The American Association of Immunologists
Oral History Project

Transcript

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Interview conducted by
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Williams: This is an interview with Dr. Richard J. Hodes for the American Association of Immunologists (AAI) Oral History Project. Dr. Hodes is the Director of the National Institute of Aging (NIA), Chief of the Immune Regulation Section, and Senior Investigator in the Experimental Immunology Branch of the National Cancer Institute (NCI). He was awarded the AAI Public Service Award in 2007. We're in Dr. Hodes' office on the National Institutes of Health (NIH) campus in Bethesda, Maryland. Today is Friday, January 8, 2016, and I am Brien Williams.

Thank you for doing this, Dr. Hodes. I'd like to have you start by telling me a little bit about your family background.

Hodes: Sure, I'd be happy to, and thank you for the opportunity to talk with you and with friends and colleagues. I grew up in a very wonderful and rich family environment. My parents left me to be the first college graduate in the family. Both are very, very brilliant people. My father, a product of the [Great] Depression, after high school went to work full-time and was a wholesale florist, went to school nights, but didn't get all the way through college. My mother was trained as a nurse and then took care of her family, but, remarkably, she went back to school after my father's early death and after we were off to school. She got her bachelor's degree after I did, in her fifties, and then got her master's as she approached seventy. My sister is an artist and teacher. We grew up around New York in the Long Island area, and, again, a background for which I am forever grateful.

Williams: What did your mother get her degree in?

Hodes: Sociology. She was really quite remarkable. Getting her master's, she lived in Queens, and as she was approaching seventy, would take a bus to the New York Port Authority Building and then a train to New Jersey to go to Jersey City State at night for her classes. I don't know how she did it. We couldn't prevent her from doing it, but she was a strong-willed and bright woman.

Williams: So it's you and your sister, the two.

Hodes: Yes. And now I should not forget to talk about the joy I have with a wife and daughter. My wife now of thirty-one years is a Ph.D. sociologist-epidemiologist, who worked for, most recently, the Food and Drug Administration. My daughter is now working as a school psychologist. Two joys of my current life.

Williams: So talk a little bit about what kind of schooling you experienced, growing up in Queens or Long Island, wherever.

Hodes: So I grew up in Long Island, went to the public school because that's what we all did, and had a great time there in Wantagh, Long Island, New York, and then was fortunate enough to get to Yale at a time when there was no need to worry about finances. We didn't have much in the way of money, but they provided full

scholarship. I wish there were more of that now. Graduated there, majoring in psychology as I transitioned to an interest from psychology to chemistry and had about the same number of courses in both, and along the way decided to move to medical school as a career, again, fortunate enough to be able to do that at Harvard.

Besides being a great environment with wonderful classmates, some of whom are now colleagues in AAI and FASEB [Federation of American Societies of Experimental Biology], it was a time that encouraged and made it easy to do things that took initiative, particularly involving research. So, for example, during the second year of medical school, a bunch of us got interested in immunology on our own and formed a little informal journal club and went through articles together. A number of those people went on to spectacular careers, but it led to an interest in immunology.

One day George Klein, who was a professor and head of the Institute of Tumor Biology at Karolinska Institute, was visiting. I gave a lecture, spoke to him afterwards, and he invited me to come, think of working there if I wanted to. The way it worked then—again, I wish it were more like this now—simply went and talked to the dean. They said, "No problem. Go off and do it and we'll find you some money." So I ended up spending two years in Stockholm at Karolinska, doing that before coming back to finish medical school, and that was the introduction to immunology. And then finished medical school, internship and residency, in internal medicine. Came to NIH for a two-year fellowship, and that was forty-three years ago.

Williams: Well, we're getting ahead of things here a little bit. Let's go back a touch. Do you remember when you began to become really turned on to science? Was there a time at some point in your life where you thought, "This is—

Hodes: There's no particular day or epiphany, but I think I always was in high school courses and certainly in college, in chemistry and physics and biology, had just wonderful instructors and coursework, and became excited there, and medical school, that simply reinforced it. Then I guess there was a time after these first couple of years in medical school, as was the case for a lot of classmates, a prospect of doing more than learning, memorizing what was already known, but actually being able to do something more investigative by way of research was exciting, and that led to the decision to take a little time off from medical school and do that.

Williams: That's the Swedish—

Hodes: That's the Swedish experience, yeah.

Williams: Contrast that environment with what's normal in the States.

Hodes: The environment in Stockholm at that time?

Williams: Well, I don't mean the city; I mean the Institute and so forth.

Hodes: Well, I think the Institute itself as a scientific venue was exciting and international, which is not so different, I think, from what's the case here, not so much in the way of difference. There are good mentors, there are good mentors here. There's a different academic system, but I don't think that the basic intellectual and scientific environment is so different. I think what was different is perhaps more that in that time it was simply easier to take the time off, find a place and do it, come back, and not be encumbered, in debt, concerned about some life trajectory. It just seemed a lot easier then, and most of us at the time were able to follow our instincts and excitement for science.

