The Philosophical Society of Texas

PROCEEDINGS

1996

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PROCEEDINGS

of the Annual Meeting
at Dallas
December 6–8, 1996

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THE PHILOSOPHICAL SOCIETY OF TEXAS
1999

THE PHILOSOPHICAL SOCIETY OF TEXAS FOR THE COLLECTION AND DIFFUSION OF KNOWLEDGE *was founded December 5, 1837, in the Capitol of the Republic of Texas at Houston by* MIRABEAU B. LAMAR, ASHBEL SMITH, THOMAS J. RUSK, WILLIAM H. WHARTON, JOSEPH ROWE, ANGUS MCNEILL, AUGUSTUS C. ALLEN, GEORGE W. BONNELL, JOSEPH BAKER, PATRICK C. JACK, W. FAIRFAX GRAY, JOHN A. WHARTON, DAVID S. KAUFMAN, JAMES COLLINSWORTH, ANSON JONES, LITTLETON FOWLER, A. C. HORTON, I. W. BURTON, EDWARD T. BRANCH, HENRY SMITH, HUGH MCLEOD, THOMAS JEFFERSON CHAMBERS, SAM HOUSTON, R. A. IRION, DAVID G. BURNET, and JOHN BIRDSALL.

The Society was incorporated as a non-profit, educational institution on January 18, 1936, by George Waverly Briggs, James Quayle Dealey, Herbert Pickens Gambrell, Samuel Wood Geiser, Lucius Mirabeau Lamar III, Umphrey Lee, Charles Shirley Potts, William Alexander Rhea, Ira Kendrick Stephens, and William Embrey Wrather. On December 5, 1936, formal reorganization was completed.

The office of the Society is located at 2.306 Sid Richardson Hall, University of Texas, Austin, 78712.

Edited by Kim Wilson, Evelyn Stehling, and Ron Tyler

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THE PHILOSOPHICAL SOCIETY OF TEXAS

Two hundred ninety-four members, spouses, and guests gathered at the Fairmount Hotel in Dallas, December 6–8, 1996, for the Society's 159th anniversary meeting. President Charles Sprague had organized a most informative meeting on "What Price Designer Genes?: The Genetic Revolution." The Friday evening reception and dinner was held at the Dallas Museum of Art, where members had the opportunity to view the exhibitions beforehand. President Sprague introduced the new members of the Society and presented them with their certificates of membership. The new members are: Michael S. Brown, William Broyles Jr., George Walker Bush, Henry E. Catto, Joseph L. Goldstein, Clifford J. Grum, George Stuart Heyer Jr., James Arthur Lovell Jr., Mary Lou Robinson, and Donald W. Seldin.

Professor Hans Mark served as moderator for the program on Saturday. We paused for lunch at the Fairmount. That evening we enjoyed a reception and dinner in the Venetian Room at the Fairmount. Frank Todd played throughout dinner.

At the annual business meeting, Vice President Jack Blanton read the names of the six members of the Society who had died during the previous year: Roger N. Conger, Margaret Cousins, Everett Holland Jones, Daniel L. Kilgore, F. Lee Lawrence, and Ralph W. Yarborough. Secretary Tyler announced that our membership stood at 197 active members, 70 associate members, and 33 emeritus members.

The following officers were elected for the coming year: Jack Blanton, president; William P. Wright, first vice president; Patricia Hayes, second vice president; J. Chrys Dougherty III, treasurer; and Ron Tyler, secretary.

President Sprague announced that Michael B. Bevins at The University of Texas at Austin and Angela Peters at Dallas Baptist University, present at the meeting, won the President's Award essay contest. Their essays are included in this issue of the *Proceedings*.

Kern Wildenthal of the University of Texas Southwestern Medical Center hosted the Sunday morning session at the school, where members were given a tour of the facilities. Following the visit, President Sprague declared the annual meeting adjourned, to be reconvened on December 5, 1997, in Houston.

Welcome and Introductory Remarks

Charles C. Sprague*

It's a great pleasure on behalf of the local committee to welcome you to Dallas for this meeting. We hope that you will find it both interesting and thought provoking. Before proceeding, though, I'd like to thank the local arrangements committee. Their names are listed in your program there. The committee was chaired by Margaret McDermott and Bill Seybold.

I'd also like, at this time, to recognize Evelyn Stehling who is seated in the back, as well as her assistant, Melinda Reese. These two ladies are really responsible for all the arrangements, and I'd ask you to join me in expressing our appreciation to them.

We had hoped that Dr. Francis Collins, who is the director of the Human Genome Project, could be with us at this meeting, but, unfortunately, he had a conflict and couldn't join us. I had the good fortune of attending a meeting in San Francisco a couple of weeks ago where Dr. Collins spoke. In his presentation he listed a number of questions that he felt needed to be addressed within the context of the Human Genome Project.

I asked him if I might present some of those same questions to the audience today because I think it would set the stage for this meeting. He graciously agreed and I would suggest that you make a mental note, or even jot down on paper, these questions. I think you'll find that each of them will be touched on in one way or another by our speakers today. The ultimate answers, however, will not be forthcoming until years in the future.

If I could have the first slide, please. I'm not going to elaborate on Dr. Collins's questions for I think they'll be self-explanatory. Will the therapeutic promise of genetics be realized? Will we successfully shepherd new genetic information from research into clinical practice? Can health care providers and the public become genetically literate in time? Will the benefits of advances in genetics be available only to a privileged few? Will we arrive at consensus about the limits of genetic technology for trait enhancement? Will effective legislative solutions to genetic discrimination be found? And finally, will we succumb to genetic determinism?

I don't know how many of you may have read an article in last week's *U.S. News and World Report* where it was stated that they now have a

genetic explanation for everything, including our behavior. And further, will we use that as an excuse to say that we have no control over our future for our genes have determined what we're going to be and how we're going to behave.

So these are the questions that Dr. Collins has posed and, as I stated earlier, each will be touched on in one way or another in today's presentations.

I'd like to close my introductory comments with a quote from Sir William Osler because I think it's appropriate for our program today:

> To wrest from nature the secrets which have perplexed philosophers in all ages, to track to their sources the causes of diseases, to correlate the vast stores of knowledge that they may be quickly available for the prevention and cure of disease; these are our ambitions.

Well, if Osler were alive today, I think even he would be surprised at the degree to which we have achieved the ambition he enunciated years ago.

As you know, we select a moderator for the program each year—someone who is not an expert in the field, but who has an understanding and appreciation for the theme, whatever it happens to be. This year we have selected Hans Mark. I think all of you know Hans as well as his background.

Hans is a bit of a Renaissance person. He is not a genetics expert, but by virtue of his own personal experience with NASA in space exploration, he has an appreciation of the importance and relevance of projects of this kind. We're delighted to have Hans serve as our moderator today and, at this point, I would like to turn the program over to him. Please welcome Hans Mark, one of our own.

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*Charles C. Sprague is president emeritus of the University of Texas Health Science Center at Dallas and is president of the Philosophical Society of Texas.

What Price Designer Genes?

The Genetic Revolution

Hans Mark, Ph.D.*

I. Introduction

A few months ago, our distinguished friend and colleague, Charlie Sprague, called me and asked me whether I would serve as the moderator of this meeting of our society. When he told me what the topic would be, I remonstrated and asked him why he thought that a former bureaucrat and ex-engineer could do this job. I told him that I knew next to nothing about genetics or biochemistry or the law or, worse yet, ethics—and all that this loaded word implies. When he told me who else was on the program, I was even more agitated. What on earth could I do to deal with a couple of Nobel laureates? Apparently, Charlie had hit the bottom of the barrel in this search for a moderator so he finally put the arm on me. He reminded me that he was a member of the search committee that brought me to Texas in the first place back in 1984 and that therefore, I owed him one! He had me there, so here I am. And, I am both very honored and pleased to have the opportunity to moderate this session of the Philosophical Society of Texas.

Now, it turns out that my connection with genetics is, in fact, genetic. What I mean here is that it has to do with my father, the late Professor Herman Mark. Many of you here today met him during the years that he lived with us at the Bauer House in Austin so you know who I am talking about. Anyway, let me explain.

II. Family Genetics

In 1925 while working at the Institute for Textile Studies at the University of Berlin, my father and his colleague, J. R. Katz, were the first to use x-ray diffraction to establish the techniques to determine the structures of large molecules of biological origin. People at the Institute were interested in establishing the physical properties of fibers used by the German textile industry. Mark and Katz pioneered the use of the then new *physical technique of x-ray diffraction* to initiate the determination of the molecular structure of cellulose (Ref.1). They chose cellulose because that compound is the major constituent of cotton, which is the

most widely used and versatile textile fiber. Later, when the structure was finally determined by Mark and Meyer, it was found that with this knowledge predictions could be made about the behavior of the fibers and the textiles made from them. It was a useful technique that substantially improved the textiles manufactured in Germany and it led to much wider applications of x-ray diffraction (Ref.2). Hopefully, this begins to establish my genetic credibility but I still have to explain the bit about Nobel laureates.

During his academic career, my father supervised two Ph.D. students who later were awarded Nobel prizes. One was Eugene Wigner, whose Ph.D. work had to do with the use of x-ray diffraction to establish the crystal structure of rhombic sulfur (Ref.3). He received his Nobel Prize for the application of group theory to the solution of problems in quantum mechanics, a theory he learned while analyzing the x-ray diffraction patterns produced by the Sulfur crystals he examined to earn his Ph.D. The other student was Max Perutz, and he is the one who is important for our discussion today because he was the one who developed the techniques that were later used by James Watson, Francis Crick, Maurice Wilkins, and Rosalind Franklin to determine the structure of deoxyribonucleic acid (DNA). In that sense, Max might be called the grandfather of the genetic revolution! In any event, I knew both of these gentlemen quite well because of my father, so I have at least some experience in talking to Nobel laureates.

Max Perutz finished his Ph.D. thesis in 1937 doing research on a problem in classic organic chemistry at the University of Vienna. Unfortunately, the thesis was never published because both Perutz and my father left Vienna shortly after the work was completed. My father saw the danger posed by the Nazis at that time since he was himself planning to leave Austria. Thus, he urged his young protégé to leave Austria as well, preferably sooner rather than later. There was a vacancy in the laboratory of Sir William Lawrence Bragg at Cambridge University. At the time, Bragg was the world's leading expert on x-ray diffraction. Perutz was worried that he knew nothing about x-rays whereupon my father said: "You will learn," and learn he did! After a painstaking series of experiments using much trial and error, Perutz succeeded in determining the molecular structure of myoglobin and later of hemoglobin, a feat for which he was awarded the Nobel Prize in 1962 (Ref. 4). Hemoglobin was a much more difficult proposition than cellulose. It is a very complex three dimensional structure and Perutz had to go far beyond what was done with cellulose, which is a relatively simple structure that has cylindrical symmetry. Perutz completed this work a few years before the structure of DNA was established using the same techniques in 1954 (Ref. 5).

III. Computers and Their Limits

The realization that DNA was the template that determines the properties of all living things using a three-digit code was the intellectual

breakthrough that brings us here today. You will hear both about the promise and the problems raised by the new insights that have been gained. The prospects are truly as mind boggling as they are varied. Instead of making lists, let me talk about what interested me most about the genetic revolution. Not surprisingly, it is related to engineering.

In 1979, when I was serving as Secretary of the Air Force, we began to wonder how much computer capacity we could put on the Airborne Warning and Control System (AWACS) aircraft. I called my old friend Walt Morrow, who was director of the MIT Lincoln Lab at the time, and asked him what he thought about the question. He replied that it has to do with the size of switching elements. Transistors that control the flow of electrons cannot be smaller than a certain size. They depend for their operation on the establishment of energy levels called Brillouin zones and, if the transistor becomes too small, then these zones can no longer exist. By doing some elementary quantum mechanics, Walt estimated that the smallest transistors must have at least 10^{12} atoms to work—that is one thousand billion. We are today about a factor of 50 away from this limit, the smallest current switches today contain about 5×10^{13} atoms. From a practical viewpoint, there is still lots of room for improvement. Every factor of two is worth lots of money so don't sell your computer company stocks! However, from a scientific viewpoint, Walt could foresee even twenty years ago that at some point, we would come up against a fundamental limit.

IV. Biological Switches

The final question that I asked Walt was what he thought could be done to overcome that limit and he then told me a most interesting story. He said that there were people in the biological departments at MIT who were beginning to learn how the switching elements in our nervous system worked. He told me that these switches were molecules containing about ten thousand atoms that are impregnated on the membranes enclosing nerve cells and that these molecules control the flow of ions (and hence electric currents) in our nervous system. If we could learn how to use and control these biological switches, Walt told me, we could build computers that are smaller by many orders of magnitude than the ones we have today. To be more precise, biological switches are eight orders of magnitude smaller than electronic switches. They are much slower since they operate on currents of relatively slowly moving ions rather than on rapidly moving electrons. However, we have since learned that it is relatively easy to overcome this problem by introducing what we call parallel computer architecture (Ref. 6). We have made much progress in learning about biological switches and what my computer friends call neural networks since I had my conversation with Walt Morrow almost twenty years ago. Walt will very probably turn out to be right that we will overcome the quantum mechanical limit imposed by size on transistors by the use of biological switches.

V. *A Speculation*

It is this last point that leads me to the speculation with which I want to wind up this introduction. The human mind is by far the most complex and sophisticated computer we know about. It has about 10^{11} (one hundred billion) synapses and each of these may contain hundreds of thousands of switching molecules, so astronomical numbers of switches exist in the brain—approaching say 10^{16}. Compare this to our best current computers which have about a hundred million (10^9) switches. The point of all this is that the way in which the switches in the human mind are wired up is contained in the genetic code. The architecture of the computer that is the human mind is hidden somewhere in the three plus billion units of the DNA molecule. By knowing the complete sequence of human DNA, will it become possible to build computers that approach the capability of the human mind? Can we understand how the architecture of the brain is encoded in the DNA molecule? If so, can we replicate the principles and use them to build artificial brains? Can we put a bunch of nerve cells in a Petri dish and then, by somehow introducing the information contained in the DNA, wire them up in such a way that they become a computer more capable than anything we now possess? My own judgement is that all of these things will eventually become possible. I believe that this is the prospect before us and the things we will discuss today only represent the first step in the Genetic Revolution.

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*Hans Mark is the John J. McKetta Centennial Chair in Engineering and Professor in the Department of Aerospace Engineering and Engineering Mechanics at the University of Texas at Austin. He is former Chancellor of the University of Texas System and was Deputy Administrator of the National Aeronautics and Space Administration, Secretary of the U.S. Air Force, and Director of the NASA-Ames Research Center. Dr. Mark is the author or co-author of more than 150 scholarly articles and numerous books.

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The Human Genome Project

An Overview

Michael S. Brown, M.D.*

Three days from now in Stockholm, Sweden, two more Texans will receive the Nobel Prize: Smalley and Curl of Rice University. And this will make the sixth Nobel Prize earned by a Texan in the last eleven years. That is really a remarkable achievement for any state. It may be the most for any state in the last eleven years, and it's a tribute to what Texas has become.

All of these people came to Texas before they received their Nobel Prizes. We used to import them afterwards. Now, we're actually growing our own. And that is a tremendous achievement. Of course, the first four of those six were earned here at UT Southwestern, by Joe Goldstein and me, and by Al Gilman and Hans Diesenhofer, and I'm pleased to report that all of us are still on the faculty and still working away actively at science. So our school is a very exciting place to do science.

The subject for today is revolution. You've heard something about it already. It's a revolution in genetics that will change the world in the twenty-first century, just as physics changed it in the twentieth. The physics revolution revealed the nature of space and time and the atom, and gave us atomic energy, computers, space exploration, but it also gave us the atom bomb. The lesson is clear. Scientific revolutions give us power, and power demands responsibility. We must use scientific power for good and not for evil. Physics gave us the power over the external world. Genetics gives us power over our own bodies.

Up to now we've had to make lifestyle recommendations that are one-size-fits-all. Genetic predictions will allow us to adopt a customized lifestyle that takes maximum advantage of each individual's potential. It will help us decide what to eat, how much to exercise, what medicines to take, what career to choose, who to mate with, and what type of children to have. Achievement will be maximized. Death and disability will be postponed.

But at what price? Will the genetics revolution produce a new rationalization for prejudice, discrimination, and loss of freedom? These evils will be avoided only if the population is educated about the powers and the limits of genetics. And that's the topic of today's program.

The genetics revolution began at the mid-point of this century with two fundamental discoveries. The first you've heard about from Hans Mark. The discovery was that genes are simply chemicals. They can be isolated and studied in a test tube. They're somewhat complicated chemicals, but they're nothing more than chemicals.

The second discovery was the deciphering of the genetic code, the working out of how these chemicals actually determine physical and chemical processes in our body. Once the code was deciphered we learned how to read genes, just like we read a recipe book. Only the genetic recipe book is the mother of all recipe books. The genetics book contains complete instructions to make a human being, including the marvelous brain that Hans Mark was referring to. And we've just begun to read this book. We're like children who sneaked into the attic and found their parents' love letters. We're learning how we came to be.

Each of us began life as a single cell, a fertilized egg. Women produce only a few thousand eggs in their lifetime, and men produce trillions of sperm. Each egg and sperm is unique, because each one contains a different assortment of genes from the parent. And the moment that a particular sperm fertilizes a particular egg a unique individual is created.

Immediately, the genes issue orders. First, the egg is instructed to divide to produce two cells, and then four, and then so on. Within nine months the single cell produces more than a trillion daughter cells. Each of these cells contains a complete copy of the genetic instruction book.

The genetic instructions direct some cells to become kidney cells and others to become liver cells or heart cells or brain cells. They direct some cells to form the right index finger and others to form the left thumb. And it manages to get a fingernail in the correct place on each one.

But genes don't only control our body's shape. They also control our metabolism. Let me give you an example that occurred in your body after that delicious dinner at the museum last night.

If you didn't have caffeinated coffee, as I did, and you happened to fall asleep, your blood sugar began to fall because you had already absorbed the food into your system. The fall was detected by cells in the pancreas gland, and they turned on a gene. The gene produced a hormone called glucagon. The hormone was released by these cells and went to your liver. In the liver, glucagon turned on other genes that made the liver into a sugar factory that resupplied your blood. Your blood sugar rose, and you slept peacefully, totally unaware of the drama that was being played out by your genes.

Now, the important thing is that everybody's blood sugar last night didn't reach the same level. Some people's blood sugar had to fall quite a bit before their genes became activated. Their genes were a little sluggish. Other people's genes were turned on very early, and they had very high blood sugars all night.

That is the individuality of the genes—the common features of genes dictate the pattern of metabolism. But the absolute levels of various chem-

icals in our blood are dictated by differences in our genes. And that's why all of us differ, one from the other.

Each human being has about 100,000 genes, each of which controls a different bodily process. When the sperm fertilizes the egg, the 100,000 genes are selected.

About 80,000 of these genes are the same in all of us. So 80,000 out of the 100,000 are pretty much standard for the human species. And this explains why we all have the same general body plan and the same general patterns of metabolism.

But 20,000 of the 100,000 are variable. They exist in different forms in different people. These variable genes explain why we're not all the same height and why we don't have the same color eyes, hair, or skin. The 20,000 variable genes are the ones that make each human being unique, interesting, and vital. Without them, we'd all be as similar as three billion identical twins. Imagine three billion identical people in the world. What a dull world. Of course, it would simplify the task of choosing a mate.

To appreciate the power of genetic instructions, we need only examine a pair of identical twins. The slide shows two men who were born as identical twins. They were separated at birth and raised entirely independently of each other. In fact, each one didn't know that he had a twin until they were reunited by a scientist at the University of Minnesota who makes a habit of chasing down these pairs of twins that were separated at birth. And when they were reunited it turned out that both of them happened to have mustaches, and both of them happened to be volunteer firemen in their communities.

When you look at these men you see how similar they are, despite their different environments. You realize the enormous power that genes have to dictate a certain level of determinism. Identical twins are extremely close in height, within a half-of-an-inch of each other, but they're not the same in weight. If we think about the weight of identical twins we can learn something about the power and the limit of genetics. People's height doesn't change very much from one year to the next, but their weight changes dramatically, as I can attest. My weight goes up and down by forty pounds, depending on how hard I work at it.

Identical twins, therefore, don't necessarily have the same weight because each one might have variable weight during his or her lifetime. But there is one thing that they do share. I am unaware of a pair of identical twins, one of whom is habitually thin and has to work to gain weight, and the other is habitually overweight and has to work to keep weight under control. If that happens, it must be rare.

So genes don't determine our body weight, but they determine how hard we have to fight to maintain our body weight. We have a will that can overcome our genetic tendencies, but the genetic tendencies are there, and they create a different background against which each of us must operate.

In the broader sense we approach all environmental challenges

equipped with a unique, and highly personal, set of genes. The environment plays upon these genes like a pianist plays upon a keyboard. And all of our keyboards are not the same. Some of us have defective keys here and there. Agents in the environment may exploit those defective keys to produce disease.

The next slide illustrates the other side of the coin—that is, how genetic differences can be. This slide is taken from an American Express advertisement that appeared several ago. The caption was, "Both of these men use the American Express card." But they don't have very much else in common. The short fellow is Willie Shoemaker, the great jockey, and the tall man is Wilt Chamberlain, one of the greatest basketball players in the history of the National Basketball Association.

These are two normal human beings. The physical differences between them were dictated when a single sperm fertilized a single egg. We've known about these genetic differences between people for a long time, and we've long since learned begun to modify our lives to account for our genetic differences and to exploit our genetic potential. It would have been absolutely ridiculous if Wilt Chamberlain had come home in fifth grade and said, "Mom, I want to be a jockey," and if Willie Shoemaker had tried out for the NBA.

Genes aren't everything. For all I know, Willie Shoemaker might have had the drive, and maybe springs in his legs, so that he could train himself to become a basketball star. There are some short players in the NBA, but they have to work a lot harder than the tall players. On the other hand, it would be technically impossible for Chamberlain to become a professional jockey. Fortunately, these two men picked careers that were consistent with their genetic makeup, and this made their life's work easier.

We've been able to make simple genetic predictions with athletes because you can look at people and decide whether they're likely to become an offensive guard of the Dallas Cowboys or a fencing champion.

But we haven't been able, up to now, to make chemical predictions—for example, to decide which person has a genetic tendency to a heart attack, and, therefore, must avoid cholesterol like the plague, or which person has a tendency to cancer, and, therefore, must avoid cigarette smoking.

The genetic revolution is going to allow us to examine the genes directly and to make recommendations for optimum lifestyles just like the recommendations that led these two men to their genetically-appropriate careers.

All diseases result from the environment playing upon the genetic keyboard. In some cases, the genetic problem is predominant. For example, in Down Syndrome, a child inherits an extra copy of a whole chromosome. That child has a very severe problem, which doesn't require an extraordinary challenge from the environment.

But if you look at another "genetic" disease, hemophilia, it's not so clear. These boys are born with a problem in their blood clotting. If they

lived in a hermetically-sealed environment, they might never have a problem. But when they run outside and fall down they have bleeding into their knee joint, which causes severe problems. So this is a disease where the defect is genetic, but it requires something in the environment, like falling down, to bring it out.

At the other extreme are diseases that are thought to be completely environmental, like auto accidents and fractures and sunburn. But I would say that all of these environmental diseases have a genetic component. Let me use sunburn as an example.

Wilt Chamberlain has a natural suntan lotion with a protective value of four. That is, if you have dark skin it requires four times as much sun exposure to develop a sunburn as it does for a fair-skinned person.

If Wilt Chamberlain and Willie Shoemaker spend fifteen minutes on the beach on a bright sunny day, Shoemaker will have sunburn and Chamberlain won't. Sunburn is clearly a genetic disease!

We don't need fancy genetic tools to tell us whether we're genetically predisposed to sunburn. Experience teaches us whether we're genetically predisposed and, if so, we put on suntan lotion.

Not all genetic predispositions are so simple to detect. Let's go back to cholesterol. Only about a third of people will ever die of a cholesterol problem. A third is a lot, but it's only one in three. That means that two-thirds of people will never have a cholesterol problem. And yet every one of you here worries, I hope, about the cholesterol in your diet, even though two-thirds of you have no reason to worry.

The problem is we don't know how to pick out the one-third that is at risk and the two-thirds that are immune. We can't look at your arteries the way we can look at your skin and decide whether you need suntan lotion. So we have to make a one-size-fits-all recommendation. That is, everybody should have a low-cholesterol diet.

It may be that a low-cholesterol diet is actually not optimum for some people. For example, women need calcium to prevent osteoporosis. Women are going off of milk in droves because of the fat content. There may well be women who give up milk and develop osteoporosis even though they were in no danger of developing heart disease in the first place.

If we can learn which women can tolerate milk and which ones should avoid milk, and which ones need more calcium and which ones need less calcium, we'll be able to make recommendations that make sense for everybody.

Let me finish by saying something about the chemical nature of genes as an introduction to some of the later talks. Each gene is a long string of chemicals called bases. There are four different bases and they are abbreviated T, A, G, and C. They're lined up in long strings like beads on a string.

A typical gene has about 30,000 of these bases lined up on a string. There are 100,000 genes, and each one has 30,000 of these bases in it. So there are a total of three billion bases in the human genome.

The genes are lined up on chromosomes, which are long strings of DNA. The chromosomes differ in size, and some have more genes than others. But there are, in general, many thousands of genes on each chromosome in the nucleus of every cell.

Each cell has twenty-three pairs of chromosomes. Every gene has a particular home on a particular chromosome, which is always the same in all humans.

