Michael Conneally

Personal Details

Name	Michael Conneally
Date of birth	04.12.1931
Place of Birth	Ireland (Galway)
Main work places	Madison, Indianapolis
Principal field of work	Human gene mapping, Huntington's disease
Short biography	See below

Interview

Recorded interview made	Yes
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Personal Scientific Records

Significant Record set exists
Records catalogued
Permanent place of archive
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Biography

P. Michael Conneally is Distinguished Professor Emeritus of Medical and Molecular Genetics at Indiana University School of Medicine in Indianapolis, Indiana, where he has been on the faculty for over 40 years. He is a human geneticist interested in finding the location of human disease genes. In collaboration with scientists at Harvard University and Columbia University, he was the first to use DNA techniques to map a human gene, namely Huntington disease. In the ensuing 25 years, he has been instrumental in locating many other disease genes and is still involved in Huntington disease. He received his bachelor's degree from University College Dublin and his Master's and Ph.D. from the University of Wisconsin, Madison.

Dr. Conneally is past president of the American Society of Human Genetics where he has served in many offices. He is Past Secretary General of the World Federation of Neurology Section on Huntington Disease. He was a member of the World Trade Center and Hurricane Katrina DNA Identification committees. He has received a number of honors including the Milton Wexler Award and the Lifetime Achievement Award of the International Society of Psychiatric Genetics. He received an honorary Doctor of Science degree from Trinity College, Dublin.

INTERVIEW WITH DR MICHAEL CONNEALLY, 28th OCTOBER 2004

PSH. It's 28 October 2004 and I am talking with Dr Mike Conneally at the Toronto American Society for Human Genetics meeting. I would like to start by going right back and ask what part of Ireland were you born and brought up in?

MC. I was born in Galway, a very poor part of Ireland. I was fortunate that I was able to get a scholarship to University from High School. There were three in the county and I fortunately got one of them. In fact I was the only one in my whole region going to college at that time, and I would say how things have changed. So I graduated from University College Dublin in 1954, actually in Agriculture and then I worked for 3 years as an agriculture instructor in west of Ireland advising farmers. I decided that I should get a little more education and I wanted to get a Masters. I was not very sophisticated at that time and it was suggested to me by somebody in the Department of Agriculture that I go to the United States and they would give me a Fellowship because I had an Honours degree. That is what happened. I was also very fortunate that I went, and my choice of university was based on the fact that many of my aunts and uncles, because there was mass migration in the generation before me, that they had come to Chicago and I wanted to go to university near there, and I went to Madison, which at that time was the best university in the country. It is chaired by Jim Crow, Josh Lederberg got the Nobel Prize, while he was teaching us actually there, and the premier epidemiological geneticist was Newton Morton, and I was his first student, and that was all the luck of the Irish I suppose, because it was not my choosing. I walked into it.

PSH. Its amazing really that Jim Crow is still around and active.

MC. Absolutely.

PSH. He must be 90 nearly?

MC. He is over 90 and he is still active.

PSH. Over 90. He was talking in our session.

MC. Yes. Yes.

PSH. And he had everything, all the computer side mastered and no problems of any kind. That's amazing.

MC. He's wonderful. He comes in essentially every day to work and, he is a widower, his wife Ann died some time ago, unfortunately. So he still carries on and is highly respected obviously, and is the doyen now of living geneticists.

PSH. But Newton also at that stage must have been a pretty young person.
MC. Yes, he had just gotten his PhD about 2 years earlier, with Jim Crow. Jim was his major advisor and he had written very seminal papers in both

segregation analysis and linkage analysis, and understanding that was something that at that time seemed difficult and were very few people working in, and so I was fortunate that it was easy to get a position because of my training.

PSH. What year was that, Mike, that you went to Madison?

MC. I went to Madison in January of '58 and I graduated in '62. I then spent 2 years at Case Western Reserve University in Cleveland with Arthur Steinberg and worked on the Hutterites, a genetic isolate in the west of the United States and Canada. I then came to Indiana in '64 and stayed on, and have just finished my 40th year there.