Williams: At the point where you graduated from Harvard, did you have a life's path sort of worked out at that point or not?

Hodes: No, I think not. As noted, I finished medical training in internal medicine and was coming to do a fellowship here at the [National] Cancer Institute, which involved some clinical work as well as a research opportunity in immunology, and I think there was a point at which I would have been excited and gratified by a career that was more clinical, more in research, but the research exposure just progressively became, I think, intriguing, seductive, exciting, and it's where I ended up.

Williams: Any particular mentors at Harvard that helped you on your way?

Hodes: Well, important during the Harvard years were principally, I think, George Klein, whom I've mentioned at Karolinska Institute, and then as my introduction from him to Bill [William D.] Terry, who was a branch chief [Immunology Branch] here at the National Cancer Institute that led to my coming down, being interviewed, and working with Bill, and Bill was just a superb mentor who was able to allow the kind of freedom to express, while providing the guidance as needed, and the richness in the environment here at NIH at a time when in immunology, in particular, things were just exploding, was a fantastic opportunity.

Some of the classmates who came with me to NIH stayed and have established careers. Ron [Ronald H.] Schwartz, Sandy [Herbert C.] Morse, people who are, in fact, still here or just recently retired, all a part of that same journal club at Harvard, became the same cohort here at NIH and followed the same research areas.

Williams: You interned at Mass General [Massachusetts General Hospital].

Hodes: Right.

Williams: What was that like, and did that have any bearing on what you thought you were going to be doing for your life?

Hodes: Well, you know, there's no question research is very different from life as an intern and clinical resident, and there were no such thing as electives during those times. It was intense but exciting and gratifying. I really did enjoy the clinical medicine. It really, the most general sense, led to the perspective we probably all have that whatever the state of knowledge in clinical medicine, it's always imperfect, and so the notion of being able to balance the gratification of clinical medicine with a chance of being a part of the effort that was going to generate new knowledge and improve our translation and our ability to care for people was the balance that was exciting. So, doing the best one could with what one knew and being a part of producing something more than one currently knew.

Williams: I'm going to leap ahead here just for a second. At Harvard was there much of an emphasis on aging issues when you were there?

Hodes: No, no, there really wasn't. For one thing, few people got old. I don't think there was not so much of a visible or organized discipline of geriatrics or gerontology, and I think even in this country overall, that didn't develop for some number of years thereafter.

Williams: So you didn't see that area on your horizon.

Hodes: I did not. I did not, not at all.

Williams: So talk about getting here and what it was like to immerse yourself in the culture of NIH and so forth.

Hodes: Well, it was the classic version of kid in a candy store, the fact that you could come to a place, NIH in particular, and have access to great minds, collaborators, resources, come up with ideas and pursue them at a time when many disciplines, but including immunology, were exploding enormously just couldn't have been better. I remember very much thinking that I really didn't have any need to take time off or take vacations or leave. Things were just so good, that it was enriching and invigorating, and there was really little more to be asked out of life. And I think to a large degree that has continued, and I only hope we manage to sustain this environment for those who are coming into next generations.

Williams: So you went into several branches of the NCI, for example, the Immunology Branch. What was that like?

Hodes: Well, it was a historical change in the name and organization, so that it was always, really from the time I came to the present, in de facto the same branch, first Immunology Branch now called the Experimental Immunology Branch, and

had superb colleagues there as senior investigators, principal investigators, great, great talent in the postdoctoral and predoctoral fellows who came through as students, and now have great pride—if we come around to asking about pride and accomplishments looking back, it's in having a chance to have worked with people who've gone on to do so well in their own careers and to have at least provided an opportunity that didn't inhibit their development.

Williams: Richard Nixon's War on Cancer was started in '71, so there must have been a connection between that infusion of funding and whatnot and what was going on here.

Hodes: That infusion to cancer research, but in addition to the National Cancer Institute, really across much of NIH, was a time of huge expansion and that had a number of implications. At the time it meant that there was a cohort of new scientists, colleagues, peers coming to expand the intellectual community, and that was great, but it also has had a consequence. There was such a large cohort at that time that when that pace of growth slowed, I think NIH and that meant the scientific workforces now experiencing this cohort who came in at around that time into research and has in surprising measures stayed in research for decades, now occupying a good portion of the workforce, so there probably isn't the same statistical opportunity for growth at the level of new investigators that there was then. So the growth at the time was exciting. In retrospect, probably unsustainable and now leaving us with a new set of challenges, I think, about how to make sure there's opportunity and incentive for bright people coming into the field now to do so and then to be retained.

Williams: So what were the circumstances that occurred for you to be appointed as director of the [National] Institute of Aging?

Hodes: That is kind of a puzzle. I was asked by the director of NIH at that time if I would be willing to be considered as a candidate for the search which had opened in that position, a relatively new Institute, the National Institute on Aging, and it was not something I had thought so much about or anticipated. In fact, the whole notion of being an Institute director was a puzzling new concept. I mean, working in the laboratory full-time with some clinical work associated with it was exciting to the point of saturation.