If we want to find a defective gene that's causing a disease, we have to map the gene, which means we must find out where it resides. Several years ago the United States government, and several other countries around the world, announced the goal of identifying the chromosomal location of all 100,000 genes. The second goal is to actually determine code letters for each one of the genes—to figure out the 30,000 bases that specify each gene.

The mapping has gone rapidly, even faster than people imagined. And the field is now at the point where they are about to determine the DNA sequence of most of those genes.

Within the first few years of the next century we will have that sequence of all of the human genes. When that sequence is obtained it will be like the star map is to the astronomers. It will be the starting point for all future biological and medical research. We will spend the next century deciding how to use all of this genetic information, which bring us back to the beginning of this talk. Hopefully, you are all now sufficiently knowledgeable so that you can appreciate the powers, and the limits of genetic determinism.

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*Michael S. Brown has been on the faculty of the University of Texas Southwestern Medical School since 1971. He is currently the Paul J. Thomas Professor of Genetics and the director of the J. Erik Jonsson Center for Molecular Genetics. In 1985 he shared the Nobel Prize in Medicine with his colleague, Joseph L. Goldstein, for their work on genetic disorders of cholesterol metabolism.

Medical Ramifications

Joseph Goldstein, M.D.*

Michael Brown has just presented an overview of the Human Genome Project, which is a technological effort to obtain the DNA sequence of all the human genes. This project officially began in 1986 and is expected to reach completion by year 2005. In my remarks today, I will discuss the Human Biology Project, which is an experimental effort to understand the function of all of the genes identified in the Human Genome Project. The Human Biology Project will become the dominant activity of biomedical science during the next century.

To understand the function of the genes, which are composed of DNA, we must discover the function of the products produced by these genes, which are called proteins. The genes are the blueprint of life. But it's the products of the genes—the proteins—that are the bricks and mortar that carry out all the business of the body. The proteins determine how muscles contract, how the stomach digests food, and when the heart beats.

When we talk about 100,000 genes in the human genome, we are talking about 100,000 different proteins in the body that are encoded by these genes. The big question for the next century is how do these proteins assemble to make the human body work. What are the interactions and interconnections of each of these proteins with each other? How many proteins does it take to product a heart? How many proteins does it take to produce a liver? And how do they all fit together? This will be the most gigantic jigsaw puzzle that has ever been put together once it is completed—much more complex than creating a map of the city of London, which is a maze of 30,000 streets.

In 1936 there was no map of London. An enterprising individual named Phyllis Pearsall took it upon herself sixty years ago to make the first map of London, the famous A to Z map. She got up every morning at 5 o'clock, walked sixteen to eighteen hours a day for a year-and-a-half, covered over 3,500 miles, and made an alphabetical list of all 30,000 streets in London. This was before the era of computers so Pearsall had to sort all her data in 500 shoe boxes. Her first A to Z listing (before she made the map) did not include Trafalgar Square because the shoe box that began with TR was lost!

Assembling the list of the 30,000 streets of London without an accompanying map that showed all the interconnections and all the interactions—how every street was related to each other street—would be analogous to obtaining the sequence of the 100,000 genes. Having this alphabetical list of 30,000 streets without a street map would be essentially useless to a Texas tourist who comes to London for the first time.

The next one hundred years of biology will be analogous to assembling the first functional street map of London from the alphabetical listing of the 30,000 streets, i.e., taking the gene sequences and the proteins that they encode and figuring out how these proteins interact with each other to form different parts of the body and how these 100,000 proteins relate to each other to orchestrate human life.

So the challenge for biologists of the future will be to learn the structure and the function of these 100,000 proteins. We now know the function and structure of about 4,000 proteins. So we have a long way to go.

When the sequence of the DNA in our genome is completed, we'll have three billion code words, which is equivalent to the information contained in forty Manhattan phone directories. The job of the scientist is to look at all of this information and figure out which regions of this DNA are translated into the proteins that are the workhorses of the body. The challenge to decode and decipher the human genome is truly enormous and approaches the surreal. One has to live in a world of dreams and fantasy to comprehend the enormity of this challenge.

And this brings me to a famous Belgian artist, René Magritte, our greatest surrealist painter. His paintings, which were done about 60 years ago, capture the style and spirit of the genome revolution. In his painting called *Clairvoyance*, the artist—this is a self-portrait of Magritte—is looking at an egg and painting a bird. By analogy, the scientist must do exactly what the artist does. He must look at some ill-defined phenomenon of nature (studying the DNA sequence of a gene) and create a thing of beauty (discovering how the protein encoded by the gene works).

Let's assume that scientists have clairvoyance and can look at all 100,000 of these DNA sequences and discover the function of their encoded proteins. This will allow us to answer *four central questions of biology.*

The *first question* is how do humans develop from a single egg? This question leads us to ask a sub-question: How is the heart formed from the genes and the proteins that are encoded in our genome? And once you know the answer to this question, then you can begin to say: How can we grow a new heart and transplant it into individuals? And how is the liver formed? Can we grow a new liver and transplant it?

We're beginning to understand how humans develop from a single egg by studying simple organisms like baker's yeast, round worms, and fruit flies. The genomes of these organisms, which are much smaller than that of humans, are being sequenced at the same time that the human genome is being sequenced. Baker's yeast is the first organism whose genome has

been completely sequenced. A yeast cell has 6,000 genes compared to 100,000 in the human, and nearly one-half of these yeast genes have an evolutionary counterpart in the human genome.

What we're learning is that the metabolic pathways inside the cell are basically the same in all organisms, whether you're a yeast, a round worm, a fruit fly, an elephant, or a human. What makes a human different from a fruit fly appears to be the regulatory signals at the beginning of a gene that instruct the gene when to turn on and how much of the protein to make. An exciting area in the future is to understand these regulatory signals that instruct the same gene in elephants to express itself differently from its counterpart in humans and fruit flies.

The *second question* is how do humans differ from one another. Michael Brown has already talked about this topic. Learning about individual genetic differences will lead us to early diagnosis of disease and ultimately to the development of medicines that are tailored to the individual—medicines without side effects, the wonder drugs of the future. The side effects of many drugs that we take today are caused by different responses of individuals to the same drug because different individuals have different genetic makeups that influence the metabolism of the same drug once it gets into the body.

Today we all take the same penicillin. When we get a prescription for penicillin, every one of us will receive the exact same chemical form of penicillin. It will have the same atomic structure. Patients with AIDS all get the same AZT. These are medicines of identity. In the future we will have medicines of variation. Once we understand the genetic differences in the way the body metabolizes the same drug in different individuals, we will then be able to take advantage of that information and design these medicines of variation.

Now to the *third question:* how do our brains work? The human brain is a small organ with an astonishing complexity, the most complicated machine that exists in nature. No Boeing or General Motors has ever produced a machine that can match the human brain. It contains 100 billion neurons or nerve cells—10^{11}. Each neuron is capable of making 1,000 synapses or connections with a different neuron. And that adds up to be 100 trillion synaptic connections in the brain—10^{14}. That's 100,000 times more synapses in each human brain than code words for DNA in our genome. Counting synapses at a rate of 1,000 per second would take an individual 30,000 years to count them all!

Understanding synapses is the key to understanding how the brain works. Understanding memory, intelligence, emotion will all come ultimately from knowing the function of all the proteins encoded by our genome and comprehending how these proteins influence all the 10^{14} synaptic connections in the brain. Nongenetic environmental factors also play a crucial role in influencing the activity of our synaptic connections. This is unquestionably the most challenging problem in biology today.

The challenge will be to discover the general principles of the brain that simplify this enormous complexity.

That brings me to a famous quotation by Albert Einstein. In 1920, when confronted with the complexities of quantum mechanics, he said, "Everything should be made as simple as possible, but not simpler."

It seems appropriate to follow this subdued quote from seventy-five years ago with a contemporary quote of a bolder nature, made by Walter Gilbert in 1990. Gilbert received the Nobel Prize in Chemistry in 1980 for teaching us how to sequence DNA. In fact, the whole revolution that we're celebrating today would not be possible if it were not for his major contribution. According to Gilbert: "In the year 2020 you will be able to go into the drug store, have your DNA sequence read in an hour or so, and given back to you on a compact disk so you can analyze it." You would then take the compact disk to your physician, and you and he or she together would analyze it and figure out which one-third of the people in this room will be susceptible to heart attacks because they have a cholesterol problem and therefore should eat a low-cholesterol diet and take drugs that lower their cholesterol, and which two-thirds would be immune to the cholesterol problem and therefore would not have to worry so much about cholesterol in the diet. You would also be able to learn whether you would be susceptible to high blood pressure, diabetes mellitus, schizophrenia, etc.

Is this a realistic possibility?

And that brings me to another famous painting by Magritte, entitled *The Human Condition,* in the National Gallery of Art in Washington, DC. It's a painting within a painting that exemplifies the essence of surrealism. The distinction between illusion and reality is brilliantly called into question in this painting. The tree in the painting hides the real tree behind it outside the room.

This is the way genomic researchers see the world, as a painted dream. Is the tree really outside the room? Will we really have drugs without side effects? Will each of our genomes really be put on a compact disk? Will we really be able to replace organs with cells produced in the test tube?

Let me now come to the *fourth and last question.* How do we convert genes into drugs? Of the four central questions of biology, this is the one that is furthest along in development, owing to the successes of the biotechnology industry. Drugs are produced by biotechnology through a sequence of events in which a human gene is cloned and then introduced into a living organism (either a bacteria or a yeast). The bacteria or yeast are then induced to manufacture large amounts of the protein encoded by the introduced human gene. This protein, called a recombinant drug or vaccine, is purified and administered to patients for therapeutic benefit.

The biotechnology industry began twenty years ago. It now consists of 1,311 companies, twenty percent of which are publicly owned. It employs 120,000 people, about one-third of whom are Ph.D. scientists.

The industry has a market capitalization of $83 billion, product sales of $11 billion, research and development expenses of $8 billion, and an overall net loss of $4.5 billion. In other words, the entire biotechnology industry is about the size of Merck & Co.—without the profits!

To date, the biotechnology industry has developed seventeen recombinant drugs or vaccines that have been approved by the FDA, including insulin, growth hormone, hepatitis B vaccine, and erythropoietin. Erythropoietin is the leading drug produced by biotechnology and one of the top ten selling drugs in the world today. It is given to patients with kidney disease who have low hemoglobin levels. Like erythropoietin, most of the FDA-approved recombinant drugs and vaccines are major contributions to therapeutic medicine, and in this sense the biotechnology industry is a success.

True to the surrealist spirit, biotechnologists are always cooking up new recipes, and I'll tell you about some of the things that are in the pipeline—that you read about in the *Wall Street Journal* and *The New York Times*. For example, there are companies working on new growth factors to treat nerve regeneration and chronic neurological diseases like Alzheimer's disease and Lou Gehring's disease. There are companies working on drugs that will slow aging, on hormones to treat obesity, and on inhibitors to prevent the metastatic spread of cancer. There are also companies working on cures for baldness and on novel approaches of gene therapy for treating cancer, AIDS, and inherited diseases like cystic fibrosis.

But let me now try to put all this information into perspective. Here is how I view the biotechnology industry today—*from the surreal to the real.* These are the *real* facts. On average, one new gene is cloned and characterized each day, one new biotechnology company is formed each week, but only one new recombinant drug or vaccine is approved by the FDA each year. So in the twenty-year history of the biotechnology industry, only seventeen new recombinant drugs have been approved by the FDA.

Typically, you will read in the newspaper that a new gene for this or that disease has been cloned and that a new drug will be available soon. This is media hype! The available facts suggest that the creation of a drug from a gene takes about ten to fifteen years if the function of the protein encoded by the gene is already known. But to create a drug from a gene when the function of the protein is not known may take twenty to thirty years.

If Magritte, the surrealist, were alive today, he might represent the situation in biotechnology as shown in his famous painting, *The Betrayal of Images,* in which he reminds us that the image of the pipe is not the same as the pipe itself (*Ceci n'est pas une pipe*). A modern version of this painting would replace the image of the pipe with the DNA sequence of a human gene to remind us that a gene sequence is not a drug (*Ceci n'est pas un médicament*).

Let me conclude by reminding you that the cloning of genes is only the

first step in putting together the gigantic jigsaw puzzle of human life. The real clues to the puzzle will emerge from learning the function of each of the 100,000 proteins that are encoded by our genes and how they interact and interconnect with each other. This is the goal of biomedical research for the next century.

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Ethical Issues in the Human Genome Project

Tom L. Beauchamp, Ph.D.*

Mark Pearson, DuPont's Director of Molecular Biology, has claimed that the human genome project will "usher in the Golden Age of Molecular Medicine."[1] But even the legendary golden age of ancient Greece had its problems, and a project of the complexity and sensitivity of the human genome initiative will inevitably be accompanied by vast moral and scientific controversy. Officials at NIH have long been sensitive to this possibility. The ELSI (ethical, legal, and social implications) project was included in the human genome initiative almost from the outset, and journalists have long found the ethics-in-medicine theme almost irresistible, as the cover of *Time* magazine in March 1989 demonstrated, upon the launching of the genome project.

Reflection on ethical issues in genetics may merit this attention, but it needs to be kept in perspective. Many critics of recombinant DNA research in the 1970s and '80s—and now of the human genome initiative—have offered sensational moral problems, many with the character of *Brave New World* nightmares. We have been told that we are on the edge of genetic engineering that would fashion the human species as a super race, that germ-line gene therapy will have disastrous effects, that we are stigmatizing the disabled through genetics research, that we will graft animal genes into humans and graft human genes into animals, that we are resurfacing discredited eugenic thinking, that we are intimidating women's reproductive decision-making, and that we may even be destroying the human species. A simple example is found in the following 1991 quotation from *U.S. News & World Report*:

> Society's knotty decisions will become even more tangled as the massive Human Genome Project lumbers toward its goal of mapping the location of every human gene, including those that govern such traits as intelligence, coordination and grace. That knowledge will expand the potential of genetic engineering far beyond the correction of disease and push it toward the realm of social engineering.[2]

It is likely true that eugenic thinking will be difficult to escape in upcoming years; and it will be difficult to distinguish constructive from destructive eugenic thinking. Nonetheless, the highly speculative nightmare accounts of ethical issues in the human genome project have thus far not been very specific or precise. Moreover, even the worst case scenarios do not suggest that the effort to map and sequence the human genome is intrinsically burdened with ethical issues. The problems are not about new scientific knowledge or the procedures used to obtain it, but about the *uses* to which such knowledge might be put, or not. It is here that the major moral problems are found—both the more speculative and the more practical problems.

From my perspective, the most interesting class of practical issues concerns the ownership and control of genetic information, and the most interesting class of speculative or theoretical problems is about scientific reductionism and causal determinism.

Insurance Implications and Questions of Social Justice

One of the primary problems is that systematic genetic testing will facilitate the exclusion of the genetically destitute from insurance coverage, and potentially from employment. It has been recognized from the beginning of the human genome project that genetic screening (that is, sorting an asymptomatic population to locate persons at elevated risk of genetic problems) would present issues of privacy and confidentiality involving employers, insurers, bankers, credit raters, and many others. Predictive uses of genetic information are not now sufficiently developed to affect a great many underwriting decisions—and they are not yet cost effective—but the human genome initiative will increasingly create a larger volume of predictive information to be added to the genetic information already available. Once obtainable, this information will encourage insurance companies to make genetic tests cost effective. Companies can then deny coverage, increase charges, initiate exclusions, and the like.

Such information is also obtainable by persons at risk of disease, and they are more likely than others to purchase the relevant type of insurance in maximal amounts because they are more likely to experience claims in excess of premiums. This circumstance and the costs of health care generally give employers a reason to avoid hiring those who may get sick and file claims. Many companies already carry limited coverage in the case of diseases such as AIDS. At the present time, so-called *group* insurance is being restricted by corporate policy to ever-smaller bundles of persons, eliminating those from the larger group who potentially will be most costly.

The private health insurance industry, not surprisingly, views these strategies and adjustments as justifiable, because insurance policies are designed to limit risk as well as to protect the healthy. But there is a morally unsatisfactory feature at the heart of the current American insurance scheme: Insurers want to avoid those most in need of insurance; the more you need, the less you can obtain, or the more you pay. The situa-

tion will worsen as genetic information accumulates. Lost in this upheaval is the moral goal of blindly pooling risks for groups in the face of the unknown lotteries of life. Now we each seek to become economically advantaged by being placed in the lowest risk group. However, if we cannot be placed in this group, our economic position is dramatically worsened, which may also affect our health care expectations. If insurance pools continue to be restricted through genetic tests, as they will be under current policies, then such tests will feed rather than alleviate problems of health care coverage, with the potential to become an American tragedy.[3]

These developments need to be put in a broader perspective of social justice. It would be incoherent to fashion either a public or a private insurance scheme that prohibited insurers from the use of *genetic* risks without at the same time prohibiting similar predictors of disease that are currently in use. An obvious question to ask about our system of access to health care is whether it is ethical to even allow risks of this sort to be assessed in contracting for insurance policies, and whether health, life, and disability insurance should be distributed more in accordance the luck of the lottery of nature. In a very different health care system than the one we now experience, it would be morally unjustified—a clear act of discrimination—to exclude persons from an insurance pool merely because they were unlucky in the genetic or any other natural lottery.

This would be less of a problem if persons were responsible for their health conditions, but genetics is the paradigm case of being ill or susceptible to illness for reasons beyond one's control. Broad principles of social justice suggest not only that exclusion of the disadvantaged is unwarranted, but that there is a social obligation to correct or prevent certain genetic defects if it is possible to do so. The logic here is that a commitment to equal opportunity requires more than the removal of barriers such as discriminatory policies. It requires positive steps to remove disadvantaging conditions.

It is morally shocking that so little of the debate about health care reform has turned on these basic moral issues about fair access, while so much of it has turned on purely economic questions of cost-containment and efficiency. Everyone is aware that the large numbers of uninsured and underinsured citizens is a massive problem in the present system. The point that I have been making is that new genetic information has the potential to enlarge the number of medical uninsurables well beyond what we are now experiencing, at the same time making new technologies available only to the wealthy and those lucky enough to have squeezed through our system of screening for coverage. So-called 'fair discrimination' in access to health insurance in the end amounts to a diminished access to desperately needed health care.

Employment, Genetic Screening, and Discrimination in the Workplace

I will now shift from insurance companies to employers and to connected problems of genetic screening. This shift is not a sharp change of

direction, because insurance and employment are closely linked in this setting. Insurers may insist that employees undergo testing, and employers may find it advantageous to exclude potentially costly employees and forms of costly coverage. Although relatively few employers currently use genetic testing, this situation will change as the benefits of testing shift and as the market fosters incentives. The genome project will accelerate the process, increasing the use of genetic screening and raising questions about what can be reliably inferred from genetic information.

Lingering worries about genetic discrimination led to a recent study by Paul Billings and associates of our *present* systems of using genetic information. He considered whether incidents involving genetic discrimination are already occurring in the workplace, thus affecting access to social services, insurance underwriting, and the delivery of health care.[4] The study was eye-opening. Respondents in the study described difficulties they had encountered in obtaining insurance coverage, finding or retaining employment, and the like. Here is a typical example involving the "asymptomatic ill," as Billings calls them—that is, those who have a disease-associated gene, but no identifiable clinical illness. A clinical geneticist treating individuals with PKU wrote:

> [Name withheld] is an 8-year-old girl who was diagnosed as having PKU at 14 days of age through the newborn screening program.... Growth and development have been completely normal....The circumstances of the discrimination that this child has experienced involve rejection for medical insurance. She was covered by the company that provided group insurance for her father's previous employer. However, when he changed jobs recently, he was told that his daughter was considered to be a high risk patient because of her diagnosis, and therefore ineligible for insurance coverage under their group plan.

This and many other cases reported in the Billings study illustrate instances of discrimination against persons who are completely asymptomatic; their only "abnormality" lies in their genotypes. Though in truth healthy, persons are treated as if disabled or chronically ill.

Problems of Reductionism, Destiny, and Determinism

I turn now to a range of more speculative problems, all of which center on questions of genetic determinism. I begin by explaining why I think such speculation might be of interest to you.

The Causal Conditions of Behavior: Reductionism and Determinism

A vision of genetics that lacks perspective can foster the belief the genes are the primary and perhaps sole causal determinant of human ills and deviant behaviors. The move in various literatures has been rapid from disorders such as Huntington's and hemophilia to schizophrenia and

manic depression, and from there to learning disabilities such as dyslexia, attention-deficit disorder, and dysfunction in language development. From there speculation has spread to the possible genetic bases of shyness, inhibition, risk-avoidance, drug abuse, sexual conduct, and all "modern maladies." At this point speculation has begun to get a little out of control. Here is an example from a recent *Time* magazine story that places its theses in a Darwinian context:

> The premise of evolutionary psychology is simple. The human mind, like any other organ, was designed for the purpose of transmitting genes to the next generation; the feelings and thoughts it creates are best understood in these terms. Thus the feeling of hunger, no less than the stomach, is here because it helped keep our ancestors alive long enough to reproduce and rear their young. Feelings of lust, no less than the sex organs, are here because they aided reproduction directly. Any ancestors who lacked stomachs or hunger or sex organs or lust—well, they wouldn't have become ancestors, would they? Their traits would have been discarded by natural selection.
>
> This logic goes beyond such obviously Darwinian feelings as hunger and lust. According to evolutionary psychologists, our everyday, ever shifting attitudes toward a mate or prospective mate—trust, suspicion, rhapsody, revulsion, warmth, iciness—are the handiwork of natural selection that remain with us today because in the past they led to behaviors that helped spread genes.

This 1994 story in *Time* was followed by another cover story in late 1995 that pointed to genetic roots for all modern maladies such as stress, anxiety, and depression.[5] Also at stake in these discussions is the idea that human destiny follows from human biology, together with the accompanying theme that what genetic medicine does is to tinker with, and that human properties are therefore the outcomes of our genetic constitution.[6] This theme continues to surface in the context of several delicate, ongoing, controversies, the most visible of which have been the homosexuality controversy, with its generally constrained conclusions about biology and destiny, and the IQ controversy—with its generally unconstrained conclusions.[7] Conclusions reached in these controversies are often allegedly supported by scientific data, despite significant gaps between the data and the conclusions reached.

So how much of the variation in IQ is linked to genetic factors and how much to environmental ones? The best way to get a direct estimate is to look at people who share all their genes but grow up in separate settings. Four years ago, in the best single study to date, researchers led by University of Minnesota psychologist Thomas Bouchard published data on 100 sets of middle-aged twins who had been raised apart. These twins exhibited IQ correlations of .7, suggesting that genetic factors account for fully 70 percent of the variation in IQ.[8]

These conclusions are also turned into a broad social agenda that demands the abolition of welfare and affirmative action programs on grounds that they are doomed to failure, that they will do more harm than good, and that many forms of social inequality are the genetically inevitable outcomes of biological differences between the bright and the dull. Opponents of these arguments fear, of course, that a social and political agenda is driving the interpretation of scientific data; it is not science, but the abuse of science. And it functions to replace the idea of the moral worth of persons with that of their biological gifts.

Conclusion

Somewhere in upcoming years the human genome project will encounter at least one massive problem that no one has yet anticipated. Obviously I do not know what it will be. But it will involve some kind of interaction between science, law, and ethics.

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4. Paul R. Billings, Mel A. Kohn, Margaret de Cuevas, Jonathan Beckwith, Joseph S. Alper, and Marvin R. Natowicz, "Discrimination as a Consequence of Genetic Testing," *American Journal of Human Genetics* 50 (1992): 476–482.

5. *Time*, Aug. 28, 1995.

6. *U.S. News & World Report*, Aug. 22, 1994.

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8. *Newsweek*, Oct. 24, 1994.

Legal Aspects

Alexander M. Capron, L.L.B.*

What might be encompassed within a discussion of the legal aspects of the genetic revolution? DNA fingerprinting and the O. J. Simpson trial? The federal regulation of recombinant DNA research? Over the past twenty some years, the Recombinant DNA Advisory Committee (RAC), which was recently almost put out of business by the director of the National Institutes of Health, moved from laboratory safety issues to spending most of its time looking at human gene therapy. How about intellectual property issues? The patenting of gene sequences has been a controversial matter; the National Institutes of Health (NIH) filed many patent applications, until the current director, Harold Varmus, came in and decided NIH would no longer seek patent protection for the strings of cloned DNA decoded by its gene sequences.

Breast cancer genetic testing raises another legal aspect, namely the role of the Food and Drug Administration in regulating the products coming out of the genetic revolution. A fifth area is anti-discrimination laws. The Equal Employment Opportunity Commission has recently announced that under the Americans with Disabilities Act the diagnosis of a genetic sequence associated with disease susceptibility could be regarded as a disability. Sixth is tort law, and seventh is medical practice acts and the licensing not only of physicians but also of genetic counselors. Another legal area is the need to protect the confidentiality of genetic information, such as through evidentiary privileges in judicial or regulatory processing. Finally, a ninth area concerns access to genetic services and the regulations that govern reimbursement and coverage decisions made by public and private insurers.

This is hardly an exhaustive list of legal issues raised by the genetic revolution. I intended it to be merely illustrative. In other parts of the world the law has already directly or in draft form gone far beyond this. The Council of Europe has put forward a proposal that would protect "the inviolability of the human genome," suggesting that the genome is something which is under attack and needs to be protected from the depredations of scientists and physicians. If this view is accepted, it would probably filter into our own legal system through finding some sort of basic protection in our Constitution under the due process clause for a person's genetic identity. That would certainly be a complex and controversial move.

