Dr. Kenneth Olden
Interview

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Victoria Harden: This is the third in a series of interviews with Dr. Kenneth Olden about his tenure as director of the National Institute of Environmental Sciences. The interviewer is Victoria Harden. The date is February 10th 2005 and the interview is taking place in the offices of NIEHS in Bethesda, Building 31.

VH: Dr. Olden we were beginning to discuss -- you and Sara Shostak at the last interview a number of the scientific fields that you have looked into. One of the things that you did as a first was to demonstrate that one can prevent organ specific metastasis of malignant cells by blocking the specific interaction between fibronectin and the integrin receptor. Could you describe for me the significance of this discovery for efforts to prevent metastases in cancer patients?

Ken Olden: Yes. The lethal feature of cancer is not so much the growth and proliferation; it's not the localized tumor. The thing that kills the patient is in most cases -- there are a few cases where the primary tumor is the cause if it's deeply imbedded in the brain for example, it's inoperable or you can't do it, get to it, but in most cases it's the spread of the disease that which is called metastasis that is the cause of death because once the cancer spreads to different parts of the body the only source of eradication you're left with is chemotherapy or biological therapy or in some cases -- basically I would say chemotherapy and biological therapy. Radiation therapy and surgery are very effective in removing or eradicating a primary tumor but if we could prevent or cure or treat metastatic disease we could in fact prevent death from cancer. So it's a huge -- would have a huge impact on the mortality from cancer if we could just treat metastatic diseases.

Now there are a lot of approaches that are being used to do that. Just this week, two days ago I heard a presentation by a fellow who is targeting angiogenesis, the new metastatic foci when tumors spread. When they reach a distant organ in order for them to grow into a new tumor, a new cancer in another organ system they have to develop a vascular, a blood supply, and our efforts by Judah Folkman and many others, to prevent the vascularization of these tumors and so that is one approach. Our approach of course is if you could prevent the tumor cells from attaching to the foreign

tissue and penetrating the foreign tissue and by using inhibitors that block adhesion by molecules you could hopefully do that and that's what we demonstrated -- that you can do in animal models.

It turns out that we were blocking interaction with one protein and there are multiple proteins that cells can adhere too, bind to, and so when you knock out one they will use -- they'll circumvent using alternate binding mechanisms. So now I'm still looking at that, but what I'm trying to do is find a critical, a sentinel event that's required for all the adhesive interactions. In other words a critical intersection and if I can identify what's involved in molecules or involved in those critical intersections then maybe we can then block adhesion to multiple molecules and really reduce the efficiency of metastasis. So it's a very exciting area of research and we've been on the end of looking at adhesion to the foreign tissue and penetration of foreign tissue but there are other strategies that are being used, but all of it is aimed at preventing death from cancer. And so that public health impact of it would be enormous when we're able to do that and with time we're going to be able to do that.

VH: Would you tell us a bit about your research on the anticancer drug Swainsonine.

KO: Swainsonine.

VH: Swainsonine.

KO: Yes. Yeah. Again earlier work by us and others had demonstrated there are surface carbohydrates or sugar groups on the surface of cells and these sugar groups are bound to proteins and they are bound to the protein that we work with. We work with an adhesive protein called fibronectin. Fibronectin it turns out has five side chains. You know the backbone of the protein is this way. And along the backbone right there are five side chains of proteins -- of carbohydrates and those carbohydrate groups have a lot of individual residues of sugars that are strung together in chains and we and others recognized that it was a unique structure of the carbohydrate group that was required for as part of the recognition -- in other words how did the tumor cell recognize the target organ? How did they recognize platelets and other cells that are required for the adhesion and recognition?

And we demonstrated that if you could use a drug like Swainsonine and you could modify the surface, the sugar, the compensation, the structure of the sugar side chains. So we altered

the structure of the sugar side chains so that you block or prevent recognition. So tumor cells once they're carried by the blood vascular system, say from the breast or lung to a distant organ they would not attach to that foreign organ or they would not recognize other cells that were required for them to aggregate. And so you could treat animals or cells with Swainsonine and eventually we would administer it to an animal and you could prevent metastasis.

VH: Okay so this is the drug then that did what you were describing before?

KO: Right.

VH: That. Okay I didn't realize that it was, but I see what you're saying now.

KO: No it is not. It is a different drug.

VH: It's a different drug!

KO: Yeah. So there's two ways involved in metastasis. There are specific proteins on the surface that bind to specific receptors. The first agent that we used was an amino acid. It was a pentapeptide and we used that pentapeptide that would bind to the receptor preventing the receptor then -- it would mask -- block the receptor. So cells then that had the cell surface masked could not then bind to anything else because it was already -- the binding had already taken place but with a little short peptide and so that was one way. So you could block metastasis by using a little peptide, but we also discovered that you could change the surface, the carbohydrate side chains on the protein fibronectin and that would also prevent recognition and that would prevent metastasis as well. So there's two ways of -- in fact there's a preventive -- more than that, but those were two that we used.

