to some extent, [ape-men] existed three million years ago. The issue of whether you could make an individual not quite human and partly chimpanzee...is something we do think about, worry about."

"People are strongly committed to the notion of a barrier around the human species," said Ritvo. She believes the roots of this are old. The chain of being, a hierarchy of the natural world that originated with Plato and Aristotle as the *scala natura*, had by the end of the 18th century become completely engrained in zoology. Though the *scala natura*, a linear "scale of nature" along which species were arranged from higher to lower (with humans or sometimes heavenly beings at the top), has long since fallen out of favor as a tool for taxonomy, we still tend to think in these terms, and the possibility for mixing different links along this chain causes anxiety.

In 1999 the American Association for the Advancement of Science published a collection of essays by ethicists, theologians, and scientists called *Perspectives on*

Genetic Patenting. An essay in the collection by Ronald Cole-Turner, an ordained minister and professor of ethics at the Pittsburgh Theological Seminary, advocates the use of a version of the *scala natura* to determine what is patentable. He calls it "the complex continuum of moral orders." On Cole-Turner's moral continuum, which stretches from noncoding DNA to coding DNA to mice on up to humans, "the stuff of each level...is neither sacred nor profane, but all valuable as God values it according to its level of complexity."

Marks links anxiety about human-ape crosses to what anthropologists call "kinship." "The common ancestry of humans and apes constitutes a historical and social narrative, a story about where you came from and ultimately about who you are," he wrote in *What it Means to Be 98% Chimpanzee*. Anthropologists call this kind of story a "kinship narrative." Learning that humans "do not stand isolated from the rest of the species on earth" is "no less disorienting" than learning that you were adopted; both force a reevaluation of one's kinship narrative. The idea of human-animal chimeras forces us to think about our relationship to other animals and to acknowledge the same things as Darwinian evolution. In the late 19th century, Darwin told us, " 'by the way, you're descended from apes—and have a nice day,' " summarized Marks. "Everyone situates themselves socially, situates themselves intellectually, on the basis of some knowledge of where they come from and who their kin are." The statement that we are related to chimpanzees, then, is "a powerful statement, obviously not a value-neutral one."

Ritvo suggested that the range of reactions we have to this statement has not changed since the Victorian era. "I think the same range of attitudes exists as then but the distribution of people across the range is somewhat different, so that there are more people now who are easy with the idea that we're close to apes, or we're a kind of ape. But there are still lots of people who don't like to be called a kind of animal. The source is the same. It comes from religion, and there's still a lot of religion around."

For better or worse, Newman and Rifkin's use of claims about the biological possibility of the humanzee to promote an agenda exploits deep-seated anxieties. Their critics would say this is typical of their extreme approach.

The human-animal chimera patent and the legislation Newman wishes for, which would ban human embryo manipulation, are not entirely theoretical. There is a real possibility that human-animal chimeras would be viable, and there are non-fringe scientists pushing for their creation.

A prominent cell biologist at the Massachusetts Institute of Technology's Whitehead Institute enthusiastically recommended the creation of human-animal chimeras to test stem cells. Due to the controversial nature of this research, he asked that his name not be used.

A question that is "terribly important right now," he said, "is whether human embryonic stem cells...are totipotent," or capable of becoming any kind of cell in the body. Scientists believe these cells have incredible therapeutic potential—stem cells might be used to cure diseases like Alzheimer's by replacing damaged tissues. These cells are thought to have the ability to differentiate into any kind of cell in any area of the body. But whether or not they really can, the cell biologist said, "can only be tested by the creation of interspecies chimeras." Scientists have seen these cells develop in a test tube into "a kind of mish mash of...beating muscle next to red cells next to a piece that looks like intestine. Not a normal embryo, but it looks like it's got pieces of a normal embryo."

