Allan Tobin

Personal Details

Name	Allan Tobin
Dates	Born 22/08/1942
Place of Birth	Manchester (USA)
Main work places	Boston, Los Angeles
Principal field of work	Neurobiology, Huntington's disease
Short biography	See below

Interview

Recorded interview made	Yes
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Personal Scientific Records

Significant Record set exists
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Biography

Allan J. Tobin, Senior Scientific Advisor to the CHDI Foundation was born on 22 August 1942 in Manchester, New Hampshire. He was an undergraduate at MIT (SB in Humanities and Science, 1963), a graduate student at Harvard (PhD in Biophysics, 1969), and a postdoctoral fellow at the Weizmann Institute and at MIT. After four years on the Harvard faculty, he moved to UCLA, where he became Professor of Physiological Science, Professor of Neurology, Chair of the Neuroscience Program, Director of the Brain Research Institute, and Eleanor Leslie Chair in Neuroscience. He is co-author of Asking About Life, a prize-winning textbook.

INTERVIEW WITH DR ALLAN TOBIN, 13th SEPTEMBER, 2005

PSH. It's Wednesday 13 September 2005; I'm talking with Dr Allan Tobin about Huntington's Disease Research and we are in Manchester UK at the World Huntington's Disease Congress. Allan, tell me first of all just to get the context. What did you do your primary science and biology training in, yourself, before you ever got as far as Huntington's?

AT. I actually grew up in Manchester, New Hampshire, so it's strange . . .

PSH. Manchester, new Hampshire. Home from Home.

AT. and I was an undergraduate at MIT in Boston where I studied literature and biology and physics. I took essentially a liberal arts degree at MIT, which is unusual and then did a PhD in Biophysics at Harvard, where I worked with John Edsall who is a protein biophysicist and chemist. Then I did further training in protein biophysics at the Weizmann institute with Ephraim Katchalsky, who later became Ephraim Katzir and then became president of the State of Israel. Then I did another year of postdoctoral work at MIT with Vernon Ingram working on developmental biology, studying chick embryos and haemoglobin, haemoglobin genes. I became an Assistant Professor at Harvard in the biology department. A friend of mine who was a pharmacologist had been invited to the first Hereditary Disease Foundation Workshop in 1971. He told me about this experience of going to multi-disciplinary workshops where people essentially played blind men and the elephant about this strange genetic disease. And I said 'that sounds like an interesting enterprise'! As you know, Milton Wexler had organised these workshops to encourage free association among bright young scientists, so I became part of the second group of young scientists in 1972. It turned out that I was very captivated by Milton and by Nancy, whom I had actually known at Harvard. She had been an undergraduate when I was a graduate student. I encountered her a couple of times. So it was 1972 when I got interested in Huntington's disease. Then I moved to UCLA in 1975 and shortly thereafter Milton asked if I would take over running the workshops, so that is how my involvement with the Hereditary Disease Foundation came about.

PSH. Had they had any scientists involved in the organisation of them before yourself, on a constant basis?

AT. Yes. Well they had a Scientific Advisory Board, which was primarily comprised of neurologists, but the initial formulation of the workshop programme came from a meeting that Milton had had with Seymour Benzer and Bill Dreyer and John Menkes. That conversation--what shall we do?—occurred shortly after his wife had been diagnosed in 1968. What shall we do about this disease that nobody knows anything about? Their conclusion was get together some bright young scientists to come up with new ideas, and so I was one of the second group. These groups were mostly assistant Professors and post docs, about a dozen of us. Some of us would continue to attend other workshops and to think about HD.

PSH. So when you came into the organisation, was there a particular theme at that time. Were people already thinking in terms of genetics or was it . . .

AT. No, in fact I think a lot of the effort was really focused on looking for peripheral biomarkers in fact, and ways of studying effects of the Huntington's disease gene in the periphery. You may recall that there was a flurry of papers at that time, suggesting that there were differences in the growth of fibroblasts, differences in the membranes, differences in the immune response and so forth. So that was the major influence on the way people had begun to think about HD. The previous person, who would effectively have functioned as a scientific director, was a man named David Barkley, a developmental neurobiologist, who had become an kind of immunologist. Just to give you a flavour of the time, I recall a comment of Tom Chase, one of the board members, a very distinguished clinical neurologist and clinical director of the neurology institute at NIH. The first thing I said when I presented myself to the scientific board as the potential scientific director was to propose a workshop on the genetics of HD. I said that there have been such advances in molecular biology and in manipulating DNA that we need to get people who know about recombinant DNA together with people who know about clinical genetics. Tom Chase said 'Well I don't understand, Allan. We know it's an autosomal dominant. What else is there to learn?' So it was part of a kind of a honeymoon deal that I got to have that genetics workshop in 1979. That workshop was also influenced by the fact that David Housman was a neighbour of mine in North Cambridge, in fact our children shared a babysitter for about 6 months of their early lives, so we had had discussions about this, and I got him to participate in the workshop planning.

