DEBATE ON VIVISECTION
BETWEEN DR. GREEK AND DR. HICKS

THE MODERATOR: Okay, we are fortunate today to have two distinguished visitors, Dr. Ray Greek and Dr. James Hicks. Dr. Greek and Dr. Hicks will be sharing there views on (inaudible) of vivisection or experimentation on live nonhuman animals.

The debate format will be as follows. Dr. Greek will speak for approximately 30 minutes, and Dr. Hicks will speak for approximately 30 minutes. Then we'll ask them to sit up here and take some questions from you all. So let's get started. I'd like to introduce Dr. Ray Greek. Dr. Greek is a physician who has published in the lay and medical literature and performed experiments on animals and research with humans. He has taught at two U.S. medical schools, the University of Wisconsin, Madison, and Thomas Jefferson University in Philadelphia.

Along with his wife Jean, who is a veterinarian, Dr. Greek has written three books on the scientific fallacy of attempting to extrapolate the results of animal experiments to humans.

Jane Goodall wrote the forward to Sacred Cows and Golden Geese: The Human Costs of Experiments on Animals, published in 2000, which was in essence a book sparked by a family squabble. Jean Swingle Greek, investigating her clinical rotations at the University of Wisconsin at Madison at Madison Veterinary School, would often come home with questions about how to treat certain cases. Her husband, Dr. Ray Greek, who was at the time teaching medicine at the university, would reply with the correct answer as if -- as it applied to humans. But in almost all cases, what cured a human did not work on animals and vice versa.

Dr. Ray Greek is president of Americans for Medical Advancement and Europeans for Medical Advancement, not-for-profit organizations dedicated to educating the public about the hazards of extrapolating the results of experiments on animal -- animal models to humans. All of the proceeds from his books go to AFMA, Americans for Medical Advancement.

Okay, please join me in welcoming Dr. Greek.

(Applause.)

DR. GREEK: Thank you, Dr. Kim, and thank you Dr. Hicks for agreeing to this debate. And thank you, audience, for showing up for class today. That was very nice of you on such a nice day. I'm from a little bit north of here in Santa Barbara, California, and I swear, I do think you have better weather than we do. Our weather is bad.

So let me get started, as any good scientist does, with a lot of disclaimers. First of all, I can't cover everything in one 30-minute lecture. Okay, it's a very broad topic.

And number two, I'm really not here to try and convince you of a position but rather to ask you to question a historical position. I'm going to go over highlights. We don't have time for any details. And there are many areas of this topic that I'm going to skip altogether.

If you want to know more about the topic, nothing beats books. Okay, sorry, but in the long run that's pretty much going to be the story with any intellectual endeavor.

Just for the record, Americans for Medical Advancement is in favor of anything that leads to cures. We are a patient advocacy group. We are not an animal rights group. We reject the use of animal models. And we'll be talking about CAMs, causal analogical models. We reject using animals as CAMs as a paradigm.

Okay, and the reason for that is when you use animals for drug testing, the animal model must be predictive to be useful. Predictability is one of the things that distinguish science from pseudoscience. Science is about predictability.

And with that we will go to the next slide.

I want to start my portion of the lecture today by asking you a couple of questions. What makes a drug good? And what makes another drug bad?

Our first example is a vaccine against rotavirus that came out about three or four years ago. One out of 2500 children in the United States suffered a severe side effect from this vaccine, called intussusception. And some of them actually died.

Now, the rotavirus is a virus that causes roughly a half a million deaths every year, mainly in what we call developing or third world countries. So because the drug was not going to be able to be sold in the U.S. because one out of 2500 children had a bad reaction, the drug could not be sold anywhere in the world, where it would have done a lot of good.

So my first question for you is was Rotashield a good drug or a bad drug?

And there's other drugs. Rezulin was a drug that was used to treat diabetes. And it worked incredibly well in the vast majority of people. Probably 99 percent of the people that took it, the drug was either effective or benign. Unfortunately, in a very small percentage of people the drug caused liver failure. Some of those people died. And some of those people had to have a liver transplant.

Was Rezulin a good drug or a bad drug?

I think a lot of us are familiar with thalidomide. Thalidomide was a drug that my mother almost took actually. It was a drug that was given to women who were pregnant in the late 1950s and early 1960s. And, unfortunately, it caused birth defects in their offspring.

Today it's used as a successful cancer treatment.

Aspirin? Every year somebody dies from aspirin because they're allergic to it. The same thing is true of penicillin. There is a drug that was recently taken off the market called Propulsid, which again treated gastrointestinal problems in people very effectively. But it was an outstanding drug for many people. Unfortunately some people died due to a heart rhythm abnormality.

Would you classify these as good drugs or bad drugs?

Allen Roses was the vice-president of genetics at Glaxo Smith Kline, which was a big drug company. And he said that fewer than half the patients prescribed some of the most expensive drugs in the world derive any benefit from them. He went on to say that the vast majority of drugs, more than 90 percent, only work in a third to a half of the population. And most drugs had an efficacy rate of 50 percent or lower.

Another point to consider is that among ten medications that were withdrawn from the U.S. market between 1998 and 2001, eight were withdrawn because of side effects that occurred primarily in women. Now, were those eight drugs good drugs or bad drugs?

What about water? Water's a good thing, right? Well, I've actually treated people who drank too much water, had seizures, and almost died. And people can die from drinking too much water. And it was anecdotal evidence like that that led people in the sixteenth century to say that the dose determines the poison. They felt that all chemicals, what we would today called drugs, were good if the dose were appropriate and bad if the dose were inappropriate.

And hopefully by the end of my lecture, I want you to consider that it is the genetic make-up of the individual and the regulation of those genes that determines the poison. A drug can be good for you and lethal for me and vice versa.

So today we're going to talk about the use of animals in biomedical research. We should know what we're talking about before we really start the discussion. Animals can be used in biomedical research in roughly nine different ways. Today we're only going -- or I am only going to talk about two of those nine ways, the use of animals to model human disease and the use of animals to test drugs.

Now, there are seven other ways that from my perspective animals are scientifically valid. Okay, animals can be used to spare parts. Your governor is currently walking around Sacramento with a valve in his heart that came from a pig. No jokes. I've heard them.

Animals can be used as factories. And they were for years. They made -- we've made insulin for human consumption from livers or from pancreases that came from slaughter houses.

Animal tissue can be used to study basic physiological processes, and it was in the nineteenth century.

Animals can be used for dissection.

They can be heuristic.

They can be used to learn things about other animals.

And they can be used to obtain knowledge for knowledge sake.

Once again, those are scientifically valid ways to use animals in biomedical science. Okay? Now, some people have ethical problems with that, and we can talk about alternatives, or the three Rs some of you may have heard of. But Nos. 3 through 9 are not my issue. My issue is solely with using animals to predict human response vis-a-vis drug testing and research for diseases like Alzheimer's, cancer, AIDS, and so forth.

The way that animals are used in Nos. 1 and 2 on the previous slide is what we call causal analogical models. Now, what this means is that the first condition that must be met in order for a thing to be considered a causal analogical model is this. X, the model, is similar to Y, the object being modeled, in respects A, B, C, D, and E.