Indeed, it's the complexity of all of these topics that would require, I suppose, not forty-five minutes, but forty-five hours to begin to delve into. But that's not the only reason why I don't believe it's helpful at this symposium to think of a "law of genetics" as the appropriate way to respond to the question, what are the legal questions raised by what we heard about this morning?

It seems to me that rather than rush onto the statute books the various methods of controlling the "genetic revolution," it would be far preferable for us to follow the precedent that was set twenty years ago when, for most people, the issue of genetics first became front page news. At that time, concerns raised within the scientific community resulted in scientists themselves imposing an international moratorium on certain aspects of the original "gene splicing" research. This effort, led by Paul Berg of Stanford and Maxine Singer of NIH, led to an international conference at the Asilomar Conference Center in Monterey, California. The conference attracted a good deal of public attention because it was an unprecedented attempt by scientists, first, to stop their work and examine it, and, then, to decide the ways in which it could go forward and to engage in a form of self-imposed regulation.

Not surprisingly, this self-regulation was doubted by some people, who called for federal legislation to limit and restrict this area of research. Hearings were held in the United States Senate, and proposals were made. I think it is fortunate that at that time the decision was made that this was an area which was not ripe for legislation. Instead, the committee I mentioned moments ago, the RAC (Recombinant DNA Advisory Committee), was established by the director of the NIH to provide advice on federally supported research, which was the bulk of all the research in gene splicing at the time. There's now a good deal of industrial work in the field, and for many years, that work was also brought voluntarily before the RAC.

Now, one might say there is only a very small difference between the establishment of a federal committee to look at the work and the establishment of laws and regulations. But if we looked at the twenty-plus-year history of that committee we would see that it was constantly able to reevaluate the standards it had set and, with experience, discover that many of the original causes of alarm were overblown. (We did not need to be protected from many, many areas of recombinant DNA research, which, indeed, are as safe, if not safer, than other kinds of virology research and the like that goes on according to accepted biomedical standards of safety.)

As burdensome as meeting with the RAC may have seemed to scientists and physicians eager to move forward faster than the committee was prepared to agree, the process they would have faced would have been far, far more complicated if we had moved quickly to legislation.

Part of the reason for this is that the law is a blunt instrument. It tends to speak in broad categories and to have a limited range of responses to

many complex situations, particularly those situations which are not themselves simply a creature of the law. One can look at certain areas of contract law and the like and say, "Of course, we need and can have elaborations from legislators and then interpretations by judges which respond to most of the problems in a fairly sensible fashion." And yet all of you from the business world know that there are many times when the business community, in the way that it is forming its commercial relationships, gets ahead of the law. And there are times when that becomes problematic, which is why you then have expensive lawyers to deal with those problems.

Besides the question of the law's bluntness, there is also a risk of using it prematurely to deal with fields not primarily of legal creation in the first place, like sales law, but rather are themselves growing out of a sister enterprise—the scientific enterprise. Indeed, in the genetics arena, most of the important issues that ought to be resolved before we legislate have not been resolved. Let me illustrate by listing eight areas which are quite unresolved.

The first one is the anxiety that attaches to this field. No one can have been a reader of popular magazines, as Tom Beauchamp just demonstrated for us, without being made aware of the risks—the genetic risks that we all seem to face and the difficulty of knowing how our society is going to respond to them.

Part of this is the uncertainty that attaches to these figures. As Mary-Claire King made clear this morning, even when we are talking about a susceptibility to breast cancer we are still dealing with probabilities. And it is, I think, a fact that any of you who professionally deal with this can attest to, that the average member of the public and, indeed, the average member of the medical community deals very poorly with probabilities. The additional factor of uncertainty about the extent of the risk results in a good deal of anxiety. Will I have disease? What does it mean to say that one in ten American women will develop breast cancer? Is that a constant risk or does it increase over life? We know that there's a high level of anxiety when people think about this subject. Ironically, the ability to diagnose a disease or predisposition pre-symptomatically in some ways increases the anxiety. If the information is there, should I go and get it?

A second unresolved issue is one which Mary-Claire King also mentioned, the guilt that arises in passing on the genes. It isn't only the women who are found to carry the BRCA1 gene for breast cancer who feel a sense of guilt. Counselors tell me that almost the first thing out of the mouth of *all* women in that situation is the concern, "Have I now passed this gene on to my daughters?" And this is magnified across the board by a whole range of genetic conditions that counselors can describe.

The flip side of that, of course, is the anger that follows from being burdened by something hereditary. Henry James notwithstanding, most people think of inheritance as a blessing, not a curse. But the notion that a gene, which could cause serious illness or premature death, has been

passed on in a family can be a source of anger or recrimination within the family.

A third point—confusion. With the flood of information that seems to be inundating a general public that does not understand genetics well, the potential exists for a great deal of misunderstanding and premature action.

Fourth—along the lines of what we heard this morning about twins—we are often told that our identity is tied up with our genes. If that is the case, and if, through genetic testing, we find that some of those genes are defective, what does that do to our sense of self-identity? This in turn raises obvious questions then about when testing is appropriate. If testing were to be done, for example, with adolescents who were going through a period when their own sense of identity is so much in flux, would we be putting them at greater risk of thinking that science had now certified and attached to something objective and measurable to them as flawed human beings?

A fifth problem—social discrimination. Not discrimination by insurance carriers or employers, but the ostracization that can follow from genetic identification. As long ago as the early 1970s, when sickle cell carrier testing was introduced on a large level in the United States and thallasemia testing was going on in the Greek Cypriot community in London, it was discovered that people who were found to be a carrier of the mutant gene (and hence, not at any physical risk themselves for the illness that would come from having the double dose of the genes) were ostracized. And today there are, in certain Hassidic communities in New York, rabbis using genetic profiles to decide who should be marriageable, or at least decide about matings of people.

These issues are not hypothetical. Ostracization and social discrimination are issues. Likewise, the question, do we have adequate personnel to test, and especially to counsel, about testing? This is not an issue for the law. This is a basic issue of our organization of medical education as well as education of genetic counselors and the devotion of resources to this field.

A seventh, broader problem is what Professor Susan Wolf of the University of Minnesota has labeled geneticism, the framing of medical and even social problems in terms of genetic rather than environmental factors. This can have its manifestation in many ways. A simple example is that physicians in the future, armed with the ability to predict individual genetic risk for particular diseases, will be able to tailor their advice to patients, so that out of the welter of health preservation and health promotion advice that we all now get, they can target that advice in a way that should be much more powerful for patients. And that sounds wonderful.

Yet there is a downsideæfor the physician-patient relationship and also for patients' healthæin adding further tests of whatever type. Already, Dr. Eric Casell has written, technology is the sorcerer's broom of

medicine. What he means is that physicians, in grasping for some certainty in the face of the great uncertainty that attaches to all attempts to talk with patients about their future health state, want to grab hold of what they regard as "definitive" and "objective" information that they can get from tests, rather than what they get through the methods that have served good physicians for so long.

Now, I would not follow Dr. Casell's view if it led to the conclusion that we don't want to have any of these tests. Nonetheless, particularly as tests are first identified and the glamour of the high-tech medicine comes upon the medical profession, the risk is that they will substituteæor even obliterateæthe existing evaluation of the individual in all of her or his manifest complexity before the doctor, to be replaced instead by a number read off a machine or a lab report identifying a genetic sequence on a chromosome.

Beyond this effect in the medical sphere, geneticism also carries the risk of altering the way in which we view human beings, both because the power of genes and their malleability is now overwhelming our thinking. However hard we try to keep in mind the interaction of genes within the environment, every time we turn to something like the twin studies, with those remarkable coincidences that seem to exist in the life of the identical twins separated at birth, we run the risk again of reifying genes and of doing what Professor Dorothy Nelkin calls, "Turning them into a kind of cultural icon."

The risk lies in thinking that we could explain individuals by knowing their genes. This goes far beyond the quote we had from Walter Gilbert this morning—because Professor Gilbert went beyond saying that in the future you would be able to go to the drug store and get a CD-ROM with your genotype. He also said he would hold the CD-ROM up and say, "Here I have the person." *Ecce homo*, this is the man on this disk. The risk then is that we will come to believe that this statement is true, and forget that what is really on the CD-ROM is a genetic message which will manifest itself in the light of particular environments as a human being. That risk cannot be underestimated.

Let me underline this point by using a very extreme example, derived from the discussion this morning of Down Syndrome. I am sure that a Down Syndrome child who did not have lethal physical abnormalities that required surgery would have had a much easier time in nineteenth-century America than at the brink of the twenty-first century. A simpler world is easier for people who don't comprehend complexity and deal with it very well. They can survive more easily in that setting.

Now, it is true that most Down Syndrome children used to die at a younger age because of the complications that came with infections and the like. But, without downplaying the advantages of contemporary medicine, I believe there are negative consequences from our current tendency to explain Down Syndrome in terms of an extra chromosome, to pretend that with this explanation we need not think about the environmental

contribution, not just to the physical manifestation of that disease, but to what we think of its burdens and problems as they are experienced by people with Down Syndrome.

Even in the case of the twins who were separated at birth, we need to remember that they shared an intrauterine environment, as recent findings emphasize these parental effects on the manifestation of given genes as seen in the baby after birth and then in the adult. Indeed, recent data have confirmed some earlier findings that the weight of a female at birth has a correlation with breast cancer. And that weight, in turn, seems to have to do with something in the intrauterine environment. So when we start talking about "genetic diseases" we should be aware that from the moment of conception we must also talk about the environment in social as well as physical terms. These factors may be more subtle and less measurable than our DNA but they are no less important.

Eighth and, finally, we come to the whole question of human nature and what it means to be a human being, which is being raised by the Human Genome Project and all the other attempts to understand genetics.

Now, when I raise these as issues and questions it is precisely because I do not think the law is going to provide any very good response to any of these. The law operates in most situations as kind of an on-off switch. We either allow something (or encourage it, through collective support) or we prohibit it. Sometimes the prohibition is modulated through regulation, allowing it in some cases and disallowing it in others. But the law does not bring to these issues much that will help us to decide about the answers we should give to the fundamental questions of genetic determinism or geneticism, or of the effect of our understanding of genes on the levels of anxiety and guilt that people have, or of the ways in which we ought to respond to the risks to our sense of self-identity.

These are problems fundamentally within a human philosophical, ethical, social sphere. And until we can address these in a satisfactory way we will not be able to write laws that will serve our society well. I would go so far as to say that the genetic information will raise questions beyond any that we have faced, but I'm not sure that we can look to the law to give us answers.

Let me end this list of things to which the law can not provide the answer by taking up a suggestion that Hans Mark made this morning. He was talking about understanding the genetics of neurons and the notion that one could take neurological cells and put them in a petri dish and in his words, wire them up so they became a computer. I want to know the point at which, when we put those neurons in the petri dish and wire them up, they become a human being. That is the issue that we will ultimately face.

Right now biologists could breed half human-half chimpanzees. In the opinion of the biologists I've spoken with, it is technically possible and it would have great payoff for developmental biology. But, of course, part of what holds people back is concern about what the resulting creature

would be. Would it be a chimpanzee or a human? Would it be entitled to vote and go to school? What would we do? How would we regard that entity?

When the Constitution tells us that there are certain protections for persons it presupposes we know what persons are. And probably the single issue that has most roiled us socially as a country for the last twenty-three years comes out of the debate over what that Constitutional provision means. Is a fetus a person? The Supreme Court answered in *Roe v. Wade* by saying, "No, it is not." It didn't say it wasn't a human being though. It's just an unborn human being, and an unborn human being is not, in the view of the Supreme Court, a person in Constitutional terms. And so the special protections that would apply to persons don't apply there. That, of course, is an enormously controversial notion in our society.

What would happen if we found ourselves able to create not the architecture of a human being, but that thing which we, most of us, regard as what makes us distinctively human, which is the human brain, that marvel of which Drs. Goldstein and Brown spoke this morning. If we could create that, at what point would we say that creation, even in a petri dish, has to be regarded differently than some other collection of cells if it can operate in a self-conscious fashion? What would that mean?

Such issues are not going to be well-dealt with by the blunt instrument of the law. So I come before you as a lawyer urging you not to press our institutions of society to move ahead too rapidly to deal with these issues as legal issues.

The law brings to all this, after all, only certain principles which rest upon a presupposition that we know the direction that we're going in. Three distinctively legal principles in our system are the principles of fairness, embodied in such things as our Equal Protection clause; procedural regularity, in-other words, due process; and the balancing of personal liberty with community well-being, which we do in all sorts of sometimes contradictory ways in the law of property, torts, nuisance, and contract, and which is manifested in Constitutional law through the notion of a protected sphere of privacy, on which the community should not intrude.

Now, all of these can supply some rules of relevance to the genetic area. Certainly, genetic testing and the use of genetic procedures ought to proceed, as all medical care does, under a regime of informed consent, which has been a contribution of the law, along with philosophy, embodying a long-standing tenant of Anglo-American law, namely protection of bodily integrity. From that has grown an important set of understandings between society and the medical profession about the ways in which information must be provided and consent sought before medical interventions go forward. And there's no reason to think that genetic interventions should be any different than this.

But that only begins to scratch the surface, because if all the complexities that I described before about the likely consequences of undergoing

genetic testing exist, what would a conscientious physician tell his or her patient about the consequences of the test? Is it, for example, necessary to talk about all those feelings of guilt and recrimination, of anger, of profound misunderstanding that can come from having a test that yields a nice, clean result that isn't so clean in its application? Is it appropriate for testing to be done only after people are warned about their risk of being discriminated against by their friends, relations, employers, or insurers? Is that part of appropriate genetic testing in this area? So that even a simple rule like the rule of informed consent becomes quite problematic?

A couple of weeks ago, at an international conference I organized in San Francisco, a group from Stanford University reported on the results of their study over a fifteen-month period of the proper grounds for going ahead with breast cancer genetic screening. I'd like to read you a couple of their conclusions, which seem, on their face, unproblematic.

They concluded, "For most people BRCA 1 and 2 mutation testing is not appropriate. For people at high risk of carrying a mutation, either as a result of family history or their own early onset of disease, testing is an option that should be discussed and that could reasonably be accepted or declined. Even for those not at high risk, testing, though not encouraged, should not be prohibited." And then they went on to say in a separate recommendation, "Marketing of genetic tests for BRCA 1 and 2 mutations should be carefully limited."

If I were sitting as the chief counsel of the FDA and saying, I want to do exactly what this thoughtful group from Stanford has urged me to do, I don't know what I would do because I'm told that it's not appropriate for the general population to undergo screening. Yet there are companies out there that are now promoting that. In fact, the FDA, at the end of October, granted approval and Myriad Genetics of Utah has now begun marketing an approved test. Previous to this, you may know that a number of companies were doing breast cancer screening. But they were doing it as a clinical laboratory test, and they were regulated, therefore, under CLIA, the Clinical Laboratory Improvement Act. They were not marketing this test, so they didn't need FDA approval. Well, FDA approval has now been given to a test and it is being marketed.

Now, is that a mistake? Suppose Myriad Genetics started taking ads out in newspapers all over the country saying to women, "Here is a way of finding out about your risk. If you are a young woman who has not yet had children, you may want to know whether you will be passing this dreaded gene on to your children." Would that be appropriate or inappropriate? Can that be limited? It should not be prohibited, it says here in one recommendation, but it should be limited. I don't know exactly what the Stanford group would be telling the FDA to do in this area. And they spent a whole year thinking about it.

Another issue: those studies that we saw displayed by Dr. King involving families requiring the gathering of information from many family

members. Indeed in some cases it was not possible to identify the gene in question until one had data from a number of affected and unaffected members of the family.

Now suppose that someone comes in for testing for a genetic condition and finds that he or she carries that gene, and then at the conclusion the physician says, "Well, we'd understand a lot more about this if we could talk to your relatives." And the individual says, "I don't want you to talk to my relatives. I don't want that information to go out of this room, and you are bound by a duty of confidentiality not to let it leave this room."

Is that an obligation if the physician knows who those relatives are because of information that has been provided previously or perhaps even the physician has other members of that family in his or her care? Does the injunction of confidentiality apply in this situation?

We generally regard people as being free to insist that medical information not be disclosed, though we make certain exceptions. One of the exceptions that has emerged in the law is where the person who has the information is regarded as having a special relationship with a potential victim. If the information is not being disclosed and its absence seriously endangers the individual's health, should the exception be invoked? Depending upon what the genetic information is, it seems to me that it is possible to construct a case in which one could say that the absence of that information to the relative seriously threatens that relative. Now, in a way, the relative is no worse off than he or she was the moment before that genetic result was uncovered. And it is also possible that whatever led the first person to come in to be tested is information available to those relatives, and if they were so moved they would go in and be tested.

Perhaps the non-disclosing relative is doing the right thing, saying, "They could be tested if they wanted. I don't want this information thrust upon them." And part of the notion that the law protects privacy suggests that we don't have to have unwanted information. What information we have about ourselves does affect us in our evaluation of our life and our prospects. And part of the notion of privacy is the ability to shape one's own life and one's own self-identify. If you don't want that information because it would be disruptive, I think a coherent case can be made that that's correct. But perhaps that's not the reason, or perhaps that's a paternalistic reason in any case.

One famous case that you may be aware of, the Tarrasoff case in California, said that in certain situations psychiatrists have an obligation to warn the potential victims of patients who have in psychiatric sessions made statements indicating that they intended to harm the victim. Among psychiatrists that was a controversial decision when it was handed down, although it turns out that psychotherapy has proceeded and has not been destroyed in California or elsewhere by the insistence that psychiatrists exercise that degree of protection of third parties. Is that the model we want to apply to this genetic information?

A good deal of reference has been made to the advantages, therapeutically, in having genetic information. One area where for the past twenty-five years genetic information has been widely used has been in prenatal diagnosis. I gather that it has been widely thought that this has been a pretty straightforward and useful medical development. And I would agree with that evaluation.

A couple of years ago the American Medical Association's Council on Ethical and Judicial Affairs addressed the issues of prenatal diagnosis because it recognized that there were ethical complexities here. In particular, the Council addressed an issue which has been controversial in medicine, the use of genetic technology to avoid the birth of a child of a particular sex, predominantly avoiding the birth of female children. The medically related issue, of course, is the use of prenatal diagnosis to discover the existence of a male fetus where the family is at risk for an X-link disease, which will manifest itself in male children, like hemophilia, but not female children. But this is the reverse. This is a situation in which the diagnosis would be undertaken because the parents want to avoid the birth of a child of the female sex unconnected to any "medical" situation.

The Council on Ethical and Judicial Affairs concluded as follows: "Selective practices, such as sex selection, may result in lasting social harms such as the exacerbation of discrimination, a tendency to view children as products, and eugenics." Likewise, recognizing the potential for social harms, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, in a report in 1982, strongly discouraged the use of prenatal testing for sex selection, stressing the need to confine such testing to "seeking genetic information in order to correct or avoid unambiguous disabilities or to improve the well-being of the fetus."

Now, you'll understand that since I directed that commission, the critical remarks I'm going to make about the utility of that statement are not casting bricks at somebody else's glass house, but recognizing that I live in one. It seems to me that our growing understanding of genetics over the past fifteen years has shown how problematic this is. Nor is it an issue only in those cases in which we have something like the use of prenatal diagnosis for sex selection.

Let me give you an example, of which I was reminded last night by Dr. Goldstein. There is a form of dwarfism called achondroplastic dwarfism, which is a dominant disorder. Most all of the achondroplastic dwarfs are so-called spontaneous mutations. There's also the tendency in this particular condition, as in any number of others, for what's called assortative mating, where people with the same genetic condition come together and end up as spouses. Indeed, in this area there's a whole organization—the Society of Little People. They live a life unto themselves. Now that the particular genetic cause of achondroplastic dwarfism is known, it is possible to do prenatal screening. It is, of course, useful to know, although not determinative, to find out that the fetus would have

gotten a double dose of the gene from both parents, a lethal condition which doesn't lead to a survivable child. Now, however, that obstetricians at some centers are able to manage the pregnancy—and I guess through Caesarian birth carry the pregnancy to term—the parents are saying, "We want to give birth to a child who has this genetic condition, not to a child who didn't inherit it from either of the parents and would be a so-called normal statured person."

This is shocking to a lot of people because it would be like sex selection—the use of a genetic technique to lead to the abortion of a child who doesn't have any genetic condition that threatens its own life or existence. And the reason given by the families is that their lives are centered around a lower height. Their houses are built that way. Their furniture is built that way. In effect they say, "This child will be an aberration in our community, and we don't want to tolerate that."

I don't think that this decision on their part is the same threat to the normal statured individuals that the sex-selection decision of people would be if it were widely carried out—as we know through studies, it would be widely carried out—to have a roughly 60–40 or 65–35 percentage of male births to female births if everyone can predetermine the sex of their children. That is a threat to our understanding of human equality because it would affect half of the population, whereas we, the normal statured, are so much the dominant in the population that we're not really threatened by a few achondroplastic dwarfs saying they want to have dwarf children.

But what their case illustrates to me is a reminder of how utterly socially determined our sense of normality is. And, in this area, until we have a better understanding of what the normal means, or, indeed, whether it makes any sense when we talk of genetic variations across all the capabilities, not just the few that have manifestations in lethal conditions, but across all the capabilities, it doesn't seem to me it is possible to talk about legislating to avoid discrimination when we would thereby be embodying a model of discrimination which exists in our usual anti-discrimination law which says, We know what the normal is. The normal is white and male.

What we have to do is protect those who are not white males by getting them treated equally to white males. That is our reigning paradigm for anti-discrimination. We say, you can't treat women differently than men, and, indeed, the Constitution says you have to afford people of color equal rights to white residents. That is the whole idea. That is our anti-discrimination paradigm.

How in the world do we apply it now that we understand the variations in genetics? In that paradigm we have to have a norm. We need to recognize that the norm does not make sense anymore, just as we have to recognize that races don't really exist. When you look at the genetic data it turns out that there is more variation on all the other genes except skin color within the so-called race than between races, so that all the other

factors that we would look at deny the notion of race, and we ought to obliterate that. But, of course, race is a social construct in our society.

Likewise, the whole notion of genetic normality, I think, is going to turn out to be a social construct. And that is a fundamental challenge. If we are going to respond as a society in a sensible way, whether it is in the issuance of insurance policies, protection of people in the work place, or our basic understanding of what it means to participate in our society, these are the issues we must resolve. And, again, I would suggest to you that the law ought to have a great deal of modesty in approaching these issues and realize that most of the heavy work that has to be done must precede any attempt to legislate.

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The University of Texas Southwestern Medical Center at Dallas

Kern Wildenthal, M.D., Ph.D.

Thank you very much, Charlie, for such an overly generous introduction. Charlie Sprague is my mentor, and he's taught me many things. When he retired and I was named to his former job, he gave me one piece of advice which is noteworthy in light of the remarks he just made. He said, "If somebody gives you credit that you don't deserve, take it . . . because somebody else will damn sure give you the blame for something you don't deserve." So, Charlie, thank you for your kind words, even if I don't deserve them.

When Charlie first told me that the Philosophical Society would be meeting in Dallas and that the topic would be biomedical, he said that the meeting would provide an opportunity to have a little advertising for UT Southwestern Medical School. So that's what my remarks will be, in part, before I introduce Glen Evans. I would like to give you some general information about our institution as a way of introducing the specific research effort that you'll be hearing about from Dr. Evans.

We are "the University of Texas Southwestern Medical Center at Dallas," one of fifteen branches of the University of Texas System. We were originally created not as a branch of the University of Texas, but as a private medical school called Southwestern Medical College.

It was war time, the country needed more doctors, and Dallas didn't have a medical school. The only two medical schools in the state were the University of Texas Medical Branch at Galveston, the sole state school, and the private Baylor Medical College, which recently had moved to Houston from Dallas.

The business and medical leaders of Dallas felt that North Texas needed a medical school and started one as a private enterprise. It was owned and operated by Southwestern Medical Foundation and had an annual budget of $250,000.

In 1949 the trustees of the Foundation realized that if they were ever to develop this fledgling school into a great institution, it would need bet-

ter financial support. They offered all of the assets of the little medical school to the State of Texas if it would become the second University of Texas medical school. The state accepted the offer and established the University of Texas Southwestern Medical School, with a state appropriation beginning in 1950 of $500,000 per year.

The first permanent building was completed in 1955, and growth was slow but steady through the l950s and 1960s. In the mid-1960s, the State of Texas made a major long-term commitment to expand and improve its system of higher education, including medical centers. Between 1965 and 1985, general revenue appropriations to UT Southwestern increased from less than $3 million per year to over $60 million, and the physical plant grew from 300,000 sq. ft. to 3,000,000 sq. ft. Similar changes were occurring at all the state's medical and general academic campuses. It was the golden age of Texas's public support of higher education.

The recession of 1986 precipitated a 14% across-the-board cut in appropriations to all of Texas's institutions of higher education. Since then, our funds from the state have grown in step with inflation but not in excess of inflation. Nevertheless, total growth at UT Southwestern has continued far more rapidly than inflation or state funding—but the increased funding for our continued expansion and enhancement of programs has to come now not from the state but from the private sector.

Between 1985 and 1996, UT Southwestern's total budget grew from $180 million to $450 million, with the state's contribution falling from over 40% to less than 20%. The physical plant has grown to 4 1/2 million sq. ft., again with the bulk of the new funds coming from non-state sources.