PSH. So was it the 1979 meeting that really started the kind of genetic studies going, would you say?

AT. Yes I think it was. I actually write about that meeting in my general biology textbook, *Asking About Life*. I can send you the chapter, but there was a discussion at that meeting. I organised to invite a group of molecular biologists. This was before the Botstein-White Paper came out [Botstein et al., *American Journal of Human Genetics 32*, 314-331, 1980] Even then, however, there was suspicion--on the basis of the haemoglobin intron sequence--that there was a lot of DNA diversity even though there was no coding-sequence diversity.

PSH. And before any DNA polymorphisms of any kind.

AT. Well there were DNA polymorphisms that had been discovered in the globin genes.

PSH. OK.

AT. So there were three polymorphisms known at the time of the meeting, all in globin genes. But from that Botstein and White calculated that if they found three in beta globin then there must be others, so Botstein on the one hand and Housman on the other got into a discussion about whether it was better to get a complete physical map of the genome and then place the two thousand genetic and described genetic diseases on that map, or whether one should start out by looking at one chromosome. David Housman argued to start out looking one chromosome at a time because one could get chromosome-

specific hybrids and then look on those for polymorphisms and map one chromosome at a time. That was David Housman's idea. Botstein was saying, 'No no, this is a whole new field!' In a way they were both right. I mean Botstein was more right in the sense that that was the programme for human genetics and Housman was right because we were lucky and as you know, it turned out that the first RFLP gel showed up a difference.

PSH. Now that was before David Botstein published his paper on the theoretical use for polymorphisms to map the genome, which I think was 1982 or 3 or something like that? Maybe '84 '85? [It was 1980].

AT. Might have been earlier. I thought that it was a little earlier, but Botstein and White were certainly working on that and I knew they were working on it and had the meeting. Raju Kucherlapati, who developed ways of looking at specific human chromosomes, was at that meeting along with others who are now established figures in human genetics.

PSH. At what stage did you get David Housman into actually starting a study, because it started off with David, while Jim [Gusella] was still a very junior guy didn't it?

AT. Right, and so Jim had just moved to Mass [Massachusetts] General in 1980 and we actually gave, the Hereditary Disease Foundation gave Jim his first grant and it was just to do this RFLP study. And it was really on the basis of the discussion that had happened at the meeting. So, Joe Martin tells a different story about the genesis of Jim Gusella's project.

PSH. I don't need to worry about that. Let's hear your story.

AT. Right.

PSH. But Jim was working with David Housman essentially as a post doc was it?

AT. Well he had just finished being a post doc with David at MIT and then he moved across the river to Mass General. And I think it was Joe Martin's insight that genetics was likely to be interesting to neurology and this was a job for Jim.

PSH. So Jim had taken the idea which had originated, so to speak, with him when he moved, is that right?

AT. Jim's big discovery in David's lab was that he could pick out human DNA against the mouse background on a Western blot.

PSH. Did they have a total human DNA library at that point, or did that come a little later?

AT. I think that came later.

PSH. So when Jim started his study, were the markers already available or did they not come until when he was into it?

AT. I think the idea was that he would develop markers at random, but the expectation was that such markers would indeed exist. I remember making a calculation at that meeting that, if there were 3300 centimorgans in the human genome, the expected value of the number of RFLPs needed to get a 10-centimorgan resolution map, would be 600-650. So the expected value for when you would find a linkage within 10 cms, you know we thought it would take two or three years work, and we might as well get started. As it turned out, it was the first gel that showed a linkage. Ira Shoulson, who was already a major player in the Huntington's disease world, had become interested in the potential for genetics in the summer of 1983. He had planned a workshop at the University of Rochester, to talk about what was the potential of the DNA-based diagnosis for the indefinite future. A week before that meeting Jim called me up and said the lod score had gone up to 3, right, and then by the time of the meeting the lod score had gone up to something like 7 or 8.

