

**Weidenbaum Center on the Economy, Government, and Public Policy
Breakfast Presentation**

November 21, 2005

Biotech in St. Louis

By William H. Danforth
Chancellor Emeritus, Washington University

Thanks very much for a really overly generous introduction. Actually, Washington University was a great place before I came. Looking around this audience, though, it's a little intimidating because this is, after all, the Weidenbaum Center, and I'm used to listening to Murray Weidenbaum talk, and here he is in the audience over here. In addition, there are people in the audience who know a great deal about this subject and certainly in some respects, in various areas, more than I do. It reminds me a little about a story of a man who lived through the Johnstown Flood. It was some years ago and as he got older he liked to tell the story. As he got a little older his words got longer and longer, and he tried to tell it to more and more, and fewer and fewer listened. As must happen to most of us, he passed on. He came to the Pearly Gates and St. Peter said "Come on in." He said, "Oh St. Peter, what I want to know is can I tell people about the Johnstown Flood?" St. Peter said, "Yes, you can." He said, "Will they listen?" St. Peter said, "Yes. they will. We'll put together a huge stage and people will come from all around heaven and listen to you as often and as long as you want." The man said, "This is the place for me." St. Peter said as he walked through, "Of course, Noah will be in the audience."

I'm here because I share the Coalition on Plant and Life Science. The name is on the slide here. This group was established by Civic Progress and RCGA to promote economic development. The basic idea was that we should capture the potential for economic development from the world-class research in life sciences; that people should not have to go to the East or West Coast in order to begin companies in the kind of science that we do so well. I

want to tell you how I, as a physician, got involved in economic development, then say a few words about our scientific assets and finally about a major obstacle in the way.

First, how did I get into this? I shared the general concern that many people have in St. Louis about loss of headquarters and need to continue to grow the economic base. Certainly that is important to all of us, and it's important to Washington University, to all of our charitable institutions, and so on. Shortly after I retired some faculty members in the School of Engineering developed a switch for getting information quickly on and off the internet. They thought that this would be a technology to build a company around and they tried for two years and failed. They then went out to the Bay Area in California and immediately were received with open arms. They got money. They got space. They got advice. They started a company and in less than a year it was sold for \$350 million dollars. Most of the money and the jobs, of course, went out to the West Coast. I thought that was terrible, and thought about the fact that we have some wonderful IT, computer work, that our major science here is life science. Here we are truly an international leader and focus especially on Washington University's School of Medicine, but other areas as well, and we should do something about it.

I talked with RCGA and Civic Progress people and others. The Battelle Group was brought in to look at what we do and to benchmark us against other communities, to say what we could do and what we needed to do if we were going to be successful. The Battelle Group, first of all, benchmarked us, confirmed what we already knew — that we had wonderful science, and sort of set out a road map that they said we would need to follow to develop companies out of this science.

The first lesson I learned was there's no magic bullet. It was not one thing we could do. We needed to do a lot of things. I'll talk about some of those. We needed to do a lot of things and we needed to do them in the right sequence. They all had to grow together. Just like a baby growing up, everything has to develop in a coordinated way. You couldn't have too much venture capital chasing too few ideas. That would be very bad. You couldn't have companies

developing and no real estate to house them. That would be bad. On the other hand, you build real estate before the companies were ready. If you did that, people would lose money and not want to invest in more real estate. Everything had to be done in a coordinated way. The Coalition on Plant and Life Science was developed and given the job of sort of overseeing this activity. This is a list of the Coalition members. You don't have to read it all, but you can see it has in it academics, scientists, business people, legal people and a variety of community leaders that we all thought would be helpful as we worked through this project.

What is the vision? What do we see that they want to accomplish? First of all, we want to have universities and not-for-profits conduct groundbreaking research in agriculture and biomedicine that improves the health and wellbeing of all. We put in agriculture here. Plant science is our specialty here in St. Louis. Plant science is a very small niche in the economy compared with what goes on in the biomedical sciences. There's enormous competition in biomedical sciences and we think we can be one of the world leaders in biomedical science. We are in the science, we think we can be one of the leaders in developing the science in the companies. If we do it right in plant science, we could be the leader because there isn't so much competition and we already have here the science in Washington University and the University of Missouri-Columbia, and Monsanto has the largest group of plant scientists of any industry. That could be a special niche and if we do it right, we are to lead the world in plant science. We wanted discoveries with commercial potential to become the basis of companies that retain economic benefits of the science in our community and our region. We wanted state-of-the-art facilities available for companies as they mature. We want adventure capital financing accessible to emerging companies so that they can remain in St. Louis and do not have to go elsewhere. We needed to train a qualified professional work force to fill what we hoped would be continuously created high-paying jobs and give individuals opportunities to pursue fulfilling careers here. Our group focused on keeping the science strong, on providing the investment capital, and facilities. We have two excellent incubators in St. Louis, one on Forest Park

operated under the offices of the University of Missouri-St. Louis, called the Center for Emerging Technologies; the other is Nidus, located on the Monsanto campus in Creve Coeur. We also needed the commercial laboratory space for companies growing out of incubators. We needed to work on state and federal policy, and we needed to work on marketing. RCGA has been in charge of the marketing effort and probably all of you have heard of the term bio-belt, which is one of the terms that they have developed.