PSH. Before we get to Indiana, can you just tell me a bit about Steinberg, because he is somebody you don't hear much about now.

MC. Arthur was well-known in the field; he was Editor of the American Journal of Human Genetics. He is still alive, but in a nursing home, although doing fine. He was very interested in, a thing he did was what I would call translational epidemiology. He tried to translate Newton Morton's segregation analysis and linkage analysis into more palatable form, that people could understand, and worked with this huge genetic isolate called the Hutterites, that unfortunately were not as productive genetically as McKusick was with the Amish, because there were not that many rare genetic diseases. The founders seemingly had a very pristine genome, which of course the Amish did not, and came back to haunt them in homozygosity later. Not so with the Hutterites.

PSH. So was Steinberg medically qualified?

MC. No, he was a PhD and his most famous graduate student was Clarke Fraser, his first student and he was hurt somewhat, because he was picked out under the McCarthy era as being you know leftish, communistic, and he was blacklisted from a lot of positions at that horrible time in American history.

Steinberg is probably not as well known, but made some seminal contributions, especially in the area of hypertension and the genetics of it in the early days, because he looked at that in the Hutterites.

PSH. I always think of him as a sort of quantitative geneticist.

MC. Yes. Right. He was, yes.

PSH. And the other person, just again before we come to Indiana, would I be right, I mean you couldn't have been much younger than Newton Morton?

MC. That's absolutely correct, because I had worked for three years after my, I think one year, two years before I met Newton. That's right, correct yes.

PSH. How was he as a person to do a PhD with, because he must have been quite inexperienced as a supervisor?

MC. Newton was very difficult to get along with, and many students would come to Newton for statistical advice in genetics and my job was, they would write everything he said and I would have to go and translate it as best I could to them, but Newton was difficult to get along with, that's why he has only had, in his total lifetime, he has had I believe 5 graduate students that have got their PhD with him; unfortunately the youngest one, I'm the oldest of course, the youngest one has passed away early on, during his post doc fellowship, but of course Newton has

PSH. Who was that Michael?

MC. I can't remember his name now, but I'll come back to that.

PSH. It seems to be a fairly general thing that most mathematical geneticists aren't very easy to understand.

MC. That's true.

PSH. And the few exceptions are really valuable, because they are so few.

MC. To go back to Steinberg. That's why Steinberg was trying to make it more intelligible to the general genetics public, but whether he succeeded I don't know, but Newton founded, of course his famous lod score, he founded linkage analysis and when the American Society of Human Genetics decided to give the Allan award, obviously for the first time they had a huge field of very important people who might get that Allan award, and Newton was chosen as the first, and so the first is much more I think significant than say the tenth, because the field has been narrowed to some extent. And it is also of historical interest that his wife, Pat Jacobs, was the first woman to receive the Allan award from the American Society of Human Genetics.

PSH. Yes. So coming on then, you got to Indiana in '64?

MC. That is correct.

PSH. And were you there first as an assistant professor, or did you go as full professor?

MC. I started as assistant. No no no. I was assistant professor on a tenure track.

PSH. Who was Chairman in Indiana?

MC. At that time the first Chairman was Don Merrit. He founded the Department. In fact when I came, for the first two years I was in medicine, a year and a half, then we had our own department. It is also of interest that Bloomington - I was at the medical school in Indianapolis - in Bloomington, where Herman Muller was a Nobel Laureate, Cleland, a famous chromosomal person on Oenothera and Sonneborn who was a very basic Paramecium

geneticist; and Don Merrit wanted to call the department Human Genetics, to model it on Michigan, but the group, the three I mentioned said, no you can't do that. We would like to reserve that for us to be Human Genetics, and so we were called Medical Genetics and I believe we were the first department to be so named, and it was only not our choice but then to this day there isn't still a department of even genetics, let alone human genetics, in Bloomington, even though they have superb geneticists there.