The experiment this scientist, who is widely respected in his field, recommends would go as follows. The scientists would inject a human embryonic stem cell or cells into a mouse embryo and let this embryo gestate inside a mouse mother. At first he said only 14 days would be necessary; he went on to recommend letting the embryos grow to adulthood. Scientists would test the resulting chimera to determine if human cells ended up in all the tissues. If this were the case, it would prove that the human embryonic stem cells were capable of becoming any kind of adult tissue.

These chimera experiments do not have to be done in mice. "Maybe a mouse isn't the best way and we should do it in a monkey, or a gorilla, you see, that's what you want to do!"

The Whitehead scientist is not the first person to recommend these experiments. At the 2002 meeting of the New York Academy of Sciences, scientists led by Ali Brivanlou of Rockefeller University proposed such tests. Many scientists raised concerns

about the technique, most of which centered on the chimeras, which would look like mice, being allowed to develop into adulthood. If they developed to adulthood, the critics warned, these creatures might produce human sperm and eggs—just as goat-sheep chimeras produced sperm of both species—and mate with one another. Brivanlou declined to be interviewed for this piece, expressing through the Rockefeller University press office that "he so easily becomes a target if interviewed on this subject."

The Whitehead scientist dismissed critics of this research. In fact, the Whitehead scientist proposed the production of human eggs and sperm by mice as an exciting application for human-animal chimeras. If you could get a mouse to make human eggs, "you would have an unlimited supply of human eggs that you could use for cloning experiments. Who's the mother? The mother's not you, it's a mouse, a mouse in a cage making human oocytes. See how important that would be? But you can't do the experiment." He laughed under his breath, as though people's uneasiness about this kind of thing were patently ridiculous.

This human-mouse chimera model has already been used by the Korean scientists led by Woo Suk Hwang who made the first human clones, announced last February. These scientists made the clones not for reproductive purposes—that is, they do not want to bring a human clone to term—but for their stem cells. If this technology progresses as they hope, scientists could use Hwang's technique to create stem cells with your genome and put them back in your body for therapeutic purposes. To test the viability of the stem cells they made, the Korean team transplanted them into mice, where they differentiated into multiple cell types. They did not, however, implant these chimeric embryos into a womb to further develop.

Another human-mouse chimera experiment envisioned by the MIT cell biologist has potential applications for diabetes. Type I diabetes is caused by damage to the pancreatic islet cells, which make insulin. "Say I took human embryonic cells, did a chimeric embryo in a mouse, grew up the mouse. Say most of the mouse's insulin-producing cells came from a human, or maybe I made a mutant mouse with a genetic abnormality so that it couldn't make its own islet cells, then all the islet cells would be human." These human-mouse chimeras could be factories for islet cells. "I can do this experiment a thousand times, harvest islet cells from a thousand mice."

However, these mice would not be like the SCID mice Stanley and Davis make, which act as a vessel for one area of human tissue. They would be like Anderson's goat-sheep chimeras—a mix of human and mouse through and through, from the pancreas to the heart to the brain tissue. The Whitehead scientist, who is aware of the issues this raises, advocated the experiments anyway. "You have something that's half-human, half-mouse, you get people who are going to ask, 'What's the central nervous system? It is a mouse, is it a human, what is it? I don't know the answers."

Bioethicist David Smith's comments about a hypothetical pig with human brain cells point to the problems with these kinds of experiments. "Would we have reason to believe that it saw the world differently from other pigs? If it ends up like Babe, I think that is a problem." Scientists have no control over the distribution of the two species' cells in adult chimeras. Generally, both animals' cells are mixed throughout the body—in the skin, in the heart, even in the brain.

Told that the Rockefeller Institute's Brivanlou refused to discuss these issues, the cell biologist responded, "Well of *course* not. This is very controversial stuff. Most people aren't going to go public with saying they want to make human-mouse or human-monkey chimeras. I'm certainly not gonna go public with it. I hope you won't—we didn't officially say this is off the record but—are *you* a reporter?" Suddenly he acted as though he thought he was just having a casual conversation, though the encounter had been described to him as an interview and a tape recorder had been running in plain sight.

