

GEORGETOWN UNIVERSITY

Joseph and Rose Kennedy Institute of Ethics

SUBJECT: Dr. Ken-ichi Matsubara
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Osaka University
INTERVIEWER: Robert Cook-Deegan

Q: How do you say the Japanese "saibukogaku?"

MATSUBARA: Saibuko, exactly. Did you have any problem finding this place?

Q: No, very simple.

MATSUBARA: So you took the right exit drive.

Q: Well, he didn't know this institute, but we asked at the stand out there.

MATSUBARA: And then the man told you where. Actually, this is the most immediately available.

Q: Yes, it's the first one, it's the first building.

MATSUBARA: And you did not miss this big construction.

Q: What is this going to be?

MATSUBARA: Medical school.

Q: A new medical school?

MATSUBARA: They are now located in downtown, and they are moving here because going downtown is so crowded and they don't have enough space. So they gave us the idea of coming out here.

Q: Is Ibaraki a suburb of Osaka?

MATSUBARA: Yes, yes, this is located about 10, 15 kilometers from the center of the Osaka City. This used to be a big bed town to Osaka, now many... are being built here.

Q: Around the university?

MATSUBARA: This is one of those, and many... are from pharmaceutical companies. It doesn't haven't to be around Osaka University. This is one of...

Q: Are a lot of the pharmaceutical companies in Japan from around here, from Osaka?

MATSUBARA: Yes, quite a few. The biggest ones, like Takeda, ..., and Santori come from all around here.

Q: I know all those four names. Oh, wonderful.

MATSUBARA: Arigatō.

Q: Well, so far on this trip I have met with Dr. Rishi, from Tokyo University, who's working with me.

MATSUBARA: What kind of conversations did you have? About...?

Q: Yes, that's mainly what I was interested in.

MATSUBARA: I haven't talked to him for some time, so you may have better information than I.

Q: Well, he says nothing is very firm yet. He says he's talked to...he's got a list of companies that he's supposed to go out and wine and dine and talk into joining a Miti project. He seems optimistic that something will happen. But I guess he's got a list of about 40 companies that he's

supposed to go approach. And he's hoping that by 1992 they'll...

MATSUBARA: Why does he have to approach? That's a job for Miti people.

Q: Well, I think they're doing it together.

MATSUBARA: Oh, I see.

Q: I gather that it's Miti and Bedek and Oishi, kind of as a club, approaching different companies. I guess it works better as a group or something.

MATSUBARA: So I think for a year from now they... have group discussions, talking of where to go and what to do.

Q: He said it got serious a few months ago, five or six months ago. And he is now meeting with the various company people, to try to get them to...to explain to them what is going on. Sounds like it will be focused on instrumentation and on the computer part--computational biology rather than mapping. Maybe it will include some...

MATSUBARA: They don't have to go into mapping business, because mapping's not a company still, you know?.

Q: Right. I don't know whether sequencing is going to be, either.

MATSUBARA: It is. I think Japan's one of the best places to start companies.

Q: Sequencing?

MATSUBARA: Yes, to do the sequencing. But not until they realize that sequencing can be... And quite...

Q: The companies in the U.S. are not...there are some companies, service companies, who do sequencing for laboratories, or whatever.

MATSUBARA: That's not the real sequencing..., you know, that's a kind of small sequencing stuff. They rely upon the... machine. But in Japan I hope to start-up several companies who, at the same time, improve the machines. Not for selling the machines, but to give the...

Q: Anyway, that's who I've talked to here, and I was just hoping to get an update on what was happening with Mombusho and anything else that you would like to...

MATSUBARA: I don't think you can read, but I have just been working over a report.

Q: You're writing a report for Mombusho?

MATSUBARA: For all Japanese. But, at the end, I have a recommendation to Mombusho--what should be done... But it takes another month before I can release it. And there may be some discussions. You know, because some scientists are quite cautious; they don't want to promise anything. But, at the same time, they want to demand many things. So, that's an odd situation. So I have to overcome this attitude in next month. And the next program for you is to translate this into English. It's pretty long report, I think maybe 30 pages--in Chinese characters.

Q: If you can, send me a copy in kanji and I'll see if I can find a translator.

MATSUBARA: Have somebody translate it.

Q: I would guess I can, especially from written. It's much easier from written to find it than to do it from this.

MATSUBARA: I can give you the formal report. This is rather long and informal one. And the formal one for Mombusho will appear, too. It's all done now.

Q: Is this the follow-up on the report that was released a year and a half ago, or two years ago?

MATSUBARA: Right, about a year, no, a year and a half ago.

Q: March of '89.