PSH. That's interesting. So apart from Don Merrit, who I remember well from my time in America, apart from him and yourself, who was there at the beginning?

MC. Katherine Palmer was our cytogeneticist.

PSH. I remember her too.

MC. And at one time trained essentially all of the cytogeneticists in the United States. Very big on training.

PSH. Is she still living?

MC. She is still living, in great health, and she was a contemporary graduate student with Jim Watson in Bloomington. Jim Watson got his PhD in Bloomington and Kate at essentially at the same time. They were contemporary

PSH. That's interesting, because one of the things which interests me is that human cytogenetics got off to really quite a slow start in America compared with Europe.

MC. Yes, that's correct, it did, yes. And you know even then it was more service and still is, very service orientated.

PSH. Would I be right in feeling that in America, cytogeneticists didn't have quite the academic standing that basic geneticists and population geneticists had?

MC. Yes, I would agree with that, because people thought of it as just a service, you know they were looking at Downs, because there weren't that many chromosomal abnormalities in those early days and looking at the level of the chromosome was not very precise at that time. Obviously it was very crude. Before banding especially.

PSH. So what was your first work when you went to Indiana?
MC. That's what brought me into Huntington's. I was working on a study on diabetes, because there was an Englishman called, I forget his name now but he said that juvenile diabetes was due to an albumen antagonist and that it was a dominant with variable penetrance, Vallance-Owen was his name, and I got a grant from NIH right away to study that, and it proved to be a red herring, and that was frustrating for me, because we now know that it wasn't correct. He had what looked like great evidence but when blind samples were

sent to him by Alan Emery he didn't do a very good job of proving his hypothesis.

I also worked on cystic fibrosis. We were very interested at that time. It looked like there might be more than one locus involved, but in fact our studies said, because it is so common, that in fact it is most likely one locus. We looked at the frequency in first cousins versus the first cousins of the affected, and Don Merrit and I set up a little methodology to do that, and it was the first time anyone looked in that kind of way at any recessive disease.

But I think the greatest highlight was when a paediatric neurologist named Les Drew came to me to welcome me there, and he had come from Michigan and he had an enormous portfolio of juvenile Huntington's disease, that's onset before 20, years and he thought they were different, that they were a little different than the regular, because of course they were much more severely affected, their duration was much less and there were many of the rigid type rather than the choreiform and so on. So he asked me to look at those pedigrees. Well, we had a fellow at that time from Pakistan, Noosat Farhib, who I was training in some basic statistical genetics, so I asked her to go and pick out these pedigrees and look at the sex ratio of affecteds, which she did and came back and it was 1 to 1, the same number of males to females; and then I don't know why, but I wanted to teach her about 2 by 2 chi square and I said, would you look at the gender of the parents, the affected parents, which she did, and she came back to me and it was clear that a vast majority of the affected parents were males, and I was highly sceptical. I said, there's some error here. There's something wrong. Noosat, would you go back and let's go and re-examine them. Well let's sit down she said, I can tell you that I thought it was odd too, and Dr Conneally, I went over it twice and that's the way it is. So indeed we wrote a little paper and Don Merrit was going to the International Congress, the International Huntington's Disease Association Meeting and I have to think now, but in Montreal I believe. It was the very first one and he presented the data there and there were a number of sceptics, but there was one person in particular, and we probably can't publish this, from Holland, who never said a word, but listened and he went back and looked at his data and found the same thing and immediately published his without any affirmation on ours, and the proceedings weren't published for maybe two years later, which is typical, and so he beat us to it for a long time until we made a crusade so that everybody realised what had happened, because many of them were at this meeting, so we eventually got the original credit for this, but it was sheer, I want to point out, there was no genius involved, it was sheer chance, and of course that hooked me on Huntington's disease.

PSH. Well you say it was sheer chance Mike, but a lot of people might not have followed up on it, or realised it was of any significance. The one good thing I think there is that people coming later like myself, nobody actually ever remembers George Bruyn's paper and if anything is cited in terms of paternal origin, it is always yours.