VH: Okay and that would then help to explain also how you're moving forward in other directions on the same problem?

KO: Right, right, right, right.

VH: All right now --

KO: Now Swainsonine has now been looked at by the National Cancer Institute still I understand and the problem with Swainsonine is getting -- it's toxic, a lot of toxicity associated with it, it turns out. And so efforts are being made to encapsulate, put Swainsonine in

something to deliver it to the tumor site where you want it to go and then release it. And so those efforts are still underway and if you can overcome the toxicity of Swainsonine, Swainsonine may still work.

VH: All right now let me follow up on that a bit. To deliver it to the tumor type -- is this a biological delivery system or an instrumental?

KO: It's a biological.

VH: What kind of --

KO: Well I gather it's encapsulated in liposomes. These are lipid soluble vesicles. You can split in little --

VH: Hmm, mmm.

KO: And lipid soluble vesicles can penetrate –- just go right through the membranes, because membranes are phospholipids or lipids. And so there's not a solubility problem. So you add it outside in the bloodstream for example. When it gets carried to the tumor cells it can penetrate and get into the cells --

VH: And you can put a monoclonal antibody or something that'll take it directly to that tumor and nowhere else?

KO: You could do that although that is not the way they're -- Yes. I mean that is -- they use monoclonal antibodies to carry, deliver drugs. This is not the approach they're using here.

VH: What are they --

KO: Well they're using -- they're called lipid vesicles. You just take you take a solution of lipid -- this is the way they're creating -- you take a solution of lipids and lipids you see it as a solution but in fact they're little, they exist as little vesicles and if you mix up say Swainsonine with this lipid mixture at the right concentration and lipid ratio these little vesicles form and when they form they entrap the drug and then if you can deliver that drug.

VH: And how do you that?

KO: Well they just put it into the blood stream and it will go a lot of places, but it should have no effect probably any other place but it will get into the tumor.

VH: But it will get into the tumor.

KO: Tumor, right. So that is the problem, specificity. Antibodies are specific.

VH: Yeah.

KO: Lipid delivery system, vesicle delivery systems, are not specific. So let's say if it gets into a brain cell -- of course there is the blood brain barrier it has to worry about that, but lets say it gets into a liver cell or a kidney cell -- will it cause a problem? And so that's still --

VH: Still being explored.

KO: Explored.

VH: Yeah, good. Thank you very much for elucidating that for me. Now in all of this obviously you have been the principle investigator of the metastasis group of the laboratory of molecular carcinogenesis even as you served as director. How did you find the time?

KO: Well I made a decision when I left the National Cancer Institute in 1980 I guess and went to Howard University as scientific director first and then ultimately becoming director -- I made the decision that I really got into science because I liked doing science, and that I always wanted to be able to do science. It's hard to be out of science for 10 years and then go back. So I made a commitment to myself that if I could do the administrative and fundraising and other things that were required and do my science I would continue run an institute, but if I discovered that my science was -- I was going to be unable to do my science I was not, I was going to give up the administrative part and go back and do some science full-time. It turns out that -- so I just made a commitment to do that and also I felt that if you're running a scientific organization you need to be a scientist, because you need to be respected by your colleagues and I found that to be true. So I just made -- you make time for the things that are important to you. And so I right now -- I mean this week and I guess yesterday or the day before I met with the head of my laboratory. He and I meet once a week for an hour / hour and half and we talk about what everybody is doing in the laboratory. So he manages the laboratory for me on a day-to-day basis. He's a staff scientist and we talk about what everybody is doing, we talk about -- we discuss manuscripts that we're

writing and then -- so I meet with him once a week and then once a week I meet with the whole group in a room like this, a conference room, and we go over the science and I hear that and have feed back of let's do this, let's do that and keep up. And so -- now that is not ideal but it's better than I think not being active in science at all. Now just this week when we met with my person -- the person who runs the lab is a staff scientist I learned that a paper that we'd just submitted two weeks had been provisionally accepted for publications in the *Journal of Biological Chemistry*, which is the best journal in our field, either the *Journal of Biological Chemistry* or *Cancer Research* and I like to get them in either one. This project was one that was more biochemistry although it is with breast cancer cells and it is cancer. I mean it's part of the project, but we got it accepted and that was good news for me, but you see when I meet with my scientist then or they see that the director of the institute is publishing papers in good journals and we have it -- a meeting this week about the intramural budget and you know this year it's going to be pretty tough. We aren't going to have a lot of money. And so the decision that I make with the scientific director about how much money does the intramural research program get effects me as well. So I can meet with the lab chiefs and say, "Guys look we aren't going to have a lot of money this year. We're going to have to -- it's going to be a difficult two years and we're going to have to do the following things, but I'm in the same boat you are."