MATSUBARA: Right, right. I don't remember, but just about that time. So, based upon that report and recommendation, Mombusho started a research team. And this research team was to survey the activities in Japan and help organize these people with some funds. The amount of... was not big enough. So we put some sequencing machines, or related machines, into the major groups. And, at the same time, we did many discussions for the possible ways, in Japanese universities and other research institutes, in near future to deal with the genome project. And now we have come to... stage working on this. And this recommendation will tell not only Mombusho but other government agencies what Japan should do. And, at the same time, at the very end, we have specific recommendations to Mombusho. And they already know

the conclusions. And another... And that report has been written already.

Q: So this is Mombusho.

MATSUBARA: Yes.

Q: It has its own, and you're the academic connection to that? It that how that works, there's an academic committee of scientists?

MATSUBARA: Right, right, because Mombusho calls more than 90 percent of the real scientists in Japan. So what Mombusho does has a real influence in academic community. And in addition STA calls some, I should say, six, seven percent of the scientists in the related fields. And they also are planning another genome project to be sponsored by STA. And Miti is also have a talk with Orishi, thinking another activity in which they are trying to gather company people most of the time.

Q: What would be the shape of the Mombusho program?

MATSUBARA: Basic research. We are not trying to coordinate people to concentrate on certain chromosomes; we just let them do. But this is a part of the basic biology in Japan.

And in the coming few years there may be some spontaneous collaboration efforts, but at this moment there won't be any specific selection of chromosomes. And also we'll let the other researchers do work over software, work over DNA cloning technologies, work over...

Q: That would be part of the genome project or that would be separate?

MATSUBARA: Yes, all of them are under umbrella of genome project.

Q: So it would include things like physical mapping, genetic mapping, cDNA mapping.

MATSUBARA: Yes, you will see the written report very soon, but we have five main projects under the umbrella of human genome project in Japan. And one is, of course, physical mapping, physical genetic mapping. And the second one is the CDNA project. And we think that CDNA project particular feat with Japanese scientific community. And the third one is DNA technology and related.

Q: Which is analytical instruments.

MATSUBARA: Not instruments, basic principles. In Mombusho, nobody is interested in developing instruments. They want to, for instance, analyze or go ahead to analyze the behavior of DNA in gels, or they want to develop specific new cloning systems and stabilize the outcome of things like that. And also there are some people who are interested in coming to work with genome informatics. And this fourth group is led by Kamihisa. Maybe you have known him.

Q: I've met him once. In fact, I tried to reach him, because I was up in Kyoto yesterday, but I...

MATSUBARA: Well, his place is not in downtown Kyoto, it's far away from Kyoto. You have to take one-hour train ride.

Q: Yes, I tried to call, and he was evidently not in or something, or my Japanese was not good enough to know what was going on, but I got the impression that he was not there.

MATSUBARA: Well, if you want to talk to him, I can call him and introduce you to him. Because I think yesterday, no, on Saturday, he was in office. I don't know what can happen with him, but.

Q: Saturday's the day I was in Nagoya, so I would have called...I think I tried yesterday. I think it was yesterday. I tried Monday.

MATSUBARA: If you are really interested in talking to him, I'll do it for you.

Q: I would like to do that before I leave Japan.

MATSUBARA: All right. Okay.

Q: Yes, maybe we could do that today.

MATSUBARA: And the fifth one is other organisms. And, in terms of other organisms, we have the E. coli project.

Q: Which is what, sequencing?

MATSUBARA: Yes. You may know Isona, co... project, and he is the main power in sequencing the E. coli. Actually, there is one group plant which has been awarded to the E. coli project since last year. This is the second year, and they have to go one more year. And they will try their best to sequence...

Q: To sequence E. coli in that time.

MATSUBARA: Right, and at the same time finding out other interesting genetic structures around the genome. So some of them will be working over segregation origins, others will be working on infr..., yet others will be working on promoters, and so on.

Q: So they may beat George Church, huh? Can be competing against George Church?

MATSUBARA: Yes. If George can analyze his gels and his films as quick as possible, he will be able to compete. I understand that he has run into problems in reading his films.

Q: He says that he thinks he has a solution, but its...

MATSUBARA: Oh, really?

Q: The latest update I heard was from...Wally Gilbert called him. We had a sequencing meeting at NIH, must have been about three months ago now. And Wally called him up, and he called Fred Blatner up, because Blatner's also trying to sequence, and got an update. And things had gone more slowly than they had hoped originally.

MATSUBARA: How about Blatner's problems?

Q: Blatner was going to push very hard. His reading technique is mainly undergraduate students.

MATSUBARA: Oh, really?

Q: So he was going to hire a bunch of people for the summer to come in and read gels until their eyes glaze over every night, and then send them home and bring them back the next day.

MATSUBARA: Oh, my.

Q: So it's not really an automated system at all.