Now, the model X also has additional property F. And while F has not been observed directly in Y, it is very likely that why also has that property.

So this is called causal analogical reasoning. X causes Y in the cat; therefore, X will cause Y in human beings.

LaFollette and Shanks said in 1996 in a book called Brute Science that since phylogenetically related species, say, mammals, have all evolved from the same ancestral species, we would expect them to be in some respects biologically similar. Nonetheless, evolution also leads us to expect important biological differences between species. After all, the species have adapted to different ecological niches.

However, Darwin's theory does not tell us how pervasive or significant those differences will be. This again brings the ontological problem of relevance to the fore. Will the similarities between species be pervasive and deep enough to justify extrapolation from animal test subjects to humans? Or will the biological differences be quantitatively or qualitatively substantial enough to make such extrapolations scientifically dubious? So that is the question that we are faced with vis-a-vis Darwin's theory of evolution.

And today we have the answer to that. Some of you may remember when the human genome was published. And the humans turned out to have between 20,000 and 30,000 genes. It kind of depends on how you count them. Recently the mouse genome was also

published, and it has between 20,000 and 30,000 genes. Matter of fact, the genes in a mouse are 99 percent similar to the genes in you.

Matter of fact, mice and humans both have genes to grow a tail. So why don't we grow tails? Well, because in mice that gene is turned on during embryogenesis, and in humans it's turned off. The difference between species is not so much in what genes each species has, but in how those genes are turned off and on.

Now, in the old days when I was in medical school, we thought that genes interacted like this diagram on the far left. We thought that a single input led to a single output. A gene makes a protein, and that's all it does.

As we learned more, we found that multiple inputs could cause that gene to put out its protein. And to the far right of the diagram today we know that genes work in networks. They can be what is called alternatively spliced. And we know now that multiple inputs actually lead to multiple outputs. So even if you have exactly the same genetic network as a mouse, you are not going to look or act like the mouse.

And this diagram on the far right tells us why.

Now, this is a little bit more complicated diagram, but this is a diagram of a genetic network in a yeast. And the only reason I'm showing you this is to show you that all of these little circles connect with other little circles, okay? Does that make sense? And what this is is this is what a species is. It's all of these little genes connecting with a lot of other little genes.

And so what this means is if you have a gene like the top yellow dot, it is going to influence all of these other genes or little yellow dots in a cascade effect. So if you have a gene in common with a mouse but that gene is turned on in the mouse and it's not turned on in you, you're going to have this cascade effect that in essence is what separates you as one species from a different species.

Does that kind of make sense? Great.

So as I said in one of my first slides, animals can be used to study basic physiological principles, okay. And in the 1800s and early 1900s we learned a lot about basic physiology from studying frogs, rats, mice, and so forth. So why can't we continue to do that today?

Well, because today our level of examination is much more fine-tuned. In the 1600s William Harvey wanted to know what that big organ in the center of the chest did. Okay? They honest to god didn't know. One thing that Harvey did was he dissected a horse. And he saw that the heart pumped blood in a circle. That was a huge breakthrough.

Today we're a little bit beyond studying what the big red organ in the center of the chest does, okay. Today we know that drugs that kill women might be safe for men. So testing those drugs on a monkey, a completely different species, is scientifically invalid. Our knowledge has increased since the hundred years ago. Today we understand gene networks, gene regulation, gene expression.

Today we understand that mammals, any mammal, is an example of what's called a complex system. In a complex system a very, very small change can lead to profound changes on down the line, just like the slide show of the cascade effect. And really we know most of this because of our study of evolutionary biology and of course molecular biology.

So the reason that we cannot use animals to test drugs or to study diseases like AIDS is because our genes are regulated and expressed differently. Even if we have one hundred percent of the same genes, it doesn't matter.

And again, I go back to the fact that among ten medications that were withdrawn from the U.S. market between '98 and 2001, eight of them were withdrawn primarily because of side effects that occurred in women. Now, this really comes down to common sense. If a man cannot predict what a drug is going to do in a woman, how, pray tell, is a completely different species going to be used successfully as a causal analogical model? That defies rational thought.

A study in Science in the year 2002 revealed that one strain of mouse could have an entire gene removed without obvious adverse effects. But a similar strain -- and strains of mice are kind of like cousins. Okay, they're closely related. Another strain, when that gene was removed, died without that gene.

Identical twins have been known for decades to physicians not to suffer from the same diseases. We have known for decades that even though twins might have -- or twins are identical and have exactly the same genes, one twin will come down with breast cancer; one will not. Today we understand why.

It's because the -- the gene that causes the breast cancer is turned on in the one sister because of environmental reasons, but not turned on in the other sister. Again, one hundred percent identical genes, and you could not have a more different outcome.

Today we are designing medications that will work on a specific genotype. Okay, they'll work on your genes, not my genes. Not your mother's, not your father's. Just yours. And this is called personalized medicine or pharmacogenomics. And this is one of the hot areas of research right now.

Now, there are a few -- when I -- when I learned I was going to be down here lecturing, I did a crisp search on the Internet to see what kind of research was taking place at UC Irvine. Because frequently when I do debates or when I give lectures one criticism that is leveled is that, well, scientists don't really use animals as CAMs, you know. My

opponent will say, "You're right, Dr. Greek. They're not CAMs. We cannot use one species to model another species in that fashion. But that's not how we use animals. We use animals as a heuristic device" or some other such thing.

So I looked up who was doing research at UC Irvine and just went through the list A, B, C, in work. This person is named Anderson. I don't know who this person is. His project title -- or her -- I don't know if it's a man or a woman -- is a new model for corneal disease. And if you'd just skip down to the bold type, it says, "This new mouse model may be important for understanding the molecular pathways that prevent keratinization of corneal epithelium and vascularization of corneal stroma. In addition, characterization of this mouse may provide insights into the pathogenesis of corneal causes of blindness and provide a potential model to test therapeutic approaches."

Okay, to put it simply, this person is using the mouse as a CAM. There's no way around that. He's not using this mouse to get an idea about what might help humans someday down the road; he is using this as a causal analogical model for human disease.

Then I pulled up this person, whose name starts with a B. And this is febrile seizure model. And again, this is an immature rat model of prolonged febrile seizures, et cetera, et cetera, et cetera. If you read the entire abstract, again, we're only to the Bs, and we have two people who are saying in their abstract that they are using animals as CAMs.

This is somebody using a new vertebrate model as a CAM, and you can read the abstract. But bottom line is "It is expected that the availability of these libraries and the data derived from them will serve to facilitate progress and the adoption of this particular fish as an important vertebrate model system." So again -- and I stopped here. I -- that's enough examples.

But this is how animals are used today in biomedical research. They are used as a CAMs. I'm not saying that every single researcher at UCI who uses animals uses them as CAMs, but a vast majority of them do. And the reason that they do this is because the general public really has a distaste for funding animal experiments. But when you put it to the public like it's your dog or your child, the public will choose their child every time.

And the criticism that I have for people who apply to the National Institutes of Health for grant money is that they say to the general public, "We're using animals as CAMs." But to themselves wink, wink, nod, nod, we know we're not using them as CAMs; we're actually using them as heuristic. But if we tell the general public that, we will not get our grants funded." And they're right. They wouldn't.