VH: I would like to explore this just a little further because I think this is something I don't know if it is common in science everywhere or just in the government but I know for example and Dr. Fauci has his lab. He is a director and Dr. Collins has his lab and you can see how someone who is outside of science would say, "Well the director's lab is going to get special privileges and they will never have to worry about money compared to the others," because that's the way a lot of the world works. Would you like to elaborate on how that works?

KO: Yes. Well the system at NIH is a good one. My laboratory is in the National Cancer Institute officially. So it's not in mine.

VH: Oh it's not in yours.

KO: It is in Research Triangle Park, but administratively it's in the National Cancer Institute.

VH: Now that's different.

KO: And I hope the other institute laboratories are also not in their institute for -- right? Now so my laboratory is reviewed by the board of scientific counselors in the National Cancer Institute and they decide whether my work is good enough to be funded and at what level. Now so they advise Michael Gottesman who is the scientific director Ken Olden's lab is let's say good enough. His productivity has been fine. He's doing good science and he asked for this amount of money and we recommend that he gets this or that or whatever. It turned out that they concurred with me that the amount of money that we had was adequate and that I should be given the amount of money that I requested. Now once that decision is made though, it's my institute -- the money comes out of my institute's budget, but the decision about whether I get any or anything is based on, is outside.

VH: I think yours is different from some.

KO: Right.

VH: That's very interesting to know.

KO: So I don't -- so when I was thinking about stepping down as -- well when I was thinking about, when I announced that I'm stepping down as director one of the things that was where do I want to be full-time? Do I want everything to be at NCI although keep staying in North Carolina? And people said to me, "Well you can switch back into the institute because you have passed peer review like everybody else so nobody can claim that just because you've been director that we're treating with favoritism because you're funded for four to five years already. NCI said that. I mean the board of scientific counselors. So four to five years you will -- we'll forget that you've been director and you have no influence over the decision that what happens to me four years from today scientifically in the institute, I suspect nobody will give a blank that I was director for a number years. Either my science is good to disserve continued funding or it won't be. So I make sure that I don't want people to say that I'm treated differently or that I fund my own lab. And so I want to go through the same peer review process as everybody else and I think -- otherwise you won't have the creditability. And so while I wanted creditability by continued to do science. I was creditability also by going through the peer review process like everybody else and I feel good about that. I mean I can tell you it was so hard carving out the time to prepare myself so that I could make an intelligent presentation and make a case for my money that I thought well maybe Ken you should just give it up and close your lab down, but I didn't do that and I got to.

I made the presentation -- it was a good presentation -- and I got funded.

VH: I think this an on going discussion about whether administrators can manage to squeeze it all in. I mean Michael Gottesman himself has his lab and that was an early tradition at NIH before World War II, but for a good while afterwards with Dr. Shannon and others they didn't even try.

KO: Didn't try, no.

VH: But it's interesting that it's coming back around and many of you are.

KO: That's right and still think that it's better -- I think -- we've hired some of our extramural people who run the extramural research program, they're program officers and we've given -- I hired one explicitly to engage in the laboratory and I wanted him to be a hybrid. I wanted him to kind of be over evaluation, how do we evaluate our science? How do we know we're making important contributions? And I wanted him to -- so we created new office. Now that person needed to be in, nested in the extramural part because that's were most of our money is so he gets the cooperation and support and access, but at the same time I wanted this person to really be a scientist and I didn't want him or her to loose their enthusiasm and knowledge of science over the years. So we put him in the intramural research program and the extramural so he has a leg in each one and he has been able to do his job administratively but at the same time he's been able to be competitive and survive the board of scientific counselors review and I said having been in a university this is no different than a university faculty who has to teach, they have to write grants, and they have to do quality research. So we're asking him rather than -- so we brought him from a university. You no longer have to teach you no longer have to write grants but you do have to do something beyond the laboratory part. And so we gave him a laboratory set up and in lieu of teaching and grant writing and other committees that he would be on at a university he has to give me information about what are we doing that's really important in the institute scientifically. So I think it's not only important for administrators I think it's important for others as well, because if you're away from science for ten years you -- most people, now there are exceptions, but most people loose their enthusiasm for it and their knowledge is not always the most current, because science, if you practice science, you're forced to remain current or otherwise your research won't be competitive.

VH: All right here's one of these final wrap up questions. When you were headed down to NIEHS and decided to move down there I would be interested in hearing sort of an overview of what intrigued you scientifically about its program, because its intramural program had been described rather derisively as NCI south and you had been apart of NCI north so you obviously has a sense about what you hoped to see in similarities and differences between the two institutes. Will you comment on that?