Growth in buildings and budgets is important, but facilities and funds, alone, don't make a great institution, of course. It is people who make a great institution. We at UT Southwestern are fortunate to have a faculty and staff composed of exceptional people. For example, we have four Nobel Prize winners on the faculty—more than any other medical school in the world. But, needless to say, it takes many more than four individuals to make a great institution, and we're fortunate to have a faculty now numbering almost 1,000 truly outstanding teachers, clinicians, and researchers.

Most people assume that medical schools have one mission, and that is to educate medical students so they can be awarded the M.D. degree. That is, of course, a central mission of medical schools, but it's only one of many.

We do indeed educate enrolled students, but not just M.D. candidates. In addition to our 800 medical students (200 per year), we educate 500 Ph.D. candidates and 400 Bachelor's degree and Master's degree candidates. The Ph.D. students are learning to do medical research. The Bachelor's and Master's degree students are learning allied health professions, such as laboratory technology, physical therapy, dietetics, and rehabilitation and counseling.

But perhaps surprisingly, enrolled students make up only half of our total number of trainees. We teach over 1,600 post-doctoral students, as well—individuals who have completed their M.D. or Ph.D. and come to UT Southwestern for additional clinical or research training.

Our educational responsibility for over 3,000 trainees is a primary mission, but like all other major academic medical centers, UT Southwestern also has other important missions as well, namely clinical care and research.

In the clinical arena, UT Southwestern's faculty physicians provide care for over 1.4 million patient visits each year. Over half of those are indigent patients at Parkland Memorial Hospital, Dallas County's public hospital, and the indigent care provided free by our faculty is currently valued at $150 million per year.

Until fairly recently, essentially all of our clinical activity was at Parkland, which lacked the space or facilities to care for the large number of elective referral patients who might want access to the expertise of our faculty specialists. Since the construction of Children's Medical Center of Dallas in the 1970s, the James W. Aston Ambulatory Care Center in the 1980s, and Zale Lipshy University Hospital in late 1989, however, we have been able to offer referral care on a broad basis, and the number of patients choosing to come to our faculty physicians has increased significantly. For example, the Aston Center had 50,000 out-patient visits in 1985 and 270,000 in 1996.

We've also had remarkable progress in the research arena over the past several years. You'll be seeing examples of that today in Dr. Evans's talk and on the tours.

Texas is fortunate in the strength of its medical research, but this is a fairly recent development. The late 1970s was the period when our state began becoming a major research force on the national scene, and I would attribute that to the major investment in its higher education institutions that Texas began making in the 1960s. It takes a little while to build up momentum.

For example, prior to 1979 scientists working in Texas were rarely elected to the National Academy of Sciences. We occasionally recruited some people who already had been elected, but the research being done in Texas was not leading to election to the National Academy.

Election to the National Academy of Sciences is probably the ultimate honor for American scientists, short of the Nobel Prize. Sixty American scientists are elected each year in all branches of science, including astronomy, chemistry, physics, agriculture, engineering, mathematics, and so on, as well as medicine. Nationally, about one-fifth of those elected each year are from medical institutions. Texas's first medical scientist in the Academy was elected in 1979 and it is interesting that since that time, one-half of all the Texans elected have been from medical institutions—a pattern quite different from the country-at-large. During that time, sixteen scientists have been elected from Texas's general academic campus-

es—two from Rice, one from SMU, two from the University of Houston, two from Texas A&M, and nine from UT-Austin. Sixteen medical scientists have been elected over the same period—three from Baylor College of Medicine, one from UT-Houston, one from M.D. Anderson, and eleven from UT Southwestern.

These numbers are something that Texans should be proud of. They serve as strong evidence that our investment in higher education has resulted not just in better education for students but also is providing the infrastructure to allow Texas universities to become research powerhouses.

UT Southwestern is fortunate in that having a large number of national and international research leaders has led to beneficial ripple effects. People of National Academy caliber attract grants competitively. They also attract other people who want to collaborate with them, both senior and junior, who, in turn, attract still other grants. They also attract the best students from across the country, who often stay on in Texas and in their own turn attract yet more grants.

So there becomes an upward spiral of increasing research activity, increasing research funding, and increasing numbers of leading researchers. The sharp rise in UT Southwestern's research activities is illustrated in Figure 1. In 1980, our faculty was awarded $25 million in competitive research grants. By 1996 that number had increased six-fold to $150 million per year.

I should point out that $150 million is not a larger total than several other medical schools in the country. However, we are also far from the largest medical school in the country. The average faculty size of the top twenty-five medical schools in the country (as ranked by *U.S. News and World Report*) is over 1,400, compared to UT Southwestern's 1,000. In terms of research grants *per faculty member*, we consistently rank in the nation's top ten, and our rate of increase is one of the fastest in the country.

Research productivity has important economic implications for Texas. UT Southwestern's ability to attract $150 million in research grants to Texas results in thousands of new jobs. Research also provides an opportunity for Texas to attract biotechnology companies, and thereby for our state to be part of one of the country's fastest growing new industries. And, when our research discoveries result in new products, Texas's medical schools can share in the proceeds of bringing the products to the marketplace.

In the mid-1980s, UT Southwestern established a technology transfer office, seeking to improve our ability to act in partnership with industry to bring research breakthroughs to the public (and, needless to say, to share in any profits). As illustrated in Figure 2, UT Southwestern's inventions in 1986 resulted in royalty payments and licensing fees from industry totaling a grand sum of $70,000. By 1996, that had risen to almost $3 million. This figure ranks seventeenth among all institutions of higher education in the country, including general academic campuses and medical centers.

Now, $3 million in the grand scheme of things is not an enormous amount, but the rapid rate of increase is encouraging. I am confident that, for all of Texas's universities and medical centers over the next decade, the numbers will continue to rise. Technology transfer efforts in universities will be an important source of revenue, and also an important means for making sure that talented faculty stay in academia and aren't forced to abandon their universities in order to see their inventions reach fruition.

But candidly, funds generated from royalties will never be sufficient to generate the revenues Texas universities and academic medical centers need to achieve and maintain excellence. So, where will the funds come from?

Clinical income is an essential and growing part of all academic medical centers' revenues. This income is vitally important to sustain the clinical enterprise and to fund charity care, but in an era of managed care it will never be a major source of funds to underwrite research and education. There are only two potential sources of sufficient funds to maintain and enhance the needed quality and scope of Texas's universities and medical schools: general revenue appropriations from the state, and private philanthropy.

As mentioned earlier, Texas led the nation in its public-sector commitment to higher education and research from 1965 to 1985. After a pause for the past decade, it is essential that we re-commit ourselves as a state—not just to maintain our current level of quality, but to provide the tax dollars necessary to build true excellence and national leadership. At the same time, we must realize that tax dollars, alone, will never suffice. We must rely on the private sector as well, if Texas is to match and surpass California, Massachusetts, etc., in terms of educational and research excellence.

We at UT Southwestern have been extraordinarily fortunate that, over this past decade of special need, the private philanthropic community has stepped forward to help us achieve our goals. Until the mid-1980s, we looked almost exclusively to state government for the provision of seed dollars for growth and improvement. Since that time we have had to look also to private donors—and they have responded magnificently. As shown in Figure 3 , UT Southwestern received $11 million from philanthropy in 1986 ($8 million from competitively-awarded grants from national foundations such as the American Heart Association and $3 million in gifts from local contributors); by 1996, that number had risen to $62 million ($22 million from national sources and $40 million from local donors). It is this remarkable outpouring of philanthropic support that has enabled UT Southwestern to continue growing and improving.

The story of UT Southwestern's rise to prominence is mirrored in many regards in a number of Texas's other leading universities and medical centers. In each, there has been an initial major boost from state appropriations, followed by a further boost from philanthropists. Both will be essential in the future if Texas is to rise to the ultimate level of achievement.

And now it is my pleasure to introduce the last speaker of our meeting. He is fairly new to Texas. His recruitment here and his success since arriving serve as excellent examples of how the investment of a combination of state and philanthropic funds in outstanding research leaders can propel Texas into worldwide prominence—and in the process, bring many more dollars into Texas than the initial investment.

Dr. Glen Evans is one of the world's research leaders in the Human Genome Project, about which so much has been said during this meeting. A few years ago, Glen was working at the Salk Institute in California. Thanks to major endowment gifts from the McDermott Foundation and the Biological Humanics Foundation (which also was founded by Eugene McDermott), plus matching gifts from anonymous donors along with core state funding, UT Southwestern was able to recruit him and his research team to Dallas. Since arriving here, his program has grown to become one of the ten largest Human Genome Centers in the country, and he and his colleagues have been awarded multi-year grants totaling over $20,000,000.

Glen serves as professor of internal medicine and of biochemistry at UT Southwestern, holds the Eugene McDermott Distinguished Chair, and is director of the Eugene McDermott Center for Human Growth and Development and the Center for Human Genome Research. It is a pleasure to introduce him to the Philosophical Society of Texas.

Sequencing of Genes

Glen Evans, M.D.

Thank you for all coming Sunday morning to hear me talk about the Human Genome Project. While I know it's hard to get up and listen to this, at least I'm convinced that anyone who's here must be really interested in this subject in order to be here this morning.

It's a pleasure for me to be able to speak with you, in part because I know you spent the last day or so discussing the Human Genome Project and have heard from a number of distinguished scientists here. So it's an opportunity now for me to give you some details about what it actually means, what it actually looks like, what we're actually doing, as well as give you some perspective from someone who's actually doing it, which may differ a little bit from those other scientists who are thinking about it.

Let me tell you from the outset, as Kern mentioned, the organization within the university, the McDermott Center for Human Growth and Development, is a research center which focuses on problems of human disease which are inherited or which have to do with genes, be they inherited diseases, cancer, birth defects, or others.

And within that we are carrying out what is essentially a large project funded by the U.S. government, predominantly the National Institute of Health, but also the U.S. Department of Energy. That project is called the Genome Science and Technology Center. A group of people that has been working on this since 1990 was translocated here from California two-and-a-half years ago, and has as a goal carrying out the Human Genome Project.

The Human Genome Project is unique in the annals of science, and particularly biology. It's the first large biological project equivalent to, in some ways, the Manhattan Project that developed the atomic bomb or the attempt and successful landing of a man on the moon in the 1960s.

The Human Genome Project has really three major goals. The first is making physical and genetic maps of the human genome. Secondly, sequencing all of the 3×10^9, or the three billion nucleotides that make up the DNA molecules in human cells. And, thirdly, and what's not always obvious to the lay public, is sequencing the genomes of selected model organisms for very specific reasons. Those model organisms include brewer's yeast (saccharomyces cerevisiae). It includes a very obscure small worm called caenorhabitis elegans. It includes the fruit fly (drosophila), the mouse, and several other organisms.

Sequencing those organisms is, in fact, as important for the future of human medicine as is sequencing the human genome. And I hope that you can appreciate from what I'll tell you why that is the case.

The Human Genome Project has a goal which will be achieved with a confidence exceeding 99.9 percent of having all of the three times 10^9 to the three billion nucleotides of the human DNA sequence determined by September 30, 2003. I'd like to emphasize to you the magnitude of that effort. The DNA sequence, is, of course, a series of letters—G, A, T, and C, all repeated one after another—in a complex, biological code. The information necessary to construct the kinds of organisms scientists are used to looking at, such as simple viruses or bacteria, is about two pages of the Dallas phone book, and would be two pages entirely composed of very small letters, G, A, T, and C, repeated in a specific pattern.

Brewer's yeast is about a third of the volume of the Dallas phone book. And other organisms occupy more. But the human genome would be eighty Dallas phone books completely filled with G, A, T, and C—several stacks of telephone books about this high—and an amount of information that, for scientists, would boggle the mind in being able to accumulate and being able to deal with it.

And the goals, in very specific terms, are to make a genetic map. That's the way we can find the locations of diseases that we find inherited through families. That's now been completed. The physical map, which is a schematic of what the genome looks like, was completed early last year. And the DNA sequencing of human and these other organisms began in earnest in January of this year.

I'll mention at least my perspective on the history of this unique project, which is quite interesting. It may differ from some of the things you've heard so far. Through a number of fairly important scientific discoveries in the mid-1980s, scientists found the ability and learned how to clone or to detect genes that cause diseases, when one didn't know anything about the gene or the biochemistry.

That is, if we could find a disease that segregated through a family, such as a kind of cancer or cystic fibrosis, or any disease that was clearly inherited from parents to children, it became possible, with a technique that was invented called positional cloning, to find that gene and to determine its sequence and figure out what caused that disease.

This was distinctly different than the recombinant DNA types of studies done in the 1970s where one had to know first about the substance, like growth hormone, and then figure out how to engineer bacteria to make it. The ability to find a gene, when we didn't know anything about it other than it segregates through a family, was a major scientific advance.

And because of that, over the ensuing ten years, scientists discovered the genes for a large number of important human diseases—cystic fibrosis, Huntington's disease, several types of breast cancer, lung cancer—hundreds of different inherited conditions. In fact, even today you read

every few weeks in the newspaper about the gene for a new disease being discovered and described somewhere in a scientific research laboratory.

This was an amazing advance. But it also created a major ethical dilemma in the way science was done in this country, which is there are 100,000 human genes, any one of which could cause a disease. Each of these large projects to discover a disease-causing gene took hundreds of people, millions of dollars, tens of years.

And the question is how could the U.S. government and the research funding agencies pay for this kind of approach for 100,000 genes. It was impossible. Then the question is, if we can't find every one, which genes are most important? Obviously, the ones that might be the most common and the ones in our country causing the most serious health problems. But, in fact, the most important disease gene to be understood is one that runs in my family, because that's the one I care about the most.

Because of this dilemma, to whom do we give the advantage when we're finding disease genes? A fairly radical idea was proposed in the mid-1980s—first proposed by Renato Dulbecco, a Nobel Laureate, who was, at that time, my boss and the president of the Salk Institute. He proposed that rather than finding diseases one after another based on the old paradigm, we should initiate a project—a crash project—to find all human genes in a very small amount of time—not to focus on diseases, but, first of all, to find the entire human blueprint.

The initial suggestion that he made was a library drawn by other scientists and became known as the Human Genome Project, and was an extremely controversial project in the late 1980s. But, in fact, a number of well-respected scientists, in particular James Watson and Francis Crick, managed to convince the U.S. Congress that this was not only a great idea, but it could be done, and it should be done.

And they established the Human Genome Project, which was officially initiated September 30, 1990. The goals of the project, as I've shown you, were to map and sequence all human genes. It was proposed it could be done for $3 billion, which was one dollar per base—three billion nucleotides, $3 billion—and it could be accomplished in fifteen to twenty years.

And my personal interest began in this way. One day at a meeting, James Watson came up after a talk, grabbed me aside, pulled me over to the side of the room, and said, "I want you to work on chromosome 11, and if you do I'll give you $2.5 million next year." We then began working on chromosome 11 for a variety of historical reasons.

As you'll see in our laboratory, the current effort is sequencing the entire chromosome 11, which is 150 million base pairs. Our criteria are that it will be 99.99 percent accurate. It will not be 100 percent accurate, and there's a very important reason for that. But we'll have no more than one percent in gaps because we know less than one percent is going to be extremely difficult to figure out. But those gaps will be well defined.

The reason the accuracy will be of this order is because not every per-

son has the same DNA sequence. And if we compare the sequence of you with your neighbor sitting next to you, it will not be identical. It will differ about one in every one thousand bases.

So if we are sequencing along, we'll never know whether these are inaccuracies or differences between two different individuals. And so at this level of accuracy, which is greater than the polymorphism rate, we would be able to extract all the information that we would need.

The final prediction of the Human Genome Project and the laboratory that you'll see later this morning came from another graduate of the Salk Institute, Michael Crichton. Michael Crichton was a post-doctoral fellow of Jonas Salk several years ago. He elected not to continue as a scientist, but became a science fiction writer, a screen writer, and a movie producer. And he wrote the book, *Jurassic Park*, in which he proposed a laboratory set up by a commercial company, which would sequence the DNA from dinosaurs, and it would extract the DNA from insects embedded in amber.

But in the book he described the laboratory, which was constructed as "two six-foot tall round towers in the center of the room, along the walls rows of waist-high stainless steel boxes. This is our high-tech laundromat," Crichton wrote. "The boxes are Hamachi hood automated gene sequencers, and they're being run by a Cray super-computer. In essence, you're standing in the middle of an incredibly powerful genetics factory."

Probably without realizing it, he described the laboratory that we constructed two years ago here at Southwestern and similar laboratories in about nine other centers around the U.S., which are designed to sequence human DNA at very high speed, using a battery of instruments that we call ABI, or Applied Biosystems—ABI 377 automated gene sequencers. You'll see a whole bunch of those. And in our case, run not by a Cray super-computer, which is obsolete, but by a Hewlett Packard Exemplar parallel processing super-computer. In essence this description from a science fiction writer is exactly what has come to pass for purposes of the Human Genome Project.

I know you've heard probably a lot about what the project is. But it essentially is taking all the human chromosomes, of which there are twenty-three, extracting the DNA, attaching it to the DNA of microorganisms, such as yeast or bacteria, as a laboratory trick in order to make lots of that material, and going through an increasingly high resolution series of lab techniques to generate maps of higher and higher resolution, and, ultimately, to come out with a complete sequence. You can see on the walls of our laboratory all of these maps stapled up on the wall as people work on different parts of it day in and day out.

It was anticipated that the first phase of the project, making the maps, would take about seven years or so. But, in fact, starting September 30, 1990, the mapping phase was finished within about five years, ahead of schedule, and, as of last year, it's completely finished.

The sequencing effort was thought then to take an increasingly large

amount of time, perhaps the next ten or fifteen years. We are now in a phase which is referred to among the organizations as the pilot project phase. That means we're trying to figure out how to do it. We know very well how to sequence DNA, but we don't know how to sequence fast enough in a large enough quantity. But we're very rapidly developing the techniques to sequence at incredible rates, which would allow the complete DNA sequence to be finished, not only on schedule, but ahead of schedule.

The initial plan was to have the human genome sequence finished by September 30, 2005, which would be fifteen years. Last year it became clear that this project was going so well that it would be possible to finish it by September 30, 2003, the current date. So I can tell you all with complete confidence that this will be finished on or before September 30, 2003. I remember that date quite well because it's my youngest daughter's birthday, who was born on the day the Human Genome Project was initiated.

These organisms, the model organisms, have already succumbed to this effort and been completed. The simplest bacteria, haemophilus influenza, was finished in July of 1995; brewer's yeast was finished in June of last year, and, as I'll show you in a minute, had some fairly profound implications for understanding of humans; the simple worm, c. elegans, will be finished in 1998; and the human sequence in 2003.

The reason these organisms are selected is for a very specific intellectual reason. The brewer's yeast is the simplest eukaryote—the simplest organism with true chromosomes—a single cell yeast that grows in liquid media.

C. elegans is the simplest animal—the simplest multi-cellular organism. It's a very small worm that has only 1,000 cells in the entire organism. So yeast will help us understand basic biochemistry and metabolism. But the worm will help us understand how animals are constructed. And all of the other model organisms are selected for very specific reason about what they tell us about the function of human beings.

I'll now tell you a little bit about the Genome Science and Technology Center here, what the people are actually doing. Our targets are initially chromosome 11, then chromosome 15, then chromosome 14. We anticipate in Dallas sequencing somewhere between fifteen and twenty percent of the entire human genome. There will be at least another five centers who will take up the other portions of the genome so that the entire thing will be completed on schedule. The Stanford group, for instance, is working on chromosome 4, another group on chromosome 17, and the effort is coordinated to avoid duplication.

This is what I referred to as a map of the chromosome—doesn't matter to you what all these things are, but these are the landmarks with which we will begin sequencing. An investigator in the laboratory would decide to take one of these markers here, and determine the DNA sequence of a large region surrounding it.

He would go to our computer data base, call up that region in the computer. Each of these dots and lines represents a fragment of DNA, or a clone in the freezer. He'd then go to the freezer, pull out the drawer, count, pull out that particular fragment, and then subject it to a process I'll discuss later.

Genome Science and Technology Center has really three main efforts. It's a well-structured and fairly large organization for an academic medical center. The mapping group determined the kind of maps I just showed. The sequencing group operates the high-speed DNA sequencing equipment, as well as the computers that assemble it and put it together and try to interpret it.

And because we're in a development phase, a large percent of our effort is in the area of automation. Our philosophy here, as opposed to philosophies at other universities is, in fact, to scale up the rate, but not to scale up the number of people. If we are able to sequence at a certain rate the best way of increasing that is just to hire more people—double or triple the size of the group.

We prefer the idea that if we can work at a certain rate, and we can utilize robots and automated equipment, we can then vastly increase the rate without increasing the number of people. That has the advantage of both getting the genome project done quicker, but also being able to sequence virtually anything. DNA is DNA. And should we decide to work on some other projects after this, the infrastructure will be in place.

The Genome Science and Technology Center is on the order of fifty people right now: the mapping group, the sequencing group, cloning support groups, and automation group, computer support, administration, and so on. I'm the director. My colleague, Skip Garner, the associate director, is a Ph.D. nuclear physicist who is responsible for all of the computer support and technology development.

And the goals we have, in fact, are to develop the laboratory you'll see and the infrastructure to carry out mapping and DNA sequencing at a rate of 100 megabases a year. We are currently probably the best DNA sequencing laboratory in the world, or at least equivalent to those, and we sequence at about four megabases a year. So we still have a substantial amount of scale-up to be done, but have a lot of technology in place to do that though, I think you'll see.

Obviously, our goal is to determine a portion of the human genome sequence as part of the Human Genome Project, about fifteen to twenty percent. We have about a third of the effort devoted to the development of instrumentation—robots, computer programs—to support high through put human genome sequencing.

So not only are we doing it, we are developing the tools. If we were sending a man to the moon, we are now in the phase of developing the rockets in order to allow us to go there.

And, finally, we are very aware that when the genome sequence is finished in 2003, which will still be within my viable scientific lifetime, we

would like to be able to use that information for the benefit of scientific research and clinical strategies in the most efficient way. One of the advantages to us in having this high-tech basic science factory in the middle of a major medical center is the potential speed which discoveries in the lab can be translated into tools that could be used in the clinic.

So the organization really is five groups: mapping; sequencing; infomatics or data processing, which you'll see; supported by a resource group and an automation group. They interact in this way. The space actually looks like this. You'll walk through. As you come out this hallway here around this floor, the mapping lab is located here. We'll walk through that, through the DNA prep lab to the DNA sequencing floor, the genetics factory Michael Crichton talked about, out this door, down this corridor to these labs, and then past the infomatics suite, which is located here.

As you'll see, the computer support for this is a substantial part of the entire operation. In addition to the traditional kinds of microcomputers and work stations, we operate the Hewlett Packard super-computer, which now holds the world's speed record for processing biological data and information. It's certainly the only super-computer in an academic center in this part of Texas.

As you walk through—I'll show you in a few minutes some of the pictures of what you will see. I would, of course, point out to you this is Sunday. There will be a few people working in the lab, though not a lot. Our usual schedule is to operate the sequencing lab twenty-four hours-a-day, seven days-a-week. But for the month of December, we've actually cut back on our Sunday runs. So it won't be occupied as it usually is.

I'll ask you please don't touch anything. But, more importantly, don't let anything touch you. Much of this is automated with robots, which occasionally like to reach out and grab someone. And I think they're all turned off. I was walking through a little while ago.

A normal laboratory technician in a traditional lab, such as you'll see on other floors of this building, will sit down in the morning at a laboratory bench and carry out some experiments with a pipette. One of the most dismal and boring things is extracting the DNA from microorganisms in order to sequence it. A normal technician will do maybe ten or twenty samples a day before they finish. And that's fine for most kinds of normal laboratory operations.

However, our laboratory uses so many samples—thousands a day—that we developed in our automation shop these three DNA automation robots, which are—they don't look like R2D2. It doesn't look like what you expect a robot to look like. But it's laboratory equipment controlled by a robotic arm and programmed by a computer, where one of the technicians, Lisa, can load in 200 samples into each of these machines, walk away, and it will generate the results of those in a few hours.

So our genetics factory actually is almost entirely automated at this step. And these machines for a while were operating day in and day out, making DNA. They currently don't work so often because we've made

DNA from virtually every DNA sample in the entire building. So they've kind of put themselves out of business.

I'll just tell you an interesting story—that these were invented by my colleague Skip Garner, who gave them—they do DNA preps—so he gave them the name Dr. Prepper, which we thought was really cute because it does DNA preps. And, as scientists usually do, they like to talk about their work. We talked about this at a number of meetings, but were surprised when a local soft drink company was not amused by that. And we received several letters asking us please to change the name so that we wouldn't take the danger of anyone confusing our robots with that local soft drink. So these are now known as Prepper Ph.D. machines.

A second, new robot was installed in the fall as a collaboration with Saigian Corporation, which two weeks ago was bought out by Beckman—so we're now collaborating with Beckman. This is called an ORCA-robotic arm. These devices are standard laboratory machines that a normal technician would use. These are pipetting machines here. These are thermal cyclers here. This is a plate sealer. This is a refrigerator which has a robotic door.

But this robot can move along this three-meter rail and transfer things from place to place under computer control, and can do the equivalent of what a laboratory technician would do, taking things from one place, putting them in another place, starting up the machine. And the goal of this machine is to be able to run twenty-four hours-a-day, seven days-a-week, preparing the samples to go in the sequencing machine, that would, at the present time, generate about 15,000 samples a day.