Oh, here's one more. Sorry. This is the dog as an animal model of human aging. Carl Kotman was the PI. "During the past five years a canine model of aging has been evaluated with emphasis on categorization of cognitive decline and links with neuropathology. The pray of the proposal seeks first to extend our evaluation of the canine model and establish that cognitive processes are particularly sensitive to aging," blah, blah, blah.

Again, this is a CAM. Okay, what this PI wants to do is -- PI stands for primary investigator. What he wants to do is look at the dog and see if he can translate those results to humans, thus getting a new drug for Alzheimer's or a new drug for some other type of dementia or to learn more about what causes dementia in humans, and so on and so forth.

So what I am saying today is that animal experiments should be abandoned in part because they do positive harm to human beings. For example, smoking was thought to be noncarcinogenic for decades because scientists could not reproduce lung cancer in laboratory animals. Millions of people died because they originally thought that smoking was (inaudible). That's not true today. But in World War II the U.S. government actually put cigarettes in every GIs little pack. Okay. Because it was safe, and it was fun. And it wasn't addictive.

Back in the old days we thought -- this is 1948 -- we thought that a high cholesterol diet was actually good for people who had just had heart attacks because we have a high cholesterol diet for dogs and I think in monkeys, and they did fine.

Asbestos was thought to be a very safe product because of animal testing. And again, when you -- when you listen to people give a scientific lecture, one thing that you should look for are these references. Because if I get up here and just, you know, say something, I mean, you don't know me. I could be a complete con artist. I could be down here telling I things that are blatantly false.

But that's why scientists, when they lecture, they put references on their little bullet points, so that if anyone is interested, they can actually go look up these articles and see if the presenter was being truthful with you or not.

So I kind of ran out of space on the references, but we've had a lot of drugs to treat stroke that worked great in dogs that killed humans. The National Cancer Institute -- they're not exactly a bastion of animal rights activity -- said in Science Magazine, I think it was 1997, that we have lost -- lost -- cures for cancer because they didn't work in animals. They probably would have worked in humans. But we threw them away because they didn't work in animals.

And again, there is a long list of things that animal models have predicted that turned out to be just the opposite in humans that have led to human death and suffering.

So why should we abandon the animal model? It's ineffective, okay. It doesn't work. I don't care what alternatives there are, if it doesn't work, it should be abandoned. Trephination, how many of you know what trephination is? Trephination is when you drill a hole in someone's skull to let out all the evil humors so the person won't be sick anymore, okay? Now, we don't have a cure for AIDS. And there's not one on the horizon. And yet I would still come out very strongly against using trephination in AIDS patients, okay? Because it just doesn't work.

So there are no alternatives to something that is ineffective in the first place. There is not an alternative to buying a used car for space travel, okay? It doesn't work.

Number two, we have better options. And the animal model has outlived its usefulness. It diverts funds from very viable research modalities. It misleads researchers. Again, we've lost cures for cancer, according to the National Cancer Institute. It does not keep bad drugs off the market. It does keep some good drugs off the market. But the bottom line is when animals are used as CAMs, invariably humans are harmed.

Okay, I'm running out of time, so we're going to skip some of these things. Some people say to me, "Why is animal use continued in light of all this?"

And there's a lot of reasons. Tradition is probably one of the bigger ones. The system is based on it. Everybody's resistant to change. Scientists are no different.

There's a lot of reasons, but I think the biggest reason is money. It is a multibillion dollar business in the U.S. and abroad, so there are a lot of people whose livelihoods would be affected by this change. It would be a human change for society.

But this is my last slide, and I will lead you with this. What a difference a little DNA makes.

Thank you.

(Applause.)

THE MODERATOR: Okay, I'd like to introduce Dr. James Hicks. Dr. Hicks obtained an MS in biology at the University of New Mexico and a Ph.D. in biomedical sciences from the School of Medicine, University of New Mexico.

He did postdoctoral work at the Max Planck Institute for Experimental Medicine in Germany from 1984 to 1985, followed by a two-year postdoctoral fellowship at the physiological research lab at Scripps Institution of Oceanography at UCSD.

Dr. Hicks was on the physiology faculty at Creighton University School of Medicine from 1988 till '92 and then joined the department of ecology and evolutionary biology at UCI in 1992, where he is currently a professor of biology.

Dr. Hick's research efforts are focused on comparative aspects of oxygen transport in vertebrates. His research has involved a broad range of vertebrate taxa and has included a variety of paradigms to understand physiological function from computer modeling to laboratory experiments to observations and experiments in nature.

His research findings have brought implications ranging from understanding the function and evolution of the cardiopulmonary system in vertebrate animals to providing insights on the metabolic physiology of dinosaurs.

His laboratory provides an evolutionary perspective into circulation and respiration and seeks to discover not only differences among organisms but the unifying principles shared by diverse organisms.

His research is currently funded by the NSF and NASA. His published research has included papers in Science, Nature, and proceedings of the National Academy of Sciences.

Dr. Hicks is currently the chair of the comparative and evolutionary physiology section of the American Physiological Society. And in January of 2002 was named editor in chief of Physiological and Biochemical Zoology, Ecological and Evolutionary Approaches. Published by the University of Chicago Press, the journal focuses on ecological and evolutionary approaches to understanding biochemical and physiological mechanisms in animals.

In January 2006 Dr. Hicks was appointed chair of the Institutional Animal Care and Use Committee, which reviews oversees, and approves all animal research at the UCI campus.

Please join me in welcoming (inaudible).

(Applause.)

DR. HICKS: Thank you, Clare. I think when I'm done with my 30 minutes you're going to find that in many ways Dr. Greek and I agree on -- on certain things, and in other things we will find that we disagree quite strongly. I think that's the way things go in a debate.

When I was -- when I was asked to be involved in this discussion, I was at first hesitant when Clare came to my office and asked, primarily because I've never done this before. I've never had to articulate or think in a public setting about why we do animal research. I guess maybe I should, but I've never done that.

And it was in the process of preparing for what would I talk about and -- and not knowing who would be speaking today except by name, Dr. Ray Greek, I went through and started reading a variety of -- of -- of books and -- and journals and the like trying to get caught up on things that maybe I should know about and don't know about. And in that process I think that I had to decide how would I go and address probably some of the issues that would come up today.

It's -- as Dr. Greek said in his talk, I'm not here to try to convince you. Probably a third of this class is probably very strongly against the use of animals in research for both

ethical, moral, or religious reasons. Probably a third of you are undecided. Probably a third of you are very pro-use of animals. And in 30 minutes, even though we live in a soundbyte society, in 30 minutes we could not, either one of us, probably convince you wholeheartedly to change your mind.

But just as Dr. Greek said in his talk, what I want to do is try to give you some -- some take-home messages, some things to think about when you hear people talk about pro- -- pro-animal research or people are against the use of animals. And as I said, you'll find in this talk that there are some things I want to agree with Dr. Greek and particularly in the sense of CAMs, because I actually have a similar -- same viewpoint. Many evolutionary physiologists have a similar viewpoint as well. But we also differ in certain things.

