

It is an honor for me to be the speaker at the first graduation ceremony for the UT Southwestern Graduate School of Biomedical Sciences that is being held separately from that of your bigger and older, but no more important brother, Southwestern Medical School. And so I am delighted to claim the honor of being the graduate school's first ever graduation speaker. As an MD/PhD, I have enormous respect for both degrees. And I extend to you, with great sincerity, my hearty congratulations. You have earned the highest ranking, most prestigious academic degree: the degree that says you are a creator of knowledge – a creator of understanding of our world. To me, there is no nobler path to follow through life.

The timing of this graduation is also of special significance to me. We share the fact that we are both having a commencement; we are both about to start something new. Today is the last day at UT Southwestern for most of you. Next Monday will be my last day as an employee of the University of Texas Southwestern Medical Center. I will retire from the faculty just two weeks short of 28 years after my first day on the job here as Chair of the Department of Pharmacology. I remember well my arrival at UT Southwestern on my first day of work here. As I pulled into the faculty garage a giant white bird swooped low in front of my car. I was unaware of the bird sanctuary on campus, and I yelped out: "My God, it's a flippin albatross!" Well of course it was an egret. And it was obviously not a harbinger of impending doom, but rather of good things to come. It has been a wonderful ride for me, and it is sad when great rides come to an end. But I am excited about my future because I am not retiring from science, I intend to continue to try to do useful things, and I am most pleased that I will continue to have my office here on the UT

Southwestern campus. More about what I'm going to do in a few minutes. For now, let's talk about you.

For several years I gave a welcome talk to incoming graduate students. I think the last time I did this was in the fall of 2003, which means that some of you probably heard that talk. I tried to paint a very rosy picture of your upcoming life as an explorer – with you as the modern day equivalent of Christopher Columbus – off to discover a new world. I talked about how the folks in charge will give you ships to sail for your journey – meaning a laboratory and money to equip it and money to hire people to work with you. And many of you will enjoy the ultimate gift – the freedom to pursue your own ideas, which will come along with a franchise to go to the taxpayers and ask them for their hard-earned money to fund your search for knowledge. You do this by presenting your ideas in the form of applications for funding. You will have the opportunity to earn your living by living your dream. That is a life-long deal that's tough to beat. You will have a sense of personal satisfaction because you are doing something of real value. Kenneth Burns said to recent graduates: “society must support science and the arts. Not because these things are needed to defend the country or the world but because these things create a country or a world that's worth defending.”

The fabulous opportunities I spoke about six years ago are still there – and they are still wonderful and unique. But there *are* some clouds on the horizon. So let's spend at least a few minutes facing up to them. The solutions to many of the problems on the horizon will be left for you and others in your generation to find.

When we talked in 2003, we were just coming to the end of a time when the budget for the National Institutes of Health had doubled over a period of about five years -- from \$13.6 billion in 1998 to \$27 billion in 2003. It felt so good. So what has happened since? What questions shall we ask to assess the current state of affairs?

Questions: Are we spending all that we need to spend or should spend? Are we as a country making a reasonable investment in biomedical research and other types of scientific research? The last six years, since 2003, have seen a total increase of only 7% in the NIH budget, and thus there has been a significant decline in purchasing power for biomedical research. We hit a stone wall in 2003. How much **should** we spend? It seems to me that a proper benchmark for biomedical research would be to look at the amount we spend on healthcare, which is currently about \$2.3 trillion dollars a year. So the federal government spends an amount equal to about 1.3% of health care spending on biomedical research. To me, admittedly biased, this is a small number, especially given the paucity of information on the real value of many of the ways that we spend money on health care. No technologically-oriented company spends so little on the research that will ensure their future. No technologically-oriented country can hope to stay at the top of the world with such a small investment in its future.

President Obama spoke recently at the annual meeting of the National Academy of Sciences. He said: "I believe it is not in our character, the American character, to follow. It's our character to lead. And it is time for us to lead once again. So I'm here today to set this goal: We will devote more than 3 percent of our GDP to research and development. We will not just meet, but we will exceed the level

achieved at the height of the space race, through policies that invest in basic and applied research, create new incentives for private innovation, promote breakthroughs in energy and medicine, and improve education in math and science.”

Questions: Are people hungry for more grant money? Are there sufficient numbers of talented people out there to spend more money wisely? There was a recent call from the NIH for so-called challenge grants – 200 or maybe 400 to be funded with economic recovery funds; 20,000 applications were received. The failure rate will thus be 98 or 99%! Additional money will be used to extend the pay line to grants that were rated in the lower half of the upper quartile. Good, I guess; that is not stooping too low. But will there be money to renew any of these grants 2 or 3 years down the road? That remains to be seen.

Question: Are we training too many people? Well, if a modestly-sized lab turned out but one terminally-trained individual every two years, the lab chief would replenish her or himself by 15-20 fold over a 30-40 year career. This obviously cannot be sustained. Perhaps labs must be smaller and populated by fewer people who strive in time to run a lab themselves. The rest must be content to be important contributors and not leaders. We need to train talented people who can work in labs and have satisfying and productive careers in research but who do not expect that they will have their own lab some day. This is a tough message to deliver.

