

## ***Our scientists are artists!***

Transcript of the French version

### **10.00.35**

*ITW Axel Kahn, Geneticist, Director of the Cochin Institute, Paris, France*

“People often talk about the harmony of life, the symphony of life, and to inspire us this evening, we’re going to listen to some music.”

### **10.00.37**

*IMAGE*

Axel Kahn

Geneticist, Director of the Cochin Institute

Paris, France

### **10.01.01**

*ITW Axel Kahn, Geneticist, Director of the Cochin Institute, Paris, France*

“A symphony means that an orchestra needs a leader, and so in life there’s one in the nucleus of our cells, our genes, and sometimes instead of the harmony we hold so dear we find a cacophony. Moving from the world of music to that of mankind, this is what a genetic disease is.”

### **10.01.37**

*COMMENTARY*

The parallel which Axel Kahn draws between the worlds of art and science runs counter to the Epinal image which likes to see scientists as the opposite of artists. Can it be that artistic creation and scientific research are driven by the same dynamic, the same engine, the same enthusiasm? What if this desire is the

driving force behind medical researchers and brilliant inventors who are always ready to dream up new ways to take care of sick children?

### **10.02.10**

*ITW Axel Kahn, Geneticist, Director of the Cochin Institute, Paris, France*

“I feel sure that the emotion which has driven me on the two or three occasions when I have had a hand in making real discoveries, arises from seeing the landscape of your field in a completely different way from how you did before the discovery was made. You have the feeling that all your work has been rewarded, a feeling you go a long way out of your way to find, and, certainly, there’s an impression that maybe this could be useful, but often it’s an aesthetic emotion – it’s just fantastic!”

### **10.02.13**

*IMAGE*

Axel Kahn

Geneticist, Director of the Cochin Institute, Paris, France.

Paris, France

### **10.02.52**

*COMMENTARY*

The Necker Sick Children’s Centre, Paris, takes care of children from all over France and sometimes even further afield.

The Arnold Munnich genetics department is looking for the causes of unknown and currently incurable diseases, like some hereditary conditions. When you’re dealing with these mysterious conditions which all too often have no name as yet, you have to try to be imaginative and creative.

### **10.03.16**

*ITW Arnold Munnich, Director, Genetics Department, Necker Hospital*

“When you discover the cause of a disease then you’ve already started to treat it, to find out what it is. Defining it, giving it a name or an explanation, describing the situation that gave rise to it, really is almost a treatment. Diagnosis is the first step in treatment.”

### **10.03.17**

*IMAGE*

Arnold Munnich Director, Genetics Department Necker Hospital
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### **10.03.37.00**

*COMMENTARY*

This large family came from Auvergne to meet Professor Arnold Munnich. His reputation is international. Around the table are seven patients from three generations, all driven by the same hope: to finally put a name to the pain they suffer every day.

### **10.03.59**

*IN THE MEETING Arnold Munnich, Director, Genetics Department, Necker Hospital*

“I have to say that this story reminds me of other similar stories, which were actually mitochondrial conditions, diseases where the organism cannot produce energy. Like a battery that should have been charged up and plugged in, the battery isn’t charging. You have what’s required, a power supply and so on, but

the battery won't charge. It's permanently flat so you have no energy. I have known several people like yourselves, but never such a large family. Now, we're moving very slowly in getting to grips with this. The first thing is that the method of transmission is not obvious. It goes through several generations, but precisely which chromosome is affected is not obvious. So we have to say we're looking at a genetic condition that affects you all. You're all together in this. The whole family has this in common, well, everybody except the in-laws."

"Yes"

"And as a matter of fact it's a kind of feature that you share, an anomaly, and we're going to try to track it down. I think we can find it. And if we do find it, then we can draw some conclusions. Can we find a treatment? Can we look ahead to being able to ease the situation, to ensure that it doesn't crop up in future generations, and so on?"

### **10.05.28**

#### *COMMENTARY*

One single chemical spelling-mistake in our inherited legacy is enough to cause a genetic disease. Among these conditions mitochondrial diseases are some of the rarest and hardest to identify, since they can affect any organ in the body. The mitochondrion lies at the heart of the cell. It works like a small factory manufacturing energy. If it breaks down, the normal life of the cell comes to an end.