MATSUBARA: How can he rely upon that accuracy? How can he sell...

Q: Well, you know, even by his method anyway there's tremendous redundancy, so I think the theory is, he's hoping to pick up errors by having sequenced things so many times.

MATSUBARA: By comparing the same sequence.

Q: And when there are discrepancies, then they go back. They've saved all the gels, so they can go back to the original gels and take a look, but that takes forever.

MATSUBARA: Is he creeping, or he is jumping all over around genomes?

Q: Shotgun. Random.

MATSUBARA: Shotgun for whole...

Q: I think so.

MATSUBARA: Ah. Kasanami has a strong objection against this.

Q: Most people have taken other strategies.

MATSUBARA: Yes, yes, because now we have accounting from physical maps. You don't have to...

Q: Yes, I don't Fred's strategy is completely random. I never read his grant proposal, so I don't know exactly what he's doing. George Church's, because of the multiplex method, it pretty much is random. That's one of the problems of the multiplex method.

MATSUBARA: Right, right.

Q: There may be one group that's going to do the primer-directed strategy, but I don't know.

MATSUBARA: Well, the nicest thing with the E. coli sequencing process is that people already know the physical maps. So even though the results, the data, are scattered, they can fix them to individual places on the genome. So, altogether, the data can make sense. But we've got physical maps like human chromosomes. You know, random sequencing makes no sense at all until they are really continuous.

Q: Thinking of physical mapping, is Kohora back in Japan?

MATSUBARA: Yes, he is.

Q: Now where is he now?

MATSUBARA: Mishima. Do you know where?

Q: I've seen Mishima on the map.

MATSUBARA: That's the foot of Mount Fuji.

Q: I think I may have gone past it on the train, between Nagoya and Tokyo.

MATSUBARA: Yes, yes, about one-hour train ride from Tokyo, two hours Osaka. But apparently you did not see Mount Fuji at this season of the year. In summer, you cannot see it.

Q: I saw the foot of it. We couldn't see the top of it, it's too cloudy.

MATSUBARA: Right, right, only in sunny winter seasons and in May and some days in September.

Q: It was a beautiful trip, that stretch from Nagoya to Tokyo, just beautiful, just beautiful.

MATSUBARA: You should visit countryside too.

Q: Well, we got out to Inoyama.

MATSUBARA: Oh, yes, yes.

Q: Which was very nice, which was very nice. And Nagoya was not very nice. But we got out of Kyoto yesterday and went around the edge of the city. We weren't really out of the city, but we were up at the end of it. You started to tell me about other organisms. We talked about coli, are there other?

MATSUBARA: And other organisms, we are going to solicit proposals. And one of them we have in mind would be fish and leaf, because Yanaida is a man who literally created all the fish and leaf... libraries. And he is distributing the library all around the world. And he himself is interested into getting into sequencing gels.

Q: Pombey or what?

MATSUBARA: Pombey. And Kohara is working on nematodes, in cooperation with the Cambridge people. Kohara was in Cambridge, did you know?

Q: Yes.

MATSUBARA: And he's back and he is... in continuing that work. But I haven't heard his written stories.

Q: The Cambridge group and the Washington University groups have both just gotten their funding.

MATSUBARA: Yes, I heard it. About how much do they get grants?

Q: I don't know what the U.K. group got. Bob Waterston, I think, was asking for over a million dollars a year, I

think. If I recall, at least in the out years, it was over a million dollars. They're buying a lot of ABI sequencers.

MATSUBARA: I see. And what do the moneys... to Cambridge for the sequencing...?

Q: I think MRC funded the Cambridge, England, part.

MATSUBARA: Yes, they do. But, at the same time, ... is not going to use the entire... money for his own.

Q: No, that's right, that's right. Some of the machines, I think, were going to be in some sort of sharing arrangement or something like that. I don't remember the exact details.

MATSUBARA: How long do you think they will take to finish up the sequencing? I think they will finish it fairly quickly.

Q: I think they were projecting that it would take... I don't remember. They said, in a grant proposal, that I have tried... Since I'm in a funny position in the NIH office, I've tried not to keep too close a track of the exact details of grants because people ask me all the time what's in the grants.

MATSUBARA: Oh, really, ah.

Q: And I'm not supposed to know because I've been part of the peer review process.

MATSUBARA: Oh, I see, yes, yes.

Q: I've been watching the peer review, so I don't know. But I think that they said something like five years or something like that.

MATSUBARA: That's a reasonable proposal. But they can't finish it up with the ABI machines. They have to invent new machines to get better gels.

Q: There are different opinions about that. There's been a lot of debate about that. Some of the groups in the U.S., as you probably know, have been reporting pretty good results with the ABI machines. Most of the initial reports were people were having lots of trouble, but three or four groups have actually gotten them to work quite well.