Now, what would be the take-home messages that I'm going to talk about today? For this I'm going to actually have to do an experiment in this class. I'm going ask for two volunteers. And I want you to think about this, who's going to volunteer. And if nobody wants to volunteer, then I'll ask Professor Kim just to choose randomly (inaudible).

But the take-home messages are two things. The first, it means just what I choose it to mean. And this will deal with the whole level of -- of when we discuss the use of animals in research and we are -- and we are suggesting that we're doing it purely from the scientific standpoint. Where are we coming from? How does our personal belief system influence just what I'm -- what I'm telling you or Dr. Greek's telling you?

And then the second take-home message I hope to -- we'll get through is that evolutionary biology is actually a very powerful paradigm, not a constraint to animal research. Or it's actually quite revealing and can reveal a whole variety of -- of new ideas about specific genes, regulatory pathways and genetic clusters which are applicable not only to understanding animals; it can be applicable to understanding human disease as well.

So again, getting ready for this -- this talk I read Dr. Greek's book on specious science. I didn't read the other books. I read that book, and I read a number of his -- of his news letters and letters that he had written to journalists.

And I thought of this quote from Through the Looking Glass, which is, "When I use a word, Humpty Dumpty said in a rather scornful tone, I mean just what I choose it to mean, neither more nor less. But the question is, said Alice, whether you can make words mean so many different things." Can you make words mean so many different things?

If you go to UCI of course you also know this individual Jacques Derrida, one of our greatest philosophers. And Jacques Derrida argued in probably his best work, which was his dissertation work Structure, Sign, and Play of the Discourse in Human Sciences, that intellectuals try to comprehend the world, but these are not value-neutral when you try to comprehend the world. There is always going to be some interpretation. Nothing is purely objective. Objectivity does not exist.

Derrida would go on to say that that's not a bad thing. But you must always remember when people are talking to you presenting prepackaged information, just as I am doing right now, prepackaged information, that we come to you with our own preferences. We are not value-neutral. We have a way of trying to convince you by selectively using information.

And this is an important -- an important message, because the selective use of information is used all the time in our society. It is used in the evolution debate. It is used in the abortion debate. You're all political science majors, right? How many wrote -- how many have read the new essay by Paul Pillar in Foreign Affairs? Paul Pillar is a C.I.A. agent, C.I.A. -- worked for the C.I.A., analyst, for seven years, Middle East. Specialty, Paul Pillar just wrote in the Foreign Affairs that it was the selective use of information by the administration that resulted in convincing the American people and the Congress that we should go to war.

Selective use of information is not necessarily a bad thing, not if you read Derrida, it's not bad to be selective. But remember, the people that come to you with prepackaged information will use that information selectively to make their point, just as I will try to do. But I'm telling you upfront that's what I'm going to do but also try to be fair at the same time.

So I need the lights on just for a second. I want to do a very simple experiment. I need two volunteers. Just two. And someone who can read very quickly.

Anybody want to volunteer?

THE MODERATOR: One more?

DR. HICKS: One more volunteer.

THE MODERATOR: How about Cathy?

DR. HICKS: What this -- when I decided to do this, this is not done in terms of -- of embarrassment. As I said, I agree with many things that Dr. Greek says. And I think you'll see that (inaudible) in the talk. But in terms of preparing for this talk, I read the books and I read many of his newsletters. This one's Pathway to Progress, which is from his Web site curedisease.com, which talks about and -- and summarizes the literature for people who are subscribe -- or you can download it free off the Internet so you don't have to even subscribe to it. And it summarizes it for you.

It turns out when I was preparing for this, though, as I was reading these quotations of various studies, there were some that I actually knew quite well from the literature myself. And I would go, "Well, that's not exactly what that study said." And when I read this Pathway to Progress, what was quite interesting was that in fact one of the studies that summarized at the end of it was actually written by a fellow colleague Michael Rose.

How many know about Michael Rose here on campus? If you know him, you won't forget him. Michael Rose, one of our most well-known evolutionary biologists in the department who works on the evolutionary biology of aging, has written a number of both popular books and scientific books on theory of evolution and evolutionary biology.

One of the studies that was referenced in Pathways to Progress was in fact by Michael Rose. So I thought, well, I know that study. I know Michael. Talked to Michael. And I thought it would be interesting to do this experiment.

So what I want you to do is I would like you -- make sure I have the right one (inaudible) -- to read this and you to read that. If you -- just a -- it takes -- it's only about 120 words. Read it very quickly. Also I know this is going to take a little bit of time. I want you to also write something down, though, too. Just a one-sentence. Can you write just one when I -- (inaudible) read or write one sentence (inaudible)?

Will you tell me when you're done. I don't have a pen. Here's a pen. Borrow. (Inaudible) and when you're done -- are you? -- I don't want to (inaudible), but when you're done will you just turn it over and just write one sentence that just -- what's the take-home message you're getting out of that summary? Just a one-sentence take-home message.

So it's taking a little longer than I anticipated. If I stand over here closer, will that pressure you a bit to like write a little faster?

Okay.

All right. Actually, you know, you can verbally say -- I've already got one written down here so -- I just don't want you to influence each other in terms of how you interpreted that paragraph.

CATHY: (Inaudible)

DR. HICKS: So if you just want to verbally say it to the class.

CATHY: Yeah. The reduction of calorie intake increases the life span in humans compared to -- but it's compared to nonhuman animals, which their life span was increased by over seven percent, but theirs is increased by -- ours was only increased by seven but theirs is like almost seven years. (Inaudible)?

DR. HICKS: Right. So this summary -- this summary says that reduced caloric intake, which is a fad diet, you (inaudible) walking around on a thousand calories (inaudible) calories a day, works in all animals, but in humans it's quantitatively less. It's about a seven percent increase in life span.

This summary says, the one sentence says, that it does not work in humans. Works in animals but does not work in humans. Essentially it says not able to relate it at all to humans, is what he wrote.

This summary is taken from Dr. Greek's Pathways to Progress. And where did that summary come from? Well, where that summary came from is actually a summary of a summary, which is not only the best thing to do but comes from this Web site. We won't go to the Web site. If you want to go we could go to it. But it come -- there's a summary of the work by Michael Rose, and then Dr. Greek summarized that summary in his Pathways to Progress.

And that summary was that even though it works in animals, it doesn't work in humans. That's the message we're hearing today.

This summary says, no, it works in humans too. It's universal. It just doesn't work as much. It's not as big, the effect. About a seven percent, five years, added on to your life.

Where did it come from? Well, let's do a little bioformatics. You know what biformatics is, comparing of information. This is the -- you don't have to read all of this. The main point here is that this is the summary that was on the Web site. And words colored in red and blue are the paragraphs or sentences that were taken out of this summary and put into Pathways to Progress, the summary that said it doesn't work in humans.

What I did for this class was I took the same summary -- oops, wrong one -- I took the same summary. And where the colors are the same we have used the exact same paragraphs. And where the colors are different I have chosen different paragraphs.

What ends up happening? There are two different meanings emerge from the exact same summary. And this just shows the rest of the article with my end point that I took.

Woops. And there's some differences here. So -- yeah, this doesn't -- I had to change computers. This is actually Dr. Greek's computer so I can't -- it's not going to show it. But the point is is what summary is closer to the intended meaning of the authors? The summary from Pathways of Progress says caloric restriction works in other animals but doesn't work in humans. The summary that I developed from the exact same summary just using different paragraphs in the same order says that caloric restriction works in all animals but is of a less quantitative nature in humans.