Let me just run through some of these activities here. First, venture capital. Venture capital as many of you know is not a single thing. It's lots of things. This is a diagram and again I don't think one needs to go through it, but just think of the complexity here. Early on you need some money that can test ideas to see if they are even worth thinking about forming a company and that requires some money that you don't expect to get a return on. With the help of state tax credits and some gifts, we have collected some money for that purpose and that is called the "bio-generator" near the top of the slide. Then if you go to the next stage, one needs angels, that is, people who are interested in investing early companies. Bob Calcaterra at the Nidus Center has taken with a person from RCGA the charge of putting together a group of angel investors, people who are interested in these kinds of investments and who work as a team and use some of the expertise we have to help them decide which technologies might be worth investing in and which might not. That is underway, and they have put together some teams of people who are interested in that. If any of you are interested in joining it or looking into it, we can arrange for that.

We have now venture capital funds in St. Louis, which we did not have before. We have Prologue, which you can see there. RiverVest, whose leader Tom Melzer is here today. Then we have Oakwood, which is a later-stage company which invests in little bit different stages of the development of companies, and finally we put together the fund of funds. This is the Vectis Life Science Fund. The reason for putting together a fund of funds is two-fold. First of all the fund of funds is safer for entities like pension funds, particularly public pension funds. It's safer

to invest in fund of funds where your risks are spread out very widely than it is to invest directly in a venture fund. Second, the fund of funds is operated by one of the leading venture capitalists in the country from Boston, Peter Brooke. He and his son John have made investments both in our local venture capital funds and national venture capital funds help to tie everything together and make available people who know St. Louis on both coasts so that there can be co-investing. Co-investing is the big thing in the venture capital business.

As I have said, we have two incubators. One is the Center for Emerging Technologies on Forest Park. You can see that their companies have about \$313 million invested in them. They are a variety of life science companies, and one has outgrown the facilities and will be ready to move to commercial space very soon. The second incubator is the Nidus Center. That's out on the Monsanto property at Olive and Warson Road and they have about \$85 million invested in their companies. All in all, we have about 24 companies here with over 400 million dollars invested so we are off to a good start. We haven't arrived anywhere yet, but we are off to a very good start.

Talking about some of the activities, and here is just a map of our community, and it outlines in the map the areas with life science activity going on. This can show that we really do have quite a lot of life science activities going on. We have Sigma Aldrich of course. We have Monsanto. We have Mallinckrodt, and we have other companies as well. Over on the eastside, we have one of the best pilot plans for developing products out of corn or soybeans in the nation. The area of greatest concentration is what's labeled as St. Louis Technopolis Area, and here is a larger map of that. This is the area where most of the life sciences, the academic kind of life sciences in St. Louis are done. That is between Kingshighway with Washington University Medical School and the associated hospitals, and St. Louis University and its medical school on Grand, and then on the north, the Center for Emerging Technologies, and on the south the Missouri Botanical Garden.

We put together a group consisting of the leaders of all those institutions plus representatives from RCGA and Civic Progress, and the City of St. Louis with Alderman Joe Roddy, who is the alderman for this area, and we have incorporated this. We raised almost \$30 million in capital, more than that now, and we have some tax credits from the state. We have begun purchasing some land and developing some land, and the first building is underway along Forest Park, for commercial wetlands space. This is a picture of how it will look when it's finished. Half of that building is rented, and we are looking hard to rent the rest of it. We're trying to grow all these things in a coherent way so that nothing gets too far ahead of anything else, and we've had some success here.