A normal technician could do maybe 200, so one machine like this can really replace a whole laboratory of very bored, uninspired people. Those bored and uninspired people can now start studying the biology of what these things mean.

Another development in the laboratory is this device, which is a DNA synthesizer. For particular parts of the sequencing project we need to sequence—once we know the sequence, we need to chemically synthesize that sequence in order to step down to the next portion. And this machine is programmed directly by the DNA sequencers, who can control this to now make the next priming step.

This is a photograph of the DNA sequencing floor. Each of these boxes is an automated DNA sequencer. It works in a way I'll show you in a minute. Each has a computer. Each is located on a moveable cart with wheels, so when it breaks down we can roll it into the shop for repairs and roll in a replacement.

We were very fortunate in moving to a institution where the administration is so forward thinking and, in fact, confident about their ability to recruit from elsewhere. Skip Garner and I had designed this entire 10,000 square feet of laboratory space. It has a lot of unique features, like these ceiling plugs. It was actually under construction before we ever committed to coming to Southwestern, which shows the confidence they had that

we wouldn't turn them down. This laboratory is the heart of the entire operation and is the one that, in most cases, except for this month, is running twenty-four hours-a-day.

How are we actually doing the DNA sequencing? What does it look like? Each small piece of the human chromosome—and there are 3,250 pieces that are being sequenced—each one is subjected to a biochemical reaction, which essentially uses an enzyme to make a copy of it.

One of the remarkable things about DNA is that it not only contains information, it contains the information of how to replicate itself. We can, in a test tube, add back this substance which will copy it. And when it copies the DNA sequence, we put into the reaction the components that are labeled with fluorescent dyes of four different colors—yellow, blue, green, and red. And as the DNA strand is copied those colored dyes are incorporated into that strand, and we can detect those in the automated DNA sequencing.

What the sequencer does is it runs these fragments that are now labeled with colors through the machine. It's detected by a laser. The laser uses a photo-multiplier to determine what the color is. And the computer then interprets that as the sequence. So the colors—here in this case it's black, green, black, blue, green—can be read off as A, G, C, C, A, G, A, T, and so on.

When the machines operate you may see, if they're in operating mode this morning, these kind of colored patterns coming out. Each one of these is a small piece of a human gene. The sequence can be read off by the colors—green, yellow, yellow, green, green, yellow, green, green, and so on. That's a difficult way for us to look at.

What the computer does is interpret it like this—as a tracing where each peak is a different base in that sequence, and the computer will interpret this as T, G, G, T, A, G, A, A, G, G, T, T, and so on, by the pattern of colors that come out past the laser.

And, remember, the two important things: it takes only three billion of these to give one the entire instructions for how to construct a human being, and it takes only one of these to be incorrect in order to cause a genetic defect, like cystic fibrosis or Huntington's disease or breast cancer or thousands of other diseases.

This again is not particularly useful on the large scale. And we've instigated a procedure using the Hewlett Packard super-computer for very rapidly interpreting the sequence as something we can understand. This is a collaboration with Hewlett Packard. And this is a picture of the machine. It looks nothing like a fancy computer. It looks like a big monolithic box. But it does have these nice colored lights on the side, which I think they put on just for our entertainment.

What that machine comes out with is a sequence that looks like this: T, T, C, T, C, A, and so on. This is a very small portion of the entire instructions for the human genome. You can't see by scanning through this anything other than an uninterpretable code. But the super-computer

can convert that into a diagram like this, which shows us actually some idea of what's there.

It marks for these boxes anything in red that is a gene we already knew about—a gene already discovered for some reason and present in a large database called gen-bank. It marks in blue any sequence which the computer predicts, based on the rules we've given it, that it must be a new gene, or it is likely to be a new gene that wasn't described before.

And those things in green are sequences that are highly repetitive in the human genome—that are repeated over and over and over again. That used to be called junk DNA, but, in fact, we know are not junk at all. In fact, they're quite important and have a lot to do with the ability to locate disease genes. So these are important mapping tools. And lots of other kinds of information can come out as well.

The reason that this is so important comes from something that was appreciated by scientists in April of last year when the sequence of brewer's yeast was completed. Yeast is, in fact, more similar to humans than we could possibly imagine, in that when the sequence of the entire yeast genome of about fifteen million base pairs was finished it was found to contain about 6,200 genes—actually the exact number is known. It's 6,183, I believe.

And when one categorized those genes, according to this pie chart, the genes in red are those that we already knew something about—or we know what they do. We have some idea of what their function is. And that's a very small percent of all of the genes present.

In fact, most of the other genes have never been seen before. Some of them we can guess as to what they might do. But there's a very large percent of genes here in purple where we, in fact, don't know anything about them. We don't know what they do. We don't know what their function is. And we never would have discovered them without this approach, through sequencing the human genome.

The bottom line is that the amount of information that will be new that will come out in the next few years will be incredible. And we can confidently tell the medical students at Southwestern Medical School that ninety-five percent of everything known about human genes will be discovered between now and 2003. So by the time they graduate, our view of human biology will be dramatically shifted.

There are two other aspects I'm going to mention briefly before we go out on the tour. The first is, like other large science projects, particularly like the NASA project to put a man on the moon, there are a lot of technical offshoots of this project that will be useful for things other than just the sequence of the human genome. There are hundreds of different discoveries that are having really enormous effects in pharmaceutical manufacturing, in genetic research, in forensics in legal settings, and in many, many things. I'm going to mention one offshoot of our work which we think will have a big impact—the idea of DNA chip—because it's something else going on here. Obviously, when we sequence the human

genome, we will conceptually have resolved the information for how to make a human being into 3,000 megabases and put it on a CD Rom in a computer somewhere. It will take up about 750 megabytes.

The next goal, or the next challenge, is how do we use that information in a very rapid way to go back into the clinic or the laboratory and read that out in any particular individual. Another way of looking at that is what we are sequencing is a generic human. Completing that project in 2003, our next goal is to figure out how to sequence a specific human, that is, how to determine the complete sequence of any individual, for medical purposes or other purposes.

A concept that a colleague of mine, Mike Heller, and I had several years ago was to do something very far out—to develop a microchip—a computer chip—that might look like this and plug into a computer and might have a test reservoir where one could put a sample of material with DNA and have that genetic material interact directly with the microprocessors. This was so far out, in fact, we couldn't get a grant to do it from any funding agency.

So we did the next best thing. We started a company, which is called Nanogen. It's in California. And they will next year release the first commercial DNA microchip. It looks something like this. It has twenty-five different test sites on this version of it. Each of these little fifty micron locations is a genetic test for a specific thing, be it an infectious disease, a genetic disease, or identity for forensic testing. The chip looks like this sitting on my finger. This particular one has sixty-four test sites in that little teeny dot in the middle.

The results look something like this. This is the set of DNA test sites. Each of these tests for a different DNA sequence. When one is positive, one of them lights up like this. It sends an electronic signal to the computer, and the answer comes out, this person is positive for this disease.

The important thing about it is it's entirely automatic and it takes about five seconds. So it makes possible, in principle, the kind of device one sees on television on "Star Trek," where one can pull out of one's pocket a small meter, rub it against someone's skin, and read out their entire genetic makeup. And we expect that that will be possible within about ten years.

The last thing I'd like to mention is that, obviously—and I'm sure one of the sources of discussion you've had—is that all new genetics, but particularly the Human Genome Project, has specific ethical issues which have been created or amplified because of the magnitude of information.

This is not a surprise to the scientists involved in it. In fact, it was anticipated from the beginning. And, for that reason, about five percent of all the money put into genome research has actually gone into studies of legal, ethical, and social issues, as well as education.

Some of those issues which are fairly well known and discussed include commercial impact and patenting, that is, who owns the genome

and should patents be allowed on it; genetic privacy—whose genome is being sequenced; genetic testing, genetic liability, predictive liability in insurance. And something which I think is not talked about at all that's a particular concern of mine is the inappropriate use of this genetic information for purposes such as biological weapons.

The conventions that have been adapted as of March of last year by an international group of scientists who are actually doing this really holds two principles foremost. The first is that we have agreed that we will not patent raw genetic material from the Human Genome Project—that that is an unethical use. It doesn't mean that patents can't be held on particular uses of the sequence, but that no one will try to patent the whole genome, or copyright it.

And, secondly, that the entire sequence will be in the public domain and will be freely available to anyone who wishes to use it, which, again, brings across this concern here about the free availability of the information, even for those that would use it unethically.

These are all questions that are being discussed and that will continue to be discussed for many years. But I'll point out that there will be many other offshoots that will have good and potentially concerning issues.

One of the scariest offshoots of the Human Genome Project, which I'll just mention to you, is, in fact, the Dog Genome Project, which was initiated several years ago to, in parallel with humans, characterize the genomes of dogs. Why would this be scary because dogs are a fairly benign organism? There are projects, of course, to work on the rice genome in Asia, the bovine genome here in Texas, and many other animals for their commercial and agricultural work.

But the dog, in my mind, has a particular concern. The concern is this. Dogs, through human civilization, have been bred for their behavioral traits and for their ability to carry out certain behavior. And their behaviors are quite distinct and quite demonstrable.

The Dog Genome Project is based on the principle of crossing a labrador with a border collie—each of whom has specific behaviors, analyzing the pedigrees, and mapping the diseases, not for genes, but for personality traits. And the kinds of personality traits that will be almost certainly located and converted into digital information will be things like eye contact with the owner, tail posture, barking, but also things like affection, response to family members in water, sociability to other dogs, aggressive behavior, and many other things.

We have learned from our studies of yeast and worms that every gene we find in the lower organism will be represented in humans, without any question. And if we find genes for affection, sociability or sociopathy in dogs, we will find equivalent genes in humans almost for sure, which would allow us, with technology ability, to actually screen individuals for the personality traits that might be desirable or undesirable.

In my mind, the idea of screening inductees into the U.S. Army for

aggressive genes is quite scary. And whether or not those things should come to pass remain to be seen.

So, with that, I'll finish. We can go onto the tour. I'll point out to you that the Human Genome Project is something that's of great excitement to all of us here. We've been working hard on it for a number of years, even before coming to Southwestern.

It sometimes strikes us as a project of immense magnitude. But, in fact, it's not all that great a thing when compared with other large structures in the universe. And when people say, "Oh, my God, three billion nucleotides—how are we going to do it?"—I just point out to them then that there are actually three times 10^{11} stars in our galaxy. So compared with that this is actually a small project.

I thank you very much, and I'll be happy to answer any questions.

WHAT PRICE DESIGNER GENES?

The Genetic Revolution

MICHAEL B. BEVINS*

SINCE THE MIDDLE OF THE TWENTIETH CENTURY, the field of molecular genetics has grown enormously, creating new ethical questions and urging the discussion of old ones. The identification of DNA as the genetic material in 1944, the discovery of the fundamental structure of DNA in 1953, and the development of molecular recombination in the 1970s stand out as the definitive events in what is often called the genetic revolution. And while most of what genetic research has allowed, and will allow, us to do already occurs in nature, this new technology will give us unprecedented control over our environment and our bodies. So much control, in fact, that some people are at the same time overjoyed by the potential benefits and terrified by the potential dangers. However, the perceived benefits and risks of any developing technology may be unwarranted, and the genetic revolution seems to be at increased risk of being misunderstood in this respect. In fact, because of the nature of the genetic revolution and the context in which it is taking place, the ethical implications of the new technology should be pursued with no less effort than the laboratory research.

The dichotomous nature of molecular genetics is that it is at the same time so esoteric and so pervasive. With this in mind, the movement of genetic research from the expert's lab to the public must be carefully ushered by evaluation and discussion of all possible implications. In the words of Harold J. Laski, "Expertise consists in such an analytic comprehension of a special realm of facts that the power to see that realm in the perspective of totality is lost." Even something as major as the theory of relativity by and large avoids this difficulty because it doesn't really change much in everyday life. Most people are ignorant of Einstein's theory and are not the least bit troubled because of it.

However, genetics will not be content to stay out of our lives; the context in which the genetic revolution is taking place makes it an impossibility. We are now more dependent than ever on increasingly specialized science and technology. Most business is dependent on complex computer systems which require experts to install and repair; when we get sick we consult a doctor who knows how to treat more of our illnesses now

than ever before; and where would most of us be without our car, and our car without our mechanic?

The genetic revolution will force us to consider how dependent we are, and are willing to become, on science. This new technology will reach into the fields of medicine, agriculture, even reproduction. As more diseases become curable, and preventable, we will go to the doctor more; as reproductive gene therapies develop, it may be considered irresponsible to have a baby without first "designing it"; in short, for any problems that arise from this new technology we will look to technology to help solve.

But what is so terrible about becoming so dependent on science? After all, as G. J. V. Nossal and Ross L. Coppel note, "Science and technology have been embraced by people all over the world for one simple reason: they work." Indeed, many of our modern conveniences are the results of scientific research, so the question to be asked may be for whom and to what end is genetic technology going to work. The responsibility for scientific discovery and development lies with the scientists, but the responsibility for its application lies with all of us. Perhaps the danger of dependence is our unwillingness, or our inability, to accept this responsibility.

Perhaps then, we have ourselves to fear more than new genetic technology. But what we must never forget is that science is a human endeavor and as such, no matter how ambitious it may be, it can never usurp our humanity; while genetic technology will surely alter the circumstances under which we make decisions, it will not render us impotent with regard to those decisions.

A major concern with regard to genetic technology relates to control and accessibility. Ideally, everyone would have equal input into all genetic technologies affecting them, but this is simply impossible, and in today's world of large corporations and governments, the line between which is sometimes blurred, it is frightening to think of what factors will motivate the development and use of genetic technology. For most people, the prospects of eliminating devastating illnesses and of feeding the world's hungry are reasons enough to pursue genetic research, and indeed these are wonderful goals. However, even if genetic technology makes it possible to feed everyone in the world, I doubt it will happen. Already, some people eat too much and some eat none, while tons of food go to waste. The problem is not that there isn't enough food for everyone, it is that some people simply cannot get the food there is. I point this out because it seems unlikely that along with new food crops we will develop exceedingly generous patent holders who, despite spending millions of dollars developing new seeds, will be willing to feed the poor and hungry of the world without making a huge profit. The corporations funding the research will hold the patents and therefore control the food supply, perhaps even more easily than they do now. Similarly, medical advances in genetics will cost billions of dollars to develop. The overall health care

costs in some cases will surely go down, as it will be less expensive to prevent disease before it starts than to treat it once it has surfaced. Arthur Caplan notes:

> It is very resource intensive—and thus very expensive—to transplant a liver from a cadaver to a child whose own organ is failing because of a congenital disease. Pediatric liver transplants require skilled surgery, long hospitalizations, many transfusions of blood, perpetual suppression of the patient's immune system and extended counseling for the family and child. Identifying fetuses at risk for congenital liver disease during pregnancy and then repairing the disorder by gene therapy should prove considerably cheaper, particularly if such therapy could be given once, early in life.

Furthermore, would it not be easier for someone to deal with the fact that their genes were altered before they were born in order to save their life than it would be to deal with congenital liver disease?

However, the new genetic technology will probably be very expensive at first, although it will surely become less so over time. Many critics cite this as a negative because few people will be able to access genetic technology. And with health care costs so high that few people can afford them without insurance, genetic engineering will force a total reevaluation of the health insurance system. For if insurance companies begin to require genetic screening for applicants, coverage may be denied on the basis of a predisposition for a disease that cannot be easily treated. Although it is impossible to precisely foretell what will happen to the health insurance industry as genetic technology develops, it is safe to say that genetic screening will be available long before treatment. The Human Genome Project is now mapping the genetic location of many diseases, but it will be many years before these diseases can be genetically treated. Therefore, insurance companies will be put in a very difficult position. To use technology that will put them at such a huge advantage over the consumer may seem good for business; on the other hand if, as has been predicted, everyone carries a few deadly diseases in their genes, who will get insured?

Consequently, socialized medicine may become more attractive, even necessary, as private insurance is compromised. Indeed, governments may have to intervene more often, as the U.S. government did in the summer of 1996 when it passed a law prohibiting the denial of coverage to someone because of a predisposition for a disease. Will future governments, who have funded so much of genetic research, be the ones to ration it out?

Perhaps I am conservative, but I really don't think most, if any, of the changes to either medicine or agriculture will be perceived as catastrophic. It is too early to tell whether genetic technology will be able to cure poverty, which is the cause of most starvation and lack of medical care. Perhaps it will make things more affordable for everyone, but I am skep-

tical. The problems, in my opinion, are much larger than biotechnology; they have a lot to do with the kind of people we are, and although my genome makes me human, it does not make me a person.

The prospect of being able to choose our children's characteristics before they are even born is perhaps the most staggering of all. Germ-cell gene manipulation is repulsive to some people simply because it degrades the miraculousness of child birth, but this is just a reaction to a shattered illusion. The selection of characteristics is simply a part of reproduction; the real problems may come from our inability to properly manage the enormous conscious control we will have over what our children will be like.

A legitimate fear is that of the selection of polygenic traits, or those determined by many genes, such as talents and intelligence. "Who will decide," Arthur Caplan asks, "whether characteristics such as short stature, baldness, albinism, deafness, hyperactivity or aggressiveness are classified as diseases rather than merely differences?"

However, no matter what their classification, I think most people have already decided whether such traits are desirable. Whose rights do they violate if a couple chooses to have a smart, tall, tanned child? None of us had any input into what we would be like, and it is ridiculous to confer rights to non-existent things, so it can't be the child's rights that are violated. It may seem cruel to admit that we would not choose certain traits in the presence of people with those traits, but no one is perfect, and no matter how much we manipulate a person's genome, no one will ever be.

My point is that we cannot give our genes as much credit as we often do; we cannot agree with James Watson's statement: "Really to understand ourselves, we're going to have to understand our DNA." Are we really willing to admit that we are nothing more than pre-programmed robots? This debate goes beyond the nature/nurture issue, for whatever good and bad comes from genetic technology, and I think there will be plenty of both, we must never lose sight of the fact that what is valuable and beautiful in people is not found in the nuclei of their cells; it is found interpersonally. The real danger of designing our children's genes is the fundamental change in perspective that it will precipitate. Will parents who selected an athletic child be disappointed when that child chooses to play the violin instead of football? I think they will, and we can anticipate a lot of lawsuits in such cases. The real danger has nothing to do with labs and mutant strains, it has to do with how we view ourselves and each other, views which, if we're not careful, will ignore the differences that aren't based on genes but on circumstances and experiences. Each one of us does wonderful things in our life, but they will seem much less so when scrutinized against the backdrop of our genetic blueprint.

Therefore, the genetic revolution is neither to be feared nor avoided. We should pursue all possibilities simply because they are possible, and with our choice intact we will come out of this revolution on top. For the scientific knowledge we acquire will be amoral; we need to concern our-

selves with how that knowledge will affect how we act with regard to each other.

For me, the genetic revolution does not degrade me as a person, rather it reaffirms what it is to be a person: my sense of self, my choice, in short, the indeterminability of personhood.

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READY OR NOT?

Designer Genes and the Genetic Revolution

ANGELA PETERS*

> *So hard for me to realize.... A mother, and all this dirt, and gods, and old age, and disease....It's almost inconceivable. I shall never understand ...*
>
> —Aldous Huxley, *Brave New World*

UNTIL 1865, when Gregor Mendel first published his results of simple genetic crosses, nobody really understood the origin of inheritance. Although Mendel worked within the context of other early geneticists,[1] it was his postulates that set the stage for the genetic revolution. Today we live in the throes of the genetic revolution. Around the year 2003, the Human Genome Project will have located, mapped, and sequenced the entire complement of human genes. We have reached a crucial point in our history—this is a time when we must define for ourselves vital questions, and earnestly seek out their resolution, if we are to avoid a baseless society prone to repeat the mistakes of other eugenic eras.

Regardless of the ideological framework in which this occurs, theologians, philosophers, and scientists can all agree, at least, on the general problems we face as we become capable of manipulating our genetic ingredients. We can now predict whether an adult will be susceptible to Huntington's disease or colon cancer; we can now determine whether a fetus will be born with sickle-cell anemia or Tay-Sach's disease; and soon, as the genetic links become more clear, we will be able to foresee who will be prone to alcoholism, to cancer, even to obesity.[2] We are now experimentally treating diseases like familiar hypercholesterolemia, cystic fibrosis, and muscular dystrophy with gene therapy. When we succeed, what next? At what price? Those concerned with the ethical consequences of designer genes, genes specifically designed to remove "undesirable" or add "beneficial" traits, must focus their attention on these questions. The genetic revolution will move forward regardless of our readiness, and the consequences of genetic manipulation touch both the individual and society: at stake is the very definition of what it means to be human, and where humanity is heading. It is imperative that this emerging science be guided by an awareness of the ethical implications of genetic intervention, the moral and practical questions it raises, along with the deeper philosophical consequences—for both the individual and society as a whole.

What Is a Human Being?

> *Learn from me, if not by my precepts, at least by my example, how dangerous is the acquirement of knowledge and how much happier that man is who believes his native town to be the world, than he who aspires to become greater than his nature will allow.*
>
> —Mary Shelley, *Frankenstein*

One of the most important questions that can be raised, if we are to find a place for genetic manipulation, is what is it that makes a human being? To what extent do the genes we carry determine who we are, to what extent does environment play a role? Is there such a thing as a "soul," or "destiny"? When does life begin, and when does it end? Certainly, as can be seen from any one of the numerous issues that can be derived from any one of these questions, or from the thousands of years of philosophic and theological tradition from which they arise, there is no ultimate answer. Perhaps what is more important is the examination of what is implied about who we are in the questions themselves.

To be a human being is to be composed of things material and immaterial. Regardless of the conditions put on that statement, or the vocabulaly applied, most would agree: we recognize the physical aspects of our existence, like cells and DNA, as well as the mental aspects, like experience and ideas. Only the mentally ill person would deny that we are composed of physical stuff, but few are comfortable with the restrictive biological meaning of life put forth by biologists such as August Weismann (1834–1914)[3]—that the function of the body (soma) is to be the protector of the germ-cell line (gametes) so that a species can be perpetuated, ensuring survival. Surely there is more to our existence than to ensure the perpetuation of our gametes? Isn't that why we have God, music, love, and poetry, and suffering, disease, violence, and racism? How do genetic manipulation and designer genes fit into this equation?

From a naturalist point of view, positive and negative arguments can both be made for human genetic manipulation. Many biologists feel that, at least at this stage of human history, altering the germ-line of individuals, which would allow the passage of traits from that individual to his or her offspring, would probably not be wise considering there is no way to tell the long-term, evolutionary effects it will have.[4] Many feel, however, that it is okay to alter somatic genomes so that disease-causing genes can have their effects removed. Examination of the literature seems to show that most biologists feel fairly confident of society's ability to regulate and control genetic manipulation.[5] Some point to the 1978 Belmont Report, which distinguished ethical from unethical research practices in order to protect the research subject, as an example.[6] The primary motivation for genetic manipulation among scientists is to see the alleviation of suffering.[7]

A question arises, however, when one attempts to define *suffering*.

The case for genetic manipulation seems more obvious when we consider such painful and debilitating diseases as Tay-Sach's, or sickle-cell anemia, or even non-life threatening but life-altering diseases such as retinitis pigmentosa (which causes gradual disintegration of eyesight into blindness). But when we become capable of identifying genetic links to conditions such as baldness, tallness, intelligence, and obesity, the word *suffering* becomes more shadowy. Here a distinction between euphenics and eugenics[8] starts to be less clear—where will the implications lead us? A return to the eugenics era, when sterilization in this country was mandated for "sexual perverts, drug fiends, drunkards, and epileptics," not to mention "imbeciles, idiots, convicted rapists, and habitual criminals"?[9]

From a more philosophical point of view, it is difficult to determine if genetic manipulation will somehow alter the dignity of humanity by usurping ontological conceptions we have about our existence. For instance, if I am a chronically depressed person—and by my depression am able to be moved into brilliance and so have made a notable and fruitful existence as a painter, thus contributing forever to human history and culture—who seeks gene therapy and becomes "cured" and now am happy, losing in the process a distinct genius in my work, where did the source of that genius lie? Was it a product of the natural components of my body, my genes, or was it something less tangible, within the realm of the enigmatic aesthetic? Some[10] argue that if we begin to identify qualities we might say belong to the "soul" as purely physical traits, capable of alteration, we become trapped by a reductionist argument of biological determinism; trapped because we lose the meaning of mental aspects of existence, becoming nothing more than vertebrates participating in an endless cycle of biological perpetuation. This raises, to the philosopher at least, a question of teleology: does humanity have a special destiny, a special place within the universe? It seems that if life is reduced to genes, and "biology is destiny" as Sigmund Freud proclaimed,[11] then what use is history, moral good, or life itself, if all we are to accomplish is procreation and survival, without embellishment? Little wonder there was a turn to existentialism in the beginning of this century. The philosopher must be concerned with how to preserve human dignity, meaning, and purpose, as we begin to meddle with things heretofore left to chance, destiny, and God.

What is the Impact on Society?

> *What did other people's deaths or a mother's love matter to me; what did his God or the lives people choose or the fate they think they elect matter to me when we're all elected by the same fate, me and billions of privileged people like him who also called themselves my brothers...[they] would all be condemned one day.... What would it matter.... ?*
>
> —Albert Camus, *The Stranger*

The freedom to make choices in North America is the highly prized

legacy of our democracy. But should we be allowed to make choices that involve interfering with our genes? When would a decision to alter some component of a person be acceptable, and what kind of precedent would such changes set for society? Are human beings capable of making responsible decisions? Are we wise enough to restrain the power to alter life? What will be the basis for those decisions? What ethical system should we use? For millennia philosophers have debated over theoretical frameworks by which we can judge the worth, or goodness, of human actions. Never before, however, has society been confronted with such an urgent need to come to some general agreement over which ethical system to use, or the criteria we should adopt, when we make decisions about the right to choose to alter our genes. Can the law keep up with the progress?[12] And who, in the end, will make those decisions?