What's the point here? The point is is that the message can be changed by selectively using information. Is this a pattern? I don't know if it's a pattern. I don't want to say that everything that Dr. Greek says has a pattern to it. I can only base it on what I have read. I've read this book Specious Science, and here's an example of where -- on page 252-51 he talked about transgenic animals and why transgenic technologies will not be useful in studying disease. And he quotes a paper. This is taken directly from the book.

Even the pro-animal model in the literature admits to the ineffectiveness of transgenic animals. Comparative medicine states that animals might be used to find out which genes cause disease in humans; however -- and then the quote from the paper by Van Zutphen -- "results to date suggest that predictive value of a candidate gene established in such an animal model is rather low. Thus far only a few genes have been allowed -- allocated as causative factors." And you can read the rest.

In other words, it's not going to work. There's too many differences between animals and man, animals and human. Transgenic technology. The message there is transgenic technology does not have positive benefit.

Where did that quote come from? Well, we can go right to the source, right to the paper. Here's where that quote came from. It came from there. Well, what if I was writing this book and I had a different spin on it? What if my book was actually called Animal Studies: How Animals Help Humans, and I decided to use this paper to make the point that transgenic technology actually is a good thing? I can pick a different quote from the exact same paper. I could pick the quote down here and not take the quote up at top. And then I would have a very different message.

I would have this message: these developments will increase the insight into transgenic pathways and gene environment interactions that are involved in the etiology of complex human genic disorder. This knowledge could be applied to select better animal models and produce specific transgenic animals, or knock-outs.

Selective use of information is the result of personal bias. If I -- I have a bias. I believe that animals are good models for experimentation in terms of understanding both human disease and animal biology. I can take the exact same information, take a different quote out of context, and make the point, very different point, almost a very -- almost 180 degrees different than Dr. Greek is making.

What's the problem here? The problem is when you're someone naive like me who has to go and try to prepare for a presentation like this, it means that every statement that will be made, you have to go to the original source and read the original data, the original paper. Because what's been quoted out of context? What's not being told to you? What's being left out?

This is not necessarily bad or good. It's what people do. It's what Derrida said, "There is no objectivity."

But what science tries to do is it tries to be objective. It aspires to be objective, but it's not totally objective. But it aspires to do that. And how does it do that?

Well, Stephen Jay Gould said, "Objectivity cannot be equated with mental blankness." You don't come to every problem not thinking or having a preference. Objectivity resides in recognizing your preferences and then subjecting them to harsh scrutiny and a willingness to revise or abandon your theory when your test fails.

So we have bias. But I want you to know as students, the take-home message is that I have a bias. Dr. Greek has a bias. The message is going to be modified, is going to be adjusted to try to convince you of our points. You can't take everything at face value. Therefore, as Dr. Greek said in his talk quite correctly and I agree with him, you have to go read. You have to read the -- the sites (inaudible) that support animal research and the sites that are against animal research.

And so I prepared for you a handout which has both pro-animal research and anti animal research sites listed for you that I'll hand out at the end of class. But it's up to you at the end of the day. Because you can't rely on somebody else giving you that information.

Now, in the last few minutes what I want to do very quickly is talk about evolutionary biology. First thing, evolutionary biology, it is not a static field. It is changing all the time. It is not the evolutionary biology of Darwin. There is no -- the evolutionary -- he was the greatest, he was a great figure of biology in terms of elucidating and articulating the ideas. But evolutionary biology is rapidly changing all the time. It's not a static field. Evolutionary biology actually depends on animal research to learn about evolutionary biology.

And there are whole new fields of evolutionary biology opening up, like evo-devo. Sounds kind of like a music group. Evo-devo, where you look at how genes influence development and how the environment influences the genetic expression of those genes and how that might flow into understanding more completely evolutionary theory in biology.

A lot of what Dr. Greek talked about was CAMs. CAMs really comes from the concept of isomorphisms. Let me state from the outset. CAMs -- I had never heard of CAMs before this talk. And I'm grateful that I was able to read his book and learn about them. Because I actually think he makes a good point about CAMs at one level. It comes from isomorphisms, and he actually went through it already. So I won't spend too much time on it here. Causal analogical models.

You have these two cones. They have common causal features. There's (inaudible) between those features. They're not causally relevantly different. There's no, as LaFolette and Shanks said, there's no dis -- you know, significant disanalogies between these two. So you can study that cone and talk about that cone and learn all about it. And if there's several differences, you might be able to learn a lot about the other cone. But if there are significant disanalogies you cannot predict anything about that cone. So that's where (inaudible) comes from.

And so Dr. Greek did a -- I mean he summarized it exactly correctly. So if you want to study babies, you study babies, obviously. That's what you have to do.

Will this tell you anything about that? Well, no, not really. Not really. Why? Because Dr. Greek already said -- and I'm just going to repeat it quickly -- because when we look

at organismal features, there are a whole variety of levels of organization from the molecular to the population. Not only are we challenged with having to integrate from the DNA all the way up to population, but we have to integrate -- that's a vertical integration -- we have to integrate horizontally over time, that time being developmental time, that time being evolutionary time. This is a major challenge in biology, how to integrate changes down here at the molecular level and equate them to what's going on up at the organ -- cell level, the organ level, the organ system level, the organismal level, the population level -- it's a big task, not easily accomplished but is a challenge in biology in the twenty-first century.

So now, I agree. Studying a rat will not tell you anything of specific information about a disease in a baby, specific information about the disease in a baby. You study babies if you want to know about babies. But causal analogical models, Dr. Greek's completely right, it dominated physiology and biochemistry for 20 -- for the -- most of the twentieth century, most of the nineteenth century. It was the result of linear thinking, that if I study a dog, it's directly applicable to the human, if I study a rat it's directly applicable to the a human, if I study a frog it's directly applicable to a human.

And who was that the result of? It was a great man, Claude Bernard, French physiologist who was the sort of father of physiology of the twentieth century. He was -- did most of his work in the late 1800s. And his thinking and his students, the people that came out of his lab that were associated with, they were not evolutionary biologists. They weren't trained. Evolutionary biology was a new science itself. They hadn't even read Darwin probably.

But so they -- they produced students who thought the same way, that there was causal linkage between studying an animal and directly relating it to human disease. And this did dominate the field for a long time.

But there are evolutionary issues. As Dr. Greek pointed out, recognizing the problems associated with comparisons of phenospecific traits among and between species is not new. It's not a new idea. This isn't even (inaudible) -- this is not even LaFolette and Shanks who wrote about it in the 19 -- 1990s. This goes back to the '40s and '50s. Evolutionary biologists knew there was a problem.

Later on physiologists also began to learn that there was a problem in the '70s and '80s. You couldn't make one-to-one relationships. It wasn't quite possible. There are species differences.

And even if organisms come from the same ancestor, organisms do change over time. Genic drift. Random mutation. Natural selection. All act to modify the genetic blueprint and the resulting phenotype. And so any two species, any two that you pick are likely to show differences in almost any phenotypic trait. Morphology, physiology, biochemistry, molecular biology -- it's almost guaranteed by random mutation and genetic drift. This has been known by evolutionary biologists for a long time. And more so by physiologists in the last 20 years.

