months. It is too early to judge the reversion. Nonetheless, indications to date are hopeful. Civil liberties continue largely unaffected. The economy continues to thrive. U.S. ship visits continue with little change and are indeed, welcomed with open arms. However, we continue to be concerned about the potential over time for the constriction of democracy, media self-censorship and the loss of hard-won rights. Chinese and Hong Kong authorities are acutely aware that the eyes of the world continue to scrutinize their post-reversion actions. That continued scrutiny is well warranted and will help ensure that all concerned continue to value and maintain Hong Kong's autonomy.

CONGRESSIONAL BIOMEDICAL RESEARCH CAUCUS

HON. GEORGE W. GEKAS

OF PENNSYLVANIA

IN THE HOUSE OF REPRESENTATIVES

Wednesday, November 12, 1997

Mr. GEKAS. Mr. Speaker, on September 10, the Congressional Biomedical Research Caucus conducted its 57th briefing on the subject of the ''University of Genes: The Bits of DNA That Make Us What We Are.'' Dr. H. Robert Horvitz, Howard Hughes Medical Institute investigator and professor of biology at MIT, and Dr. Philip Heiter, professor of medical genetics of the University of British Columbia, Vancouver, spoke about the similarity of genes across species and how this discovery assists in biomedical research.

I was particularly pleased to have Dr. Horvitz participate because as a member of the Joint Steering Committee—a coalition of five basic biomedical research societies: the American Society for Cell Biology, the American Society for Biochemistry and Molecular Biology, the Biophysical Society, the Genetic Society of America, and the Association of Anatomists—he has played a significant role in supporting the caucus briefings.

Congressman JOSEPH KENNEDY of Massachusetts introduced Dr. Horvitz and was joined in attendance by myself, Congressman STEVE HORN, Congressman JOEL HEFLEY, and Congressman TOM PETRI, as well as a room full of senior health staff.

I believe our colleagues will find Dr. Horvitz's remarks useful.

ALL CREATURES GREAT AND SMALL: THE UNIVERSALITY OF GENES

I. INTRODUCTION

First, I would like to thank the organizers of this Caucus for inviting Phil Heiter and me to talk with you today. The title of this Caucus is ''All Creatures Great and Small: The Universality of Genes.'' What we are going to discuss today is one of the most striking discoveries in the history of biomedical research: genes—the bits of DNA that make us what we are—genes are so remarkably similar among different organisms that we can study what they do in a microscopic worm or in a yeast that is used to make beer to learn how they work in us.

II. GENES

Let me start with a few introductory remarks about genes. Genes define hereditary traits. Each gene can exist in different forms, and such variations in the forms of genes result in variations in traits. Some such variations we consider simply to be what make us different from one another: for example, eye color and blood type are defined by genes. Similarly, our sexual characteristics, whether we are boys or girls, as David Page put it in an earlier Caucus, are determined by our genes. Variations in other genes result in variations in other traits: for example, dwarfism, deafness and color blindness can be caused by variations in genes. Variations in still other genes results in variations in our traits that we label ''disease'': Huntington's Disease is caused by one such gene; variations in other genes cause or predispose one to cancer, cardiovascular disorders, asthma, cystic fibrosis, premature aging, Alzheimer's Disease, bone loss, and many, many other diseases.

So, genes are important to us, and crucial to our health. How can we learn about our genes, what they do, and how they sometimes go wrong? One approach is to study our genes—human genes—directly. Biologists do this. (I do this.) But the study of human genes is in many ways very slow and inefficient. Furthermore, some types of genetic studies are simply impossible to do with people. For example, the classic method of genetics is to cross individuals with different gene variants (called mutation); this we cannot do with people.