KO: There are -- yeah I was a bit concerned because clearly our institute was not going to be highly visible and perceived as being successful as long as we existed in the shadow of a big institution like NCI. So the question was how could we live up to our mandate to look at the role of the environment in the development of cancer, and at the same time create a separate image for ourselves in addressing other diseases as well as cancer. So I was concerned and I think the issue was that we -- I guess the institute was established because of public concern about the impact of the environment in terms of cancer and somehow we had never kind of moved much beyond that. Now we always had a mandate within our mission to do anything else, address any other disease like Alzheimer's, Parkinson, but all that you heard about from our institute was cancer. Well when members of congress think of cancer they think of NCI. They don't think of us, but now -- so I felt that the issue was not -- was the areas of emphasis needed to be expanded, but we also needed a different message. We needed to communicate -- we needed a communication strategy to get us visibility. So I created -- spent a lot of time with people who are experts in communication to help us craft what is now as everybody calls a brand for our self. So we, I wanted to brand NIEHS as being apart of the NIH, important to the mission of the NIH, but different from NCI. So we created this -- what we call a mantra, this triangle, that said human diseases are caused by genetics, environment and behavior and we began to push that. It's caused by the interactions between, and this morning Alan Spiegel presented at the institute directors meeting some science and up there was a slide from NIEHS dealing with this gene environment interaction part. And so we've had to -- so it was -- it had most to do with communication but also the agenda was too narrow. So I expanded the agenda -- on walking over from the institute director's meeting I walked over from a fellow, the director for mental health and he wanted to talk to me about autism. Well 12 years ago or 13 years ago autism wouldn't have been on our radar screen, but autism is now on our radar screen and he wanted to talk about some work that we're supporting at

Columbia University and at the University California Davis, so we're on the radar screen for lots of things now, autism, Parkinson, Alzheimer's, osteoporosis, breast cancer. And so we're a player, but it had to do with diversifying the portfolio and a communication strategy, branding.

VH: Well also the fact that the institute was just beginning during the great war on cancer years may have also had an impact on focusing on cancer and you had the great opportunity to do the diversification.

KO: Right, right, right.

VH: As we're coming to the end of our conversations here I want you to be able to explore anything that you think of that we haven't covered and let me just say that in 1996 you wrote an editorial on the occasion of the 30th anniversary of the institute in which you discussed challenges and I wondered if that would give you a frame work to go into the things that you are proudest of, the things that you really would like people to remember as far as your directorship and you spoke about three things and let me just -- I'll read them to you one at a time and let you comment if you will. First "teasing apart the genetic causes of disease to help discover genes modulated by the environment."

KO: Well yes I'm very -- that's one of the developments that I'm most proud of and the one that I think I will -- that's a major part of my legacy is that I created the, what we call the environment genome project. Which is kind of like the human genome project except the human genome project was trying to determine the sequence of the alphabets and the letters in the alphabets for the whole human genome and we're going back and saying which -- and what we identified was called a reference sequence it's the average for the American population, but I know -- we know there is dramatic variation among individuals among groups. So the genetic code is -- we're 99 point 9/10th percent identical. We're 1/10th percent different and 1/10th of a big number is a lot and so now we're going back and saying of those genes that we know are involved in causing environmental diseases how many of those have what we know and call polymorphisms and variations and are those variations responsible for the enhanced susceptibility of populations, of individuals? I mean why is it some people who smoke never develop lung cancer and others do and or people who consume too much alcohol or whatever don't develop kidney disease and cancer? So a lot of these things have to do with genetic susceptibility and that's what we were talking about

autism. One of our investigators at Columbia University discovered that she administered mercury, a derivative called thimerosal, that's in vaccines to something like five different strains of mice. Now mice are inbred but the strains are strain differences kind of like difference in humans and she discovered that one of the strains was susceptible to thimerosal. In other words it developed phenotype behavior and so forth similar to autistic children. The other four did not and so she concluded that based on a limited study that this suggested that it is indeed the genetic background that determines whether you develop autism, a kid develops autism, when exposed to thimerosal. Now we're having that study repeated. So what we went after is to try to understand why is it some people are susceptible to environmental exposures and others are not and we suspect that most diseases are the direct consequence of interaction between a susceptibility gene and the environmental trigger. And so -- and that's where everybody -- that's where NIH is, but we started that in 1997. In order to tease apart -- that's the point; if you want to know how genes and environmental agents interact you need to know both. You need to know what is the genetic risk factor, which gene, which variation and which environmental agent does that gene interact with and the only way you can do that is the [unintelligible]. The most straightforward is the approach that we took and now NIH, human genome, and everybody is looking for susceptibility genes because that's where the excitement is going to be. And so we were out front on it. We've got a lot of good press. One of the Nobel Prize laureates, Lee Hartwell wrote an article about our environmental genome project in *Nature*. A young woman who is a journalist for *Science* wrote on in *Science* about it. And so we've -- there's been a *Nature* article -- two *Nature* articles. So we got a lot of creditability for that. So we're doing that. Now it's certainly not finished so the new director his own work is in that area. So it's something that will be continued for a number years but I would say in five to ten years we're going to have lots and lots of data to begin to figure out how to prevent and identify which populations are susceptible and we can either decide what sort of action to take in terms of public policy. So I'm very proud of that.