PSH. Yes I can remember that. But just going back a bit, you had the American families and then the Venezuela family. Had the decision to get the DNA from those, was that part of something separate or was it run entirely as part of Jim's project?

AT. No. So the first family was a family from Iowa, and we arranged to collect the lymphocytes from that family, specifically to test in a blinded fashion the hypothesis that there were differences in the properties of the lymphocyte membranes and in DNA repair of lymphocyte membranes, which had been reported in non-blinded studies. The idea was to collect these samples. Mike Conneally and Ray Roos, (not the neurologist from Leiden but the other Ray Roos neurologist, from the University of Chicago), went to a family reunion of an HD family in Iowa and collected blood and I think fibroblasts. I don't know that they immortalised lymphocytes or merely spun them down but the purpose of that was to look at the actual lymphocytes. I think that they must have been immortalising lymphocytes even then.

PSH. I guess with Mike Conneally there, he would have ensured that the right samples were collected which you could do a linkage analysis, rather than just studying the affected folk.

AT. That's right. At that time Mike had done a study that had ruled out something like, excluded some 12% of the genome.

PSH. And that was all using classical blood group markers?

AT. That was all using classical blood group markers, exactly.

PSH. Well I'm just trying to think then, at this particular point what markers Jim actually had available to test. I know it was only a handful. Some of these were from
Ray White, is that right?

AT. I think that Jim was generating his own markers. I think he was just looking for things that were polymorphic so he must have been cloning them.

PSH. And was it out of a Maniatis library do you think or . . .?

AT. Must have been. Must have been, because the Maniatis library was there. That's where the beta-globin and alpha-globin sequences came from.

PSH. So basically, at the time G8 came along, G8 was just one of the first, probably the first that Jim had generated and I'm trying to remember how many they ran in the first run. I know it was a very small number.

AT. There was one gel as I pictured in my mind's eye, it looked like it had 12 lanes, but Jim will know that.

PSH. So at this point then, from the point of view of the Hereditary Disease Foundation, was this still one single, possibly speculative project among a range, or had it become the main theme?

AT. From Allan Tobin's point of view it was a major new direction. From the terms of the funding that we put out, it was one project of say 8 that was being funded by the Hereditary Disease Foundation. I believe the amount was something like $16,000 dollars. It was not a huge grant, but it was enough to do whatever it was that Jim wanted to do.

PSH. So then once the linkage had appeared, and I remember very vividly this, because Jim had visited us in Britain a few months before, when linkage was very weak and we all agreed linkages usually went away, and then we all came to Rochester for the meeting and the people were running around. But at what stage, thinking from the point of view of you as the scientific co-ordinator at the HDF, at what stage did you make this into, it must have been fairly obvious that this was becoming a main theme, but was this a conscious decision or did it sort of happen?

AT. I think that everybody who thought about genetics or molecular biology knew that the key to understanding Huntington's disease was going to be to get a hold of that gene and to find out what it did. Now the hope was, that when we saw what the gene was we would say "Aha!". So effectively there were candidate-gene approaches that were running alongside this for a very long time, indeed including my own work. I guessed there was going to be something wrong in the GABA system. I think you know that my lab subsequently cloned about a dozen genes from the GABA system, none of which were involved in causing Huntington's disease, as we had hoped. That was my candidate system and actually it wasn't until much later in the early eighties that I made the transition to working directly on HD. So HDF engaged more and more with genetics but it really wasn't until we supported people to continue working in Jim's lab, and by that time Jim had NIH funding as well. Who else was supported in the early days? I can't remember.

PSH. John Wasmuth?

AT. No. But I'll tell you about John Wasmuth. The John Wasmuth story is an extremely interesting story. So after the gene was located on chromosome 4, the question was, how do we find the gene itself? So in January of '84 I organised a meeting and I brought people with different technologies together.