III. UNIVERSALITY

Fortunately, biology has provided us with an approach that is feasible: genes are strikingly conserved among organisms, so we can study genes in experimental organisms and in this way learn what genes do in us. Let me show you an example from my own research. I study two organisms, human beings and the nematode roundworm known as *C. elegans*. My focus in humans is on Lou Gehrig's Disease, or ALS, the devastating disease that killed Lou Gehrig, Jacob Javlts, David Niven, and many others. Four years ago, with a team of collaborators, we found a gene responsible for ALS, a gene known as SOD1. SOD1 in humans is strikingly similar to SOD1 in my worm, as can be seen by the large number of boxed identities in the sequence of the protein products of these genes. Such similarity is seen in SOD1 in many organisms: the gene in spinach is essentially the same as well. To understand what SOD1 does, and how it goes wrong in ALS, one can study the gene in whatever organism is best suited for a particular line of inquiry, and SOD1 is now being studied in worms, in brewer's yeast, in fruit flies and in mice in attempts to understand how it causes ALS in humans. Let me generalize from this example and show you more broadly the degree to which genes are conserved among organisms.

The next slide is from an article written by Phil Hieter, our next speaker. This table shows a list of 84 human genetic diseases, from A to Z (really from A to W: achondroplasia or dwarfism is No. 2 on the list, while Wornor syndrome, which results in premature aging, is 4 from the bottom). The columns show matches (in color) with genes found in those organisms commonly used for laboratory studies of genetics: the mouse, the fruit fly, the nematode roundworm, brewer's yeast, and the intestinal bacterium *E. coli*. What you can see is that almost all of these human genes have a counterparts in the mouse, that many do in the fruit fly and worm, and that quite a few do in the yeast and bacterium. This table underestimates the degree of similarity with mice, fruit flies and roundworms, since many genes remain to be characterized in these organisms and some will no doubt provide additional matches. It is now clear that almost every human gene has a mouse counterpart, that the majority have fly and worm counterparts and that many have yeast counterparts. These kinds of observations, coupled with findings that genes that look similar act similarly, have led to the use of experimental organisms as models for human biology and human disease.

IV. ORGANISMS

If all organisms have similar genes, how do scientists decide which organisms to study? The short answer is that different organisms have different experimental advantages and that by studying a variety of organisms biologists obtain different types of data that together help us understand what genes do. To provide some concrete examples of how studies of these simple organisms are helping us to understand as well to prevent and cure human disease, Phil Hieter and I will now talk about work involving ''our'' organisms, the brewer's yeast and the roundworm. The next slide summarizes my perspective on using roundworms to study human disease, given what we know about human genes and worm genes: ''Worms are little people in disguise.'' So let me start with the neurodegenerative disorders, such as Alzheimer's Disease, and on cancer.

V. ALZHEIMER'S DISEASE AND THE PRESENILINS

First, let's talk about Alzheimer's Disease. Some, but not all, cases of Alzheimer's Disease are clearly genetic, i.e. pass from parent to child. Most genetic or ''familial'' AD is caused by changes in a single gene, known as PS–1, for ''Presenilin gene number one.'' In 1995 this gene was isolated biochemically. What does it do? How can we find out? Simply having access to a gene is not enough to tell us what it does unless it is sufficiently similar to a gene we already know about.

PS–1 is similar to four other known genes. One, called PS–2, is a second Alzheimer's gene isolated in 1995. The other three are all in the roundworm *C. elegans*. How similar are these worm genes to the human genes? In one experiment, researchers at Columbia University in NYC showed that the human PS–1 gene could work in the worm, substituting for one of the worm genes it looked like. This finding says that the human AD gene and the worm gene are functionally interchangeable. They are very similar. Thus, figuring out what the worm gene does should give us a very strong clue about what the human gene does. Studying this worm gene is now a important effort in both academia and the biotech industry.

VI. CANCER AND THE RAS PATHWAY

Let me turn now to cancer. Cancer, like familial AD, is caused by variants in genes. The first human cancer gene was identified in 1981. This gene was called Ras. Biomedical researchers actively analyzed Ras and desperately wanted to know what it does and, in particular, wanted to know the pathway through which Ras acts. This concept of pathway is key for the development of pharmaceuticals: if you can block the action of a disease gene, either directly or indirectly, i.e. either by acting directly on that gene or by acting later in the gene pathway through which that gene acts, you should be able to prevent the disease.