So I remember turning to the one good friend I had at the time who had experience with this, Tony [Anthony S.] Fauci, to ask him what he thought of this and how it could possibly work, and I'm forever grateful for Tony, who's still a wise and revered colleague and perhaps dean of all of us here, and with his encouragement, gave it a try, and to my own sense, I thought maybe I'd see what happened for a couple of years, whether it was possible to both do that sort of job as a director of an Institute and to maintain the laboratory experience. So now it's twenty-two-plus years into that experiment, and we'll see how it works out. [laughs]

Williams: Well, so far has it worked out?

Hodes: So far it's been great, yeah. It's quite a privilege to be able to both continue being active in science and to play a role in supporting a large area of science beyond the scope of one's own work.

Williams: Just for the record, who was the director of NIH at the time?

Hodes: Bernadine Healy, who was, in fact, a medical school classmate.

So Tony was a great figure, an immunologist. A year after I took the position as director of NIA, I remember Steve [Stephen I.] Katz, another member of AAI, an immunologist, who was asked if he would be interested in considering the position as director of NIAMS [National Institute of Arthritis and Musculoskeletal and Skin Diseases], the Institute that deals with musculoskeletal, skin diseases, a lot of autoimmune areas. He and I were good friends, so, in turn, he came to me to ask what I thought of this sort of possibility. Steve is just one year behind me now. He must be twenty-one or twenty-two years in that position as well.

Williams: So where does NIA fit into the sort of fabric of this place?

Hodes: In terms of the fabric of NIH, interesting. You know, it's not one of the disease- or organ-oriented Institutes. It obviously is one that deals with a life course, but by that nature, it has intrinsic, close relationships across many of the Institutes. Both at a science and at a personal level in terms of the gratifying interpersonal interactions with other Institute directors, it's been one of the great delights of being here and with the Aging Institute to have a chance to continuously and even increasingly interact with the other Institutes. Not all the research that needs to be done relevant to aging can or should be done by the National Institute on Aging, be it cancer or diabetes or arthritis or the immune system. You know, they're all affected with age, and I think increasingly that perspective for realization is being translated into collaboration in research efforts.

Williams: Is that kind of a new development?

Hodes: I would say it's accelerated and enhanced. Yes, I think that the notion that aging was an underlying process, biological as well as clinical and sociologic, that might well be related in an intimate way to other disciplines has become more recently increasingly evident. For example, the controls on cell growth, the senescence at a cellular level, the relationship of those events as they might occur in aging to what happens in cancer or other tissues, the fact that for most of the diseases and conditions of aging, that it's actually age, which is the risk factor that trumps everything else. So trying to understand processes going on in health and disease in multiple organs and tissues as they interrelate to the changes that happen with aging is a challenge which has gone from maybe a grudging

acknowledgement in the most vague of sense to one which now has cellular, molecular, genetic substance to it, and so has become much more tenable as an area of science.

Williams: Did you have to push for and campaign for crossing institutional lines here to develop this sort of interdisciplinary approach to things?

Hodes: I think maybe the most important reason behind the increased collaboration or crossing of boundaries really was driven by the science itself, and so if there was a role to be played in promoting this, it was to emphasize by both the support of research at NIA and then identifying compelling collaborations with other Institutes around what was an emerging scientific rationale, not just a political correctness for a collaboration across Institutes and Centers.

Williams: With the growing senior population, has there been a real shift in research priorities at the NIH, do you think?

Hodes: I think yes. I think that, in general, as we've gone from having become rather better at treating or preventing a number of the more acute infectious and noninfectious diseases, that increasingly the burden of chronic noninfectious diseases has been appreciated, and emphasis is steered in that direction. There have been particular examples, maybe the most current around Alzheimer's disease and dementia, which as there's an increase in the number of older people at risk, has exploded in terms of the public health imperative. In recent times, especially these last years and the current year, has led to a very substantial increase in funding this area, which is a brand new kind of challenge to have a very dramatic increase in funding for a particular discipline with the opportunities that create, to now recruit into this science the research area behind it whole new generations and disciplines of researchers.

Williams: What is your take on disease-specific appropriations?

Hodes: In principle, I share what has been voiced with great unanimity probably by NIH directors, Institute directors, and that's that the decisions about where funding goes ought to be driven by scientific priority-setting, not by politics. Having said that, I think we all appreciate the fact that the public and policymakers understand the purpose of the research we do in a way that is driven home frequently most effectively by specific diseases and conditions. So we appreciate that, we appreciate the fact that at NIH in particular, the research we do, critically basic as well as translational, is done with an eye, long term as well as short term, towards its relevance. So, appreciating the reason that diseases are cited and appreciating the support that comes, I think we all share the commitment to making sure that the basic underlying science, sometimes free of any obvious disease-related hypothesis, has been and will continue to be a critical driver of the most effective sort of research portfolio.

Williams: You're probably referring to NAPA [National Alzheimer's Project Act of 2011] as the big infusion of funding, right?