The Whitehead biologist and UC Davis's Gary Anderson both repeatedly insisted that anyone who opposed chimera experiments was a religious lunatic or simply did not know the science. For scientists such as these, either you know the science and make a rational decision that animal chimeras raise no ethical issues, or you are irrational. They do not recognize much grey area. When asked why he thought some people felt ambivalent about the creation of chimeras, Anderson asked, "Do you think I'm a monster?"

Newman and Rifkin on the one hand and Anderson and the Whitehead scientist on the other all seem to oversimplify the issues—something they accuse each other of doing. "The public doesn't understand [the science]. If they understood it better, they would be less frightened. I believe we need to do outreach," Anderson said. A few

seconds later, however, he cited studies that showed that while Europeans were better-educated about biology and genetics than most Americans, "they are also more frightened by biotechnology."

Scholars working on these issues seem to agree with Rifkin and Newman on one thing, if on nothing else: the way scientists look at these issues is often inadequate, their ideas about what they are entitled to do too broad. "I think a that a lot of scientists get outraged that you might want to tell them what they can't do, but people tell bus drivers what they can't do," Newman said. "You can't drive over people's lawns even if you can get your passengers to their destination faster." Newman said there should be no limits on, for example, what artists can do. "And scientists—they might not like the analogy—but they think of themselves like artists: we're doing good stuff and we should be as free as possible to do anything we want."

Scientists do not want to be constrained by what they perceive as others' irrationality. Marks, whose recent research has centered around issues in genetics, said scientists who think like this see ethics as a stumbling block to their pursuit of knowledge. "I think in general scientists don't want to deal with bioethicists," he said. His work on a chimpanzee chromosome exposed him to many geneticists; most of them "wish bioethicists would just go away and allow them to do whatever they want." Murray agrees that bioethicists are annoying. "I take it as a compliment that people who do the work I do are occasionally annoying to entrepreneurs. We're also occasionally annoying to scientists, government officials, surgeons—*frequently* annoying to surgeons, *forget* surgeons. We're annoying to each other. I try not to be annoying to my family, but other than that they're all fair game."

"I think there is this feeling in academic science that it should be objective, should be disconnected from society—which are all 19th century modernist pipe-dreams," Marks said. The role of bioethics is not simply to perform damage control after scientists given free reign perform the scientific equivalent of running the bus over the lawn. "Who's to stop Monsanto" from creating a humanzee, Marks asked. "And I think the question is, should there be regulations if Monsanto wanted to do it? It needs to be decided before it happens, before lives are at stake, and welfares are at stake."

Anderson dismissed people who disagree with him as uninformed; Jonathan Marks and Newman think scientists like Anderson and the Whitehead scientist need to be better-educated. They both see a failure in the way scientists are trained. It troubles Marks that "the training of a scientist doesn't include a curriculum or much attention towards community repercussions and social interactions and ethical questions, to the extent that community members are concerned about those things."

Whittemore voiced his concerns about the way our society views science. "We live in a culture that expects scientists to be continually producing new and good things," he said, "and that creates enormous incentives and many microdecisions that are made which make it very difficult to even imagine how you would slow things down."

In Pliny's *Historia Naturalis*, which he wrote in the first century AD, Pliny noted the importance of civilization for man's success given what he saw as our physical vulnerability. "Man is the only living creature whom Nature covers with materials derived from others.... All other animals know their own natures: some use speed, others swift flight, and yet others swimming....No creature's life is more fragile." For millennia, what Pliny might call our hairless and slow species has succeeded primarily by changing the world around us to suit our needs and desires.

This human tendency to manipulate our environment, coupled with our society's expectations of science, is what makes bioethics so important—what makes even people like Rifkin "useful," as Ritvo put it. Scientists like to say, "This has to be done," Smith noted. "Well—no, it doesn't. Nothing *has* to be done. The question is what *should* we do and what we *want* to do."