MATSUBARA: You mean...

Q: The 24-track.

MATSUBARA: They can read, yes, with the 24-track can read longer than others.

Q: They can't routinely get over 500, but a couple of gels that I've seen go out to 700 and it's still fairly good.

MATSUBARA: Well, there is a trick, you know, to get such a nice ladder. You have to work really hard to begin the preparations. So the results are the same--either spend more time in preparation of good DNA, or spend lousy time in preparation of DNA but do the gel around twice. So it's about the same.

Q: The other thing is the calling software, that's been the major...the computer filter baseline.

MATSUBARA: Right, right, right, it's been improved dramatically.

Q: Yes. The new program has, I guess, helped things quite a bit. So we've got some projects in the U.S. that are going to use those machines, and we'll see what they can do. They'll really only be tested for the first time this year.

MATSUBARA: I hope, in Japan, we could introduce new principles in automatic DNA sequencing. But not in near

future, maybe in a few years from now, in cooperation with Oishi... I still don't understand why Miti is so much interested in instrumentation. It's a small job as compared to general instrumentation activities related new... But somehow they want to stop with DNA sequencer...

Q: I think they may be right, in the sense that no matter what you do in biology in the future, it's going to involve sequencing. So it's a real core technology from which other things will come out. I mean, the computer stuff will have to fit with that, and most of the other analytical techniques are going to have to somehow fit with DNA sequencing. So I think it may make sense to focus on that first and then build out.

MATSUBARA: Yes, that's a good reason, because there they see the biggest market. The thing is that many Japanese companies still don't understand what genome project is. So I'm doing campaigns all over, independent of Oishi. Oishi is gathering some companies recommended by Miti, and he's educating these people. And I'm speaking out in other areas like pharmaceutical sciences and health-related industries, computer sciences. And after a year or so, it's been quite successful. Now, quite a few of them know at least what genome is. And next year they will start trying to collate

their activities with genome project. But I'm doing this for starting the HUGO Pacifico primarily.

Q: What's happening...Diane, incidentally, sends her regards. At the very last minute, I think I told you, their computers broke down. And this is the end of their fiscal year at Hughes, Howard Hughes Medical Institute, and she is still at Howard Hughes Medical Institute. She's half-time HUGO, half-time Hughes.

MATSUBARA: Is she happy now?

Q: I think she'll be happier when things settle down a little bit. HUGO is still not a...there's a lot of work to be done, even in the America's office. They got the million dollars from Hughes, and they got almost that same amount for the European office, but...

MATSUBARA: What is the major problem in American office?

Q: Well, they need to build a structure.

MATSUBARA: Oh, I see. So...

Q: There's a lot of paper work. As of right now, Diane is the only permanent staff.

MATSUBARA: Oh,... I'd... to invite a lady to join our discussion. Would you mind?

Q: Oh, no, that's fine.

MATSUBARA: She was waiting, I forgot.

Q: Okay, sure. I'll put a halt on this.

MATSUBARA: Her husband worked for...how many years?

Lady: Many, many years...National Capital Institute.

Q: At NCI?

Lady: Yes.

Q: In Frederick or in...

Lady: No, in... I'm sure you are familiar with that.

MATSUBARA: Actually, her late husband ran a group of research activities.

Lady: ...going to be..., but he was offered the...

Q: So he came back for the second...

Lady: For the second, but he deceased two years ago. He was only fifty years old.

Q: Heart attack?

Lady: No, the cancer... I thought that was terrible.

Q: Oh, gosh. Oh, what an irony.

Lady: Yes, it is.

MATSUBARA: And then Walter recommended, in our conversation last year. However, she might be able to help with the HUGO activity and related genome research activity here, because she knows many people there and here, and also she has been educated as a scientist. She is coming here now only once a week, but I hope that she is becoming full time. ...setting up the HUGO activities.

Q: Well, let me explain a little about what I understand. It would be much better if Diane could be here because she could give much more information. But, as I was explaining to Dr. Matsubara, Diane, at the last minute, could not come because she was...it was very hard for her to arrange the

first time. And we wrangled an invitation to this meeting and it was in Tokyo last week, at the very last minute. But then their computers broke down at the Howard Hughes Medical Institute, and so she lost about a week's worth of work and she had to completely do it over again.

Lady: I understand.

Q: And it was the end of their fiscal year, so she could not come. But it's my understanding that they have filed papers in the America's office. Hughes has given them this grant, a descending grant that goes four hundred thousand this year, three hundred, two hundred, one hundred, so it's a four-year grant that goes down every time. They also donated a building, but before HUGO can move into that building, it has to achieve a certain tax-free status-- 401c(3) status. They've filed the papers for that, but then it takes a while for the bureaucracy to move, so they have not gotten that tax-free status, as we've said here.