Hodes: Yes.

Williams: That occurred, I guess, in 2011. Before then—I think I picked this up in my reading—your budget was one of the smallest of the Institutes at NIH. Has that changed because of the funding?

Hodes: I think historically, until the last couple of years, we were probably rather the median almost perfectly as a mid-sized Institute. The big changes have come in these last couple of years. This year was the most remarkable, when across all of NIH there was a $2 billion increase, which is about 6 percent, which we appreciated enormously. The National Institute on Aging budget actually increased by 33.4 percent in one year, the majority of that being targeted for Alzheimer's-related research.

Williams: So as director, what are your goals for the Institute? What do you see yourself focusing on?

Hodes: The goals in the most general sense are to recruit the very best of science into the disciplines that will drive discovery for its own beautiful and scientific sake, and discovery that will ultimately be translated into the public health and clinical imperatives that we face today.

So we've actually, interestingly, been required—this is internally, not by imposition—to be a lot more specific and strategic—and "strategic planning" is a bit of a dirty word to a lot of us as scientists—in the face of what has now happened, namely a national program or commitment for a public to address Alzheimer's disease in particular, and the need to find a way to assure that a very rapid expansion of funding in this area is used to support outstanding research. The fields won't always necessarily expand spontaneously in this regard, so we've been, I hope, very careful in identifying the areas of research that are of high scientific priority. We do this by having a very comprehensive input from scientists at true scientific summits to identify the critical areas, and then letting people know that there's funding available in these areas, and the areas range, again, from the most basic molecular and cellular studies of the brain and of aging and all organs and tissues through clinical trials and everything in between.

Williams: And where is Alzheimer's in the general mix of your activities here? Is it the dominant area of interest?

Hodes: Well, for NIA, given the specific allocation of funds with congressional targeting to Alzheimer's disease, certainly it's become by far the largest individual area of research. It is targeted and mandated in a way that no other area of research is. Again, I stress in doing due diligence and full responsibility to the aim and

target—that is, to find effective interventions for Alzheimer's disease and dementia—it is also clear that to do that, not knowing what the most successful eventual strategy's going to be, that we need to be supporting research that identifies the normal and age-related changes in neurons, in brain development, in interaction between neuronal cells in their glial environment, inflammation related to immunology certainly playing a very important and visible part in examples of the kind of multideterminant factors that are probably influencing health and disease in the brain, including dementia and neurodegenerative diseases. So, an example of a way in which basic science, immunology included, not only can be but *must* be a comprehensive part of trying to understand effectively complex multideterminant processes that occur.

So it's a chance to try to encourage the best of people in fields like immunology, neuroscience, molecular biology, genetics, to be thinking, not giving up what the exciting areas of interests are themselves, but thinking of ways in which this may be truly, plausibly, and compellingly relevant to specific areas so that that research can be supported.

Williams: It looks like you've done things in an innovative way in terms of structuring the Institute. Is that an example that other Institutes in NIH and other places are following or taking the same kind of lead?

Hodes: Oh, I wouldn't want to take credit or claim or even accept the suggestion that the way in which we've been organizing things in this Institute are exceptional or the exception. I think that colleagues across NIH are all wrestling in a very intelligent and proactive way with the best way to manage their resources in pursuit of their own priorities and in collaboration across NIH.

Williams: What about the balance between research that's being done here and extramurally?

Hodes: Well, as with most of the Institutes at NIH, as you're expressing, we have intramural and extramural research supported. The intramural programs, meaning scientists who are direct government employees either here on campus or at some other locations, but direct federally funded, constitute approximately, historically and to this day, maybe 10 or 11 percent of the budget, something now probably less than that for NIA. So that the rest of the budget is supporting research across academic institutions and organizations across the country and to a more limited degree even internationally, and it all needs to be coordinated. So for any of the Institute directors who are looking at the balance of resources they have, it's perhaps 10 percent for intramural research and all the rest for extramural, with an attempt to coordinate those two components as best we can.

Williams: And as director, how do you keep in touch with the extramural activities?

Hodes: Well, we, of course, have very, very gifted and committed professional staff, scientists themselves, most of whom had very substantial and successful careers of their own till they came to NIH to serve as directors of a division or a branch that, in turn, deals with supporting extramural research in a given area. As an Institute director, you have the obligation, the opportunity, the luxury of learning about all of these areas in, I'm sure, an inadequate way, but through the staff here, but also by, to the degree possible, direct interaction through scientific meetings, workshops, and the literature in all those areas.

But implicit in the question is sort of an interesting dichotomy for any of us who are Institute directors and also working in a laboratory, and probably still is the majority of Institute directors currently, you have laboratories, although when I chose to do it, Tony Fauci was the only one. The distinction between attempting to be familiar in enough depth with one's own area of research, to be capable of research in that area, versus the importance of understanding broad areas of research, to be a part of the decision-making and priority-setting process for such a large domain and breadth of research that one couldn't possibly have that same level of intimacy. So I think for most of us, it's a challenge but also a set of complementing kinds of gratification to be able to work in an area of science and be highly informed in that specific area and balancing that with the ability to attempt to be a part of the judgment that supports a far broader area of research and science.