Now if you remember that in 1984 the idea of megabase molecular biology was brand new. Up until then, the size that you could put into a Lambda clone was in the order of 15 or 20
kilobases so the idea of dealing with pieces of DNA that were longer than that was an issue, and it was also the age-old problem of shear. At that time, people didn't know how to deal with large pieces of DNA, and people were increasingly aware that gene-sized pieces of DNA were big and needed to be treated specially. There were a few methods for dealing with such large pieces. So I rounded up a small group of people who had developed such techniques. These included Charles Cantor, who had developed pulsed-field gel electrophoresis. We also had Len Lerman, who had developed ways of scanning DNA for mutations based on its conformation. And David [Housman] of course, Jim Gusella, and a young scientist from Children's Hospital Los Angeles, Keith Fournier, who had been able to get single-chromosome hybrids. You know, when you have single chromosome on a mouse background, you can study one human chromosome at a time. So we tried to assemble the different techniques for walking, and then for jumping, along the chromosome. Two things happened, though I am not sure which happened that first year. We heard about a post doc at Yale who had developed the idea of a jumping-gene library. He was about to start to be an assistant Professor at University of Michigan. So I called him up and invited him to this meeting, and his name was Francis Collins. I found Hans Lehrach by quite a different route: it happened that I was on some trip to Israel, where I had done a post doc at the Weizmann Institute. I had been invited to a meeting in Israel, but because of a screw-up by a new travel agent, I ended up stranded in Frankfurt on my way to Israel. I called up Hans Lehrach, with whom I collaborated on the haemoglobin project when Hans was a post doc and I was an assistant professor at Harvard and I said "I'm going to come and have dinner with you".

PSH. Was he in Frankfurt then?

AT. He was in Heidelberg. So I took the train to Heidelberg and had dinner with Hans and his then wife. He was talking to me about his jumping libraries, and I remember calling Nancy after dinner and saying, we have to invite Hans to this meeting. So Hans was there. Then just a few days before this meeting Ralph Bradshaw, who was a member of the Scientific Advisory Board, a growth-factor person, been working with determining the sequence of NGF [nerve growth factor], and chair of biological chemistry at University of California Irvine. Ralph called me up and said 'I've got an assistant professor in my department who is interested in chromosomes. You should invite him to this meeting. That was John Wasmuth. And then John Wasmuth shows up and he had been studying chromosome 5 in Cri du Chat syndrome, but he had read about a 4/5 translocation. He had tried to get hold of cells with this translocation because of his interest in chromosome 5, but he couldn't get a return phone call. And here is a place where Nancy was indispensable. At the meeting we said how useful it would be to have that translocated chromosome, with the tip of chromosome 4 [where the HD gene was located] isolated from the rest of chromosome 4. Within a few days Nancy had got in touch with the geneticist in Texas who had reported this translocation and managed to get it to John.

PSH. Was that Mike Siciliano?

AT. Don't remember. I think it was a woman.

PSH. Ok.

AT. So that was the beginning of a consortium the where people had complementary technologies and that became the major focus. Very divergent personalities. Again going back to my experiences as a post doc. In order to learn Hebrew and to indulge my socialist leanings, I spent a month in a kibbutz before I started my post doc. One of the things that I noticed was that people were just as nasty to each other in the kibbutz as they were anywhere else, but they actually pulled in the same direction. They took care of each other. It wasn't necessary for people actually to get along! I mean this is Allan as a socialist and still a vestigial socialist. My attitude was a self-conscious comparison that I made over the ten years of holding this consortium together.

PSH. Because that's what I think is so unique. There have been lots of collaborations and almost all of them work quite well when nothing's happening very much and then fall to pieces near the end. But really, how you managed to overcome that I think is really pretty unique.

AT. So, there were several things going on. First of all, at the beginning, there was the need for the complementary technologies, which drove the initial effort, and at the beginning, people were learning a lot from each other. When people started getting DNA, however, there was a lot of tension about who was sharing what—both information and DNA itself. In particular, the people with technologies conflicted with the producers of clones. The former were seen as consumers and so there was a lot of tension. And there was particular tension between Jim and John, who were both producers but who didn't really want to share. Hans [Lehrach] was the most productive in terms of generating clones. I remember calling Hans about the tension. Hans was very angry because he was convinced that Charlie Cantor and Cassandra Smith were just going to take his DNA and use it and get all the credit for it. Or that Francis Collins would do so. And they were very very worried that they wouldn't have relevant DNA with which to work. Hans had just gone through a job transition, as you may know. Again, from my peace-activism days, I had been aware of the idea of unilateral initiatives, which I am sure you have heard about. And I called Hans, and had an hour transatlantic call with him, explaining the concept of the unilateral initiative and suggesting that he bring his clones to the next meeting. And so Hans showed up -- I remember this moment – he showed up with six ice-cream cartons and distributed the clones. That then became a ritual for every subsequent meeting. Everybody showed up with ice cream cartons and so that ritual became a cementing of relationships. There was another moment, and I don't remember whether it was earlier or later than the introduction of the ice-cream cartons, where John and Jim were not speaking with each other. We were having our quarterly meeting at MIT, and we had a double seminar room that could be closed off for two seminars. We had the meeting table in one half and the coffee in the other. During the first coffee break, John was in one room and Jim was in the other room and "he said he was going to send me this and he didn't." "I said I