Lady: They have not gotten that yet.

Q: No, they haven't. [tape ended]

MATSUBARA: ...to the young people. So I don't know whether or not they can be really successful.

Q: This would be for Japanese postdocs?

MATSUBARA: Both.

Q: Both. So would this be the beginning of a postdoc system in Japan?

MATSUBARA: Well, there are some postdoctoral fellowship systems in Japan. But they use postdocs; we propose ten for the first year, at least, earmarked postdoctoral fellowships for genome activities. So if everything goes all right, out of the grants we have another budget for establishing centers and also these activities. And they are not counted on the grant system. We don't know how much money will be paid--maybe three, four times as much money we can use from grants. Because we have to build a new center for... and put a few number of equipment to deal with materials and computers, setting up networks, and also hire new people, which is proposed to be about twenty people, to be filled in three years from now. Now, you know, we are not in the front to negotiate with the minister of finance people, but Mombusho people must do this. So if they are defeated, that grant will be substantially shrunk; but if they succeed, that'll be fine. They all know that this activity's important and they are now fighting during this summer, and by fall, we'll know the results.

Q: And then your budget gets passed in the fall for next April?

MATSUBARA: Right. Not fall, late fall, maybe early December sometimes, depending upon conditions.

Q: That's when we'll get our budget to start in October.

MATSUBARA: So that's the story about Mombusho. And also STA is also discussing about its own project and with its own grant money. And most of the activity's concerned with the developing machine systems, or sequencers. And also they are considering to increase some research activities around by Riken. You know, Riken is a major..., where Ikawa used to be. And they are...

Q: Ikawa is no longer at Riken?

MATSUBARA: He is a part-time employee at Riken now. He moved to Tokyo Medical Dental School as a professor.

Q: Oh, I didn't know that.

MATSUBARA: Very recently, from this April.

Q: I just saw him at this meeting in Tokyo, very briefly, just said hi. I didn't even find out that...I assumed that he was still at Riken.

MATSUBARA: He still has an interest in things. During April, I saw him and he seemed to be quite busy. And I asked him whether he was fine, and he said he was okay. But he did not know, until he accepted the job position, that he had to teach, from the April. So he kept himself quite busy.

Q: I bet. Boy, that's a lot of work.

MATSUBARA: Yes, well, he doesn't matter, though, he doesn't care, because he used to be so busy all the time, adding more, adding up much heavier duties. It doesn't bother him at all.

But anyway, STA is also considering to add more grants to support Riken projects where they are... chromosome 21 physical maps, and also some wide-range physical mapping projects like physical mapping of immuno..., and one or two other projects which I don't remember.

Q: Is there any connection between, like when Dr. Shamis, he's working on chromosomes 21 and 22, right? He collaborates with Riken, or how does that work?

MATSUBARA: Yes, he puts his both legs--one on Riken project; one on Mombusho project. And that's fine.

Q: Oh, so he's also part of the Riken project?

MATSUBARA: Yes.

Q: He supplies materials for them or something?

MATSUBARA: No, he just contributes scientific activities.

Q: Like a consultant or something?

MATSUBARA: Actually, he gets grants from both.

Q: Oh. Oh.

MATSUBARA: All the same work and splits the results into two halves and give half to Riken, another half to Mombusho.

Q: That's how it works in the States.

MATSUBARA: Yes, it really works. It's just like getting grants from DOE and NIH.

Q: That's right, although so far I don't know anybody who's succeeded in doing that other than George Church. They did that early on, but now they're trying to decide which agency funds it and then just leave it to that one agency, most of the time.

MATSUBARA: Because in our country the amount of grants to be awarded is not big enough, so getting your feet wet on both sides is our out. And sometimes that works fine because the same one is working for both agencies and he can somehow coordinate these.

Q: Is there any connection between the projects that you've outlined, we've talked about STA, Mombusho, and Miti. There were two other genome projects that we've heard something about. One is Health and Welfare. Now what are they doing?

MATSUBARA: They just appointed a chairman to that activity. And the name of the chairman was Oya, and he was director of National Institute of Health in Japan. And I think he has organized people working on related fields on human disease into seven groups. I don't remember which groups or what groups have been proposed, but gathering these seven groups, they will spend about two hundred million yen for five years to study disease-related human genes. So this is not the genome project but a subsidiary of the genome activity. And

most of the money will be spent by researchers under control of the National Institute of Health and the Cancer Research Center.

Q: Where is that?

MATSUBARA: Cancer Center is in Sukizi, Tokyo, and National Institute of Health is in Noguro, Tokyo. And also there's another, National Institute of Cardiac Disease, nearby, and one group of people also joined there.