Williams: It's a good segue into my next question, which is what do you feel laypeople should know about your research activities?

Hodes: It's a good question. For those of us whose research, own research, laboratory research is in basic science, the question often asked by friends, neighbors, relatives, "What do you do?" The first instinctive answer is, "It's immunology." And when pressed further, it's pretty specific with a sense that, "I don't know if you really want to hear this."

But the answer usually come round to is explaining that in the case of the work in my own lab, what it's been, what it is now, is an attempt to look at molecular and genetic levels of the mechanisms that regulate the immune response, and to do that with enough precision and insight that eventually it lets us understand how whole organisms, even humans, respond and how the immune system is a part of our defense and preservation of health. But trying to convey to the lay public what it means to have great excitement about discovering a new cell surface molecule that works to interact with this receptor and co-stimulating the response in the T cell to an antigen-presenting cell is a challenge.

Williams: So are there discoveries that you and your lab have made that have had translational value so far or not?

Hodes: I think only in the broadest and most general sense of it. For example, having been, I would just say, a part of the early years when there was so much excitement in understanding the nature of immune response, of T cell recognition of antigen, and MHC [major histocompatibility complex] restriction and cooperation between T cells and antigen-presenting cells, and having a part of the discovery or identification of some of the co-stimulatory molecules and pathways, all of that has become a part of what is now important designing immunization strategies, in designing intervention strategies for cancer that are targeted at removing some of the inhibitions on anticancer responses. And, sure, one could point to specific discoveries in labs, including our own, of a particular molecule, of a particular interaction that way downstream, then reflecting the input of scores and hundreds of scientists over the years and decades, eventually got to be somewhere as a result of all that work. In that broad sense of translation, it's been a privilege to have been a part of that.

Williams: You're being very cooperative here. [laughs] Aging, of course, is something that everyone either knows about or will soon find out about. So what's your feeling about the current status? Are you on the verge of major discoveries, or is it a long vista ahead?

Hodes: First I would say, just looking back over the last ten and twenty years, the amount of progress there's been in understanding the kinds of changes that occur with normal aging and with pathologies that can accelerate some of the aging processes has been huge, the insights we have, really exciting.

As is usually the case in science, if you ask whether we're on the verge of discovering what aging is, the answer is increasingly that it's not going to be a simple, single thing. There's been a recent movement or a recent naming of a movement, something called geroscience, which originated with leadership of folks here at NIH, at NIA. Felipe Sierra, who's been recently division director of Division of Basic Biology of Aging, has been instrumental in leading this conceptualization, and basically it says that there are aspects of aging that underlie the aging processes and are relevant, therefore, to many of the diseases and conditions that are associated with aging. And these are basics such as inflammation, autophagy, protein folding, cell senescence. There now is in some recent publications identification of perhaps seven pillars of geroscience. So the notion that all of these and probably more are contributing to what we call aging and to the relative success or the relative complications of aging by conditions and disorders.

So the way in which your question might be reformulated or challenged now, anyway, asked whether we're on the verge of the discovery about what aging is, is a relatively new excitement about the possibility that if you accept that there may well be underlying commonalities that occur with aging and that are responsible for susceptibility to multiple diseases, that we will find interventions that target aspects of this basic aging process, and, in doing so, will not just prevent or delay

a single disease or condition, but will have an effect on multiple age-related conditions simultaneously.

I would say this is an area that has received a lot of excitement. It is intriguing. There's a basic science underpinning for its plausibility, and it will remain to be seen just at what pace and how effectively ultimately this gets translated into real clinical translation. There have been, though, for example, even conversations with the Food and Drug Administration, FDA, about how one might work to qualify, test an agent, the intent of which is to delay processes that underlie multiple diseases. You can see it's a conceptual challenge from many respectives, but just the very fact that scientists—NIH, FDA— are thinking in these terms is itself a bit revolutionary.

Williams: So, geroscience is an exciting concept. Is it a concept or is it—

Hodes: I think so.

Williams: —an approach?

Hodes: It's a concept that leads to an approach. In terms of what the "it" is of geroscience here at NIH, there's a geroscience interest group that began a few years ago. I got a few of my NIH Institute director colleagues together to talk about this notion that we might form an interest group committed to looking into the commonalities of science behind it. They were the immunologists including Steve Katz and Tony Fauci and a set of others, and that has matured now into a group of Institutes, with support of their Institute directors, who do meet regularly. So there's been a Geroscience Summit to discuss the science behind this, workshops, meetings of an interest group.

Most recently in the formulation of one FOA [funding opportunity announcement], that is, a funding announcement that is attempting to promote the recognition that aging is a variable in many of disease and other models that we pursue by simply offering with a large amount of—the support coming from NIA, to take the current models of heart disease, of arthritis, of diabetes, which are often studied in young mice, because, you know, it's very hard and very expensive to generate old mice or animals of any sort, and to essentially cost-share, to encourage pursuing any of these models which are already of interest to a scientist, but taking into account the age variable in the systems in which they're looking. This is an example in which in a modest way to begin with, I think if we can gain increasing appreciation of the relevance of aging as a variable in a wide area of research.