would send him that, and I did" I remember literally shuffling back and forth 3 times and then the two of them came together, so that kind of thing went on all the time. And Nancy of course did her bit of the same sort, but I don't think she was so attuned to the specifics, but she was . . .

PSH. No but she could see the chemistry of interactions and what needed doing too.

AT. To an extent yes, and I think she, and she continues to be, psychologically attuned. She would say, 'We are all in this important struggle together and we all love each other, kind of.' I was less impressed by that argument. You know I admired her ability to the extent she could do that, but as somebody who is an academic myself, and at that time I was not a tenured academic, I was aware of the needs of individual people to solve specific problems.

PSH. At what point did you come up, because I remember there was a formal agreement that when the gene was finally found, it would be a joint publication in the name of the collaboration, rather than everybody doing it just as their own groups. When did that evolve?

AT. Now an important component in making the collaboration continue was Dennis Shea You knew Dennis?

PSH. I remember Dennis.

AT. Dennis was a wonderful man whose wife had Huntington's disease and his children were at risk. He raised money for HD research and treatment. He put on a dinner in Wall Street. He was a bond broker in Wall Street and he put on a dinner on Wall Street that raised a million dollars. So whereas, up until that point and after that point, the budget of the Hereditary Disease Foundation was basically around half a million dollars a year, in those years it went up to a million, over a million dollars. So originally we funded one post doc in each of these seven or eight laboratories and then it got bigger than that as a result of Dennis's intervention. But more importantly I think than the money, Dennis had us to his estate in Florida. Did you go there?

PSH. Yes I did.

AT. So he engaged his friends to cook. I remember him saying, 'these people think that having good potato salad is going to accelerate the cure and they believe that and that's what makes them come out and work.' In fact having the potato salad did accelerate the cure, because people wanted to go to Islamorada and they liked that togetherness. So the idea was we were going to have an Islamorada meeting.

Now in the end, things happened fast, with the discovery of a fuzzy band on a Southern blot [representing a much expanded CAG repeat in DNA from a child with HD]. It happened just before Nancy was off to Venezuela for a month, and Jim and Marcy wrote the paper very quickly while Nancy was in Venezuela. And it's a beautiful paper. It's a beautifully written paper. So you

wonder what would have happened if the paper had been written by committee instead. It's really, I think, a beautiful paper. Maybe I'm being too frank about these things?

PSH. No, and of course I was partly there, only partly and not involved in any way in the behind-the-scenes side. One of the things which does intrigue me, it was a long haul and in the latter part there were a lot of people outside who were getting quite negative, saying oh it just shows you can't find DNA things this way, you know, and maybe as a bit of a reaction from some of the early hype, not from the inside . . .

AT. There certainly was hype and I remember Frank Ruddle was quoted as saying, and this got back to all of the boys "If I have to listen to another presentation about Venezuela I'm going to vomit".

PSH. But was there any particular way in which you handled this keeping of such a long standing collaboration of quite difficult folk on the rails over these years where, really, it looked at times it wasn't going anywhere very fast?

AT. I think the key to it was getting these face-to-face meetings. We had face-to-face meetings with the investigators 3 or 4 times a year, and then once a year we had a big meeting with the post docs, 50 or 60 people. A lot of people groused about credit. It was always put in terms of protecting junior scientists: 'I'm worried about credit for my post doc.' So there was a lot of discussion. Jim really took the lead in sorting out what progress papers could come out. So that actually made a big difference. Interestingly the people who have since succeeded the best in their careers, were the people that were most co-operative when they were post docs in this consortium. I'm thinking of Marcy MacDonald, Leslie Thompson, Gill Bates, and Michael Altherr, who has disappeared from the HD world, from the world I have travelled in, but I think he has done very well at Los Alamos. So there's an object lesson there as well. The other thing that kept people together, I think, was that the junior consortium members had privileged access to senior people who were emerging by that time as major figures in human genetics. So it was a special treat to go and spend a weekend with Francis Collins, David Housman, Richard Mulligan, and Bob Horvitz. We didn't know, of course, that Horvitz was going to win the Nobel prize, but people knew he was a significant person to talk to. So I think that was also a draw to keep people coming.