We also felt that we had to work with our governments because government policy is very important. We worked with Governor Holden and his staff. We worked with people in Kansas City. We worked with the University of Missouri, and we hired Battelle to do a statewide strategy, "An Opportunity to Build Missouri's Economic Future." That was released in January of 2003, with bipartisan support and a lot of enthusiasm. We got a newly established legislative caucus and a Joint Committee on the Life Sciences. That was started with a lot of fanfare, and since that time though, we've had some changes. It all seemed to be going really well but we hit a new, at least to me unforeseen, road block and that is efforts to criminalize a branch of medical research called Somatic Cell Nuclear Transfer that gathered a lot of momentum in the legislature. It looked like in this last legislative session as if it might pass. Those who were favorable felt that they had a clear shot that certainly it would pass this year. As you might guess, I was on the other side. I was very opposed as were some of our colleagues. We did escape criminalizing it in the last state legislative session thanks to Governor Blunt's help and the help of some key legislators.

I wanted to say a word about why I have opposed these efforts to criminalize stem cell research. A part of it is economics, and I'll go into that in a minute, but first I am a physician. I use to be a medical scientist in the past and I believe in medical research. If you go to old

cemeteries, you'll see lots of graves of babies. You don't see that anymore. If you go to old cemeteries you'll see lots of graves of young women who died around the time of childbirth, and you don't see that anymore. The first summer I was a young physician we had a polio epidemic in St. Louis. I remember one of my early patients, a young man almost my age, and I had to put him into an iron lung from which he never returned. I remember my second patient was a young woman who ended up with a paralyzed leg. Young doctors don't see that anymore. You don't see many of the diseases of childhood — measles, whooping cough, scarlet fever. You don't see much rheumatic heart disease anymore. Exploratory surgery is out, and that used to be terrible. Doctors used to have to open up to see what was wrong with people. Medicine was very primitive fifty years ago and progress is moving faster than ever, and I think that's a good thing. The major reason for wanting to criminalize this branch of medical research is the philosophical belief that cells in a Petri dish are as valuable as my children or my grandchildren.

I have to take a little bit of a detour here because not everybody knows what stem cells are. I won't give you a full course, and there won't be a quiz, but I want to give you a sort of an overview. People talk about two kinds of stem cells. First are adult stem cells. What are adult stem cells? If you scrape your skin, your skin will grow back. You have some skin stem cells under the skin, and they grow back and regenerate skin. If someone comes and takes a part of your liver out, your liver will re-grow because there are some liver stem cells. Now one interesting thing is that the skin cells cannot produce liver cells and the liver cells cannot produce skin cells. That might be kind of surprising because every cell in your body has all the genetic information that your first cell had, exactly the same, but that genetic information is for one reason or another — nobody fully understands why — unavailable so that skin cells can form only skin cells and liver cells can form only liver cells, and some cells can't reproduce at all. That's what adult stem cells are, and adult stem cells have been very useful medically. Particularly, you have heard about bone marrow transplants. Now early, or embryonic stem cells, are young stem cells. They are like the earliest stem cells and they can form any kind of

tissue. They can form skin, or liver, or nervous system, or heart muscle, or what have you. They have the potential of accessing all of that information in the genes and so the early stem cells have lots of promise for being able to understand things like cancer, how cells develop, how they develop normally and abnormally, birth defects, and things like that. Scientists are very anxious to study these early stem cells for that reason.

There's another reason, a long dream that scientists have and that is that some day they would like to be able to replace damaged tissue. Let's say you have had a very bad heart attack and you destroy a lot of your heart muscle. Wouldn't it be neat if scientists knew how to turn on the genes in your heart or to take some of your cells and put it into your heart and re-grow that tissue? Similarly, Parkinson's disease is a result of loss of certain cells in the brain; wouldn't it be wonderful if you could replace those cells. This is the dream that is called regenerative medicine.

Now these early stem cells come from two sources. The first source is left over products from in vitro fertilization. A couple is not having any kids and they go to their obstetrician, and say they are very anxious to have kids. The physician gives the woman some hormones, collects some of the eggs, and mixes them with the husband's sperm. Then in about a week or five to six days these cells grow into what are called blastocysts and some of the blastocysts are implanted in the woman's uterus in the hope that a pregnancy results. There are usually more cells than are used, and if a pregnancy results then there are these leftover blastocysts. They are a little tiny clump of cells. If you took your pen and made a dot on a piece of paper, they would be smaller than that. They have no differentiation at all. At first laboratories just discarded the leftover blastocysts, and then some people felt they might be valuable or they may be needed for second babies so they put them and keep them in liquid nitrogen in the deep freeze. But they know that over a period of time the blastocysts deteriorate so what do you do with them? The question has been and gets asked, can you use them for medical research? That's one way of getting early stem cells.