MC. Now I want to mention another person who had a lot to do indirectly with the history of genetics. That's Julia Bell. Julia Bell had collected families and she had collected Huntington's, including Huntington's juveniles and when we went through her, I forget what you call them, Treasury of Human Genetics.

PSH. Treasury of Human Inheritance.

MC. Treasury of Human Inheritance. When we went through her Huntington's pedigrees we found exactly the same thing as we had found in Michigan, so that convinced that was our replication and we had done that already before the meeting, so we had replicated the findings, thank goodness, Julia Bell had.

PSH. Do you know that is something I don't think I ever knew, even though I have been very interested in Julia Bell's work and I have got her Huntington's monograph, and you know she did one on myotonic dystrophy?

MC. Yes, I knew she did.

PSH. But did you know also that if you think of parental origin in myotonic dystrophy, well we might come onto the maternal inheritance of the congenital

MC. Congenital

PSH. But she looked at the origin of the adult cases and she also found excessive paternal origin in that, and it was only years later that I found it and published it not realising it; Hans Brunner had found the same, also not realising it and then if you go back it's there in her work. I think she was an amazing person.

MC. Absolutely. No as far as I know, unfortunately for her and unfortunately for us, she did not look at juvenile Huntington's in her day. If she did, she did she didn't publish it, because we did but in any case

PSH. The really important lesson I think from her is, she gave all her raw data in great big tables and so you can go back to the raw data and look for something even though she hadn't realised it. The actual data are all

MC. All there. Absolutely.

PSH. Can I ask Mike, had you set up a linkage lab already by that stage, or did that come a bit later?

MC. Well, yes we had. We had a genotyping lab and in fact we were looking at families of different kinds and trying to map them, but I had a superb graduate student Peggy Pericak-Vance, who has since gone and just became invested in the Institute of Medicine, which is very prestigious and has won very many international awards, but it was obvious that Peggy would be doing linkage because that was my area, and at that time we had a Huntington's clinic because of our work with the juvenile and that, I became hooked on, so to speak, Huntington's disease, so we started a monthly clinic with Huntington's patients coming in. So I suggested to Peggy that we would have access to lots of families and I knew the National by then, the National Huntington's Association and so I said, Peggy it's tough but I think we should have a project for Huntington's disease. That was fine with Peggy. You know at that time graduate students did what they were told and all that, although I

didn't push her obviously. And so we started collecting families throughout the United States with the help of the national organisations, there were two at that time in Huntington's, and we got lots of good families and we had our genotyping lab and of course that was the very weak link. I think we ended up with, and I am guessing now, 42 markers or something, the blood groups and all of the protein polymorphisms and every time, especially Harry Harris, would come out with a new protein polymorphism we would set it up. And it was very tedious because no two of them, you know, you use that specific enzyme substrate and all this kind of thing and it took time to get them set up and then time to type them and set gels and . . .

PSH. What year are we in now Mike?

MC. I'm guessing we are getting into, I can't remember, the seventies. I may have to come back

PSH. Before the DNA era?

MC. Oh long before the DNA era, that's correct, and so it was then that we also started my collaborations and we of course had tremendous collaborations with both you and Lou Went in Holland and we would get together because you were trying to do the same thing and we would get together and compare notes, and unfortunately none of the markers were on the short arm of chromosome 4, so we were none of us getting anywhere.

PSH. I remember that very well.

MC. Which was very sad. I very fondly remember working with you and going to Wales and to Cardiff and to Leiden and having meetings there with all of you, and that started something that I have been doing all my life ever since, collaborations, which I strongly recommend to any graduate students, or any new faculty, I should say, not graduate students.

PSH. How did you come to meet up with David Housman and also with Nancy Wexler for the Huntington's?