VH: With good cause. The second point you made was understanding carcinogenesis of environmental agents and you've talked a lot about that already. Is there anything else that you'd like to add to that?

KO: Well again the approach is – well it turns out that we don't have methodology for identifying carcinogens. So I created a program

in 19 -- in 2000 called toxicogenomics approach and it is a high throughput approach to identifying which agents are carcinogenic, which agents in the environment or drugs are carcinogenic and which ones are not. And it's a gene and protein expression profiling procedure and it's a way of looking at thousands of genes and thousands of proteins at the same time. And so that's how it gets to be high throughput. Right now it takes us about five years, a cost of about 2 to 6 million dollars and about 1800 animals to identify a single carcinogen. Well I think using toxicogenomic approach, gene protein expression approach you can do this in probably a manner of weeks and that's what we hope at a nominal cost and maybe with no animals or one or two animals. So that's going to be -- so what we're doing is using toxicogenomics is to develop then approaches that are fast and cheap and use fewer animals and in the end are more informative than our current test. And so that is going full swing. We have six university wide centers, base centers, that are -- and they are toxicogenomic centers and we're investing millions of dollars to generate those profiles or fingerprints so that we can identify a carcinogen and in the end we hope to do it exactly the way the FBI does with fingerprinting. So we're going to put in a signature in a database some place and any chemical that has that signature you know will be a carcinogen and you can make a prediction very fast. The FBI can do it in one or two days or I guess they can do it as soon as you can send it through the computer they can get a computer match. So that's what we are -- we plan to do. Is to pick up offending environmental agent in a matter of a day because it's in the database. And so I'm happy about that and that again is -- well I gather that the March issue of *Environmental Health Prospective* is put -- apparently the editor asked different people to tell them what they think my legacy is and write a little one pager or whatever on it and toxicogenomics is one of those that they asked somebody to write on, and it will be interesting but they're asked to write about the environmental genome project, and so it will be interesting. It's a very interesting concept. So I guess there'll be a special issue what are the areas that I developed it and that's my legacy.

VH: I know about this issue and I think it will be a fine issue to have. It's also interesting however just to hear it from your own mouth -- what you think. That brings us then to the last two points which are really apart of the same, one is animal models, using animal models and the other is developing new ones.

KO: Right, right, right, absolutely that's exactly right. I like many other people abhor the use of animals in medical research, although I recognize like a lot of other people that there is no alternatives

either you let people die from devastating illness or we make some effort to find cures and we need animal models. So I use them, but to the extent that we can, I am eager to find alternatives and now we can create alternatives and we can make animals more sensitive so that you don't have to use a hundred, maybe you can use five and I'm not sure in my lifetime that we'll ever get to the point where we don't need an animal, but we may need 800 per chemical. So I am concerned about the number of animals that are used. I want them to be -- experiences to be more humane and so the only way you can do that is to develop alternatives, and we're investing and toxicogenomics is an alternative because I think you can do it with just tissue from an animal, not the animal -- you don't need the animal anymore. So and I think there are also ways to make the animals more sensitive and so you don't need the same number because they're reliable. They're genetically manipulated to be susceptible to this or that and so you don't need -- the reason we use 800 because there's so much variation from animal to animal and we don't know what the genes are, but if we knew what the genes were and we could actually create an animal model with that gene variation and then everyone that you expose to let's say to a carcinogen in cigarette smoke would develop cancer so you don't have the statistical problems. So we are doing that. We've made a huge investment in developing alternatives to animals not just through toxicogenomics, but through creating genetic, manipulating the gene, the chromosomes, the genes in the genome of the mouse and still use a whole mouse, but many fewer, they're called transgenic animal models that's what I was trying to think of. So we've created transgenic animal models that are far more useful and informative in carcinogenicity or toxicity testing than the typical rodent model.

VH: We've covered a lot of area in these three and fourth interview that Sara did with you also and I know it's hard to remember back over all these different -- these months, but I wonder if there is anything that you think of that we haven't talked about that you would like to get on the record?

KO: Well we've talked about it but it is one that still I think we don't do very well at the NIH and I'd like to come back to it.

VH: All right.