The other method is called somatic cell nuclear transfer. That is, if you go for the same procedure to collect some ovum, and instead of fertilizing them with the sperm you take the nucleus out of the egg and you put in a nucleus from a normal body cell, say a skin cell. If you treat it the right way, you can trick the egg into thinking that it ought to be dividing, and it begins dividing and forms a blastocyst. What is the advantage of that? Let us say you have a disease like Parkinson's and it has advanced far enough that you know how to form these cells to create L-dopa in the brain. Then there's an egg and you take one of your skin cells, take the nucleus out, put it in the egg, and begin to grow different types of tissue. That tissue is just like you. It will have all of your genes in it, and your body will not reject it. If you take some of my skin and put it on your body it will be rejected for immunological reasons, but this will not be rejected. That holds great promise for the future and many people are thinking that will be very wonderful.

The reason that people give for criminalizing this procedure is that some believe these groups of undifferentiated cells are really basically the same as a baby, and that they should have all the protections as any human being. Why oppose criminalization? Because a lot of people don't believe those are human beings and don't see any evidence for that and believe that taking care of people and improving human life is a noble and a moral cause that should be pursued. Those are the two differences.

What would be the effects of criminalization? First of all, medical care and research would suffer in Missouri. Missouri would become a place where these procedures were criminalized and not just for research but also for patient care. If any good treatments come out of this research, and I'm sure that eventually they will, physicians and hospitals would not be able to use them on patients, and scientists would not be able to pursue this kind of research. Kansas City has an institute for medical research. Mr. Jim Stowers, who has done very well, has put \$2 billion into building a medical research institute. He and his wife are cancer survivors; they have done a terrific job. They believe in the importance of research, and he would move his activities out of the state of Missouri. That would be one effect.

On Washington University, I think it would be clear that Washington University would not be able to pursue this kind of research. Scientists now move around in their research. They want to have the tools available to use that needed for their problem. If you begin to limit the tools this sends a very strong message that if you need those and try to find them in Missouri you'd be sent to jail. We would become a place where scientists would not want to go. We'd have a hard time recruiting scientists, and eventually they would leave. Stowers has already had a hard time recruiting scientists who won't come because of this.

Washington University Medical School, as you might guess, I'm partial to it. It's been built and maintained for over a hundred years by enormous toil and treasure. It's provided us with medical care second to none, and research from Washington University benefits the whole world. The advances have helped us and will do the same for our grandchildren and great grandchildren so that their lives can be healthier than ours. It benefits not only the people here in St. Louis but the research benefits help those in Europe, Africa and Asia as well. I think that it would be irresponsible to take apart what I think in human terms is one of the most responsible and beneficial institutions. On looking at the economic front, Washington University Medical School plus BJC are the largest employers in the region. It would certainly be a blow to the things that I've talked about, the economic hopes for St. Louis.

I asked the leaders of some of the companies in the two incubators we have, the Nidus Center and the Center for Emerging Technologies. I did this very quickly and some were out of town so I don't have full results but I think this will give you a pretty good indication. We asked the leaders of the science companies who are here in St. Louis, what if SCNT were criminalized? Four said it would not affect the future plans for my company. Eleven said my company would be less likely to stay in Missouri, and zero said my company would be more likely to stay in Missouri. We asked what about companies like yours? Zero said Missouri would be a better place for companies like mine. Thirteen said companies like mine would

probably avoid Missouri, and three said criminalizing would make no difference to companies like mine.

Through a lot of efforts something has been formed called the Missouri Coalition for Life Saving Cures and it has announced that it will be seeking enough signatures to make possible a referendum on stem cells in November 2006. The referendum on stem cells would ask for a level playing field. Missouri would be governed by federal rules about stem cells rather than enacting more restrictive rules on it's own. That would basically mean that Missouri patients, physicians, and scientists would have the same opportunities as those in other states. Federal rules would apply. There would be no cost to the state other than monitoring the agreement.

The federal government has not yet done a very good job of regulating stem cell research so we have things that would regulate what could be done and what could not be done. For example, one could not put into a woman's uterus anything except a normally fertilized blastocyst as they do for in vitro fertilization. One could not pay women in order to produce ovum for experimentation. One could not create blastocysts just for experimentation and so on. We've built in some pretty tight rules that ought to cover any kind of medical research.

It may seem like a risky project to move ahead with a referendum because we don't want to lose, but we decided to go forward anyway. Polling looks very good. Most Missourians favored going ahead with stem cell research. That's true of most Republicans, most Democrats, and most Independents. It's true of various religious groups. Even the very conservative right-to-lifers are split on the issue, although more are against it than for it.

We are also working very closely with the Stowers Institute in Kansas City. Jim Stowers is older than I am and he's anxious for a quick decision so he's pushing very hard to go ahead at this time. He wants to decide where his place is going to be before he passes on. So we have first-rate consultants, and our challenge is to win, and that's where we stand at the moment. Thank you.