MC. Because we were mapping Huntington's, Nancy had a meeting in San Diego on Huntington's disease and we went there to present our findings and right away, the next Hereditary Disease Foundation workshop or maybe two times after, then I started going to the workshops. At this stage RFLPs, people knew about what RFLPs were, and they had read the Botstein and Skolnik and Ray White paper, I forget the order, about how RFLPs could be used as polymorphisms, and so that excited us. So David Housman and I were at the foundation, at the meeting, at the workshop, and of course I was talking about linkage and how we hoped someday to be able to do RFLPs, we were going to have to gear up for that, a whole new technology, and David said, well I have a post doc, he is just finishing and he is going to be my post doc. His name is Jim Gusella, he is fantastic, extremely bright and I am sure I can persuade him to work on Huntington's. So Jim was working on RFLPs, he was molecular, he had all the technologies, and with David of course at MIT, and he needed families, so we had a large number of good families and by the way, at this stage we had also the National Huntington's Roster,

because Margery Guthrie had got Congress to agree to have permission to investigate Huntington's and make recommendations.

They did, and one recommendation was that there would be 'centres without walls' which were in Hopkins and Boston and the second was that there would be a national roster to collect families and other data on Huntington's. We got that so we had a lot of very good families and I sent these families to the group, and I sent them the obviously good ones and they agreed with my estimation that this family in Iowa was by far and away the best family that should first be looked at. So I went out with Ray Roos, not Ray from Leiden, but Ray from now Chicago, and he and I and a couple of workers toured Iowa over a long weekend and collected samples from this large family. Nancy had persuaded the mutant cell bank, which at that time only took at most 3 people from a family, the individual with a chromosome abnormality and both parents who would be the maximum. She had persuaded them to take 25 samples I believe. I can't remember.

We sent 34 on that day and of course obviously they couldn't refuse them. So this was the first large family ever immortalised by the mutant cell bank. Jim got these families and he then used 13 probes, and we weren't very optimistic that he could hit it with 13 probes, we were smart enough to know because of our experience with 30, they weren't all that polymorphic as a group as the ones Jim were using.

So Jim sent for me and said, I have some data that looks promising, so we mapped the Iowa family, that's what we had done and we got a lod score, I believe, of approximately two. To be significant you need a lod score of three, but this was by far and away the most promising thing we had seen and this was the marker known as G8, that's what they were called, could have given it a better name how famous it became. So we said we've got to try and get some more samples and we had already by then samples from Venezuela. So Jim looked at the Venezuelan, he then typed the Venezuelan samples for G8, and of course that was the beginning of an end for Huntington's disease, because that showed without any doubt that the Huntington's gene was right next to G8. Then we had, take me a minute to remember, she is now in San Antonio, who was the expert in assigning and lighting up probes - Sue Naylor. So Jim said to me, you know we need to know where G8 is now and at that time we weren't interested unless there was a linkage. So I said, send it to Sue, and sent it off to Sue and she did it in very short order, and found it was close to the telomere of the short arm of chromosome 4 and that was fantastic. From then on we never looked back.

PSH. It is an amazing piece of history that, and one of the things which I remember very vividly, I remember two things, I remember that summer, Jim came over and visited us in Cardiff and I asked how things were going and he said well, we've got some positive lod scores, but they are bound to go away like they always do, and nobody was then terribly excited, but the other thing I remember was, there was the World Federation Huntington's meeting, I think in Rochester in September, and by that stage I think the Venezuela families had been looked at and it was very clear, and everybody was in a terrible state as to whether to say anything to the press, and Nancy was wanting to rush out and publicise it, and everybody else was wanting to be cautious and

it really took everybody quite by surprise because am I not right that it first surfaced in August and everyone was on vacation?