Even within single species, as Dr. Greek pointed out, there is a lot of variation that will influence the phenotype. This is a whole new field, as he pointed out, pharmacogenetics or genomics where you have drugs specifically designed for your genotype. Why? Because there's genetic variation. We know this animal, what came out of this animal through domestication? That animal. And that animal. There's a lot of genetic variation under -- that's underneath all of us. And it does have an influence on phenotype and physiology and biochemistry.

And so it is -- he's absolutely correct that what goes on at this level, small changes can affect what goes on at this level, which changes what goes on at this level, all the way up.

But we know that. This is not new. Evolutionary biologists have known this for a long time. The challenge is understanding it. We don't know everything at the molecular level. We don't know everything at the cell. We don't know how this connects to this in an integrative, quantitative, predictive sense. But we believe we can understand that, can in the twenty-first century.

Yes. There are causal analogical models. They did dominate it. And Dr. Greek says in his -- in his presentation -- and he stole some of my thunder. Because I actually think it's a straw man. It doesn't really exist. In the past 20-plus years with the explosion of molecular biology, gene sequencing, comparative function genomics the view has changed among life scientists. They do think of them as HAMs.

He said it in the following way when he was up here. They'll tell you what they're going to do, but then wink, wink, they're saying they're using it for heuristic devices. It's not a wink, wink. Scientists use animals as heuristic devices. A lot of scientists use animals as heuristic devices. And the quotes that he used from the animal studies done here, I know those investigators. I've reviewed their proposals. They're not using them as CAMs. They're using them as heuristic devices.

What's a heuristic device? How do you generate new knowledge? How do you generate new ideas? How do you generate novel approaches? You can do it on animals. Why? Because the underlying biology is similar enough to reveal patterns and processes. But everyone knows they don't directly correspondent. And if they do they're naive. Evolution not only reveals differences but reveals similarities. Discovery of novel genes, regulatory (inaudible) pathways and functions, and these insights can be applied to all animals, including humans. We know this through phylogeny, the connection of animals through genetic history over time.

This is called a cladogram. And we can compare things by cladograms. The wider animals are separated, the more we might be able to know about some of the very common features. What are the core sets of proteins in multicellular organisms? How do they -- and as these animals become more close related how does the sequences in their genes tell us something more specific about their organ- -- these organisms? We can apply cladograms, molecular phylogenies, for mapping phenotypic traits and

understanding and predicting similarities and differences in organisms by using phylogenies.

There is a lot of similarities in the animals. And they do tell us a lot about how animals work. Here's a homeobox gene, sequence of genes that code for pattern, developmental pattern. It was discovered in a fruit fly. This actually -- the discovery of homeobox genes that are involved in the development and color coded for what parts of the animal they are coding for, that of the -- that was the big birth of comparative genomics essentially, understanding that at the gene level there are conserved genes that code for similar kinds of structures, functions, or pathways.

And now they found that homeobox clusters in a whole variety of animals. And do they do the exact same thing? No, they don't do the exact same thing. It would be silly to think that they do the exact. But they gave insight into -- into developmental biology.

If you take a fly, a fruit fly, and mutate one of the homeobox clusters, you get appendages coming out of its head. This is the result of a mutation of homeobox clusters in humans. It's not the same thing, but it's an underlying pattern that starts to give you some insights.

Chondroplasia, short-lived dwarfism, in humans, it's the result of a mutation in the FGFR or the fiber op- -- the fiberglass growth factor receptor. There's three different subtypes. There's a mutation on one of those receptors. It's the result of actually a single base change in a gene that results in a glycine, an amino acid, being converted to an arginine. 95 percent of these dwarfs have that genic mutation.

I'm not -- if you take the same or similar gene in a mouse and mutate it in the same region to create the same kind of mutation in the FGFR receptor, you get dwarfism in mice. Is it the same? No. They'll be differences. But there's enough underlying similarity that the single mutation can be used to try to study the genetics, how the genes coalesce and how they move from populations, and they can be used as heuristic devices to try to understand or come up with novel approaches that you can study in an animal that might not be easily studied in a human.

Many biologists and some of the biologists that he quoted today from UCI just don't study animal models. They have parallel human studies that they do as well, always knowing that you got to connect back. You just can't blindly look at an animal and say, "Oh, yeah, this is exactly what's going to work in the human."

So I'm just about to finish here. There's 30,000 genes in the human genome. Less than 50 percent have a known function. And with the discovery -- as we begin to discover all these sort of interesting clusters through genomic analysis -- and this is the hot area, genomic analysis, bioformatics, (inaudible) genomics -- how will we know what these genes do?

Well, there's a bunch -- there's a variety of technologies available. Transgenic technology, knock-out technology, where you knock genes out, put genes in. You do

comparative genomic, function genomic, function genomic where you look at big gene sequences across populations. You can do epidemiology. And you can do experimental evolution. UCI has one of the centers of experimental evolution in the country, if not the world.

What is experimental evolution? Well, transgenic technology just modifies the genotype. One gene, you look at the result. Actually it's not the very good way to do things. If you had to do this, it will take you a million years to ever figure out the whole -- all the genes that are available or what they're doing.

So another way in order to do it is called experimental evolution. You can do evolution in the lab using fruit flies, mice, zebra fish, rats now even, animals with fairly short generation times. You can select on the these animals, know their back- -- the selection. You can do quantitative genetics on them. You can begin to understand phenotypes and genotype connections at a level that's not presently understood.

And you don't have to read all this. The most important thing is that these methods used in experimental evolution begin to reveal correlative responses, the interdependence of phenotypic traits on a specific genetic background.

The thing that I come away from when I read the work by Dr. Greek is the feeling that we already know everything about animals. They're not even applicable humans. So why do we even bother to study them? We know very little about how phenotypic traits correlate on a specific genic background.

Are human studies, will they be insightful? Yes. And animal studies will be insightful as well.

We are entering -- this is the last slide -- really the most exciting period in biology. You know, this twentieth century was really the century of physics. This is the century of biology. We have the challenge to try to understand life from the DNA level to the organismal level. And as someone said at NIH, you know, if you want to study oranges, if you want to know about oranges, you got to study oranges. But you can learn a lot about fruit by studying fruit, all kinds of fruit.

And the same applies to human biology. We can look, try to integrate the challenge of integrating across these local levels of organization both vertically and horizontally and just say, you know what, we don't need to study any more animals to try to understand this. It's all done. But I don't think we're going to get very far if you just do that. We have to bring all the tools that we have available, epidemiology, more human studies, better designed human study, better designed animal studies. But we don't -- we don't toss out animals just because there's examples sometimes of where they have not worked. We have to use all these and bring all the tools to understanding biological systems.

Because at the end of the day, you have this, lots of life. And there's enough underlying conservatism in life -- evolution doesn't reinvent the wheel -- there's enough underlying

conservatism that just as they said at NIH, you want to know oranges? You got to study oranges. We can learn a lot about fruit by just studying all sorts of fruit. And that's what you will study and find in this situation.