The impact on society that new genetic insight into diseases has had is already apparent. In an interview with Vicki Quade, the editor of *Human Rights* magazine, attorney Theresa Morelli asserts that without legislative protection, those who are at risk of genetic disease, or who have a genetic disorder, will be uninsurable and forced onto Medicaid or welfare.[13] As an example of the power of insurance companies, there have been examples of HMOs telling parents that if they carry a fetus to term with a known genetic disease, they will not pay for the baby's medical expenses or for the pregnancy.[14] Most states do not have laws regarding genetic testing; Wisconsin was the first state to outlaw it.[15] If we give the power to insurance companies, who are concerned mainly with the economics, to make these precedent-setting decisions over good genes and bad genes, then could it be possible that someday those who carry the "bad" genes will be forced to change them via gene therapy? Maybe not forced, or culturally mandated, as in *Brave New World*, but forced in that it will become economically necessary, for both the individual and for the insurance companies? In other words, will we be left with no choice?

Following the same line of argument, if society makes these kinds of judgments under the pretext of economics, what can we say about the value of those who carry genetic disorders, and are either incapable or unwilling to change them? Should it be forced upon them? Should they be "terminated"? Should they be ignored, and left to brutal nature? Who should take care of them? If one can imagine this future, it seems highly likely that nobody would feel a need to value such individuals, because what makes such individuals different, in some ways disadvantaged, would be seen devoid of its humanity, would be seen as a blatant badge of defect in every biological and economical sense. Is this a slippery slope? No. One needs only to be reminded of Hitler's Nazi Germany. Furthermore, these kinds of attitudes lie dormant in everyday culture. When paging through a medical textbook, under headings like "deformity" and "defective," there are pictures of Down-syndrome adults, adults with hemophilia, children with sickle-cell anemia, thalidomide babies. The current critical issue of euthanasia is making it more socially accept-

able to find reasons—practical, economic, moral, or otherwise—why someone with a disease should die. Society must remind itself of the not-too-distant jump from gene therapy to eugenics. Even those who argue that gene therapy should be done only when medically necessary[16] should ask themselves "what do we mean by medically necessary?" "What are we saying about those individuals who carry genes that are bad enough to recommend changing?" What message will the *medical community* send to the insurance companies? Should doctors decide what are the good genes and what are the bad?

The person that does suffer from a genetic disorder, like Huntington's disease or retinitis pigmentosa, will pay no attention to these abstract arguments, however. That is because their concern is more pragmatic. The person with Huntington's disease wants to have control over his or her faculties, and the person with retinitis pigmentosa just wants to be able to have normal vision. There is no strength in adversity for most of these individuals—they want a normal life, and most of us would understand and accept what they mean by *normal.* Do they not have the right to choose? But how do we extend the definition of a normal life to those who want gene therapy for non-medical disorders, like baldness, tallness, intelligence, and obesity? If plastic surgery is socially acceptable, even desirable, for personal enhancement, then why not genetic enhancement? Do we not have the right to choose?

What Should Be Done?

> *Every craft and every investigation, and likewise every action and decision, seems to aim at some good; hence the good has been well described as that at which everything aims....Then surely knowledge of this good is also of great importance for the conduct of our lives, and if, like archers, we have a target to aim at, we are more likely to hit the right mark. If so, we should try to grasp... what the good is...*
>
> —Aristotle, *Nicomachean Ethics*

It is unlikely that we will ever be able to say with any certainty what should and shouldn't be done with the power to alter our genome. We are not, after all, God. What can be said, however, is that society needs to be aware of the issues, and not be content to let decisions be made on the basis of one particular directive, supported by one particular group. The stakes are too high, and the lessons of history too formidable. We need to continue the conversation, guided by an awareness of the issues. Scientists and philosophers can at least agree on the problems: how do we define a human being and where do genes fit into that definition; by what criteria is gene therapy warranted and how should we decide it; and without sacrificing human dignity and freedom, how should gene therapy be regulated in society and who should regulate it? By at least recognizing these problems, society has a target to aim at in its pursuit of principles.

Awareness of our mistakes will also be a tempering force in the forging of a new genetic era. No critic, however, can stop the genetic revolution; nor can we deny the potential benefits to be obtained by it. Can we, however, make the right decisions? Will we aim for the *highest* good, however we define it, in our decisions? What kind of legacy will we leave for the future? That may be for them to judge, but it is for us to determine now.

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Endnotes

1. Interest in genetics goes back to ancient Greece, where a distinction was made between physical substance and the generative force. The preformation theory (a sperm or egg contains the preformed individuals of all succeeding generations) was dominant in the seventeenth century. William Harvey is credited with the first statement of epigenesis (an individual is derived from substances from both parents). Darwin set the foundation for modern genetics, with *Origin of the Species,* by recognizing that blending (a mixing of traits from both parents creating intermediate results) could not explain variation and diversity of species. From Gerald Audesirk and Teresa Audesirk, *Biology: Life on Earth* (3rd ed.; New York: Macmillan, 1993), 209; Bruce M. Carlson, *Patten's Foundations of Embryology* (6th ed.; New York: McGraw-Hill, 1996), 1-3; and William S. Klug and Michael R. Cummings, *Concepts of Genetics* (4th ed.; New York: Macmillan, 1994), 2-5, 51.

2. Audesirk and Audesirk, *Biology,* 309-324; Klug and Cummings, *Concepts,* 569-589; and Kathryn L. McCance and Sue E. Huether, *Pathophysiology: The Biologic Basis for Diseases in Adults and Children* (2nd ed.; St. Louis, Mo: Mosby, 1994), 192.

3. He made the distinction between soma and gametes a century ago (Carlson, *Patten's Foundations,* 3). Many scientists will speak of life within the context of this biologic determinism.

4. Audesirk and Audesirk, *Biology,* 303; and "Changing Your Genes" (editorial), *The Economist,* in *Biomedical Ethics: Opposing Viewpoints,* ed. David Bender and Bruno Leone (San Diego, Ca.: Greenhaven, 1994), 273.

5. One textbook states, "What, if any, are the rights and responsibilities of society in these decisions. . . . In a free society, probably the best solution is to give people the best information possible about their genetic constitution and that of their future children" (Audesirk and Audesirk, *Biology,* 326); another says, "Applied research in genetics has provided other medical benefits. . . . Human genetic engineering . . . is being used to alter the genetic constitutions of individuals harboring genetic defects and to correct such defects in the developing fetus. Although such processes present ethical questions, the ability to correct serious genetic errors in member of our species ensures that such approaches will become commonplace in the near future" (Klug and Cummings, *Concepts,* 13); and again, "Our society has repeatedly demonstrated that it can draw a line in biomedical research when necessary" (W. French Anderson, "Genetics and Human Malleability," Hastings Center Report, in *Biomedical Ethics,* ed. Bender and Leone, 276).

6. Ibid.

7. Audesirk and Audesirk, *Biology,* 309-326; Klug and Cummings, *Concepts,* 413-435.

8. Eugenics, a termed coined in 1883 by Francis Galton (a cousin to Darwin), refers to artificial selection of human characteristics by controlling human matings, and restricting the reproduction of individuals with undesirable traits. It is used to describe Hitler's ideas for producing a superior race, and has a strongly negative connotation. Euphenics, a modern term, refers to medical and/or genetic intervention designed to reduce the impact of defective genotypes on individuals (Klug and Cummings, *Concepts*, 10).

9. Ibid.

10. Robert J. Nelson, "What is Life," *Christian Social Action* (Jan., 1991), in *Biomedical Ethics*, ed. Bender and Leone, 263-269.

11. "Changing Your Genes," 271.

12. "Although it has been said that scientific knowledge doubles every ten years, one estimate holds that the doubling time in genetics is less than five years." Klug and Cummings, *Concepts*, 1.

13. Vicki Quade, "Protecting the Essence of Being," *Human Rights* (Winter, 1993) in *Biomedical Ethics*, ed. Bender and Leone, 288.

14. Ibid.

15. Ibid.

16. Anderson, "Genetics and Human Malleability," 276-280.

MEMORIALS

Roger Norman Conger
1909–1996

Roger Norman Conger, son of Dr. Ralph E. and Margaret Conger, was born in China Spring, McLennan County, Texas, on September 26, 1909, and died in Waco on February 13, 1996, of Lou Gehrig's disease. When Roger's father, a doctor, died on March 1, 1922, the family was forced to sell their fifteen-room home in China Spring and move into a small three-bedroom home in Waco. Roger was twelve at the time and sister Luella was sixteen. Their mother went to work selling insurance.

Roger entered Waco High School in 1922 and took his first paying job as a delivery truck driver for a retail grocery store. After graduation from school in 1926, Roger went to work for the Cooper Grocery Company where, as an eighteen-year-old, he "earned a man's salary." In 1928 he worked half-time at Cooper and attended Baylor University part time. After five years with the Cooper Grocery Company, Roger took a job with Southern Cotton Oil Company of New Orleans with an assigned position in Dallas. He married Lacy Rose Hammond in 1933 and, with children Roger Lacy and Claire, lived in University Park and was active in the Highland Park Presbyterian Church.

Roger started what he considered his "second career" in 1941 when he and his family moved to Waco, where he set up a national sales and distribution organization to market products manufactured by Hammond Laundry-Cleaning Machinery Company of Waco. During World War II the company provided products for military ships and submarines. At the end of the war, the company provided equipment for the expanding laundry and drying cleaning business. The nationwide operation expanded further into Europe, India, Soviet Russia, Mexico, and Latin America.

Roger had plans for son Roger Lacy to take on the position of operating the firm. Tragically this dream did not take place when young Conger was killed in an automobile accident in 1960 while on a business trip in Germany. The Hammond business was sold, and Roger then found time to do other things he wanted to do. He viewed "public service" as his third career. He was a Waco city commissioner 1962–65 and mayor 1964–65. He was an elder and Sunday school teacher for many years at Waco's First Presbyterian Church.

As a Waco and Texas historian, Roger rose to the top of the ranks and was known as "Mr. Waco History," according to Kent Keeth, director of

Baylor University's Texas Collection. On the state level Roger was active and served as president of the Texas State Historical Association. Fortunately, much of the history Roger wrote during more than fifty years has been printed and listed in *Waco's Champion: Selections from the Papers of Roger Norman Conger* (Marion Travis, editor and bibliographer), published by Historic Waco Foundation in 1990. Roger's historical writings, along with his activities in the Historical Waco Foundation, Texas Ranger Museum, Sons of the Republic of Texas, Tri-State Chisholm Trail Centennial, Texas State Historical Association, and Texas Historical Commission, earned for him the coveted Award of Merit from the American Association for State and Local History.

At the time of his death Roger was a thirty-three degree Mason. He was buried in Waco's Oakwood Cemetery. He is survived by his wife Lacy Rose Hammond Conger, daughter, Claire Conger Garner, and granddaughter, Rosalyn Lacy Conger.

D.H.W.

Margaret Cousins
1905–1996

On July 30, 1996, the Philosophical Society lost a dear friend and fellow member, author and editor Margaret Cousins. Cousins gained prominence and recognition in literary circles for her work as a magazine writer and author of children's books. A native Texan, Cousins was born in Munday to Walter Henry and Sue Collins on January 26, 1905. After graduation from The University of Texas with an A.B. in 1926, she began her literary career as an associate editor of the *Southern Pharmaceutical Journal* in Dallas, and became its editor-in-chief.

In 1937 Cousins moved to New York City and joined the staff of Hearst Promotion Service as a copywriter. While at Hearst, Cousins was responsible for serving as courier in transporting the Anne Frank diaries to the United States for publication. She was quite moved by Frank's emotional writings and convinced the owners of Hearst to serialize the writings. She left Hearst after four years of service, and in 1945 accepted a position with *Good Housekeeping* magazine, serving as managing editor until 1958. Cousins was then hired as managing editor of *McCall's* until 1961 when she took the position of senior editor at Doubleday and Co.

During her time at *Good Housekeeping,* Cousins began to write children's stories. Her first children's story, *Uncle Edgar and the Reluctant Saints,* was published in 1948 and she continued to produce such works as *We Were There at the Battle of the Alamo.* As well as writing children's stories, Cousins wrote many short stories that found their way into our homes and lives. One of her many well remembered short stories, "The Life of Lucy Gallant," was produced as a movie in 1955. Cousins wrote more than two hundred short stories, which were published in the United States and in seventeen foreign countries during her twenty-five year career.

Cousins had strong ties to Texas and in 1972, after her publishing career, moved to San Antonio, where she lived until her death. She moved to San Antonio after close friend and interior designer Bill Pahlman relocated there. Cousins moved downtown into the Clifford Building on the San Antonio River where many of her friends, who all shared a common love for literature, also lived. Although she never married, Cousins had a wealth of friends who truly appreciated her engaging personality. One group of her friends consisting partly of architects and designers became known as the "River Rat Group," as all became friends because of their relationship to the San Antonio River. Cousins is also noted as being a member of the San Antonio Reading Club, and met with the distinguished group every week to read and critique a variety of literature. Cousins was a member of St. Marks Episcopal Church in San Antonio.

Cousins held membership and leadership positions in several other clubs over the last forty years. She served as member of the Board of Governors of the Authors Guild from 1959 to 1974, as the secretary of the American Authors League of America, and member of the Board of Directors of the Arts Council of San Antonio. Her membership in various social and literary clubs also included the Cosmopolitan Club, the San Antonio Fine Arts Commission, the San Antonio Conservation Society, and the American Institute of Interior Designers.

Margaret Cousins' many years of work as an editor and writer have not gone without recognition and reward. She was given the George Washington Medal by the Freedoms Foundation of Valley Forge in 1969 and the J.C. Penny-Missouri School of Journalism award in 1968 for her magazine writing. She was also honored in 1973 with the Distinguished Alumna Award by The University of Texas at Austin.

In an interview with *Contemporary Authors*, Cousins credited much of her success to her mother and father. Self-educated and prodigious readers themselves, they exposed her to the classics at an early age and shared their love for literature with her. Because she did not know another child until her brother was born when she was five, Cousins spent much of her time listening to her father read her anything from Edgar Allen Poe to the *Saturday Evening Post*. She attributed her love for short stories to the fact that her father read to her all nine volumes of the O. Henry stories.

Margaret Cousins was most definitely an accomplished editor and writer who had a great influence on American literature. She shared her passion for literature through her great work and leadership of American periodicals and through her creative children's and short stories. She had a love for Texas that ran thick in her blood and she used a pen and paper as the canvas for her expression. Margaret Cousins is missed by her friends and loved ones, but her loving personality and engaging character will live on through her work.

A.B.D.

Newton Gresham
1905–1991

Newton Gresham passed away at his home on Wednesday, June 5, 1991, at the age of eighty-five. He was born on July 21, 1905, on a farm near Jewett, Texas, in Leon County, the son of Edward A. and Beulah Selman Gresham. He was named for his uncle, a well-known agrarian leader in Texas who founded the Farmers Union in 1902. Gresham grew up in Uvalde, Texas, where he graduated from Sam Houston State Teachers College in 1924. For the next six years, he alternated teaching in public schools and attending The University of Texas Law School.

Receiving his law degree in 1930 when jobs were scarce, Gresham took the only job the firm of King, Wood & Morrow could offer at the time—employment as a legal stenographer. In 1937, Gresham became a partner of that firm. After undergoing major changes in the early part of the 1940s, the firm of Gresham, McCorquodale, Martin & Buck (with heavy involvement in the defense of insurance cases) merged with the firm of Fulbright, Crooker, Freeman & Bates, which later became known as Fulbright & Jaworski L.L.P.

Gresham will be remembered as a gentlemanly, low-key, brilliantly analytical lawyer. He was probably the most beloved of his firm's lawyers among the judges, clerks, bailiffs, and court reporters who worked in the rural counties where he tried some of his lawsuits.

A member of the board of regents of the State Teachers Colleges of Texas from 1959 to 1965, Gresham served as president from 1963 to 1965. His distinguished service on the coordinating board of the Texas College and University System spanned the period from 1965 to 1983, during which time he served as vice chairman from 1965 to 1980 and as chairman in 1983.

Newton Gresham was a trustee of St. Luke's Episcopal Hospital, Killson Educational Foundation, and Sam Houston Foundation. He was a fellow of the American Bar Foundation and the American College of Trial Lawyers, and a member of the International Association of Insurance Counsel, Federation of Insurance Counsel, State Bar of Texas, Houston Bar Association, and American Bar Association. Gresham was president of the Houston Bar Association in 1984 and president of the State Bar of Texas in 1956-57, and was selected as Distinguished Alumnus of Sam Houston State University in 1977. He also held membership in Alpha Chi, Alpha Tau Omega, Order of the Coif, and Phi Delta Phi. He was a senior warden of St. John's Episcopal Church and active in its affairs.

He was married to Mary Frances Stone on July 3, 1933, and they had one daughter, Susan Frances Oaks, and two granddaughters, Elizabeth Clarke Oaks and Mary Gresham Oaks.

J. S. B. & H. L. W.

Everett Holland Jones
1902–1995

Bishop Jones was born in San Antonio, where he went through the public schools and spent most of his life. After graduating from the University of Texas in 1922, he taught a year at the Texas Military Institute before continuing graduate studies in journalism at Columbia University. While in New York, gaining experience as a reporter, he began taking courses at Union Theological Seminary. Later he enrolled in Virginia Theological Seminary from which he received the degree of Master of Divinity-1927. After ordination as an Episcopal priest he served parishes in Cuero and Waco and as canon chancellor of the National Cathedral in Washington, DC. In 1938 he returned to San Antonio as rector of St. Marks Episcopal Church where he had been baptized, confirmed, ordained, and finally consecrated as bishop of the Diocese of West Texas.

In 1940 he was married in St. Marks to Helen Miller Cameron, a widow with one child. From her custom of always wearing red at annual diocesan meetings, she became West Texas's "Lady in Red." Her ministry to the clergy wives helped build the diocesan sense of family. Her generosity is still reflected in many parts of San Antonio and the state.

He brought the program of Alcoholics Anonymous to San Antonio while he was rector at St. Marks. As bishop he was one of the three co-founders of the Ecumenical Center for Religion and Health in San Antonio. He also led in developing the finest young camping program.

He wrote several small books. One of them, "A Bishop Looks at Life," was a compilation of sixty of his newspaper columns which were carried in more than forty newspapers in Texas.

Bishop Jones received honorary degrees from the University of the South, the Virginia Seminary, and Trinity University in San Antonio.

He died in San Antonio at the age of 93 on November 21, 1995.

W. D. S.

J. Erik Jonsson
1902–1995

J. Erik Jonsson was born to Swedish immigrants in Brooklyn, New York, in 1902. He earned a mechanical engineering degree from Rensselaer Polytechnic Institute in 1922, and moved to Dallas in 1934 with Geophysical Services, Inc., the forerunner of Texas Instruments. The Jonssons had one daughter, Margaret Jonsson Rogers, and two sons, Philip Jonsson and Kenneth Jonsson. Margaret and Philip reside in Dallas, and Kenneth lives in Los Angeles. Mrs. Jonsson predeceased Mr. Jonsson, having died in 1984.

Mr. Jonsson's business genius helped create one of the world's most successful corporations. He and his partners, Eugene McDermott and

Cecil Green, took Texas Instruments as a small electronics company in the early 1950s and turned it into a multi-billion dollar giant.

As significant as his accomplishments were in the world of business, perhaps even more so was the leadership he provided for Dallas during its darkest hours. He became mayor of Dallas in 1964 just months after the assassination of President John F. Kennedy. His seven-year tenure as mayor totally reshaped the image of Dallas. Among his accomplishments were the very successful Goals for Dallas program, construction of a new city hall designed by I. M. Pei, the Martin Luther King Jr. Center in south Dallas, the new downtown library, and his concept of developing the West End as an entertainment district. His crowning civic achievement, however, was the partnership with Fort Worth that led to the construction of the Dallas/Fort Worth International Airport, now the second busiest airport in the world.

Mr. Jonsson, with his business associates, had a keen appreciation for the value of quality higher education and were responsible for what is now the University of Texas at Dallas. In addition, he was a major supporter of a number of institutions of higher education including the University of Texas Southwestern Medical Center where he is often given credit for making it possible to retain the services of two of the institution's Nobel Laureates, Dr. Joseph Goldstein and Dr. Michael Brown.

Mr. Jonsson died at the age of ninety-three and few, if any, have had a greater impact on the development of the city of Dallas.

C. C. S.

F. Lee Lawrence
1926-1996

I take comfort in knowing that my friend, F. Lee Lawrence, who died on July 10, 1996, has been presented his crown of righteousness, but knowing this does not fill the vacancy his death leaves in my life. It is a gap that only he was uniquely qualified to fill. That he would trust me with the task of writing his memorial may not have been his wisest request, but it is certainly one of my highest compliments. And it is a formidable task. Let me try to define him by drawing the circle of all he touched, and talk about the important ways he touched me and why F. Lee Lawrence was, to me, a very special hero.

Our lives crossed thirty-six years of shared adventure. We had three passages in our relationship. The first was my rite of initiation as I tried to prove myself a worthy addition to the Lewis family or, more importantly, worthy to be Lee's brother-in-law. In Spanish, we are called *contigos*, non-blood brothers, but there was enough transfusion between us of life's essence that we developed a bond as deep as blood.

In the beginning, the fourteen years of age that separated us seemed too wide a gulf for us to ever cross, but Lee became like an older brother to me. One to be admired, emulated, imitated, but never excelled. In the Lewis family, there were four brothers-in-law. You may recognize this as

the perfect number for a golf outing. The only problem was that Lee did not play golf, so his vacancy was filled by our father-in-law, A. Y. Lewis, the head of the Lewises. I have often wondered how different all our lives might have been if we could have convinced Lee to have been our companion in such play.

However, it was far away from the golf course, around a subject that was a life-long passion for Lee, that our relationship developed. It was Lee's love for history—the Civil War, Texas, and especially the history of East Texas. It was truly his love for history that best defined him. Importantly, it was not just history for history's sake, but what he loved in history. For him it was the heroes of history, those people who stood above the madding crowd and gave their all for a cause, a forlorn cause: heroes like those of Hood's Texas Brigade, which suffered 70% casualties at Chancellorsville, or Terry's Texas Rangers, who, at the conclusion of that great conflict, refused to surrender and turned their horses west, back to Texas. Lee had no time for compromises or compromising souls of those living out their lives in quiet desperation. He always wanted to stand for something and to stand up for something.

Sometime, about ten years ago, we entered the third phase of our relationship. It was a time of mutual admiration and shared commitment. Like all of us, he had a sin nature. He could pick far too long at some of the bones of life. But, deep down, he was a man full of tenderness and compassion and integrity. A conversation with Lee would frequently begin, "Now (fill in your name), tell me about your (fill in your subject)." This was his invitation for you to share your life with him. He listened to your answers, never hurrying you to conclusion, always ending with some meaningful insight into your situation, and always with respectful approval of your efforts. I observed this process on a thousand occasions. It never felt staged. I frequently asked myself, "Why did he do this?" and, finally, one day, I understood. He truly cared about you, your life, your struggle. Not only could he sympathize with your failure, but he could applaud your success. That is truly a rare talent.

Lee did not give the impression of being tough or one to whom physical strength was important, though he had an inner toughness, strength, and courage. He was unwavering in his convictions, conservative in his politics, but liberal in his generosity to friends and family. Lee was a great lawyer, in part, because he believed so fervently in his clients and their causes. But his friends and family were beneficiaries of that same unconditional affection and commitment. It was once asked of the famous Texas Ranger, Captain McNally, what type of adversary he feared the most. His answer: "A man who knows he is right and never stops coming." Lee was a man who pursued causes that he knew were right, and I can tell you, based on his life, he never stopped coming.

I watched Lee serve in numerous leadership roles—president of the Texas State Historical Association, the Texas Historical Foundation, the East Texas Historical Association, and, twice appointed by Texas gover-

nors to the Board of the Texas Historical Commission. In all these roles, he captured the respect and admiration of all those with whom he served because of his excellent judgment and insight and his willingness to make a financial commitment. But I think, most importantly, he gained respect because Lee, in pursuing his passion for history, served not his own selfish interest in life, but a true interest and love for history. There is not one of those organizations that is not distinctly better for his service to their cause.

If Lee believed in you, he would always be there for you. Throughout our thirty-six years, he never failed me or deserted me. He was the first man I called for advice when I was faced with a difficult task or just wanted to hear the voice of a friend. He was the first person I called when I became president of the Texas State Historical Association. He was the first person I called when I was seeking new members to the Board of the Texas Historical Foundation, and he gave generously of his time and money. He was the first person I called when I planned a large fund-raising effort for the Texas State Historical Association. He was the first person I called when I decided to restore and expand the Gage Hotel in Marfa, and he was the first man I talked to when I made the decision to take my former job in Canada. He supported my nomination to the Texas State Historical Association and the Philosophical Society of Texas. He introduced me to the Greek revival architecture of East Texas and, most significantly, he infected me with his passion for history.