What is the Ras genetic pathway? The answer emerged not from studies of human Ras but from very basic and apparently unrelated studies of animal development, in particular studies of the development of a sexual organ of the roundworm and of the eye of the fruit fly. It turned out that a gene that controlled worm sexual development as well as a gene that controlled fly eye development were both strikingly similar to human Ras. The levels of identity were approximately 80 percent. Furthermore, at the time it was discovered that a Ras-like gene was involved there had been very extensive studies of these processes; as a consequence within a few years detailed gene pathways were

completed. Together these studies, which were done in my laboratory at MIT, at CalTech, and at Berkeley, revealed the pathway of action of Ras. Now cancer biologists and drug companies alike are using this knowledge of the Ras pathway both for further studies of how Ras causes cancer in people and for the development of drugs, drugs that can block the various steps in the Ras pathway.

VII. PROGRAMMED CELL DEATH, NEURODEGENERATIVE DISEASE AND CANCER

The third example I'll offer from worms relates both the cancer and to neurodegenerative diseases, which include AD. This example again is one in which studies of a basic biological phenomenon in the roundworm have had a major impact on our understanding of and approach to human disease. The biology in this case involves a phenomenon called ''programmed cell death.'' For many years, biologists assumed that cells died because they were unhappy, i.e. because somehow they had been injured. However, a variety of studies revealed that many cells die during the normal course of development. For example, as our brains form, as many as 85 percent of the nerve cells made at certain times and certain parts of our brains die. Such death is a natural phenomenon and for this reason is often referred to as ''Programmed Cell Death.''

Given that cell death is a natural aspect of development, some years ago my colleagues and I reasoned that like other aspects of development, PCD should be controlled by genes. We sought such defined a 15-gene genetic pathway that controls programmed cell death In the worm. It now appears that a least some of these gene correspond to human genes that caused disease. For example, we talked earlier about neurodegenerative diseases, such as AD, Huntington's Disease, Lou Gehrlg's Disease and Parkinson's Disease. Many researchers believe that these diseases, which are characterized by the death of nerve cells, are diseases in which the normal process of PCD has gone amok. Specifically, the normal pathway that causes cells to die by PCD during development for some reason may be unleashed in nerve cells that are not meant to die.

How might we stop such deaths? By blocking the killer genes responsible! And what are the killer genes? We have ID'd two such genes in the worm, genes we call CED–3 and CED–4, for ''cell-death abnormal.'' Given these worm genes, others have gone on to find similar genes in humans that also act to cause cell death. These genes have now become major drug targets: many companies in the pharmaceutical industry are attempting to block the action of these killer genes, with the goal of preventing such neurodengenerative diseases.

It turns out the genetic pathway for PCD we have defined is relevant not only to neurodegenerative disease but also to cancer.

Let me explain. What is cancer? In brief, cancer reflects an uncontrolled increase in cell number. How can you get such an increase? One way is to make too many cells. This is precisely what happens when the Ras gene, which we just discussed, is mutated. However, it turns out there is another way to make too many cells. The number of cells in our bodies is really an equilibrium number. Cells are always being added to our bodies, by the process of cell division, but cells are also always being taken away, by the process of programmed cell death. So, we can generate too many cells—as in cancer—not only by too much cell division but also by too little cell loss.

How can we bet too little cell loss? One of the genes we identified as controlling cell death in the worm is not a killer gene but rather a protector gene—it protects cells from dying by PCD. If a gene like this is too active, too many cells would survive, and cancer would result. In fact, there is a human cancer gene that is very similar to this worm protector gene, so similar that the human gene can work in worms to protect against worm cell death and to substitute for the worm gene. Given such protector genes, how might one prevent? Again, this is precisely the approach that is now being taken in the pharmaceutical industry, and there is great nope that by learning to control such protector genes it will be possible to control certain cancers.

VIII. CONCLUSIONS

Let me conclude very briefly by summarizing what I've said. First, a gene is a gene is a gene. Genes in humans are fundamentally no different from genes in other organisms and are so similar in many ceases that a human gene can be put into another organism and work just fine. Second, genes are much easier to analyze in experimental organisms than in people. In few years, the Human Genome Project, sponsored by the NIH, will tell us what all of our genes look like. But what do they do? To find out, we must study experimentally tractable organisms. Third, time and time again truly basic studies of genes in experimental organisms have proved directly relevant to human diseases and disease genes, once we knew what those human genes looked like. An investment in such basic studies is an effective investment indeed, as it means that knowledge will proceed at an enormous pace once a human disease gene is identified. Finally, knowledge of what the counterparts of human disease genes do in an experimental organism can be directly used both in the understanding of what that gene does in people and also in the application of that knowledge to the development of a treatment of cure. I thank you for your time.