Q: What was this director's name again? I'm sorry.

MATSUBARA: Oya.

Q: And then there was an Irato project?

MATSUBARA: Yes, it's run by Geta and it's going fine, but I have hardly any details yet. I'm expecting to hear this fall from them.

Q: And then there was a Dr. Endo.

MATSUBARA: Dr. Endo is taking the major part of the Riken... to construct an autosequencing machine, starting

with DNA into the computerized data. He's trying to robotize all the steps.

Q: So is he the inheritor of the original Wada idea?

MATSUBARA: That's something which Endo doesn't like to hear. But that's what it is.

Q: So I should be careful. Thank you. I will. And then there was a Ministry of Forestry and Fisheries project on the rice genome. Is that connected at all?

MATSUBARA: Yes, a few days ago they publicly announced that they are organizing rice genome project. But I don't know the details.

Q: That'll be a very big project. Isn't the genome like...

MATSUBARA: The same size as human genome.

Q: Or a little bigger even maybe. It's very big.

MATSUBARA: Yes, but approximately the same. I don't know how much they are going to spend. I had a chance to talk with the man responsible for that grant..., and he was not

brave enough to give me the figures. He just wanted to keep it secret. Now you will know it by the end of this fall.

Q: Well, yes, when the budgets come out.

MATSUBARA: Because all these governmental agencies start negotiating simultaneously with the Ministry of Finance, and at the end they will be all publicly announced.

Q: It's like our budget cycle, except that here it's the Ministry of Finance, in our case it's Congress.

MATSUBARA: Right, right.

Q: Like our budget is very much up in the air this year, NIH's budget, because of...

MATSUBARA: And, you know, the curious situation in Japan is that these governmental agencies don't want to make their budget proposals publicly known, because, if they fail, that means a failure of the administrator in charge of it. And, at the same time, people from Ministry of Finance are very much efficient slicer of the budget proposals. So this side doesn't want it publicly known the amount they propose, but at the very end they will happy announce... for the coming year. So there is some problems.

Q: Are there any other activities going on in Japan? I don't think NIH needs to focus too much on the rice genome thing, because I think NSF is handling the plant stuff in the U.S. Their arabidopsis, they're spearheading.

MATSUBARA: It depends, there is no arabidopsis update, except for Shimura. Do you know his name?

Q: I know his name. I do know his name somehow.

MATSUBARA: Shimura is the only one working on arabidopsis. And he's supported by a special grant from Mombusho, so he's all right. But we don't have those special plant in... And the last time I asked Shimura whether he might be interested in coming to join human genome program, to propose one of the other organisms, and he said no. Apparently he is concentrating on other possibilities. So the Japanese other genome projects may be E. coli as a top priority, and fish and leaf, and some bacillus... Kohara wants to come join... And other things I don't know. And rice project will be entirely different project, sponsored by agriculture fishery.

Q: They should, logically though, plug into...I mean, the technique, the basic RFLP-generation technique and all that

would be quite similar to what you're already doing. One would hope they wouldn't...

MATSUBARA: Yes, so what they actually have in mind is to follow human genome project three or four years behind and...

Q: Use the same techniques.

MATSUBARA: And follow the same course, yes.

Q: So they'll start with the genetic linkage map and then move to a physical map.

MATSUBARA: Right, right, so they don't have to develop special computer systems, better technology, or whatever. So they can achieve it with less than one-tenth of the effort. That's a good thing...

Q: That's a good strategy.

MATSUBARA: ...in the human genome project, you know.

Q: Is there anything else I should ask you?

MATSUBARA: So we talked about... genome activities.

Q: HUGO.

MATSUBARA: And HUGO in Japan, and governmental status. Oh, one thing you might be interested in is that we are organizing second Japanese human genome workshop this coming...when was it, September or October?

Lady: September.

Q: *This year or next year?*

Lady: This year, this year.

Q: *This year.*

MATSUBARA: Oh, yes. ...end of September.

Q: *Oh, this is a repeat of this conference that David Swinbanks reported on last year?*

MATSUBARA: Last year, yes. This is a second one.

Q: *What do you expect to have happen there?*

MATSUBARA: Tokyo. And I don't know, last year we had a big, pretty busy number of public... I don't know what will happen this year.

Q: What was the result of that meeting last year? The only thing I ever read about that workshop was what Swinbanks report in Nature.

MATSUBARA: I don't remember how he reported, though.

Q: Well, he said there were basically different points of view, with one group, I presume it was Oishi, saying Miti should do something big, and others saying Mombusho needs to keep the lead. And it wasn't clear what came out of the meeting.

MATSUBARA: No, but actually the workshop was organized for presenting scientific progress.

Lady: I think this meeting you are talking about is a different meeting.