MC. I'll tell you a little story about that, because we were going in August to what is now called HUGO but was called gene mapping then, and the gene mapping conference was in Los Angeles at UCLA and my wife Mary and I and our two kids decided to drive out there on vacation. Just before I left, the data from the Venezuelan family had just come in and I looked at it and I knew it looked very good. I knew, but I had no idea of course what the lod score was, but here we are in the Grand Canyon State Park and we had come back from touring the Grand Canyon. I had just made a fire by the camp ground and I had opened a bottle of beer, a six pack of cold beer for us and some pop for the kids, and we were sitting relaxing by the fire and the next thing I see what looked like a cop looking at my registration on my car and it was a park ranger and then he comes over and he says are you Dr Conneally, Indiana? I said I am, and he said we have a very urgent message for you down at Headquarters. By this time I think its well into11 pm and that would have been 1 am in Indiana and I thought, oh my, well you know, I am not going to call back. I knew exactly what it was, but of course I was elated, so I had an extra beer that night and went to bed and got up in the morning, and then I felt so embarrassed because they had stayed up all night to await my call. They wanted me to know. By the way they had tried to get Jim, they could not get Jim. They got Nancy but Jim was up in Canada on vacation and nobody knew exactly his whereabouts, so Nancy and I knew I think a day or two before Jim did. So then we of course went to LA and to the meeting and were mapping genes and talking about them and obviously everybody knew now, the word was out, and Victor said to me, now we need to put this in a workshop and I said well, you will have to ask Jim. So Jim and Nancy said no, it's got to get to Nature first and I know Victor was very perturbed because we were withholding information. Well there was no one else could really have beaten us, but that's the way it was and so we wrote the paper right there during the workshop, Nancy and Jim and I deposited ourselves in one of our rooms and wrote the paper and had one of the foundation people type it up and then rang home, made figures and got it together out to Nature, and of course they accepted it and it got out. One aside that I always felt terrible about was that Margery Guthrie, who founded CCHD, had died in the Spring of that year and didn't live to see the great discovery.

PSH. Yes, that's sad, because she was a wonderful person.

MC. She was, and were it not for her a lot of this would not have happened.

PSH. That's true. You see these are the kind of things, Mike, which never get into the published literature, and yet I think, looking back in the future, people will want to know the background, you know all these things, including the mix-ups and confusion which is so often part of science, but it gets edited out and never appears in the final version.

MC. Absolutely.

PSH. After that, and I remember very well how everybody assumed that having found the linkage so quickly it would only take another year or two before finding the gene.

MC. Yes, that was amazing. Yes of course, I was convinced a year, at most two years. This by the way, of course the reason this got so much notoriety, the mapping and not the cloning; the mapping, it was the first gene to be mapped using this new DNA technology and it proved that the technology would work. Now everything is mapped. All Mendelian genes are mapped, but at that time.....I would also like to say that during this time, this anomalous inheritance of juvenile Huntington's, where the vast majority, say under 10 is 100% inherited, under 10 I mean onset under 10, 100% of it is inherited through the father. We had the most complicated explanations for this phenomenon and I worked with many many good people in both England and Wales and helping them, giving them data to test their hypothesis and obviously after that C.A.G. repeat was discovered we now know what the real thing is but ...

PSH. It was always much more difficult thinking of a reason for a paternal effect than it was for a maternal one.

MC. Exactly, but I think if you had asked me when I was with Wisconsin, do you think there are complicated situations with trinucleotide repeats or something, and I only want to bring up another anecdote while I was in Wisconsin, and that was another paediatric neurologist working with Les Drew was Paul Dyken and Paul had these families with myotonic dystrophy and he kept saying to me, they are getting worse every generation. Absolutely. And I said, Oh Paul, it is an artefact, and I explained the way we defined anticipation at that time and I explained the whole thing to him and I know he was saying, you're crazy, that can't account for it, and I said, well maybe you know there's some kind of chromosome defect, and so we looked at chromosomes. I didn't believe him but I thought, let's look at them Paul, to help him, so we looked at the chromosomes in succeeding generations, at one very particular pedigree where there was enormous anticipation and found nothing, and even I suppose if it was chromosomal, because of the techniques then in cytogenetics we wouldn't have found them, but I'll always remember when I then went to the Hereditary Disease Foundation with you and heard about myotonic dystrophy and how it was inherited and the whole situation. I remember I couldn't wait and ran out of the room and called Paul Dyken and I said, "Paul, do you remember when I told you you were crazy to be thinking of anticipation?" and then I said "You got a few minutes?" He said yes, so I explained the whole situation to him and always remember Paul saying, "Mike, you sure made my day".