KO: Because it was discussed this morning at the institutes director's meeting again, in a way of information and I didn't speak up because, but and that is we -- this was an EEO thing about how do we -- we have a mandate that we're going to get minorities and

women into the NIH and women not only in, but promoted up through the ranks. Now for women that's -- whatever the issue is, issues/ barriers are they're removable. We can do something about that, because women are trained. They're just as good as the men who show up and why is it that they don't become institute directors or lab chiefs or title 42s or SESs. There's a barrier and we can identify those barriers and we can remove them, but they had African-American scientists up there and the presenter presented it as if the barriers are the same and they aren't. The problem with African-American scientists is a pipeline and no matter how hard you or I try we can't find enough people out there with the training, qualifications and experience to populate NIH the way we'd like to see it populated. In other words people who are competitive for the jobs that are announced here and it has nothing to do with my interest or the willingness of the NIH to do it. And so we keep going out there with advertisement and calling people and it ain't ever going to work until we have a pipeline that every time you advertise that 10% or 15% of the applicants are well qualified African Americans. So --

VH: So what can you do about this and from your position I know you've been very concerned about this and very active in it. Specifically what do you hope you have to been able to accomplish?

KO: Well I'm going to strike that, the person who made the presentation in an email and send Zerhouni a carbon copy of it and that it's the pipeline issue and just last week I was in Puerto Rico and I'm going to tell Dr. Zerhouni about that. There are two programs in the United States that's really having an impact on the pipeline. It's just, in my case, I think there are others who make incremental contributions, but two programs are really successful. We many years ago, I bought into one of them as soon as I heard about it, and I think that was more than 10 years ago. And so that one is at University of Maryland called the Meyerhoff Program. It's at the University of Maryland, Baltimore campus and they don't have a graduate program. They are training minorities and low income others, from other groups who are not represented in science, and they're providing them with an environment in undergraduate school so that they can first become excited about science but also go on to graduate and professional schools and come out and become practicing scientist and competitive. They've been successful at doing that. So I have been giving them 500,000 dollars every year and now in fact I think we're at 650 or 700 now. We started with 500,000 a year and we do it through the National Science Foundation, a partnership and now we have a

track record. Well, I was just in Puerto Rico and discovered that program though which was created by NSF not by NIH and phasing out, it was a 10 year program. It's been in place 10 years and now it's phasing out as of next year. Well at NIH we have not been a part of that. I mean NIH hasn't. We have been, NIEHS has been, but the other institutes and we keep supporting this program and that program and you say in the end what are we doing it for? And so I'd like to see us just step back and say -- I mean it's going to take a while. I mean let's just be -- this liberal approach won't get us there. Let's just step back and admit what the issue is, that there are not enough black scientist that are well trained in the best institutions that are going to be competitive at NIH. So how do we get them? Let's take the long haul look and say if we invest in programs like Meyerhoff and the MEI program at Mendez University in San Juan, Puerto Rico we are one day going to have this population. We're going to populate the field. Now you're going to be criticized by black colleges and universities because they want some of the money to run their programs, but they've been running their programs and it hasn't worked. So until we can get African-Americans going to Stanford, Yale and Harvard and Princeton like everybody else going through those programs, coming to the NIH through a four to five year post doctoral training program, and then go out there and compete like everybody else we're never going to solve this problem, but if you want to -- you make people happy and the noise goes away if you contribute if you support a program at Morehouse College or Meharry or wherever, Howard. You don't hear a lot of noise, but our problem is not solved and we are not solving the problem of the African-American Community.

KO: Now there's --

VH: Wait let me ask you the question on tape here. I had talked with Dr. Kirschtein about women and why more of them have not followed in her footsteps as the first woman to be a director of an institute and she said she was somewhat disappointed that there weren't more and I'd like you to comment on the same thing with respect to African-American scientists.

KO: Like Dr. Kirschstein I too am very disappointed, but I -- I want to say I don't blame the system. I think that there is very little that we can do at this point, except to try. We're expecting somebody else to do the pipeline issue and we want them as they are coming out. Well nobody is going to come out unless somebody goes in and you've got to find good programs that are going to create the kind of person that we're going -- and I maintain that most of the --

VH: Is it good enough to do it at the college level or do you need to drop back to high school or elementary school?