Question: Are we training the most talented people to be our research leaders?

Another quote from President Obama: “Our schools continue to trail other developed countries and, in some cases, developing countries. Our students are outperformed in math and science by their peers in Singapore, Japan, England, the Netherlands, Hong Kong, and Korea, among others. American 15-year-olds ranked 25th in math and 21st in science when compared to nations around the world. And we have watched as scientific integrity has been undermined and scientific research politicized in an effort to advance predetermined ideological agendas.”

Young people have turned away from science in the United States. One reason: *It takes too long to get a job that does not pay that well.* We graduate 50,000 lawyers each year, but only 17,000 physicians, and decreasing numbers of US citizen scientists. The *average salary* of a major league baseball player was \$2.8M a couple of years ago; the minimum salary was \$390,000. The average salary for an independent major league biomedical scientist is about 5% of that of major league professional athlete. Two-thirds of all current doctoral engineering students in the United States are from foreign countries. One-third of all science doctorates awarded in the United States go to non-citizens.

Question: Are we giving young people the opportunity to realize their capabilities? We must support young people’s research efforts. Most people probably do their best, most important work before they are 40, and surely before they are 50. There are exceptions of course, and age may bring wisdom, but it usually does *not* bring creativity. Fame acquired before or around age 40 while running a smaller lab translates into more money to run a bigger lab and a less efficient lab when the creative genius is waning. United States science was a great

success *because* we gave people their independence and freedom when they were young. *We have lost this advantage.* It takes longer to find a job, and so training is extended for artificial reasons. It then takes longer to get a grant. The percentage of NIH funded investigators under age 40 has now fallen to a very small number. What a shame. Recently, one of our faculty members tried to convince me that money should be specially earmarked to support senior investigators. I disagree completely. Better ways should be found to take advantage of the wisdom of senior investigators, but they surely don't need special consideration for research funding. The young people do need such consideration.

Obama said to the National Academy of Sciences membership (an aged group): "let's create new pathways for experienced professionals to go into the classroom. There are, right now, chemists who could teach chemistry, physicists who could teach physics, statisticians who could teach mathematics. But we need to create a way to bring the expertise and the enthusiasm of these folks -- folks like you -- into the classroom."

Chris Buckley, a humorist and satirist, wrote a book called *Boomsday*. Buckley describes an America near disaster as the hoard of baby boomers begins to retire, bankrupting the younger generation. The heroine of the book is a young woman professional who blogs all night, calling for an economic Bastille Day. Her followers attack gated communities and destroy golf courses in protest against the retired old folks. To solve the Social Security problem, she promotes legislation to require senior citizens to kill themselves in exchange for estate tax breaks or other inducements (*e.g.*, farewell cruises). She calls it "voluntary transitioning". *In the absence of*

mandatory retirement, perhaps we need to encourage more voluntary transitioning from the aging scientific community. Shrink the size of laboratories. Become a more active citizen of the University. Do more teaching. Tenure should not last forever. Maybe even accept lower salaries! I am ***not*** making many friends among my colleagues with these suggestions!

Question: Are we buying the right kind of science? When funds are tight the tendency is to become conservative – to fund things that are sure to work. This means that incremental work gets funded rather than transformative research. So much preliminary data is required that projects are usually finished before they are funded.

And so there are major issues, and the mood is not that bright – not in science or medicine and for the last year not throughout the entire economy and not throughout the world. A cartoon in the Dallas Morning News two weeks ago showed a chap like me on the stage at graduation saying: “And with your diplomas this year we have included a map to the unemployment office.” And 60 minutes correspondent Scott Pelley said to the graduates at Texas Tech: “You picked a hell of a time to graduate. Did nobody in this class take Timing 101? I know you’re looking up here at my generation and you’re thinking, ‘Great, thanks, just when it was our turn, you broke it.’ ” Well, I don’t think we have broken it, but there surely are stresses and strains.

So back to Barack Obama at the National Academy of Sciences, where he said: “At such a difficult moment, there are those who say we cannot afford to invest in science, that support for research is somehow a luxury at moments defined by necessities.” Obama said:

“I fundamentally disagree. Science is more essential for our prosperity, our security, our health, our environment, and our quality of life than it has ever been before.”

Question: Where might more money come from to pay for biomedical research? There have been suggestions that a specific tax on health insurers would be a proper way to fund more research. The health insurers of course object. They have no real stake in prolonging your life and giving you the opportunity to rack up more medical bills. They want you to remain perfectly healthy until you are ready to check out; you should then die swiftly, preferably before you can reach a hospital. It strikes me that the life insurance companies might be willing to share the burden. In contrast to the health insurers, they profit from your longevity; they might be motivated to help fund life-prolonging research.