Q: Oh, it's a different meeting?

Lady: A microbiology meeting. ...big discussions.

MATSUBARA: Oh, I see, yes, yes. So certainly Swinbanks reported about our debate in Japanese Microbiology Society annual meeting. And there were big debates, quite fun.

Q: That's what happened in the United States for three years, as you know. It's still happening. In fact, it's intensified this year.

MATSUBARA: Yes, I saw a headline in certainly article, blaming Jim Watson for...

Q: Yes, there was a very nasty piece done by New Scientist magazine.

MATSUBARA: Oh, yes, that...

Q: Robert Wright was the author of that. Yes, and he really went after Jim. It was quite personal.

MATSUBARA: Was it? Somebody sent me the copy, and I took it around and showed it to someone, and he immediately grabbed it--before I read it.

Q: I had a copy of it with me at one time, but I think I've shipped it home.

MATSUBARA: That's all right, though.

Lady: Do you approve the things that the House approves appropriations?

Q: You know, it was uncorrelated with that.

Lady: Uncorrelated, because it was quite a big number, ...one hundred and sixty-six...

Q: That was another problem. I mean, I don't think it's going to stay at that number, but... Have you seen this? Have I shown you this?

MATSUBARA: No, I don't think so.

Q: Well, you can keep that and circulate it through...

Lady: Yes, we have it. Yes, we read this.

Q: Do you have it?

MATSUBARA: Not this piece, though.

Lady: No, because it was copied...

MATSUBARA: Oh, both pages, yes.

Q: I thought I had maybe sent you... This is probably a slightly newer draft.

Lady: Yes, it is. Maybe a little revised. It was too... something.

MATSUBARA: So this is a revised one. Thank you.

Q: You can use that or do whatever. There's no restriction on that; you can let anybody see it who wants to see it.

MATSUBARA: Oh, one more important thing I have to tell you. Because, in Japan, usually independent governmental agencies don't communicate well, and... human genome project-related activities are sponsored by five, at least five independent governmental agencies, so we have several difficulties in coordinating these. And now Dr. Mori, the head of the Science and Technology Council, concerned this very much. And he seems to.... to coordinate these, and he seems to be the best window towards foreign countries or...

Q: His name is Mori?

MATSUBARA: Mori Wagaru.

Lady: He used to be the president of...

Q: I think I may have met him this week.

MATSUBARA: Yes, I think so.

Q: And I met Dr. Okamoto, who is the head of the Council, is that right?

MATSUBARA: He used to be. And Okamoto retired, Mori took over the position. And Mori knows quite well about human genome project, worldwide, because I have frequent conversations with him. And he used to be a member of the Science Council in Mombusho, and he was one of the strong proponents of the Mombusho program. Now he moved to the Science and Technology Council as the chairman. Not actually the chairman, but a representative. And he is just going to organize these activities privately. You know, this is the important part. He can never do it officially, but on private basis he can achieve it. And I'm sure that he will become the window towards other countries. So, in a half a year or so, he will be quite successful, because I am all for that activity and other people will also support it. So if you want to have some special contact, he will be the best one.

Q: Maybe I should meet with him when I go to Tokyo.

MATSUBARA: Yes, that will be a good idea. But he is extremely busy, so you need to have appointment well ahead.

Q: Maybe we can handle it by fax for now. Well, I'll see if I can... Do you happen to have a phone number?

MATSUBARA: Yes, I do. Now I don't have the fax number, though, only phone number.

Q: I'll just try the phone. I need the fax number when I go back to the United States.

MATSUBARA: Tokyo, 035813861. That's his office, and his secretary will be easy to reach, so she will let you know.

Q: And how do you spell his name?

MATSUBARA: Mori.

Q: And what's his...

Lady: Wagaru.

MATSUBARA: He is a gentleman, so you must wear a tie.

Q: I'm seeing Dr. Wada on Thursday. And, you know, he met me the same way you did, at OTA. The first time I met Dr. Wada I was in shorts and a tee shirt, because that's how I work, and Dr. Wada told me that I had to wear a coat and tie when I came to visit him, because he was going to take me someplace. "Since they don't let you in unless you have a coat and tie," he said. When I'm in a foreign country, I dress.

MATSUBARA: Well, this is damn hot.

Q: Well, I will at least try to reach Dr. Mori, and I will try to reach Kanahisa.

MATSUBARA: You have his fax number?

Q: I do not have Kanahisa's fax number, I have only his phone number.

MATSUBARA: I'll let you know. You have his phone number, right?

Q: I'll tell you what phone number I have for him. I kept the names and addresses of the people that I still have to meet, in here. ...323111.

MATSUBARA: Yes, but you need to use extension. He has a dial-in phone number. That's 077433, that's dial in, 0239. And his fax number, 0774328235.