KO: Well, I mean sure. It would be nice to go all the way, but it's already been demonstrated. I mean Meyerhoff Program now they pick and choose. You've got to have ability so they try to identify innate ability and drive and basically what they do is take kids who in the top 10 percent of their class, wherever they've been, at least that says something about a kid. He or she has taken advantage of the environment of which he or she has been in and then they bring them in and they kind of herd them all together and there is -- you know kids learn from each other and they acquire a lifestyle that's very different from the other cohort of kids. And so they've been very successful. We now have one of there, as a postdoctoral fellow in our institute and this is a woman who went through Meyerhoff here at the University of Maryland. She went to Georgia Tech and got a PhD in engineering and she is in imaging, and she is now a post doc with us and she works jointly with a person at NIEHS and a professor at Duke. This woman is very good. She came and gave a seminar, very poised, knows what she's doing and NIH was very happy to get her. Now this woman -- we did have to make exceptions for her and my guess she is motivated enough, she's smart enough, well trained enough she will be somebody that will go up through the ranks some place if not NIH and be a full professor. So it can be done, and that's what Meyerhoff has demonstrated. Now in Puerto Rico they demonstrate the same thing. I was just down there and there's a young woman that -- but there are other examples, but I'll say this one. She went to MIT, she worked with a National of Academy of Science person. We funded her program at MIT. They've got her -- she's got her Ph.D. they've brought her back to Puerto Rico at the Mendez University and she's got -- it's just amazing, the equipment, the lab, the enthusiasm, the quality of the undergraduate education at that institution. Now Mendez University admits it has open admission, they take any kid and they try again to identify those characteristics, and these are not the top of the -- I mean the best kids don't go there. I mean, well supposedly. The upper middle class --

VH: Right, economic.

KO: Economic don't go there. These are the kids who probably wouldn't be going to college at all by their own initiative but they take these kids and they turn them into real stars and I've talked and interacted with at least five of those stars.

VH: It sounds exactly like the City University of New York taking in --

KO: Right in the olden days.

VH: So in that sense what really is needed is perseverance and just hanging in there with the programs.

KO: Right, right and getting students excited about science and understanding what the lifestyle is. It is -- I think if you're interested in science, you like science and it's not working. You're doing what you enjoy doing. I just think -- as I'm going to say to Zerhouni and all until we make a long-term conscious investment in the pipeline, we're never going to have these people. Now he could say, "Well I won't be here Ken 10 years from now why should I --" and I understand that or I can say, "I'm not going to be here," but I've made investments for 10 years this is the first one of the post docs, or first two, that I could even compete for. So I've said to both Meyerhoff, I'd like for you tell me everyone of your students that's out there so I can write them, stay in touch with them at least offer them a position when they get out. Now they don't have to come to NIEHS, but since we've been part of there -- and I know these people are well trained and I did it because I want to increase the pipeline for us, and others, I at least want to call them up and say whomever -- we have a position here would you consider it and let them come down and look at it and make a decision, but the point is whether they come to NIEHS, the NCI, heart, lung and blood or the University of Maryland these people are going to be well trained and be -- and that's how it's going to happen. It's not going to happen the other way around.

VH: Well, all right as we end you obviously are far to animated and interested in various things in life to just go sit in a rocking chair. So what are you planning to do for the next 30 years?

KO: Well I'm going to write and lecture at probably some historical black colleges and universities and I want to do that because I think I have had experiences and training that could be very important for students to kind of understand and get acquainted with somebody like me I think. A few of them have asked me to do that. And let's say writing I've just wrote an article that we hope that *Science Magazine* we think is going to publish and it's on healthcare and this is an issue that I care about and I'm challenging a tactic to the health care delivery system and I think we've -- I read what hope is the final version on the plane last night, but I think it makes a compelling case that we're never going to solve

this issue of health disparities. We have a way in this country of just working at things around the fringes and when in fact its the infrastructure that's the problem, and infrastructure is difficult to change but you've got to start someplace. In fact I gave a talk to the president's cancer advisory panel and I made that case, and the very day I gave the talk it turns out I came back, got on the plane, opened up *USA Today* and they had a cartoon that I now have that said healthcare, it compared healthcare with social security, and social security is broken. Now you can improve it and that's what they showed. They showed President Bush putting curtains around social security, but behind the president was these two windows, broken, and health and care was at the top, you could see it, and so this is the opinion of many people that healthcare is indeed broken, but that social security is not. So we need and we're running out of time with healthcare. We have the best science, we have the best trained people, we have the best research in the world but yet we have, we rank number 37 in terms of healthcare delivery. And why is that? There is a disconnect and so that's what I am discussing, why is there that disconnect? And until we address that disconnect -- and just yesterday I finished the article because I incorporated another paragraph because the president just came out with an agenda about two or three days and I just fell on my desk and I looked at it and he's talking about healthcare and exactly what he said is exactly what I've got in my article. So I conclude by pointing out that this is absolutely consistent with the president's agenda on the healthcare and quoted him, which is exactly what I said about him. But he is not focusing on the infrastructure and he's not going to get there. So things like this. I have time hopefully now to really think about some of these big picture issues and that's what I said, what we need here is leadership, somebody who is visible enough and so I'm sure I can get this written in -- I want it to come out in *Science*, and that will reach one audience and we think that they're going to do it. But there is another audience, and I'm not sure, but at least if it gets out there in the press it will get debated and get started the debate. And that's -- and I can tell you I didn't get into New York to testify before the president's cancer advisory panel but I sent my testimony because they asked -- they're putting together a white paper with everybody's testimony. Well a woman that I don't know from New York wrote to me after -- she was there in the audience because the panel was meeting in New York City, the weekend they had the big snow. She wrote to me and said, "Dear Dr. Olden I read your statement that you submitted that President's Cancer Advisory Panel, you know they handed them all out even although I was an unable to be there in person, and I can say that I heard all the others, and you're the only one that really proposed