I was only twenty years old when he encouraged me to give my first historical speech before the Texas State Historical Association on my relative, Moses Austin. I will share with you today, in all honesty, that it was a miserable speech. But Lee, as I watched him, never flinched. Afterwards, he made me feel that I had just delivered the equivalent of the Gettysburg Address. From that date forward, for thirty-five years, Lee suffered through many of my historical speeches and always found something positive to say to encourage me.

They say there are three things a man should do to endure past his grave. Have a child, plant a tree, and write a book. Lee did all three of these with wonderful style. He had three outstanding children—daughters. He planted a tree. As a matter of fact, he planted many trees, especially on their Mountain Creek Ranch at Comanche. The Mountain Creek Ranch was the original Texas homestead of Lee's relatives, the Cunninghams, who settled in Comanche County in 1855. Lee, through good fortune, was able to buy that homestead in 1984, and, with the help of his family and friends, he carefully and lovingly restored it to its original status. Then, as was the case with most things Lee did, he significantly improved on it. This was not just an outstanding example of a historical restoration, but a restoration done with profound respect and sympathy for those ancestors who had passed before him, who gave birth, shed blood, and suffered death on that very spot. I know Lee gained inspiration in this task from the hero images of his ancestors. This was not just

a piece of God's earth that Lee was restoring. To him it was sacred ground.

Lee authored not one, but two books. Both subjects reflected a different part of his historical passion. The first, *Camp Ford*, is a book about the Confederate prison camp that was located in Tyler, and the second, *Texas War Horses,* is a delightful book about Texas horses who, loyally and with stamina, carried their riders into the jaws of conflict over three generations of history. These books say volumes about Lee. Space permits only two observations. In *Camp Ford,* the dedication was not to a variety of inspiring supporters who had helped with this work, but simply to the men of Camp Ford, both Union and Confederate, who lived out their drama on that location more than 100 years ago. It was compassionate recognition by Lee of the struggle suffered by both prisoner and guard as they tried to maintain their human dignity in the most difficult of circumstances. In *Texas War Horses*, you see Lee's affection for horses as he acknowledged their loyal commitment to themselves as animals and to their riders.

I will close by reading the following from Lee's *Texas War Horses:*

> Most frontier horses were expected to do their jobs with only the nourishment they could gather themselves from whatever range was available. And yet they performed incredible feats that no modern rider would expect his horse to accomplish even under the best of conditions. It is difficult to comprehend. The answer must lie in the inherent vigor common to all who survive physical adversity. It is the same vigor we have admired in their riders; so the story of the old time Texas War Horse is parallel to and coincidental with that of the Texas pioneer who rode it. The adversities, hardships, and privations they both endured on the prairies of Texas produced people and horses possessed of astonishing stamina and grit. The frontier lifestyle that created these rawhide horses and riders has long since vanished, and so have they. We will not see their like again.

And I say similarly, that I know I shall never again see the likeness of a man such as my friend and hero, Lee Lawrence.

J.P.B. Jr.

Leonard F. (Mc) McCollum
1902–1993

Distinguished businessman, citizen, and philanthropist "Mc" McCollum was born in Tennessee, but grew up in South Texas, graduating from Cuero High School in 1920 and from The University of Texas in 1925 with a B.S. degree in geology.

That same year he went to work for the Humble Oil and Refining Company (an affiliate of Standard Oil of New Jersey) as a scout and geol-

ogist. In twenty-two years he advanced from scout to head of the world-wide production of Esso, now Exxon.

In move that he called "the hardest thing I did in my life," he left Esso to become president of Continental Oil Company. "Mr. Mc" transformed the medium-sized domestic company into an integrated international energy firm with $2.3 billion in assets and 32,000 employees. "The hottest brand going" was the gasoline trademark of his Conoco years. He was a "go-getter" who joked abut the fast pace: "I kept four company planes at my disposal to go north, south, east, and west. I couldn't waste time turning around."

"Mc" bred cattle on his 1000-acre ranch near Brenham which became a gathering place for cattlemen, business executives, heads of state, and friends from all over the world.

In addition to his positions of leadership in the petroleum industry and varied other businesses, he was devoted to education and public service.

For his contributions to The University of Texas as a member of the Chancellor's Council, the Committee of 75, and the Centennial Committee, and his place as a national business leader, he received the Distinguished Alumnus Award in 1965.

He served as a member of the Visiting Committee of the Harvard Graduate School of Business Administration. The McCollum Center at the school is named for him and his wife, Margaret.

He was a trustee of the California Institute of Technology for many years.

Beginning in 1969 he served with distinction as a member of the Board of Directors of the Texas Medical Center, Inc. For four years he served as chairman of Baylor College of Medicine. "I was persuaded to accept the job because I believed, from talking with some people at Baylor, that I could be helpful to the school."

In 1973, Dr. Michael E. DeBakey wrote: "Under L. F. McCollum's guidance Baylor has quadrupled its endowment, doubled its student body, strengthened its faculty, and implemented a 10 point program originally expected to require a decade for completion."

This is only a partial list of his many interests and accomplishments and honors he earned.

"Mc" McCollum was preceded in death by his first wife of 45 years, Margaret Wilson. He is survived by his second wife, the former Eleanor Searle Whitney; a son, L. Franklin McCollum Jr. and his wife Lauran; a daughter, Olive McCollum Jenney and husband Robert M.; a step-son, Cornelius Searle Whitney of San Francisco; a sister, Macie Bell Midgett of Donna; five grandchildren, and eight great-grandchildren.

May he rest in peace.

W. D. S.

Herman P. Pressler Jr.
1902–1995

Herman Pressler, Houston attorney and civic leader, died May 2, 1995, at his home in Houston. He was born in Austin. After graduation from its public schools, he attended Virginia Military Institute and graduated from The University of Texas, both its undergraduate and law schools. He was a graduate of the Advanced Management Program at Harvard University Graduate School. At both Texas and Harvard, he was president of his graduating class.

He came to Houston to practice law in 1925 and later joined the legal department of the Humble Oil and Refining Company (now Exxon). He later served as vice president of that company until his retirement in 1967. After retirement, he practiced law and handled family investments.

Herman Pressler served as president of the Houston Bar Association (1950–51), president of the Texas Medical Center (1976–1982), and founder, charter member and trustee of Texas Children's Hospital. He served as chairman of it from 1976 to 1982 and chairman emeritus from 1982 until his death. He also was chairman of the Houston and Harris County Chapter of the American Red Cross (1952–1954) and was a trustee of Baylor College of Medicine. Mr. Pressler was a founding member of River Oaks Baptist Church. He was a member of the Houston Country Club, Bayou Club, Petroleum Club, the Eagle Lake Rod and Gun Club, and a member of other social organizations. He served on many other professional and charitable boards during his lifetime of service to his community.

Various honors were awarded him, including having a street in the Medical Center named "Herman Pressler Street" and the west lobby of Texas Children's Hospital named the "Herman P. Pressler, Jr. Lobby." Sheltering Arms awarded him and his wife, Elsie Townes Pressler, its Distinguished Service Award. The Houston Bar Association presented him with the Leon Jaworski Award for outstanding community service. The City Council of Houston adopted a resolution designating "Herman Pressler Day."

He was an avid hunter until the time of his death. Few birds which came within the range of his gun survived. He hunted often with his wife, sons, grandsons, and friends. He also thoroughly enjoyed the mental stimulation and camaraderie of the Philosophical Society meetings. He was a very well rounded person.

Mr. Pressler was survived by his wife of sixty-six years, Elsie Townes Pressler, two sons, Judge H. Paul Pressler III and his wife, Nancy Avery Pressler, and Townes Garrett Pressler and his wife, Bette Craddock Pressler. He was also survived by six grandchildren and nine great-grandchildren. He always took time for his family in spite of his heavy involvement in business and charitable activities. Since his death, his number of

great-grandchildren has grown to thirteen. He worked hard to make this a better world for them to enjoy.

H. P. P.

Harry Mayo Provence
1914–1995

A native Texan, Harry Provence was born on September 9, 1914, and graduated from Denton High School. He received his bachelor of arts degree from Baylor University in 1937 and a year later married his college sweetheart, Frances Bludworth, who preceded him in death in 1988.

During his days at Baylor, Provence was editor of the *Lariat*, the student newspaper, and immediately following graduation he began working at the *Waco Tribune-Herald* on June 11, 1937. He served as copy editor, night news editor, day news editor, and managing editor before taking over the reins as editor in August 1951. In 1954 he was appointed editor-in-chief of Newspapers Incorporated, which owned the newspapers in Waco, Austin, Lufkin, and Port Arthur. He became vice president of the Corporation in 1963 and, in 1976 when Cox Enterprises purchased Newspapers, Inc., Provence continued as editor-in-chief of the *Tribune-Herald* until retiring October 1, 1979.

Harry Provence was a committed citizen of the State of Texas and gave of himself selflessly to a number of worthy endeavors. After James Connally Air Force Base in Waco was closed in 1964, Provence was instrumental in getting the base converted into what is now Texas State Technical College (TSTC). TSTC recognized his vital role through the years by naming its communications building the Provence Communications Technology Building. Additionally, Provence was a friend to many influential state and national leaders, including President Lyndon B. Johnson and a succession of Texas governors. He was a frequent visitor to the White House during Johnson's presidency and authored *Lyndon Johnson, A Biography*, a personal look at the chief executive culled from years of personally accumulated material.

Provence served as a distinguished member of the Texas Higher Education Coordinating Board from 1965 until 1979, and was appointed chairman of the board in 1973 by Governor Dolph Briscoe and was reappointed chairman in 1975. He always felt that this was one of his most meaningful pursuits. In recognition of Provence's outstanding service to Texas higher education, Baylor University conferred an honorary doctor of laws degree on him in 1978. A number of other institutions also recognized Provence in various ways for his lasting contributions.

Provence was a sportsman and spent much time fishing and hunting. He was also a jazz enthusiast and a scintillating conversationalist. He also served faithfully and well on the board of Waco's Community Bank and Trust for twenty-four years, beginning in 1971.

Harry Provence left an important legacy when he died on August 3,

1995. He is survived by his three daughters, Eugenia Provence, Harriett Provence Spitzley, and Lesley Provence Grohe, two sisters, and four grandchildren. An obituary to Provence stated that "at six feet five inches tall, Harry Mayo Provence's size was matched only by his influence for good." Bob Lott, his successor as editor at the *Waco Tribune-Herald,* stated that on the personal side he knew Harry as a "thoughtful, gentle and considerate man," which is echoed by all who knew him.

B.R. and H.H.R.

James Udell Teague
1909–1995

James Udell Teague, oil field roustabout to independent driller, Rice student to Chairman of the Trustees, was born on October 23, 1909, in Caldwell, Texas, to Oliver R. Teague and Mary Frances Rollins. He was elected to the Philosophical Society in 1979.

Jim graduated from Caldwell High at fifteen, worked in the oil fields in West Columbia for a year, and entered Rice. While a Rice student, he earned extra money by running a radio repair service in West Columbia. "In those days [late 1920s] a radio was quite an unusual thing. I built my first radio when I was still in Caldwell, and of course word got around that the Teague kid could fix radios. After that I persuaded a radio manufacturer to let me be the West Columbia dealer." After graduation he worked in the field as a roustabout for Humble Oil—"That is the way we all came up in my day—by actually working on the rigs in the field." Jim said of a meeting with Mr. Will Hogg during his Rice days, "I'll never forget going into that great man's presence. He was a very big man and I was terrified." In 1940 he left Humble and joined the Hogg Company, but soon left to serve in the U. S. Navy in the Pacific reaching the rank of Lt. Commander. He returned to Texas in 1947 to found his own company, Columbia Drilling, and developed it into a prosperous enterprise. "The oil industry is a highly technical field, and it is unfortunate that misunderstandings have developed with people who have no interest in oil other than getting a tank of gasoline at the lowest price. Although we have tried to publicize the crisis in oil supply for years, we have never been able to overcome the Cinderella image of a few people in the industry." "In reality it's not that way at all. Much of the wealth of the industry is divided into the relatively small earnings of hundreds of people—small investors and landowners who collect only modest royalties from the wells drilled on their property. I'm optimistic about the future."

Jim served many professional societies: American Association of Oilwell Drilling as director and president, American Association of Petroleum Geologists, American Institute of Mining and Metallurgical Engineers, American Petroleum Institute, Mid Continent Oil and Gas Association, Texas Independent Producers and Royalty Owners Association, and the Independent Petroleum Association of America. He served as director of First Professional Bank N.A. of Houston, First City

Bank-Medical Center, The Howell Corporation, and Falcon Seabord Drilling Co. as president and director. He was also president of the Houston Petroleum Club. Through his lifelong association with the oil industry, Teague developed a real dedication to the industry and a strong desire to see present problems worked out. In Houston civic affairs Jim was a director of the St. Joseph's Hospital Foundation, Holly Hall, and was president of the DePelchin Faith Home.

Jim and his wife, Margot Elizabeth Terry, had two children, James Oliver Teague and Margot Terry Teague Fry. Mrs. Teague died in 1990. Jim later married Lara Ruth Lindholm.

At Rice between 1966 and 1979 he served as chairman of the Academic Affairs Committee, co-chair of the Corporates and Foundation Committee for the $33 Million Campaign, vice chairman and chairman of the trustees. He was awarded the Rice Academic Gold Medal for Distinguished Service in 1976. On his role at Rice, "The beautiful part about being a Trustee of a University like Rice is the feeling of being part of an institution that is going to go on so much longer than your own lifetime. We sit down there in the board room for a while, try to make decisions for the good of the University, and then are gone. But the University lasts in perpetuity. Oh yes, I think that Rice has a great future!"

W. E. G.

(W. E. G. thanks the Development Research Office at Rice University for archival material used in this memorial.)

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*	Mirabeau Buonaparte Lamar	1837–59
*	Ira Kendrick Stephens	1936
*	Charles Shirley Potts	1937
*	Edgar Odell Lovett	1938
*	George Bannerman Dealey	1939
*	George Waverley Briggs	1940
*	William James	1941
*	George Alfred Hill Jr.	1942
*	Edward Henry Cary	1943
*	Edward Randall	1944
*	Umphrey Lee	1944
*	Eugene Perry Locke	1945
*	Louis Herman Hubbard	1946
*	Pat Ireland Nixon	1947
*	Ima Hogg	1948
*	Albert Perley Brogan	1949
*	William Lockhart Clayton	1950
*	A. Frank Smith	1951
*	Ernest Lynn Kurth	1952
*	Dudley Kezer Woodward Jr.	1953
*	Burke Baker	1954
*	Jesse Andrews	1955
*	James Pinckney Hart	1956
*	Robert Gerald Storey	1957
*	Lewis Randolph Bryan Jr.	1958
*	W. St. John Garwood	1959
	George Crews McGhee	1960
*	Harry Hunt Ransom	1961
*	Eugene Benjamin Germany	1962
*	Rupert Norval Richardson	1963
*	Mrs. George Alfred Hill Jr.	1964
*	Edward Randall Jr.	1965
*	McGruder Ellis Sadler	1966
*	William Alexander Kirkland	1967
*	Richard Tudor Fleming	1968
*	Herbert Pickens Gambrell	1969
*	Harris Leon Kempner	1970
*	Carey Croneis	1971
*	Willis McDonald Tate	1972

*	Dillon Anderson	1973
*	Logan Wilson	1974
*	Edward Clark	1975
	Thomas Hart Law	1976
*	Truman G. Blocker Jr.	1977
	Frank E. Vandiver	1978
*	Price Daniel	1979
	Durwood Fleming	1980
	Charles A. LeMaistre	1981
*	Abner V. McCall	1982
*	Leon Jaworski	1983
	Wayne H. Holtzman	1983
	Jenkins Garrett	1984
	Joe R. Greenhill	1985
	William Pettus Hobby	1986
	Elspeth Rostow	1987
	John Clifton Caldwell	1988
	J. Chrys Dougherty	1989
*	Frank McReynolds Wozencraft	1990
	William C. Levin	1991
	William D. Seybold	1992
	Robert Krueger	1993
	Steven Weinberg	1994
	William H. Crook	1995
	Charles C. Sprague	1996
	Jack S. Blanton	1997

* Deceased

Meetings of the Philosophical Society of Texas

1837 – Founded at Houston, December 5
1840 – Austin, January 29
1936 – Chartered, January 18
1936 – Reorganizational meeting – Dallas, December 5
1937 – Meeting and inaugural banquet – Dallas, January 29
1937 – Liendo and Houston, December 4
1938 – Dallas
1939 – Dallas
1940 – San Antonio
1941 – Austin
1942 – Dallas
1943 – Dallas
1944 – Dallas
1945 – Dallas
1946 – Dallas
1947 – San Antonio
1948 – Houston
1949 – Austin
1950 – Houston
1951 – Lufkin
1952 – College Station
1953 – Dallas
1954 – Austin
1955 – Nacogdoches
1956 – Austin
1957 – Dallas
1958 – Austin
1959 – San Antonio
1960 – Fort Clark
1961 – Salado
1962 – Salado
1963 – Nacogdoches
1964 – Austin
1965 – Salado
1966 – Salado
1967 – Arlington
1968 – San Antonio
1969 – Salado
1970 – Salado
1971 – Nacogdoches
1972 – Dallas
1973 – Austin (Lakeway Inn)
1974 – Austin
1975 – Fort Worth
1976 – San Antonio
1977 – Galveston
1978 – Houston
1979 – Austin
1980 – San Antonio
1981 – Dallas
1982 – Galveston
1983 – Fort Worth
1984 – Houston
1985 – College Station
1986 – Austin
1987 – Kerrville
1988 – Dallas
1989 – San Antonio
1990 – Houston
1991 – Galveston
1992 – Dallas
1993 – Laredo
1994 – Austin
1995 – Corpus Christi
1996 – Dallas
1997 – Houston

PREAMBLE

We the undersigned form ourselves into a society for the collection and diffusion of knowledge—subscribing fully to the opinion of Lord Chancellor Bacon, that "knowledge is power"; we need not here dilate on its importance. The field of our researches is as boundless in its extent and as various in its character as the subjects of knowledge are numberless and diversified. But our object more especially at the present time is to concentrate the efforts of the enlightened and patriotic citizens of Texas, of our distinguished military commanders and travellers,—of our scholars and men of science, of our learned members of the different professions, in the collection and diffusion of correct information regarding the moral and social condition of our country; its finances, statistics and political and military history; its climate, soil and productions; the animals which roam over our broad prairies or swim in our noble streams; the customs, language and history of the aboriginal tribes who hunt or plunder on our borders; the natural curiosities of the country; our mines of untold wealth, and the thousand other topics of interest which our new and rising republic unfolds to the philosopher, the scholar and the man of the world. Texas having fought the battles of liberty, and triumphantly achieved a separate political existence, now thrown upon her internal resources for the permanence of her institutions, moral and political, calls upon all persons to use all their efforts for the increase and diffusion of useful knowledge and sound information; to take measures that she be rightly appreciated abroad, and acquire promptly and fully sustain the high standing to which she is destined among the civilized nations of the world. She calls on her intelligent and patriotic citizens to furnish to the rising generation the means of instruction within our own borders, where our children—to whose charge after all the vestal flame of Texian liberty must be committed—may be indoctrinated in sound principles and imbibe with their education respect for their country's laws, love of her soil and veneration for her institutions. We have endeavored to respond to this call by the formation of this society, with the hope that if not to us, to our sons and successors it may be given to make the star, the single star of the West, as resplendent for all the acts that adorn civilized life as it is now glorious in military renown. Texas has her captains, let her have her wise men.

MEMBERS OF THE SOCIETY

(As of August, 1997)

(Name of spouse appears in parentheses)

ADKISSON, PERRY L. (FRANCES), former chancellor, Texas A&M University System; distinguished professor of entomology, Texas A&M University, *College Station*

ALLBRITTON, JOE LEWIS (BARBARA), lawyer; board chairman, Riggs National Corporation, *Washington, D.C.*

ANDERSON, THOMAS D. (HELEN), lawyer, *Houston*

ARMSTRONG, ANNELEGENDRE (TOBIN), former U.S. ambassador to Great Britain, *Armstrong*

ARNOLD, DANIEL C. (BEVERLY), private investor, *Houston*

ASHBY, LYNN COX (DOROTHY), former editor, editorial page, *Houston Post*; member, Houston Philosophical Society; author, columnist, *Houston*

ASHWORTH, KENNETH H., commissioner of higher education, Texas College and University System, *Austin*

ATLAS, MORRIS (RITA), lawyer; senior partner, Atlas and Hall, *McAllen*

BAKER, JAMES ADDISON, III (SUSAN), former U.S. secretary of state; former U.S. secretary of the treasury; former White House chief of staff, lawyer, *Houston*

BAKER, REX G., JR., lawyer, *Houston*

BARROW, THOMAS D. (JANICE), president, T-Bar-X, Ltd., *Houston*

BARTON, DEREK HAROLD RICHARD (JUDITH), professor of chemistry, Texas A&M University; Nobel Prize in chemistry, *College Station*

BASH, FRANK (SUSAN), director, McDonald Observatory, The University of Texas at Austin, *Austin*

BASS, GEORGE FLETCHER (ANN), scientific director, Institute of Nautical Archaeology, Texas A&M University, *College Station*

BELL, HENRY M., JR. (NELL), banking consultant; retired senior chairman of the board, First City Texas, Tyler N.A.; chairman of the board, East Texas Medical Center Foundation, *Tyler*

BELL, PAUL GERVAIS (SUE), president, P. G. Bell Company; president, San Jacinto Museum of History, *Houston*

BENTSEN, LLOYD (BERYL ANN "B.A."), former U.S. senator and U.S. secretary of the treasury, *Houston*

BERDAHL, ROBERT (MARGARET), president, The University of Texas at Austin; author; historian., *Austin*

BLANTON, JACK S. (LAURA LEE), president, Scurlock Oil Company, *Houston*

BOBBITT, PHILIP C., professor of law, The University of Texas at Austin; author, *Austin*

BOLTON, FRANK C., JR., lawyer; former head of legal department, Mobil Oil Company, *Houston*

BONJEAN, CHARLES M., Hogg Professor of Sociology and executive director of the Hogg Foundation for Mental Health, The University of Texas at Austin, *Austin*

BOWEN, RAY M., president, Texas A&M University, *College Station*

BRANDT, EDWARD N., JR. (PATRICIA), physician-medical educator; Regents Professor, University of Oklahoma-Health Sciences Center, *Oklahoma City, OK*

BRINKERHOFF, ANN BARBER, chair, UTMB Centennial Commission; Hogg Foundation national advisory board; vice president, Houston Community College Foundation, *Houston*

BROWN, MICHAEL S. (ALICE), professor of molecular genetics and director, Jonsson Center for Molecular Genetics, the University of Texas Southwestern Medical Center at Dallas; 1985 Nobel laureate in physiology or medicine, *Dallas*

BROWNELL, BLAINE A. (MARDI ANN), provost and vice president, University of North Texas, *Denton*

BROYLES, WILLIAM, JR. (ANDREA), author; founding editor, *Texas Monthly;* former editor-in-chief, *Newsweek;* co-creator, *China Beach;* author, *Brothers In Arms;* co-screenwriter, *Apollo 13*, *Austin*

BRYAN, J. P., JR. (MARY JON), president, Gulf Canada Resources Limited; former president, Texas State Historical Association, *Houston*

BUSH, GEORGE (BARBARA), former president of the United States; former director, Central Intelligence Agency; former ambassador to United Nations; former congressman, *Houston*

BUSH, GEORGE W. (LAURA), governor of Texas, *Austin*

BUTT, CHARLES C., chairman of the board and chief executive officer, H. E. Butt Grocery Company, *San Antonio*

CALDWELL, JOHN CLIFTON (SHIRLEY), rancher; president, Aztec Foundation; former chairman, Texas Historical Commission; director, Texas Historical Foundation, *Albany*

CALGAARD, RONALD KEITH (GENIE), president, Trinity University, *San Antonio*

CARLETON, DON E. (SUZANNE), director, Center for American History, The University of Texas at Austin, *Austin*

CARMACK, GEORGE (BONNIE), former editor, Houston *Press,* Albuquerque *Tribune* and *Travel;* editorial writer, San Antonio *Express-News, San Antonio*

CARPENTER, ELIZABETH "LIZ," former assistant secretary of education, Washington correspondent, White House press secretary; consultant, LBJ Library; author, *Austin*

CARSON, RONALD (UTE), Harris L. Kempner Distinguished Professor in the Humanities in Medicine and director of the Institute for the Medical Humanities, the University of Texas Medical Branch at Galveston, *Galveston*

CASEY, ALBERT V., former U.S. postmaster general; chairman and C.E.O., AMR Corporation and American Airlines, Inc.; director, Colgate-Palmolive Company, *Dallas*

CATTO, HENRY E. (JESSICA), former U.S. ambassador to Great Britain and El Salvador; vice chairman, Aspen Institute; vice chairman, National Public Radio, *San Antonio*

CAVAZOS, LAURO F. (PEGGY ANN), former U.S. secretary of education; former president, Texas Tech University and Texas Tech University Health Sciences Center, *Port Aransas*

CHRISTIAN, GEORGE (JO ANNE), writer and political consultant; former press secretary and special assistant to President Lyndon B. Johnson, *Austin*

CIGARROA, JOAQUIN G., JR. (BARBARA), physician, internal medicine and cardiology, *Laredo*

CISNEROS, HENRY G. (MARY ALICE), former mayor, San Antonio; faculty member, Trinity University, *San Antonio*

CLEMENTS, WILLIAM P., JR. (RITA), former governor of Texas; former chairman, SEDCO, Inc.; former U.S. deputy secretary of defense, *Dallas*