Kanahisa is working very hard to coordinate human genome activity in fifth generation computer... And he is very good...

Q: Yes, he's trained at Los Alamos, right? He was at Genbank at about the time it was started up.

MATSUBARA: Right, right. Well, his program now is to recruit as many young scientists, inframatic scientists, as possible. Because he has been awarded another grant, presumably three hundred million yen, to run for five years. No, more than that. Two hundred million yen per year for five years. That's a big grant.

Q: That's very big.

MATSUBARA: So he is going to set up computer networks.

Q: Who is that from? Is that from STA or from...

MATSUBARA: No, from Mombusho.

Q: Mombusho.

MATSUBARA: Yes, independent of the grant I just talked to you. All are under the umbrella of human genome effort, but, you know, Mombusho did not have enough grants, frame of grants to include everything, so they used two frames: one for... and one for...

Q: His database used to be supported by the Ministry of Health and Welfare, though, right? The DNA database of Japan?

MATSUBARA: No, supported by Mombusho.

Q: Oh, it was Mombusho.

MATSUBARA: Yes, but you don't have enough money, and the comment he says not in charge of it. But Miagrawa is. And he apparently has run into problems, because the money was short and the supporting staff is not big enough.

Q: That's the problem they ran into at Genbank for years.

MATSUBARA: Oh, really.

Q: Very serious personnel problems, and they couldn't hire enough people to meet the workload.

MATSUBARA: So they are now trying to improve this situation. And I wanted to help them, too, by combining that DNA database with the human genome database. And somehow they did not like this idea, so they are going to do on their own, which will start sometime next year or a year and a half from now.

Q: The other thing I wanted to tell you about is, it's my understanding, and I don't know the exact details of this but Wyngaarden would, the genome project was raised... I think we had a fax back and forth last year about this disaster, Janet Dorrigan and all. I don't know if you know all this stuff, where there was the bilateral science and technology agreement between the U.S. and Japan, and it was knocked off the agenda by the U.S. side.

MATSUBARA: Right, right. For some reason.

Q: For stupid reasons. It was put back on, and it was discussed again. STA, and I presume it was Kanaka, was the principal Japanese contact. On the U.S. side, it was the OSTP, so it was Wyngaarden and Rachel Levinson. And, in fact, the person who's likely to take that position in the future, handling those issues, is somebody that you know-- Pat Hoban, because she used to work at OTA. But it's my understanding that in those negotiations for the whatever it

is that's finally signed, the genome project is mentioned, or something like that, but the U.S. side asked for there to be a specific coordinator in Japan. And I don't think there's any money stipulated or anything, there's just kind of a we agree to agree kind of...

MATSUBARA: Just general.

Q: Yes, very vague. But I gather there is some language in there, or something, at this point. And I think that the STA people stipulated that the Science and Technology Council would be the coordinating focus in Japan.

MATSUBARA: That's a reasonable, reasonable and plausible way to control it, except that Science and Technology Council cannot govern over Mombusho. Mombusho is outside of their control, so that creates problems every time.

Q: Mombusho is not part of the... The Science and Technology Council is...

MATSUBARA: Supposed to coordinate governmental activities related to science and technology. And Miti...

Q: But all your basic scientists are outside of it?

MATSUBARA: Yes, but not Mombusho. And, worst of all, Mombusho carries 90 percent of the scientists.

Q: That's what I was thinking, it's kind of like having a Science and Technology Council that doesn't have NIH in it, that has NSF and DOE and...

MATSUBARA: Right, right, right. That's why, as I said, Dr. Mori must do this job personally. Otherwise, Mombusho...

Q: His relationships with Mombusho are good, because he was from there?

MATSUBARA: It is good. Otherwise, Mombusho will never follow that program. And because I worked quite hard for Mombusho in setting up the project, I have been stamped as Mombusho people. And STA sometimes don't want to tell the real details to me. But Dr. Mori will do this.

Q: My hope is that... Yes, what we found, actually, it's not just Japan. Sometimes, like when we were doing the OTA project, we found that U.S. agencies were finding out about, NIH was finding about DOE through OTA. And, more recently, we found that we can talk to factions in different countries from the NIH office. So... in a way that people within the

country don't. I hope that HUGO will begin to be able to do that to some extent also.

MATSUBARA: Yes, that's really important. Actually, that happened while two Japanese groups were sequencing..., they were competing each other.

Q: And they didn't know it?

MATSUBARA: So much that they did not communicate to each other. But somebody outside of the country got postdated, and they are comparing their results through this ad hoc agency. That's how it happens most of the time. But let me ask you one or two things.

Q: Sure.

MATSUBARA: First one is the coming human genome mapping workshop [tape ended]