anything that remotely is relevant or interesting. Most of the others were just whining, and you came and said, "Let's do something different and important." And she was the woman who was interested in breast cancer, and she said, "I was very impressed with what you said that you have [unintelligible] prevention, helped promotion, as a way to bring down health care costs and changing the system." And it was, she said, "It was compelling and I applaud you." Now I don't this woman, now so, but I had a platform, I used it.

So that's what I'm going to do, is use the platform that I have to try to focus attention on some of these important issues. And in part, I couldn't say or do because I'm an institute director, but once I'm no longer institute director I can say, for example, that continuing investing in historical black colleges and universities, the way the NIH has done over the years, is not going to solve the problem. And then they can't, you know, they can't call up Zerhouni and say, "One of your institute director is --." So I'm going it as a private citizen, I can say that.

VH: Right.

KO: And it needs to be said, it needs to be said by an African American.

VH: Right.

KO: And if you think about it, we've had all this time. Ruth is certainly one of the -- at the forefront of creating a minority program, but she has to be disciplined with what the product, the return, it just hasn't worked. But I would say on the women's issues, I think there's five woman institute directors, and that's good.

VH: That's coming along, yes.

KO: That's coming along. Now it was a long time in coming, but it -- and the reason that there are five is because there are lots of women out there who qualify to be directors -- just needed a director of the NIH who would pick them.

VH: So if you extrapolate that you have just a few -- fewer relative to all women.

KO: Right.

VH: African American males and females, but you do have the Ken Olden's and the Colin Powell's and the Condoleeza Rice's who have reached a level, but there's the pipeline.

KO: Right, there are so few that do make it up the pipeline and when they -- everybody has -- we all want to live in different parts of the world, we want to do different things and just scatter us all around, there isn't enough to go around. I mean I hear, people write to me all the time, universities because they think, you know I'm black, they think I know others, and I just nominated a fellow for the Chancellor -- they're looking for a Chancellor of University of Tennessee, Memphis medical center. And I nominated a young black, and they just called me on Saturday. I was driving, pulled into a parking space and I get a phone call, and they called me and said, "Look, can you -- you nominated somebody, boy he's good. He is one of the final two or three for the position." And that's why they appoint me. I mean they -- I don't think that they don't want to select an African American, but typically there isn't going to be one in the pool.

VH: That's right, or come up on the radar screen.

KO: Or come up on the radar screen, so I nominated this fellow and they said, "This guy, he is very good, whether he gets it or not still," and I think it's an open fair process. And I'll just tell you this, one of the place -- I'm a Tennessean, I applied for the position, that's the reason they called me about the position. I applied for the position of the President of the entire wide system, and again, I was a finalist. And I think it had nothing whatsoever to do, the fact I didn't get it, that I was black. They were impressed that I was qualified, how I handled myself in the interviews, and I made friends and gained their respect. And again, just one person knew me and wrote to me and said, "Look, I hear you're stepping down as institute director, would you consider this?" And I did and went through the long drawn out process but in the end when they ranked the people, there's no way you could say that I wasn't qualified to do the job. It was just a matter of my going down and convincing them that I could do the job, and there were convinced of that, but in the end I had never run a university and the person who got it was Vice Chancellor or Provost at University of Wisconsin -- oh not Wisconsin, Connecticut. And he had run a university on a day-to-day basis and I hadn't, and the question was do you -- so somebody had to make that --

VH: Sure.

KO: And it was a ballot, and then there was my age, the guy's ten years younger than I am, and that's an issue. So it is an issue and so you can take all these things, and I think they made a good choice. I think times have changed to the point that if you're qualified, you can, in most cases,

not all, you can through the door, women or minorities. I mean there are some people who obviously wouldn't hire me because I'm a minority and wouldn't hire you because you're a woman, but I think that's passing. But my going down had some real importance because now they know me, they respect me and they respect anybody that I nominate. So I nominated, and there was thirty or so people and they went through the process and narrowed it down to two or three, and there are some outstanding applicants because I looked at them. And this fellow is one of the outstanding applicants. So those are the kinds of things I'm going to do. Try to.

VH: Well I thank you very much for talking with us, and when we do the editing you certainly should feel free to add anything else that --

KO: All right, all right. And thank you very much, I appreciate your interest.

End of Transcript