About the Author

Katherine Anne Bourzac previously attended the University of Southern California in Los Angeles, where she ate a lot of tacos and graduated with a BA in biology and comparative literature in 2003. She won USC's 2003 Comparative Literature Prize, was a USC Presidential Scholar, and graduated magna cum laude as a Renaissance Scholar. She would like to do freelance magazine writing, write books, and move back to California in the next few years.

Acknowledgments

Thanks to friends and family on both coasts for 3 am phone calls, coffee breaks, and lots of venting. I learned so much from listening to and especially reading the work of my peers—before this year I would never have opened a piece "The wild-eyed creature wandered...". Special thanks to Akta Patel, Mara Vatz, Courtney Humphries, and SC1, my roommate down the street, for helping me find life on planet MIT. I'm grateful to BD Colen, my thesis advisor, for having some idea what I was getting at even when I was wandering and for both wild ideas and reality checks. This piece would not be what it is if not for thoughtful edits from Marcia Bartusiak, Megan Ogilvie, and Nick Buchanan—even though they were all very busy.

Notes on the Research and Writing

During the spring of 2003 I worked on my undergraduate thesis in comparative literature—about the Tower of Babel in modern art and literature—for six or seven hours a night. I walked around in a mental fog, surrounded by the dim shapes of Borges's monsters and Escher's impossible buildings, puzzling over Kafka's version of the Great Wall of China and Dürrenmatt's Babylon. I came up with chimeras as an MIT thesis topic one of those nights when I was up late writing.

Though this year's thesis became a magazine-style piece of science writing, my thinking was always informed by the writers I studied last year. I want to thank those dead white men, even though most of them did not make it into my bibliography.

My topic and I were well-matched for several reasons: my interest in cell biology and bioethics; the need to place chimeras in the context of history, literature, art, myth, anthropology, etc.; and not least, my own ambivalence about chimeras, which allowed me to both examine the science critically and to temper my emotional responses and doubts.

A bibliography follows; however, I'd like to note some of my more important sources. Serendipity brought me molecular anthropologist Jonathan Marks's book *What it Means to Be 98% Chimpanzee*, which I found while browsing around the Harvard Coop. (This happy accident makes me wonder what potentially useful books I never came across.) In lively, clear language, Marks plows through a history of our reactions to the great apes, from myths to pseudoscience to genetics, which are so often intertwined in primatology. Marks and MIT historian Harriet Ritvo—who writes so gracefully she keeps the reader from tripping over a word like "synecdoche"—provided important historical and anthropological background for me.

Like so many classic authors who are not read much anymore, Pliny is surprisingly readable and relevant. I highly recommend both his *Natural History* and Borges's *Book of Imaginary Beings*, which I used for ancient examples of chimeras in ancient science and mythology.

The interviews for this piece were a mixed bag. Like Ritvo and Marks, Stuart Newman spoke in sentences (a plus when transcribing). Newman was persuasive. For about seven days after interviewing him and reading Jeremy Rifkin's vision of a

biotechnological future dystopia when human values and norms are slipping, I felt negative and scared. Talking with bioethicist David Smith, who has such faith in humanity, buoyed me up again.

I am grateful my interview with the MIT cell biologist came late in the year and late in my thesis research, after I had confidence in my knowledge of the topic and several other interviews under my belt. He treated me with contempt, assumed I was out to sensationalize the science without listening to what my project was actually about, and directly insulted me for having lived in Los Angeles, which he called "the cauldron of Hollywood"—presumably where I learned about making people like him look like monsters. But I'm glad I didn't throw a glass of water in his face because in the process he gave me some great material. Because he declared the interview off the record in medias res, I could have used his name; however, my thesis advisor asked me to respect his wishes because of institutional concerns.