EXTENDING CERTAIN PROGRAMS UNDER THE ENERGY POLICY AND CONSERVATION ACT

SPEECH OF

HON. HENRY J. HYDE

OF ILLINOIS

IN THE HOUSE OF REPRESENTATIVES

Sunday, November 9, 1997

Mr. HYDE. Mr. Speaker, I ask that this exchange of letters between me and Chairman BLILEY be placed in the RECORD following debate on H.R. 2472.

HOUSE OF REPRESENTATIVES,
COMMITTEE ON COMMERCE,
Washington, DC, November 8, 1997.

Hon. HENRY J. HYDE,
Chairman, Committee on the Judiciary, U.S. House of Representatives, Washington, DC.

DEAR HENRY: Thank you for your letter regarding H.R. 2472, a bill to extend provisions of the Energy Policy and Conservation Act (EPCA) through September 1, 1998.

EPCA is one of the legislative cornerstones of our national energy security policy. Among other things, it authorizes the operation and maintenance of the Strategic Petroleum Reserve and provides limited immunity to American oil companies to participate in activities pursuant to the International Energy Agreement. In light of current actions in the Middle East and the important activities authorized by this Act, prompt passage of this EPCA extension is necessary.

I appreciate your interest in H.R. 2472 and I acknowledge that I will bring it to the House Floor in the form of a simple extension through September 1, 1998 without any substantive change to the antitrust provisions. I also acknowledge that your action in allowing this legislation to go forward does not affect any future rights of the Committee on the Judiciary. Consistent with the Judiciary Committee's jurisdiction over antitrust issues under Rule X and with the Commerce Committee's jurisdiction over energy issues under Rule X, I would be pleased to work with you to develop legislation which ensures an effective national energy security policy.

In keeping with your request, I will place your letter and this response in the record of the debate on H.R. 2472.

Sincerely,

TOM BLILEY,
Chairman.

HOUSE OF REPRESENTATIVES,
COMMITTEE ON THE JUDICIARY,
Washington, DC, November 8, 1997.

Hon. TOM BLILEY,
Chairman, Committee on Commerce, U.S. House of Representatives, Washington, DC.

DEAR TOM: I understand that today or tomorrow you intend to move to suspend the rules and concur in the Senate amendment to H.R. 2472 with an amendment.

The version of H.R. 2472 you plan to bring up would extend through September 1, 1998 certain provisions of the Energy Policy and conservation Act, 42 U.S.C. §6201 *et seq.* Under Rule X, the Committee on the Judiciary has jurisdiction over provisions of the Act: the antitrust defense provided in Section 252, 42 U.S.C. §6272, the participation of the antitrust enforcement agencies in activities under that section, and any amendment, extension, or expansion of these provisions or any other antitrust immunity provided in the Act.

Because of the urgency of passing this important national security legislation, I am willing to waive this Committee's right to a sequential referral of H.R. 2472. I will allow this legislation to go forward so long as it remains a simple extension through September 1, 1998 without any substantive change to the existing antitrust defense or the participation of the antitrust agencies. However, my doing so does not constitute any waiver of the Committee's jurisdiction over these provisions and does not prejudice its rights in any future legislation relating to these provisions or any other antitrust immunity provided in the Act. I will, of course, insist that Members of this Committee be named as conferees on these provisions or any other antitrust immunity provided in the Act should the bill go to conference.

If the foregoing meets with your understanding of the matter, I would appreciate your placing this letter and your response in the record during the debate on H.R. 2472. Thank you for your cooperation in this matter.

Sincerely,

HENRY J. HYDE,
Chairman.

INSTITUTE FOR COMMUNITY LIVING

HON. NYDIA M. VELÁZQUEZ

OF NEW YORK

IN THE HOUSE OF REPRESENTATIVES

Wednesday, November 12, 1997

Mr. VELÁZQUEZ. Mr. Speaker, I rise today to pay tribute to the marvelous work of the Institute for Community Living, on the occasion