COOK, C. W. W. (FRANCES), company director, former chairman, General Foods Corporation , *Austin*

CRAVEN, JUDITH LYNN BERWICK (MORITZ), professor of public health administration, The University of Texas Health Science Center, Houston; director of public health, Houston, *Houston*

CRIM, WILLIAM ROBERT (MARGARET), investments, *Kilgore*

CROOK, MARY ELIZABETH (MARC LEWIS), author; member, Texas Institute of Letters, *Austin*

CROOK, WILLIAM HERBERT (ELEANOR), former U.S. ambassador to Australia; former president, San Marcos Academy; commissioner, U.S.-Mexican Border Development, *San Marcos*

CRUTCHER, RONALD A. (BETTY), professor of music and director of the School of Music, The University of Texas at Austin; cellist, *Austin*

CUNNINGHAM, ISABELLA C. (WILLIAM), professor of communications, The University of Texas at Austin , *Austin*

CUNNINGHAM, WILLIAM H. (ISABELLA), former president, The University of Texas at Austin; chancellor, the University of Texas System, *Austin*

CURTIS, GREGORY (TRACY), editor, *Texas Monthly;* author, *Austin*

DANIEL, JEAN BALDWIN, former first lady of Texas; author, *Liberty*

DARDEN, WILLIAM E., president, William E. Darden Lumber Company; former regent, The University of Texas System, *Waco*

DEAN, DAVID (MARIE), lawyer; former secretary of state, Texas, *Dallas*

DEBAKEY, MICHAEL E., surgeon; chancellor, Baylor College of Medicine, *Houston*

DECHERD, ROBERT W. (MAUREEN), president, A. H. Belo Corporation, *Dallas*

DELCO, WILHELMINA (EXALTON), former member, Texas House of Representatives; civic leader, *Austin*

DENIUS, FRANKLIN W. (CHARMAINE), lawyer; former president, the University of Texas Ex-Students' Association; member, Constitutional Revision Committee, *Austin*

DENMAN, GILBERT M., JR., lawyer, partner, Denman, Franklin & Denman; chairman of the board, Southwest Texas Corporation and Ewing Halsell Foundation, *San Antonio*

De Wetter, Margaret Belding (Peter), artist and poet, *El Paso*

Dick, James, founder-director, International Festival-Institute at Round Top; concert pianist and teacher, *Round Top*

Dobie, Dudley R., Jr. (Saza), of counsel, Brorby & Crozier, P. C., *Austin*

Dougherty, J. Chrys, III (Sarah), retired attorney; former Honorary French Consul in Austin; former trustee, St. Stephen's Episcopal School, Austin; the University of Texas Law School Foundation; Texas Supreme Court Historical Society, *Austin*

Dougherty, J. Chrys, IV (Mary Ann), assistant professor, Lyndon Baines Johnson School of Public Affairs, The University of Texas at Austin; director, School Information Project, Just for the Kids, *Austin*

Doyle, Gerry (Katherine), former chairman, foreign trade committee, Rice Millers Association, *Beaumont*

Dugger, Ronnie E. (Patricia Blake), author, *Wellfleet, MA*

Duncan, A. Baker (Sally), chairman, Duncan-Smith Company, *San Antonio*

Duncan, Charles William, Jr. (Anne), chairman, Duncan Interests; former secretary, U.S. Energy Departmen; deputy secretary, U.S. Defense Department; president, The Coca-Cola Company; chairman, Rotan Mosle Financial Corporation, *Houston*

Duncan, John House (Brenda), businessman; chairman, board of trustees, Southwestern University, *Houston*

Elkins, James A., Jr., trustee, Baylor College of Medicine; trustee, Menil Foundation, *Houston*

Erickson, John R. (Kristine), author; lecturer; owner, Maverick Books publishing company, *Perryton*

Evans, Sterling C., ranching and investments, *Castroville*

Farabee, Kenneth Ray (Mary Margaret), vice chancellor and general counsel, the University of Texas System; former member, Texas Senate, *Austin*

Fehrenbach, T. R. (Lillian), author; historian; former chairman, Texas Historical Commission; former chairman, Texas Antiquities Committee; member, Texas State Historical Association, *San Antonio*

Finch, William Carrington, retired dean, Vanderbilt Divinity School; former president, Southwestern University, *Nashville, TN*

Fisher, Joe J. (Kathleen), chief judge emeritus, U.S. District Court, Eastern District of Texas; former district attorney and state district judge, First Judicial District of Texas, *Beaumont*

Fisher, Richard (Nancy), managing partner, Fisher Capital Management; former executive assistant to U.S. secretary of the treasury; adjunct professor, Lyndon Baines Johnson School of Public Affairs, The University of Texas at Austin; democratic nominee for U.S. Senate, 1994; founder, Dallas Committee on Foreign Relations, *Dallas*

Flawn, Peter T. (Priscilla), president emeritus, The University of Texas at Austin, *Austin*

Fleming, Durwood (Lurlyn), former president and chancellor, Southwestern University, *Dallas*

Fleming, Jon Hugh (Cheryl), educator; consultant; businessman; former presi-

dent, Texas Wesleyan College; former member, Governor's Select Committee on Public Education, *North Zulch*

FONKEN, GERHARD JOSEPH (CAROLYN), former executive vice president and provost, The University of Texas at Austin, *Austin*

FROST, TOM C. (PAT), senior chairman of the board, Cullen/Frost Bankers, Inc., *San Antonio*

GALBRAITH, JAMES K. (YING TANG), professor, Lyndon Baines Johnson School of Public Affairs, The University of Texas at Austin, *Austin*

GALVIN, CHARLES O'NEILL (MARGARET), centennial professor of law, emeritus, Vanderbilt University, Nashville; of counsel, Haynes and Boone, L.L.P., Dallas; adjunct professor of law, The University of Texas at Austin, *Dallas*

GARNER, BRYAN ANDREW (PAN), author; lecturer; lawyer; president, LawProse, *Dallas*

GARRETT, JENKINS (VIRGINIA), lawyer; former member, board of regents, the University of Texas System; former chairman, board of trustees, Tarrant County Junior College, *Fort Worth*

GARWOOD, WILLIAM L. (MERLE), judge, U.S. Court of Appeals, Fifth Circuit, *Austin*

GILLIS, MALCOLM (ELIZABETH), president, Rice University, *Houston*

GOLDSTEIN, E. ERNEST (PEGGY), formerly: professor of law, The University of Texas at Austin; special assistant to President Lyndon B. Johnson; senior partner, Coudert Fréres, Paris, France; currently: advisor to the director, Harry Ransom Humanities Research Center, The University of Texas at Austin, *Austin*

GOLDSTEIN, JOSEPH L., professor of medicine and molecular genetics, the University of Texas Southwest Medical Center; Nobel laureate in medicine or physiology, *Dallas*

GORDON, WILLIAM EDWIN (ELVA), distinguished professor emeritus, Rice University; foreign secretary (1986–1990), National Academy of Sciences, *Houston*

GRANT, JOSEPH M., executive vice president and chief financial officer, Electronic Data Systems, *Plano*

GRAY, JOHN E. (MARY), president emeritus, Lamar University; chairman emeritus, First City National Bank, Beaumont; former chairman, Coordinating Board, Texas College and University System, *Beaumont*

GREENHILL, JOE R. (MARTHA), lawyer; former chief justice, Supreme Court of Texas, *Austin*

GRUM, CLIFFORD J. (JANELLE), chairman of the board and chief executive officer, Temple-Inland, Inc.; former publisher, *Fortune* magazine, *Diboll*

GUEST, WILLIAM F. (AMY), attorney; chairman, American Capitol Insurance Company, *Houston*

HACKERMAN, NORMAN (JEAN), former president, Rice University; former president and vice chancellor, The University of Texas at Austin, *Austin*

HALL, WALTER GARDNER, chairman of the board, Citizens State Bank, Dickinson; former president, San Jacinto River Authority, *Dickinson*

HAMM, GEORGE FRANCIS (JANE), president, the University of Texas at Tyler, *Tyler*

HANNAH, JOHN, JR. (JUDITH GUTHRIE), U.S. district judge, Eastern District of Texas, *Tyler*

HARDESTY, ROBERT L. (MARY), former president, Southwest Texas State University; former assistant to the president of the United States; former chairman, board of governors, United States Postal Service, *Washington, D.C.*

HARGROVE, James W. (MARION), investment counselor; former U.S. ambassador to Australia, *Houston*

HARRIGAN, STEPHEN MICHAEL (SUE ELLEN), author; contributing editor, *Texas Monthly*, *Austin*

HARRISON, FRANK, physician; former president, the University of Texas Health Science Center at San Antonio; former president, the University of Texas at Arlington, *Dallas*

HARTE, CHRISTOPHER M., investments, *Portland, ME*

HARTE, EDWARD HOLMEAD (JANET), former publisher, Corpus Christi *Caller, Corpus Christi*

HARVIN, WILLIAM C. (HELEN), lawyer, *Houston*

HAY, JESS (BETTY JO), chairman, HCB Enterprises, Inc.; chairman, Texas Foundation for Higher Education; former member, board of regents, the University of Texas System, *Dallas*

HAYES, PATRICIA A., president, St. Edward's University, *Austin*

HECHT, NATHAN LINCOLN, justice, Supreme Court of Texas, *Austin*

HERSHEY, JACOB W. (TERESE), board chairman, American Commercial Lines (retired); past chairman, advisory committee, Transportation Center, Northwestern University, *Houston*

HERSHEY, TERESE (JACOB), civic leader; Houston Parks Board; Texas Women's Hall of Fame; former board member, National Audubon Society; Trust for Public Lands, Texas Parks and Wildlife Commission, *Houston*

HEYER, GEORGE STUART, JR., emeritus professor of the history of doctrine, Austin Presbyterian Theological Seminary, *Austin*

HIGGINBOTHAM, PATRICK E. (ELIZABETH), judge, U.S. Court of Appeals, Fifth Circuit, *Dallas*

HILGERS, WILLIAM B., attorney; former chairman, Supreme Court of Texas Grievance Oversight Committee, *Del Valle*

HILL, JOHN L. (BITSY), attorney, former chief justice, Supreme Court of Texas; former attorney general, Texas; former secretary of state, Texas, *Houston*

HILL, LYDA, president, Hill Development Company and Seven Falls Company ..... *Dallas*

HILL, JOSEPH MACGLASHAN, physician; director, Wadley Research Institute; former president, International Society of Hematology, *Dallas*

HINES, GERALD DOUGLAS (BARBARA), chairman, Hines, *Houston*

HINES, JOHN ELBRIDGE, (retired) presiding bishop, Protestant Episcopal Church; trustee, Episcopal Seminary of the Southwest; former member, State Board of Hospitals and Special Schools, *Highlands, NC*

HOBBY, DIANA (WILLIAM), *Houston*

HOBBY, WILLIAM PETTUS (DIANA), lieutenant governor of Texas, 1973–1991; Radoslav A. Tsanoff Professor, Rice University; Sid Richardson Professor, Lyndon Baines Johnson School of Public Affairs, The University of Texas at Austin, *Houston*

HOFFMAN, PHILIP GUTHRIE (MARY), president emeritus, University of Houston; former president, Texas Medical Center, Inc. , *Houston*

HOLLAMAN, ELIZABETH E., headmistress, Trinity Episcopal School, *Galveston*

HOLTZMAN, WAYNE H. (JOAN), professor of psychology and education; president, Hogg Foundation for Mental Health, The University of Texas at Austin, *Austin*

HOOK, HAROLD SWANSON (JOANNE), chairman and chief executive, American General Corporation; trustee, Baylor College of Medicine, *Houston*

HOWE, JOHN P., III (JILL), physician; president, the University of Texas Health Science Center at San Antonio, *San Antonio*

HUBERT, FRANK W. R. (MARY JULIA), chancellor emeritus, Texas A&M University System, *Bryan*

HUEY, MARY EVELYN (GRIFFIN), president emerita, Texas Woman's University, *Denton*

HUGHES, VESTER T., JR.; lawyer; founding partner, Hughes & Luce, *Dallas*

HURLEY, ALFRED FRANCIS (JOANNA), chancellor, University of North Texas, *Denton*

HUTCHISON, KAY BAILEY (RAY), U.S. senator; former state treasurer, Texas, *Dallas and Washington, D.C.*

INMAN, BOBBY R. (NANCY), admiral, U.S. Navy (retired); investor, *Austin*

JACK, JANIS GRAHAM (WILLIAM DAVID), U.S. district judge, *Corpus Christi*

JAMAIL, JOSEPH D., JR. (LEE), attorney; philanthropist, *Houston*

JAMES, THOMAS N. (GLEAVES), cardiologist; president, the University of Texas Medical Branch at Galveston, *Galveston*

*JOHNSON, CLAUDIA TAYLOR (LYNDON B.), *Stonewall*

JOHNSON, RICHARD J. V. (BELLE), chairman and publisher, Houston *Chronicle*, *Houston*

JOHNSTON, MARGUERITE (CHARLES W. BARNES), journalist; author; former columnist and editor, *Houston Post*, *Houston*

JORDAN, BRYCE (JONELLE), former president, Pennsylvania State University, *Austin*

JOSEY, JACK S., president, Josey Oil Company; member, board of governors, Rice University; former regent, the University of Texas System, *Houston*

JUSTICE, WILLIAM WAYNE (SUE), judge, U.S. District Court, Eastern District of Texas, *Tyler*

**KAIN, COLLEEN T., retired executive assistant, The University of Texas at Austin, *Austin*

KEETON, PAGE (MADGE), former dean, School of Law, The University of Texas at Austin, *Austin*

KELSEY, MAVIS PARROTT (MARY), retired physician; founder and former chief, Kelsey-Seybold Clinic, *Houston*

KELTON, ELMER (ANNA), fiction writer, livestock journalist, *San Angelo*

KEMPNER, HARRIS L., JR., trustee, H. Kempner; president, Kempner Capital Management, Inc.; member, Texas Governor's Task Force on State Trust & Asset Management, *Galveston*

KEMPNER, RUTH L., member, Kempner Foundation, *Galveston*

KESSLER, JAMES LEE (SHELLEY), Rabbi, Temple B'nai Israel; founder and first president, Texas Jewish Historical Society, *Galveston*

KING, CAROLYN DINEEN (JOHN), judge, U.S. Court of Appeals for the Fifth Circuit, *Houston*

KING, JOHN Q. TAYLOR, SR., chancellor and president emeritus, Huston-Tillotson College; major general, AUS (retired), *Austin*

KING, MAY DOUGHERTY (JOHN ALLEN), investor, oil exploration and development; founder, Dougherty Carr Arts Foundation; Equestrian Order of the Holy Sepulchre, *Corpus Christi*

KNEPPER, DOROTHY WARDELL (DAVID W.), former director, San Jacinto Museum of History, *Houston*

KOZMETSKY, GEORGE (RONYA), professor and administrator, The University of Texas at Austin, *Austin*

KRIER, CYNDI TAYLOR (JOSEPH), former member, Texas Senate; partner, Vallejo Ranch, *San Antonio*

KRUEGER, ROBERT "BOB" CHARLES (KATHLEEN), U.S. Ambassador to Botswana; former U.S. senator, congressman, ambassador to Burundi, ambassador-at-large to Mexico; former Texas Railroad commissioner; vice provost and dean of Arts and Sciences, Duke University, *New Braunfels*

LABOON, ROBERT BRUCE (RAMONA), managing partner, Liddell, Sapp, Zivley, Hill & LaBoon, *Houston*

LANCASTER, SALLY RHODUS (OLIN), consultant to the nonprofit sector, director emerita, The Meadows Foundation, *Dallas*

LAW, THOMAS HART (JO ANN), lawyer; former member, board of regents, the University of Texas System, *Fort Worth*

LEBERMANN, LOWELL H., JR., president, Centex Beverage, Inc.; member, board of regents, the University of Texas System, *Austin*

LEE, AMY FREEMAN, chairman, board of trustees, the Wilhelm School, Houston; artist; critic; lecturer, *San Antonio*

LEHRER, JAMES CHARLES (KATE), co-anchor, MacNeil/Lehrer NewsHour, *Arlington, VA*

LEMAISTRE, CHARLES A. (JOYCE), president emeritus, the University of Texas System Cancer Center M. D. Anderson Hospital and Tumor Institute, *Houston*

LEVIN, WILLIAM C., physician; former president and Ashbel Smith Professor, the University of Texas Medical Branch at Galveston, *Galveston*

LIEDTKE, J. HUGH, president, chief executive officer, chairman of board, Pennzoil United; trustee, Rice University, *Houston*

LINDSEY, JOHN H., businessman; art collector; civic leader; former member, board of directors, Museum of Fine Arts; director, Alley Theatre; member, board of regents, Texas A&M University System; former member of the board of the United States Military Academy at West Point, *Houston*

LINDZEY, GARDNER, former vice president for academic affairs, The University of Texas at Austin; psychologist; author, *Palo Alto, CA*

LIVINGSTON, WILLIAM S. (LANA), former vice president and dean of graduate studies, The University of Texas at Austin, *Austin*

LOCHRIDGE, LLOYD (FRANCES), lawyer; former president, State Bar of Texas; former member, board of governors, American Bar Association, *Austin*

LOCKE, JOHN PATRICK (RAMONA), president, Locke Holdings, Inc., *Dallas*

LOMBARD, RICHARD S., lawyer, *Dallas*

LORD, GROGAN, chairman, First Texas Bancorp; member, Texas Securities Board; trustee, Southwestern University, *Georgetown*

LOVE, BEN F. (MARGARET), retired chairman and chief executive officer (1972–1989), Texas Commerce Bank, Houston, and Texas Commerce Bancshares, *Houston*

LOVELL, JAMES ARTHUR, JR. (MARILYN), astronaut in Apollo 8 and 13, Gemini 7 and 12; recipient of the Presidential Medal of Freedom in 1970 and the Congressional Space Medal of Honor in 1995, *Horseshoe Bay*

LOVETT, HENRY MALCOLM (MARTHA), lawyer; former chairman of the trustees, Rice University, *Houston*

LOW, GILBERT, lawyer, *Beaumont*

LUCE, TOM (PAM), lawyer; of counsel, Hughes & Luce; partner, Luce & Williams, *Dallas*

MCCOLLUM, LEONARD FRANKLIN, president, Continental Oil Company, *Houston*

MCCOMBS, B. J. "RED" (CHARLINE), chairman of the board, Southwestern University; chairman of the board of visitors, the University of Texas M. D. Anderson Cancer Center, *San Antonio*

MCCORQUODALE, ROBIN HUNT; author, *Houston*

MCDERMOTT, MARGARET (EUGENE), *Dallas*

MCFADDEN, JOSEPH M., president emeritus, University of St. Thomas, *Houston*

MCGHEE, GEORGE CREWS, former U.S. ambassador to West Germany, *Middleburg, VA*

MACKINTOSH, PRUDENCE M. (JOHN), author; member, Texas Institute of Letters, *Dallas*

MCKNIGHT, JOSEPH WEBB (MIMI), professor, Southern Methodist School of Law; legal historian; law reformer, *Dallas*

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BENJAMIN FLOYD PITTINGER
GEORGE FRED POOL (1984)
CHARLES SHIRLEY POTTS (1963)
HERMAN PAUL PRESSLER JR. (1996)
HARRY MAYO PROVENCE (1996)
MAURICE EUGENE PURNELL
CHARLES PURYEAR (1940)
CLINTON SIMON QUIN (1956)
COOPER KIRBY RAGAN
HOMER PRICE RAINEY (1985)
CHARLES WILLIAM RAMSDELL (1942)
EDWARD RANDALL (1944)
EDWARD RANDALL JR. (1970)
KATHARINE RISHER RANDALL (1991)
LAURA BALLINGER RANDALL (1955)
HARRY HUNTT RANSOM (1976)
EMIL C. RASSMAN
FANNIE ELIZABETH RATCHFORD
SAM RAYBURN (1961)
JOHN SAYRES REDDITT (1972)
LAWRENCE JOSEPH RHEA (1946)
WILLIAM ALEXANDER RHEA (1941)
JAMES OTTO RICHARDSON
RUPERT NORVAL RICHARDSON (1987)
JAMES FRED RIPPY
SUMMERFIELD G. ROBERTS (1969)
FRENCH MARTEL ROBERTSON (1976)
CURTICE ROSSER
JOHN ELIJAH ROSSER (1960)
JOSEPH ROWE
JAMES EARL RUDDER (1969)
THOMAS J. RUSK
McGRUDER ELLIS SADLER (1966)
JEFFERSON DAVIS SANDEFER (1940)
MARLIN ELIJAH SANDLIN
HYMAN JUDAH SCHACHTEL (1991)
EDWARD MUEGGE "BUCK" SCHIWETZ (1985)
VICTOR HUMBERT SCHOFFELMAYER (1966)
ARTHUR CARROLL SCOTT (1940)
ELMER SCOTT (1954)
JOHN THADDEUS SCOTT (1955)
WOODROW BRADLEY SEALS (1991)
TOM SEALY (1992)
GEORGE DUBOSE SEARS (1974)
WILLIAM G. SEARS
ELIAS HOWARD SELLARDS (1960)
DUDLEY CRAWFORD SHARP
ESTELLE BOUGHTON SHARP (1965)
JAMES LEFTWICH SHEPHERD JR. (1964)
MORRIS SHEPPARD (1941)
JOHN BEN SHEPPERD (1989)
STUART SHERAR (1969)
PRESTON SHIRLEY (1991)
ALLAN SHIVERS (1985)
RALPH HENDERSON SHUFFLER (1975)
JOHN DAVID SIMPSON JR.
ALBERT OLIN SINGLETON (1947)
JOSEPH ROYALL SMILEY (1991)
A. FRANK SMITH JR. (1993)
A. FRANK SMITH SR. (1962)
ASHBEL SMITH
FRANK CHESLEY SMITH SR. (1970)
HARLAN J. SMITH (1991)
HENRY SMITH
HENRY NASH SMITH
THOMAS VERNON SMITH (1964)
HARRIET WINGFIELD SMITHER (1955)
ROBERT S. SPARKMAN
RALPH SPENCE (1994)
JOHN WILLIAM SPIES
TOM DOUGLAS SPIES (1960)
STEPHEN H. SPURR (1990)
ROBERT WELDON STAYTON (1963)
ZOLLIE C. STEAKLEY (1991)
RALPH WRIGHT STEEN (1980)
IRA KENDRICK STEPHENS (1956)
ROBERT GERALD STOREY (1981)
GEORGE WILFORD STUMBERG
HATTON WILLIAM SUMNERS (1962)
ROBERT LEE SUTHERLAND (1976)
HENRY GARDINER SYMONDS (1971)
MARGARET CLOVER SYMONDS
WILLIS M. TATE (1989)
JAMES U. TEAGUE (1996)
ROBERT EWING THOMASON (1974)
J. CLEO THOMPSON (1974)
BASCOM N. TIMMONS (1987)
LON TINKLE (1980)
CHARLES RUDOLPH TIPS (1976)
MARGARET LYNN BATTS TOBIN (1994)
JOHN G. TOWER (1991)
HENRY TRANTHAM (1961)
FRANK EDWARD TRITICO SR. (1993)
GEORGE WASHINGTON TRUETT (1944)
RADOSLAV ANDREA TSANOFF (1976)
EDWARD BLOUNT TUCKER (1972)
WILLIAM BUCKHOUT TUTTLE (1954)
THOMAS WAYLAND VAUGHAN (1952)
ROBERT ERNEST VINSON (1945)
LESLIE WAGGENER (1951)
AGESILAUS WILSON WALKER JR. (1988)
EVERETT DONALD WALKER (1991)
THOMAS OTTO WALTON
FRANK H. WARDLAW (1989)
ALONZO WASSON (1952)
WILLIAM WARD WATKIN (1952)
ROYALL RICHARD WATKINS (1954)
WALTER PRESCOTT WEBB (1963)

HARRY BOYER WEISER (1950)
PETER BOYD WELLS JR. (1991)
ELIZABETH HOWARD WEST (1948)
CLARENCE RAY WHARTON (1941)
JOHN A. WHARTON
WILLIAM H. WHARTON
WILLIAM MORTON WHEELER (1937)
GAIL WHITCOMB (1994)
JAMES LEE WHITCOMB
WILLIAM RICHARDSON WHITE (1977)
WILLIAM MARVIN WHYBURN (1972)
HARRY CAROTHERS WIESS (1948)
DOSSIE MARION WIGGINS (1978)
PLATT K. WIGGINS
JACK KENNY WILLIAMS (1982)
ROGER JOHN WILLIAMS (1987)
LOGAN WILSON (1992)
JAMES BUCHANAN WINN JR. (1980)
JAMES RALPH WOOD (1973)
DUDLEY KEZER WOODWARD JR. (1967)
WILLIS RAYMOND WOOLRICH (1977)
BENJAMIN HARRISON WOOTEN (1971)
SAM PAUL WORDEN (1988)
GUS SESSIONS WORTHAM (1976)
LYNDALL FINLEY WORTHAM
FRANK McREYNOLDS WOZENCRAFT (1993)
FRANK WILSON WOZENCRAFT (1967)
WILLIAM EMBRY WRATHER (1963)
ANDREW JACKSON WRAY (1981)
RALPH WEBSTER YARBOROUGH
RAMSEY YELVINGTON (1972)
HUGH HAMPTON YOUNG (1945)
SAMUEL DOAK YOUNG
STARK YOUNG
HENRY B. ZACHRY (1984)