PSH. It was actually, that's how I met you first. I was at Hopkins working on myotonic dystrophy.

MC. That's right yes.

PSH. You remember, with Marion Rivas and you know we came over and looked at the Indiana families and you helped us; I remember we used to

bring all the samples back to your lab and you would get them separated out , but it was then also that I met Paul Dyken and he was not only hooked on the anticipation, and quite right too, but again there was this maternal effect, which he had, in just a small number, but then when we got my data from other centres, it added up that the congenital ones were almost all maternal, and it was the two of us that then put the data together and published it, which put the maternal inheritance of myotonic dystrophy on the line, but what we never dreamt was that it would join up with the Huntington's work and all be the same thing.

And I remember also coming to the Hereditary Disease Foundation meeting and we would keep saying to the people there, look at the data on myotonic, because it's really showing something, and I remember most of the folk there, apart from yourself, were saying, oh no we are not interested in muscle disease. It is nothing to do with Huntington's.

MC. Yes, sure. There you go.

PSH. And then we got the anticipation in both, and when the myotonic gene came out it was just crying out loud, there must be something the same.

MC. Absolutely yes.

PSH. Except for those telomeres if you remember. I think I am right that the idea that Huntington's was on the telomere was simply because those recombinants hadn't been properly been examined.

MC. Examined, in fact there were two individuals, two Huntington's phenotype as Huntington's that were two real Huntington's experts say they are absolutely Huntington's, and Jim would say are you absolutely sure, because they were really screwing us up. It looked like double cross-overs, which were in a very narrow region as rare as hen's teeth, and in fact this went on for a long time, until we insisted they go back and re-examine them and they said well you know, maybe it isn't Huntington's and that always bothered me how difficult the clinicians were, experts in Huntington's, and then proved to be wrong.

PSH. Well that set things back about 3 or 4 years.

CM. It certainly did, two. I always said two but it probably did yes. That really screwed us up in shortening it.

PSH. And I remember again, the only time people believed it wasn't at the telomere was when disequilibrium came up

MC. Yes exactly.

PSH. And when our probe right at the end of the chromosome by the telomere didn't show any and the ones further down did.

MC. Yes, in fact we had one workshop, and it was held at Stanford specifically on telomeres.

PSH. I remember.

MC. Remember that? Yes.

PSH. And it taught everyone a lot about telomeres, but nothing about Huntington's

MC. Exactly. That's right, yes.

PSH. Anyhow I think it was an amazing period of work, and I think the thing which I always feel Nancy deserves huge credit for was keeping that collaboration on the road for 10 years.

MC. And it was very difficult. There were a fair number of prima donnas in there. David Housman and there were four of us, I'm sorry, not David. David was a member of the research. There were three of us. C. elegans, just got the Nobel Prize, Bob Horwitz and myself, and Nancy of course with us, and I will remember the fourth person in a moment. Our job was to have to take care of the little in-fighting and meet individually with them and we had the terrible experience of having to ask one pair of researchers to leave the collaboration because they had published something without, and were doing things on their own.

PSH. That was the pulse field gels wasn't it?

MC. Yes. And I guess I can name names on this.

PSH. I can't even remember who it was.

MC. Minor things, but we had fabulous meetings and they were delightful, and they were often at a time in the year when it was cold up north and beautiful in Islamorada, and of course we had wonderful workshops in Los Angeles as you know and they were all at famous film star's homes. I think we were three years in a row at Julie Andrews' house.

PSH. Well, Mike, I think that is probably a good time to close, but thank you very much indeed.

MC. You are welcome Peter, more than welcome.

End of tape