One of the most surprising and fulfilling things about this project was realizing it did not stand alone but had its genesis in so many of my past projects. A few months ago I found an essay I wrote my junior year of college about Mary Shelley's *Frankenstein*, Darwin's *Descent of Man*, *Genesis*, stem cells, and human nature (which wasn't quite as bad as it sounds). In this essay—which I wrote for a literature and popular culture class and then forgot about—I wrote a paragraph on the Tower of Babel, which would go on to be the focus of my undergraduate thesis, and one on chimeras, which would be the subject of my masters thesis. One piece seems to lead to the next, even though I may not realize it at the time. I wonder which thread I will pick to weave my next major project but I am so in love with this topic I may write a book about chimeras in the next few years.

Bibliography

Alighieri, Dante. *The Divine Comedy: Volume I: Inferno*. Mark Musa, trans. New York: Penguin, 1984.

Anderson, Gary. Personal Interview. 16 January 2004.

Bazopoulou-Kyrkanidou, Euterpe. "Historical Review: Chimeric Creatures in Greek Mythology and Reflections in Science." *American Journal of Medical Genetics* 100 (2001): 66-80.

Boread Painter, attr. *Spartan black-figure clay vase, Bellerophon, Pegasus, and Chimera*. J. Paul Getty Museum, Los Angeles, CA.

Borges, Jorge Luis. *The Book of Imaginary Beings*. Trans. author and Norman Thomas di Giovanni. London: Vintage, 2002.

Chapman, Audrey R., ed. *Perspectives on Genetic Patenting: Religion, Science, and Industry in Dialogue*. New York: American Association for the Advancement of Science, 1999.

Davis, Paul. Personal Interview. 6 April 2004.

Dowie, Mark. "Gods and Monsters." *Mother Jones* Jan/Feb 2004: 48+.

Fehilly, Carole B., S.M. Willadsen, et al. "Interspecific chimaerism between sheep and goat." *Nature* 307 (1984): 634-36.

Filingeri, Licia. "The Hybrid as Symbol of the Transformation." *Paleolithic Art Magazine*. <http://www.paleolithicartmagazine.org/pagina75.html> Accessed 25 March 2004.

Flabert, Gustave. *The Temptation of Saint Anthony*. quoted in and translated by Borges (99); see above.

Frels, W.I. and Janet Rossant. "Interspecific Chimeras in Mammals: Successful Production of Live Chimeras Between *Mus musculus* and *Mus caroli*." *Science* 208.4442 (1980): 419-21.

Giudice, Linda. Comments at "Creating a World We Don't Want to Inhabit?" a seminar at the American Association for the Advancement of Science annual meeting, Washington State Convention and Trade Center. 15 February 2004, 2:30-5:30 pm.

Gray, Malcolm. "New Life from the Lab." *MacLean's* 14 September 1987: S10.

Haraway, Donna. email correspondance, 31 March 2004 and 1 April 2004.

---. *Primate Visions: Gender, Race, and Nature in the World of Modern Science*. New York: Routledge, 1989.

Hwang, W.S. et al. "Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst." *Science* 303.5664 (2004):1669-1674.

Kamenetsky, Hannah. "Chimera conflict: Human-mouse hybrid plan faces patent challenge from activist Rifkin." *The Scientist* online, published 10 December 2002; accessed 18 August 2003. http://www.biomedcentral.com/news/20021210/04

Lodish, Harvey :P How to cite?Personal Interview. 7 April 2004.

Marks, Jonathan. Telephone Interview. 9 February 2004.

---. *What it Means to Be 98% Chimpanzee: Apes, People, and Their Genes*. Los Angeles: University of California Press, 2002.

Meinecke-Tillman, Sabine and B. Meinecke. "Experimental chimeras—removal of reproductive barrier between sheep and goat." *Nature* 307 (1984): 637-8.

Monmaney, Terrence and Mary Hager. "Should Man Make Beast?" *Newsweek* 4 May 1987: 64.

Murray, Thomas. Personal conversation, 15 February 2004.