Where else do we find money being spent on biomedical research and development? The US-based pharmaceutical industry spends over \$50 Billion dollars a year - or nearly 70% more than the NIH. Yes, much of that is for development of products rather than for discovery research, but that is none the less important, difficult, and interesting. They spend 15-20% of their sales for Research and Development, in contrast to public spending of 1.3% of the health care budget. Scientific careers in industry were viewed with some suspicion when I was starting my career. This was simply not something that the better people did. But things have changed tremendously. Pharmacology, my field, used to be a bit of a dirty word. But now everyone wants to develop drugs and, foolishly, everyone thinks they can. People love pharmacology, although they like to clean up the old girl a bit before bringing her home to meet

the parents. So they invent cool new names like chemical biology or chemical genetics and pretend they are bringing new insights to a very old subject – the study of the interactions between biological systems and chemicals. Many of the best biomedical scientists now pursue careers in industry, working at huge old pharmaceutical companies or successful or fledgling biotech companies. Some of the best science is carried out in these settings. Resources and facilities may be superior, opportunities for collaboration abound, individual fame and glory is less likely, but compensation is better; take your pick.

But clouds also surround the pharmaceutical industry, and its vocal critics find support for their accusations from a poorly informed public that thinks the pharmaceutical industry is responsible for our country's very high health costs. It's simply not true except in some individual cases. The cost of drugs accounts for 12% of the nation's health care spend. If that percentage number were really high – 70%, for example -- it would likely mean that drugs fixed everything except trauma. But the critics say there is little innovation, that too much money is spent on promotion, that prices are too high, that industry cannot be trusted and clinical trials should be taken over by a federal agency, and that patent protection should be shortened to six years, even though a mouse trap gets 20 years. To those of you who choose to work in industry, reject this poppycock and prove to all that the most strident critics are wrong.

And where else can we find support for research? A few states in the United States are pursuing vigorously the notion that investment in high technology is good for society, both for the health and welfare it can bring to its citizens, and also because it can bring special advantage

to the state making the investment by creating more jobs, better jobs, and better paying jobs. Not surprisingly, California led the pack by creating the California Institute of Regenerative Medicine, with the mandate to invest \$3 Billion over a ten-year period on stem cell research. More surprisingly, Texas has jumped into the game with the creation of CPRIT – The Cancer Prevention and Research Institute of Texas, empowered by a constitutional amendment supported by a generous majority of the voters of the state to spend \$3 Billion over the next decade on cancer research.

And that brings me to phase II of my own voluntary transitioning. Phase I was moving to the dean's office, and phase II will begin next week as I become the Chief Scientific Officer of CPRIT, charged with giving away hundreds of millions of dollars a year for research. When I first mentioned this to Dr. Podolsky (President of UT Southwestern Medical Center) he wisely quipped, "Well, you won't be lonely." I think I'll have many new friends, at least for a while.

What can we do...to do CPRIT right and show the rest of the world that Texas is the place to be?

1. There will be no politics in the distribution of funds. In her talk to the Texas Academy of Medicine, Engineering, and Science last January, our Senator Kay Bailey Hutchison stressed that the money must NOT be given out by congressional district. Funds will be distributed according to a pay list prepared by superb peer reviewers, all of whom will be non-Texans to avoid conflicts of interest.
2. We will not fund the left-overs from the National Cancer Institute. We must focus on innovation and importance. We must be willing to encourage risk and to share in that risk.

3. We must fund the entire spectrum of research: basic, translational, and clinical. The people of Texas are each going to pay hundreds of dollars for this program. They have a right to expect both health benefits and economic benefits. We must make fundamental discoveries and we must bring them to patients in the form of prevention and better treatments.

4. We must bring more talent to Texas. Is money the real limiting step for science in Texas or is it people? We must train the brightest to pursue the mysteries of cancer. We must recruit the brightest to make the discoveries and establish the companies that will stimulate growth in Texas. Recruitment of young rising stars and established rock stars is the thing we can do that will last well beyond the 10 years of funding envisioned by CPRIT.

5. And to the legislature and to the public, we ask for patience. We will cure nothing in the first few years. New drugs take over a decade to come to market. The first war on cancer was declared by President Nixon, now 40 years ago, and the war goes on. We will not under-work, but we must not over-promise.

Now for the last minute or two, let's return to thoughts about you with a few more serious words. Since I am now an aging curmudgeon, it seems to me that people who make their living by living their dream sometimes get a bit spoiled. They forget what a great deal they have. They forget what a privilege it is to go to the tax payers and ask for their money to pursue their individual dreams. Some seem to believe that it's "all about me" and my fame and glory; that it's all about numbers of publications or the size of my lab or the number of grants. **It's not about that.** It's about fundamental knowledge and understanding gained; it's about deep thought and

honesty. And it's also about institution building and fabulous citizenship. No one works in isolation. Great work comes from great institutions that come only from interactions among thoughtful people. And since I hope you are grateful to at least some of your teachers, and I hope especially to your research advisors, remember that gratitude and instill it in others as you undergo the marvelous transition from student to teacher.

I started some of you off six years ago with stories of Christopher Columbus. I'll close with an equally nautical theme. Mark Twain said: "Twenty years from now you will be more disappointed by the things you didn't do than by the ones you did. So throw off the bowlines, sail away from the safe harbor. Catch the trade winds in your sails. Explore. Dream. Discover."