Williams: Looking at some of the work that was being done in the conferences and so forth, there's a global aspect to this whole matter of aging issues, isn't there?

Hodes: Mm-hmm. Yes, it certainly is worldwide. And in addition to the basic science that we see, and maybe as an immunologist and an AAI member in this conversation are focusing upon, there's a lot of interest and a lot to be learned at the global level, meaning this globe, this planet, at a universal level, the comparison what goes on in different countries as they pursue aging as both a clinical and a sociologic phenomenon in different ways is really an opportunity to learn from one another. So in that respect, at NIA, the Aging Institute, among the diverse programs there are some that are looking very specifically at just that, populations representative of different nations in the world, harmonized studies that look at the biological and other variables in these populations in parallel, to look for similarities and differences and to learn from that.

So when you do studies like that and find out that in Europe or U.K. [United Kingdom] there are areas of major disease in which apparently not explicable just by socioeconomic level, for example, there are major differences, and in some of these cases, U.S. just not doing as well as other countries, it's a natural experiment of sorts that allows one to start trying to learn from these comparisons and understand how to best interpret and configure what we're doing here in this country and what all countries are doing to better inform their approaches.

Williams: Is the global approach, which is so important to this area, relatively new, or has there always been a very international flavor to science and research?

Hodes: Well, the answer probably depends upon the kind of science one is thinking of. So in the most basic kind of laboratory research, which is done in individual laboratories with small collaborations, there's been in recent history pretty good communication and collaboration through meetings, publications. This still goes on. So this is global, but probably not so much more global than it always was.

It's in cases where there's something to be gained by explicitly collaborating, taking some expense and commitment. So population science, clinical trials that you can do with greater power across countries than any one country, genetics, population genetics, a very clear example, where by studying different populations in the world, you're going to learn a lot more than in any individual domain with its more limited genetic as well as environmental exposure. So the place where there's probably been the greatest explosion has been in the large-scale science, that is, population genetic, genomic, as well as a continued, I think, very healthy international collaboration in the more basic areas of science.

Williams: Thinking of Alzheimer's specifically, was there a moment in time when it sort of had its "AIDS moment," sort of the light bulbs all went off at the same time? Or am I wrong about that?

Hodes: It was not quite so acute, which makes sense. In AIDS/HIV appeared as a de novo, relatively de novo epidemic, and so the appreciation of it and the concern, the fear that it engendered happened quickly. Alzheimer's disease, quite

different. It's been around, so far as we can tell, probably with relatively similar age-adjusted prevalence for quite some time, but it's only in the last half century or so that it was really even appreciated very much as a disease as apart from normal aging. Certainly in my own time in medical school, there was very little to be learned at all. It was dementia, it was premature if it happened early, but otherwise there was very rarely a diagnosis made, never called a cause of death. And we have both had an explosion in the number of people who reach the age at which they are susceptible to and therefore develop Alzheimer's disease, and only in the past half century or so at which the biochemistry and underlying genetics have been understandable. Until that last half century or so, it's largely the plaques and tangles that Alzheimer described in 1906 that are seen in the brain at death and very little to be done other than that postmortem diagnosis. So, not the same pace as AIDS/HIV, but in the large scale, in the last ten to twenty years, there's been an exponential growth in appreciation, press, and near exponential, probably, in funding now as well.

Williams: Having seen several of your appearances on YouTube, it strikes me that maybe this is a relatively new role for directors of Institutes at the NIH, of being the public spokesman. Do you feel that that's the case or not?

Hodes: I don't know that it's any newer. I think that all of us are attempting to responsibly and effectively communicate to varying audiences, whether it's to our scientific constituencies, the public, advocacy groups, Congress, and other public representatives. I think we all do it and have been doing it. I suppose YouTube and current communications for those who tweet or blog has made it a lot more visible and a lot easier to do it and reach larger audiences.

Williams: Well, Dr. Fauci has been such a person to go to for information and whatnot, and I would think you're in a similar situation for the area of aging, and that that might be somewhat new, that a scientist needs to be an advocate and an instructor and an educator.

Hodes: I think it is a role that has become even more important. It should always have been the case, and I think always has been, but I agree with you, the public—and I take this to the good—is more sophisticated and increasingly more interested in health, disease, in underlying biology, and I hope—and this is perhaps the biggest challenge—in the most basic science that underlies it all. We're all, I think, trying to be very consistent in emphasizing in the message we deliver that the importance for supporting research that is true discovery-focused, that will ultimately but unpredictably have its impact in a more applied way, is in some sense the most difficult message to get across to a public.

Williams: What about getting that message across to members of Congress?