PSH. One of the things that has always intrigued me is, that as I saw it during this time, you were always on the lookout for people who could bring in new approaches and technologies and there were some people who kind of came and then went, according to the change in technology. But there were a remarkably high proportion of people who stuck with HD, and I get a feeling that that's much bigger than from most other situations, this kind of loyalty to the disorder and that people have come in, perhaps not knowing anything much about the disorder and they were hooked and stuck with it.

AT. Well I think a lot of that had to do, as you pointed out in your lecture at the beginning of this conference, I think a lot of it had to do with the charisma of Nancy and of Milton. I mean, so often scientists don't feel like anybody

cares about what they do, and here were these Hollywood-type people acting differently toward us than the way people interact at most scientific meetings.

PSH. Yes, I remember you had some quite young gauche scientists and then you would find Hollywood celebrities treating them as if they were celebrities, which probably never happened to them before.

AT. I remember the first meeting I went to in Los Angeles in January 1973. There was a party at the studio of a then relatively unknown architect named Frank Gehry. And I remember two incidents from that, where I was a beginning assistant professor at Harvard, and a beautiful young woman came into the room and one of the other workshop fellows, much bolder than I, said "Oh, you must meet Allan Tobin". I thought this is a joke, right, somebody was there, and it was Candace Bergen, a famous actress and I remember her and I said "Hi, I'm Allan Tobin". "Oh you must be one of the young geniuses" and that was the way we came to be treated, especially having been in an institution that does not treat you that way!

PSH. The other thing which intrigues me very much is, when the gene had finally appeared and didn't give really any clues from its immediate structure, it almost seemed like everyone was sent back to the starting line to begin the race all over again, and again some people decided to leave at that point and other people decided to re-learn everything, and that must have been a really tricky transition for the Foundation at that point. How was that approached?

AT. Well, along the way I have been trying to build a parallel understanding of the neurobiology of Huntington's disease and getting a broad transition. This is actually a lesson for Euro HD, which I hope they will understand. The single most important innovation that I made at the Hereditary Disease Foundation, was to convince Milton and Nancy that the terms on the Scientific Advisory Board should be limited and non- contiguous. So people would serve for 4 years and they needed to be off the board for a year, and then they could be re-elected or not. So the result was that the board turned over completely several times. There were some people who continued on the board throughout those decades, but gradually we recruited younger people who were expert in molecular biology on one hand or cell biology and neurobiology, and I think that we engaged neuroscientists to say " OK, how can we use this information, now that we have a gene." Now by that time neuroscience and neurogenetics had advanced in other areas, because it took 10 years to get the gene and muscular dystrophy, dystrophin was known already and other genes and so people had thought down this road already, but I think that once we had the gene it didn't take a great deal of genius to figure out that one wanted to have transgenic mice. Again we were blessed with a serendipitous finding that Gill's first mice had a strong neurological phenotype, but they were never designed to have a neurological phenotype. So I think the transgenic mice and the transgenic cells, the engineered cells, were really important innovations and they brought in cell biologists on the one hand and neuroscientists on the other. The dialogue or the polylogue among the neuroscientists, the cell biologists and the geneticists is interesting because you still see that there is not as much cross talk as you would like, but it is increasing. That's where I think the action is.

PSH. Alan, how long altogether was it that you were with the Hereditary Disease Foundation.

AT. Almost 25 years.

PSH. That's an amazing, . . . It's a pretty unique kind of scientific life having had your own career and then this alongside it. I can't think of anyone else who's done quite the same, can you?

AT. Is that true? Gee, I never thought of that.

PSH. Well I can't anyway.

AT. No it's true. Certainly there have been people who have had a lot of influence on voluntary foundations.

PSH. But not in terms of direct scientific . .

AT. Yes.

PSH. Well, look, thank you. I've taken up most of your time talking instead of eating, so very many thanks and I am going to turn this off.

End of recording.