Nesmith, Jeff. "Bioethics: Age of biology's dark prophet; Jeremy Rifkin preaches on pitfalls of playing god." *Atlanta Journal-Constitution* 24 March 2002, Home Edition: 3F.

Newman, Stuart. Telephone Interviews. 9 February 2004 and 18 February 2004.

---. "Carnal Boundaries: The Commingling of Flesh in Theory and Practice." *Reinventing Biology: Respect for Life and the Creation of Knowledge*. Birke, Lynda and Ruth Hubbard, eds. Bloomington, IN: Indiana UP, 1995.

---. "The human chimera patent initiative." *Medical Ethics Newsletter* 9 (2002): 4, 7.

---, Ruth Hubbard. "Yuppie Eugenics: Creating a world with genetic haves and have-nots." *Z Magazine* March 2002: 36-39.

Oppenheim, S.M., G.B. Anderson, et al. "Evidence Against Humoral Immune Attack as the Cause of Sheep-Goat Interspecies and Hybrid Pregnancy Failure in the Doe." *Theriogenology* 55 (2001): 1567-1581.

Pearson, Helen. "Human genetics: Dual Identities." *Nature* 417 (2002): 588.

Polzin, V.J., G.B. Anderson, et al. "Production of Sheep-Goat Chimeras by Inner Cell Mass Transplantation." *Journal of Animal Science* 65 (1987): 325-330.

---. "Production of Sheep<->Goat Chimeras by Blastocyst Injection." *Theriogenology* 25.1 (1986): 183.

Rifkin, Jeremy. "Patenting Forms of Animal Life: Is Nature Just a Form of Private Property?" *New York Times* 26 April 1987, Late City Final Edition: 3.2.

---. "Halt Before We Reap the Whirlwind." *Sydney Morning Herald* 25 July 2000: 15.

Ritvo, Harriet. Personal Interview. 18 February 2004.

---. Conversation. 11 December 2003.

---. *The Platypus and the Mermaid and Other Figments of the Classifying Imagination.* Cambridge, MA: Harvard University Press, 1997.

Schneider, Keith. "Where There Can Be a Patent on Life." *New York Times* 30 October 1987, Late City Final Edition: A10.

Schwerin, Noel, dir. *Bloodlines: Technology Hits Home.* Backbone Media, 2003.

Shelley, Mary Wollstonecraft. *Frankenstein, or The Modern Prometheus.* New York: Oxford UP, 1998.

Smith, David. Telephone Interview. 9 April 2004.

Smith-Hughes, Sally. "Making Dollars out of DNA: The First Major Patent in Biotechnology and the Commercialization of Molecular Biology, 1974-1980." Isis, Vol. 92, No. 3. (Sep., 2001), pp. 541-575.

Stanley, Samuel. Telephone Interview. 8 April 2004.

---, Paul Davis. "Breaking the species barrier: use of SCID mouse-human chimeras for the study of human infectious diseases." *Cellular Microbiology* 5.12 (2003), 849-860.

Strain, Lisa, John C.S. Dean, et al. "A True Hermaphroditic Chimera Resulting from Embryo Amalgamation after in Vitro Fertilization." *The New England Journal of Medicine* 338.3 (1998), 166-169.

Van Biema, David. "Biotech Gadfly Buzzes Italy." *Washington Post Magazine* 17 January 1988: W13.

Veitch, Andrew. "Mixed-Up Geep Sweats it Out: Focus on the world's first goat-sheep chimera created two years ago by Cambridge scientists." *The Guardian* 31 July 1985.

Wade, Nicholas. "Stem Cell Mixing May Form a Human-Mouse Hybrid." *New York Times* 27 November 2002, Late Edition – Final: A21.

Whittemore, Gil, Esq. Personal Interview. 8 April 2004.

Yeats, W.B. "The Second Coming." *The Collected Works of W.B. Yeats Volume I: The Poems: Revised Second Edition*. New York: Scribner, 1996.