Hodes: I think, by and large, Congress, in a very bipartisan way, has been appreciative and accepting. There have always been areas of controversy, particular research

areas that will be cited as more or less virtuous by particular areas. There was a time when AIDS, HIV/AIDS research, you know, had its real controversies, but overall and to the current time, I think rather uniformly—in fact, I can say completely uniformly in my own experience, I have yet to not have had a very receptive and supportive interaction with any and all of the policymakers, Congress and otherwise, of whom had a chance to integrate.

So I think the will is there, I think NIH is a priority, NIH-supported research is a priority, and these days I think probably the largest constraint on the research support is the broad macroeconomic one. You know, where are we going to find the funds to do all the things that need to or ought to be done? But relatively little restriction based on concerns or limited enthusiasm, I would say, by policymakers. I think they do understand.

And that's a continuing and ongoing effort. It's not just NIH Institute directors, but it's the professional organizations. Here, I think, you ask whether this is sort of a new role for Institute directors or leaderships to be spokespersons, to be visible. I think it's perhaps an even newer role for the large community of scientists who appropriately—and in many ways, I envy all who really are just able to focus on their own work, minimal administrative responsibilities, but that group is in many ways going to be one of the strongest advocates we have—probably underutilized. I know AAI makes real and laudable efforts to organize and orchestrate it.

But I have to emphasize that. Scientists—and I resonate with it—are a little self-conscious about advocating for the importance of supporting their own work. It looks sort of self-serving and self-interested. But it is a community that I think is highly respected and needs to be out there speaking about the importance of what they do.

Williams: You're prescribing some behaviors here, correct?

Hodes: Yeah. And I think this is not a new message. I think that AAI in particular is organized with very specific efforts in this regard that have been effective.

Williams: You joined the AAI in 1975. What attracted you to the organization?

Hodes: It was never a question; it was the natural thing to do. As a part of a scientific community, one wanted to belong. Now, at that time if you wanted to get the journal [*The Journal of Immunology* (*The JI*)] and go to meetings, it was all made much easier by joining. And at that time I think that's what it meant to me. It meant being a colleague in meetings and having the journal. Only more recently, quite more recently, have the more organizational and programmatic aspects of AAI become apparent in the way it's encouraged, encouraged trainees, has informed and educated the public, has become more visibly to me as a member of

a public service organization as well as a convenience organization for convening meetings and publishing a journal.

Williams: Any recollections about your stints as an editor for *The JI*?

Hodes: Ah. Yeah, boy, I'd almost forgotten you've got that down way back. That was a very challenging educational and stimulating experience. Up until that time, of course, as with all of us have had an opportunity to be asked to review a paper here and there, but to be at a central point of identifying reviewers and then mediating or editing the reviews that came in, it gave another level of appreciation, probably at that point a real increment, in what it meant to be trying to judge and regard science to be a part of community more broad than one's own research area.

Williams: You also served for a while on the Program Committee of the AAI. Any observations on that service?

Hodes: You know, it's a great area of participation to be able to try to match the science and scientific programs to the areas of current and emerging science, a great challenge and a privilege to be a part of it.

Williams: I noticed that in '07 you received the AAI Public Service Award. The significance of that award to you?

Hodes: Oh, I was, you know, gratified, flattered. I don't know why or how I particularly deserved it. As an Institute director, I guess there was an opportunity in doing right by that job to be supporting areas of science, including immunology, and to be a spokesperson for research. In my position, it was aging research that included immunology, but, again, I was very gratified, but don't know that at the time I was able to understand exactly what the criteria would have been, other than somebody who was committed and did best, as so many of us did, to promote the ends of the Association.

Williams: I was intrigued by some of the other winners of that award who were not scientists, several members of Congress and so forth.

Hodes: Yes.

Williams: So it an interesting colleague or cohort. [laughs]

I also noticed that the Alliance for Aging Research awarded you the Indispensable Person of the Year Award in 2013. My lord, how—

Hodes: Yeah, how about that as a term? Yeah.

Williams: That is really—I am truly honored to be here. [laughs]

Hodes: Indispensable maybe just for that year.

Williams: Oh, I doubt that.

I guess in some of the publications I've read, it's been projected that in 2025 your goal is to have, effectively, treatment and prevention.

Hodes: So, that's interesting. As scientists, we all cringe at the notion, I think, of making predictions about a cure for this or that, and certainly as Institute directors, rather routinely in congressional hearings, will be asked that question, "Doctor, when do you think we'll have a cure for this?" Or, "How much more money would you need to have a cure for this by that year?"

And I, along with almost all of my colleagues have been rather steadfast, politely so, in saying, "We really can't make that kind of prediction." So I never said 2025, I never suggested 2025, but I understand it. You know, the advocates and policymakers made the case that although they acknowledged that science is not predicted, it's not engineering, there's no timetable, that making this a goal and so-called aspirational goal, aspiring to do this was itself motivating, and that having a plan in place that projected how research might progress with the capability of making that achievement by that time was itself motivating and therefore self-justifying, and that was the judgment, and so we live by or with it.