If my last slide will work. Oh, it doesn't. But I'll show you anyway.

So it's -- it's a mosaic of a picture of an egg.

At the end of the day you will -- you'll ultimately have to figure out how it all works in the baby. You can learn a lot about the baby by understanding what's going on in all these organisms. And so with that I finish. I agree with Dr. Greek on a lot of levels, but I disagree with him in terms of evolutionary biology and in terms of presenting himself.

I don't have -- I'm not bi- -- I have a biased view and I would just wish in his writings and in his newsletter that he would state upfront that he has a very biased view and therefore is picking and choosing information he wants you to hear. And for us to seriously debate means I'm going to have to go back and read hundreds and hundreds of papers all the way through to figure out exactly what was left out and what was left in.

Thank you.

(Applause.)

THE MODERATOR: Okay, question? Gina.
QUESTION: My question is for Dr. Greek. I know that in your lecture on line you mentioned the importance of using the three Rs in order to eliminate (inaudible). And I was wondering exactly how you proposed proceeding with reducing animal testing when there are so many people who believe that it is a good model for human testing (inaudible)

DR. GREEK: I -- I think the only way that you can use the three Rs is to make the distinguishing -- the distinction that I've made on that slide where I said Nos. 3 through 9 you can use the three Rs.

The only way that people are going to stop using the animal model is when they stop confusing CAMs with HAMs. And I'm not a big fan of the philosopher Derrida. I think science is somewhat objective. And science is also self-correcting.

And so evolutionary biology in contrast to this lecture, I think is pretty much proof positive that you cannot use animals as CAMs. If you read NIH grant requests, that's pretty proof positive that that's how they are used.

So I think the answer to your question lies in education. And I think it was Einstein that once said something to the effect of "Old paradigms don't change; the scientists who use them die off, and that allows the new paradigms to come in." And that's what I think's going to happen.

The slide that Dr. Hicks showed about my quote from van sup ton, the point of that quote from van Zutphen is that even a person who believes strongly in the animal model admitted that there were these flaws. And the last paragraph where he sung the praises of the animal model was not substantiated in that article. That was opinion. Pure opinion.

Now, the study that he quoted in the article was not opinion. It was peer-reviewed science. It was published, and so on and so forth.

So to answer your question, I'm afraid it's going to be time.

THE MODERATOR: Other questions.

QUESTION: For Dr. Hicks, do you believe that all experiments are beneficial in some way or another to humans?

DR. HICKS: No.

QUESTION: And then --

DR. HICKS: Actually (inaudible) asked the question all experiments specifically all (inaudible)?

QUESTION: Yeah, (inaudible) on animals were they beneficial in some way or another to humans? Like --

DR. HICKS: No. And I don't want to be contrite and say no. Let me qualify that. No, not every experiment that's ever done is beneficial, not only (inaudible) humans; it may not be beneficial in the greater sort of scientific question.

I think one of the problems, and it addresses this and it's what I think that Dr. Greek talks about CAMs, you have to ask, first of all the (inaudible) is not -- CAMs is not a common philosophical term used. It's -- was -- as far as I can -- and he can correct me if I'm wrong, but as far as I can tell it was invented by LaFolette and Shanks, and there's some papers they wrote in the 1990s.

But what happens in terms of CAMs is that what -- what he's attacking is the way scientists talk to the public. And this is a problem. And so when you ask me does every experiment result in a benefit to humans, you know, every time I'm interviewed by reporters -- and I've done -- some of the research that I have done in my lab has had interest by the popular press. Every time they'll ask me that question, well, what benefit is it for humans? That's the common question.

Well, do you ask that of a physicist who's studying black holes? Biologists are studying, trying to understand nature, how nature works, how life works. Some of the information will have benefit towards humans. A lot of the information won't have direct benefits to

humans but will increase our understanding of the natural world. That's what motivates a lot of people.

What motivates a lot of biomedical scientists is using animal models to generate novel and new ideas. However, what has happened -- and Dr. Greek is entirely correct -- is that to sell the idea, quote, unquote, sell it, I would -- I would agree that many biomedical scientists can be accused of overpromising and underdelivering. But the overpromising is what's required or the -- or is what they have to define why are you doing this research and how's it going to directly benefit humans?

What scientists have not done well in the twentieth century and what they don't I think do well now is explain what is the scientific process? Where do ideas come from? Do they just come out of the air? Are you sitting here one day and suddenly go, "Oh, that's a great idea. I will I'll use that. Yeah, that's -- that's how the cell cycle works. That's fantastic. Now I know where it's come from"?

No. They do experiments. And many experiments lead nowhere. But in defending they're doing the experiments they often will tell the public or tell the granting agency or tell the Congressman the end point, "I'm doing -- I'm studying cell cycling because it's going to cure cancer." Well, you know, cell cycling, how cells determine how they're going to divide, that is important to cancer biology. But will that specific project cure cancer? Well, probably not. But it will -- might lead to some new insights into the cell cycle, which then later on might lead into some additional insights into the cell cycle, which then might lead on -- and this can take a long time.

So I do think scientists are guilty of overpromising and underdelivering. And they shouldn't be excused from it. What I tell my students, what I tell my postdocs is that when you're asked that question do not fall in the easy trap, "Oh, I'm studying this because it's really important for heart biology." Tell me why you're studying it. What excites you about the question? What is -- why are you really doing it? And if they want to continue to write something about how it's going to help heart biology, that's the reporter's problem, not the scientist's problem.

So I agree with Dr. Greek in one sense, I think scientists have done this for too long and we have not done a good enough job of explaining to the public what we're really doing.

The quotes that he used, I know Bogey Anderson, quite well. He wouldn't come in -- he would say it's not -- "I'm not using this as a CAM. It's a heuristic device." And yet he said, you know, scientists will say that and then they wink, wink, don't -- then they explain this CAM. Well, no, it's just they have fallen into the trap themselves of always trying to give the end point and not talking about the pathway to -- to ultimate understanding. Because people don't want to hear about the pathway. It's too long. It takes 50 years to get there, not two years.

THE MODERATOR: Another question?

QUESTION: I'm going to try and word this as best I can. It's actually -- it's still a whole bunch jumbled in my brain.

Dr. Hicks, you stated that animal -- and I believe also that understanding, you know, the similarities between animals and humans and also the difference between animals is very important. I guess my question is we had a debate on animal experimentation the other day. There was a point made. Penicillin, how to (inaudible) was first on mice, little effect; second, rabbits, no effect; and the third subject was a person instead of a guinea pig, because there was an emergency situation. The person survived. So, you know, experiment (inaudible) the result. (Inaudible) people and the result historically it did. The fourth subject, a guinea pig, died. The fourth subject, the guinea pig was supposed to be the third subject. So it's saying if the third -- if the guinea pig were used before the human being penicillin would not have been used and, you know, history would be a disaster.

Now, I'm guessing a lot of experiments now, I mean, as you said, there's been so much history with research done on animals. Lots of the similarities between people and humans have been found. And right now where I believe that a lot of experiments that are supposed to be used on humans are being done on animals first. And to me those are results of just on animals. How would you defend -- I mean should it be legal to even test, you know, medical treatments on animals at such a high complex level and using them as viable results on humans?