But I think it's important to distinguish, I think everyone recognizes we really can't make a prediction like this, and worry a bit about the risk, whether it was cancer predictions twenty years ago or whatever it might be now, of the public being displeased by false promises or promises not fulfilled. So it's a great aspiration, it's possible, it would be quite extraordinary if we can do it, but it should be regarded as a goal and target and not anybody's—certainly not my own—suggestion of, "Here's a date by which I know we're going to be able to accomplish something."

Williams: At this point in your career, are you looking back with satisfaction on your career?

Hodes: I feel extraordinarily fortunate. It's been a privilege to do what I've done. It's been gratifying throughout. I've enjoyed being a part of smaller and larger successes. So, absolutely. It'd be hard to imagine a more gratifying and privileged opportunity.

Williams: Any regrets or any downsides?

Hodes: No. You know, the regrets were at each stage having to give up something. So I remember when it was clear that I couldn't both carry out the kind of research career I wanted to do and be a clinician. For a while I prolonged that. In fact,

several years after I was in the laboratory as an independent investigator, I did an oncology fellowship here at the National Cancer Institute, so the labs in the evenings and then seeing patients in the day, and that was exciting for a while. The time came when I knew that I wasn't going to be able to do that, it hurt, you know, because I enjoyed working with patients, clinical medicine. So I don't regret the decision. I regret the fact that there had to be a decision, and none of us can do everything. The fact that I've been able to continue in a laboratory as well as playing the role I am at NIA as one of the NIH Institute directors I think is just an extraordinary privilege. So one only regrets those things that one had to give up, but, boy, that in itself is rather a positive statement, isn't it, that one regrets only not having been able to do more of the wonderful things that one had a chance to do.

Williams: Are you optimistic about the future of biomedical research in the U.S.?

Hodes: Sure. If this is a yes/no question, then the answer is yes. I think we've been very fortunate in that the support for basic research has largely superseded political issues. I think that the level of support for biomedical research is largely going to be dependent upon broad economic issues in what the country decides it can afford.

I think that I can point, as an administrator, if you will, to frustrations with administrative processes. So we speak of this all the time, the fact that rules are imposed, some of them absolutely critical—protection of human subjects or of animals, absolutely critical, avoiding conflicts of interest, enormously so. But I think all of us have seen an expansion of the administrative hurdles one needs to step through that deserve some re-attention to see whether, in fact, we can make the whole process as well as our daily lives more efficient by looking for economies and processes that don't compromise appropriate oversight, but let us do a more effective job of accomplishing what we're supposed to be doing.

Williams: Do you see improvements in that direction, or is that a battle that lies ahead?

Hodes: The battle, the challenge remains.

Williams: [laughs] What advice are you giving students that you come in contact with about careers in immunology, study of aging, whatever?

Hodes: Well, the very first is that from my own perspective, and I think a relatively objective one, there's never been a more exciting time in terms of scientific opportunities for someone who enjoys the creative challenge of discovery, of invention, of science. This is an extraordinary time. The most exceptional of approaches and technologies are now available to most scientists in a way that wasn't true and would support enthusiasm and excitement for that.

I think one, to be responsible in mentoring these days, has to acknowledge the reality that support is highly competitive, that one ought to really love it. You know, you don't do this because it's an easy life, an easy way to get rich, and people have to go into it with eyes open, understanding the challenges. But if you love it and your heart and soul are in it, then it's just an extraordinary time, and people ought to leap to it, and we who already are in the field ought to be doing everything we can as a very highest priority to try to facilitate and make it easiest for people coming in now to succeed at their entry and to succeed in their continued career development.

Williams: How have you balanced family life with your professional life?

Hodes: I guess you'd have to talk to my family. I think well. I work, like most of my colleagues here, work pretty long and hard hours, but most of the time when I'm not here, well, I'm either in the gym or with my family, and that's always been the way. The time has been valued by all of us, I think, in intents.

You stimulated food for thought once again. I would hate to think that I'd compromised the quality of time with my wife, with my daughter by work. I don't think so. I think they've appreciated and shared the enthusiasm for what I do, and we spend every opportunity for quality time together. We need to complement that.

Williams: And what do you do for fun? [laughs]

Hodes: Well, besides work, you mean.

Williams: That's right. [laughs]

Hodes: Well, you know, day to day, week to week, the work is a large component of the time, always been involved in physical activity, largely in a gym, so a few days a week, a few hours a day, I'm there for a good part of that time. You know, travel that comes for work or as a means of escaping for a little while with family is something I enjoy as well. When the weather's right, we do a good bit of gardening and keep ourselves in vegetables for the season. Recently had to add a deer fence to our armamentarium in the backyard, but that's something I enjoy doing too.

Williams: Anything else you want to contribute to this record that I hadn't prompted or you hadn't thought about it?

Hodes: No, I think you've really covered the area very widely, and thank you for the opportunity to participate with my colleagues.

Williams: Very good. Thanks so much, Dr. Hodes.

Hodes: Thank you.

[End of interview]