DR. HICKS: I mean it's -- it's a loaded question. First of all, the whole thing about penicillin. I can't answer that, your initial opening statement about penicillin. Because I don't know the history of that. I don't know the detailed history of it.

DR. GREEK: Actually, let me just jump in.
Penicillin was tested on a rabbit in 1928 by Fleming -- 1929. It excreted penicillin so rapidly from its kidneys that Fleming put it back on the shelf. Then 11 years later you get into the sequence that you talked about.

So I don't know who said that, but the sequence was wrong. The concept that you've related was correct. But the timing with the species was slightly different.

DR. HICKS: Yeah, so in terms of trying out new tech- -- I mean I think it depends on the question, it depends on the technique, it depends on the therapy. All right, there can be some -- there can be some therapies, for example, you know, okay -- so let me gave you an example anyway from UCI that I'm only aware of. As I said, I don't do this, you know, go out and give lectures on this. So I don't have a rich array of studies that I've read all the history of and can connect all the points together.

But here at UCI there's a guy named Frank LaFerla. Frank LaFerla is in neurbiology and behavior. A few years ago it was said that, you know, transgenic models would never be any good for studying Alzheimer's in patients because you can't reproduce the phenotype. Alzheimer's has both this plaques, these deposits of these beta amyloid proteins and these

tangles, the way the -- the neurons will sort of come (inaudible) due to changes in the biochemistry. Couldn't recreate that in an animal model.

So studying animal models only had one phen- -- one of the phenotypes or the other. It was a complete waste of time. And transgenics didn't work very well.

Frank stumbled upon developing a transgenic, triple transgenic, animal which he has both amyloid plaques and tangles and the animals it showed declines in memory tests that are done, standard memory tests for mice, over time.

Frank also works with, is involved with human Alzheimer studies as well. But in his lab now he's got a model that has some of the similar phenotypes. So now he can start saying, okay, you know, what if we tried this particular cholinergic agamous? It's a -- cholinergic agamous is a neurotransmitter. What if I gave this to this mouse? What will it do?

He -- he found out, it was announced this week, that in fact what it does is A, their memory improves and there is a -- a disappearance of the plaques and tangles. Frank will be the first one to tell you this is -- doesn't mean it's going to work in humans, but it's a new idea now. It's a new avenue of approach that people hadn't thought of before with this particular drug. So let's start seeing if that will be worthwhile. At that level it might be worthwhile.

The other thing is that what Dr. Greek said, you know, that it -- it doesn't work in animals so it doesn't -- no. Forget it. We're not going to use it in humans. I think that that -- with all due respect, I think that's very naive. I think historically that may have happened. But I think people now, because of the explosion of molecular biology and -- and our appreciation of evolutionary biology, that just because it doesn't happen in one animal, nobody's going to shelve anything. Because they know that variation exists, they know that there could be a lot of genic and phenotypic variation; and therefore they're going to try to repeat and see if this is a pattern that's developing, not a single instance of it developing.

So I think it depends on the question. I do agree with Dr. Greek that -- that if someone directly thinks that there is a -- that they're using a CAM -- a real model, that they're studying a rat, that's really going to cure hypertension, I think that that's bad science. But I just don't -- the scientists that I interact with, the ones that I discuss things with, the ones that I talk with at meetings, they don't think that way.

THE MODERATOR: Would you like a chance to respond?
DR. GREEK: Yeah, thank you.
I think that what this discussion has led to -- and Dr. Hicks can correct me if I'm wrong -- but I think we have both agreed that many people who conduct research on animals lie to the American taxpayer. And I don't care what your motivation is. I don't care what your cause is. If you cannot stand in front of the American tax-paying public and say, "I'm

going to use your money for the following reasons," you're being very disingenuous at best. All right.

Now, Dr. Hicks attacked some of the quotations that I used. I would strongly recommend that you do exactly what Dr. Hicks said. Go read the original source and see if I preserved the content, the concept that I am saying that I preserved. Did I quote the entire article? Of course not. Were there parts of the article have Van Zutphen said, for example, the animal model is a great thing? You bet. How do you think van Zutphen earns his living?

Okay? When somebody with a vested interest stands up and says, "Gosh, my vested interest is saving lives," please, are we so naive that we're just going to take that at face value?

But when somebody like Van Zutphen stands up and says, "You know, this transgenic thing just isn't working out," ah, now, that's going to get my attention. And yes, you can find thousands of people whose livelihoods depend on animal based research who have said in peer review journals that it's a great thing. Is that a shock? I don't think.

And with regards to the caloric study, this is a very good way for those of you who are not science majors to decide who's telling the truth in this debate. When you go back to your living quarters, Google caloric restriction in humans and read the first ten things that pop up. Now, if those first ten things say that, by gosh, it does work. It just doesn't work as much as it works in animals, then believe Dr. Hicks.

But the reason that I chose that particular study to summarize was because there were ten others just like it.

DR. HICKS: But the point is, Dr. Greek, you did not mention ten other studies.
DR. GREEK: I did not interrupt you. If I could please (inaudible).

So yes, you do need to research these things for yourself. But let's face it, a vast majority of you are not going to do that. Okay. I wish you would. I'm the one who provides the references to the slides and so on and so on. I encourage you to do that.

But at the end of the day use your common sense, okay. If drugs that are tested on men act differently on women, then you are not going to get any bright ideas out of giving those drugs to rats. It just doesn't work. The premise of the whole thing is flawed.

Dr. Hicks was right, Claude Bernard was a creationist. That could summarize my argument.

Go ahead.

DR. HICKS: Well, what I was going to say, but what you don't do, when you say -- is that you don't give them the ten other articles. What you do is you have -- I truly believe

that you strongly believe -- and I am not going to call into question why you believe this - - I strongly believe --

DR. GREEK: Oh, that's not true. You have called that into question.

DR. HICKS: No. No, I strongly believe that you do not think that animals should be used in research. But what you do is that you do not provide all the information. So that quote of the Michael Rose study you -- you left out the significant quotes that would have indicated that it does, from their study, works in humans. If you had said that this is consistent -- here's a quote and this is consistent with ten other articles that show that it doesn't work in humans, that would be honest. But what you do is you have an objective. The objective is to bias the information so that you can make a convincing argument. And the Rose quote is a perfect example of that, because Rose --

How I said to the students you want to find out which of the quotes is closer to the truth, go ask Michael Rose. He's right here on campus. Because that's who you'll find out what is the intention of the author, the person that wrote the paper. And Michael Rose is not a biomedical physiologist or (inaudible). He's an evolutionary biologist.

THE MODERATOR: Okay, since we have to actually let them go in a just a minute, Dr. Greek, would you like a final chance to say something more?

DR. GREEK: Well, again, I'd like to thank Dr. Hicks. In all honesty, this is the best debate that I have ever participated in. Most of the time the ad hominem attacks are much greater and the science is much less. So I think that you have gotten a very good representative debate today on the subject of animal models, you know, from a scientific perspective in research.

And if you'll go to our Web site, which is CureDisease.com, you will find links to the opposite opinion as well as a lot of information about why we think what we think. And I would just encourage you to read more.

Thank you.

THE MODERATOR: Thank you very much.

 (Applause.)

(End of debate.)