### **10.06.00**

*IN THE MEETING Arnold Munnich, Director, Genetics Department, Necker Hospital*

Arnold Munnich: “I’d like to have a discussion about this family, these twelve related individuals I’ve seen...”

Arnold Munnich: “I’m not aware of many conditions which cause both muscular and digestive problems.”

Jean-Paul Bonnefont: “Are they very seriously handicapped?”

Arnold Munnich: “When you see them like this they look like a really happy, really together family and you don’t get much of an impression of all the suffering. But when you interview them individually you find that in actual fact the kids are perpetually dribbling, they have stomach and muscle pains around the clock, they get tired really easily and that in general their lives are pretty tough”.

#### **10.06.34**

*ITW Arnold Munnich, Director, Genetics Department, Necker Hôpital*

“This is how we work in our area: you make an extraordinary observation and you pass it on to your colleagues, telling them what you’ve just seen. It’s a bit like an unbelievable story that just really happened to you, and you’re giving your colleagues the keys to recognising similar cases.”

#### **10.06.50**

*IN THE MEETING Arnold Munnich, Director, Genetics Department, Necker Hospital*

“First hypothesis, it’s a mitochondrial mutation. But I don’t know how to investigate it. I’d like to know what you think.

But we can’t exclude the hypothesis of a dominant disease.”

#### **10.07.02**

*COMMENTARY*

What is developing right in front of our eyes is a service which is almost unique in Europe. Doctors and researchers are working together on the same floor, they meet every day, reinforce their discoveries and form a united front in the face of previously ignored genetic diseases which are still all too often mysteries.

#### **10.07.22**

*ITW Arnold Munnich, Director, Genetic Department, Necker Hospital*

“You can’t tell me that scientific thought in our field follows a rational, straight line. That’s nonsense, it’s not true. The way scientific thought travels is on an uneven, hectic, rocky road, full of surprises, of coincidences, trial and error...”

#### **10.07.56**

*COMMENTARY*

Scientific thought is all of that, and much more. It’s also the way many people will join together to advance as a group ...In the case of mitochondrial diseases where there are very few patients in each country, European-level cooperation is essential.

Here in Milan the Besta Institute gets DNA fragments containing the famous mitochondria from France. The Italian researchers are working on mice which suffer from the same condition as that of the children we’ve met at Professor Munnich’s department.

#### **10.08.34**

*ITW Agnès Rötig, Geneticist, Genetics Department, Necker Hospital*

“We’re working with an Italian group based in Milan. This particular laboratory has identified a new gene for mitochondrial disease. I don’t know which gene it is. It’s a state secret, because people keep their little secrets right up until they’re

completely certain. But we all know it's just a game we play. We all know each other, we know what areas people are working in, we have a rough idea what will emerge, we know where such and such a result is going to come from, if something's happening, and if there's something interesting, you'll be involved in the outcome."

#### **10.08.46**

##### *IMAGE*

Agnès Rötig Geneticist, Genetics Department Necker Hospital
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#### **10.09.06**

##### *COMMENTARY*

The discovery of a gene responsible for a disease paves the way to a possible treatment. This is why Massimo Zeviani, director of the Milan laboratory, is in such close contact with the Necker team.

#### **10.09.20**

*ITW Massimo Zeviani, Director of the Mitochondrial Diseases Centre, Milan, Italy*

"I met Arnold quite a few years ago when we were still very young and we were both interested in diseases of the metabolism; we've been collaborating ever since."

#### **10.09.24**

##### *IMAGE*

Massimo Zeviani Director of the Mitochondrial Diseases Centre
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Milan, Italy

### **10.09.39**

#### *COMMENTARY*

Research is fundamental at the Besta Institute, whether it's carried out on the laboratory bench or by computer imaging. It's a step closer to the world of the artist with its intuitive, creative and forward-looking approach.

### **10.09.53**

*ITW Giorgio Battaglia, Neurologist, Besta Institute, Milan, Italy*

“Here's a very nice picture of epileptic rats which has made it possible for us to show the basic principles of epilepsy. Look – in my opinion there's nothing more satisfying than examining these beautiful images under the microscope”.

### **10.09.57**

#### *IMAGE*

Giorgio Battaglia,  
Neurologist, Besta Institute  
Milan, Italy

### **10.10.50**

*ITW Axel Kahn, Geneticist, Director, Cochin Institute, Paris, France*

“A good scientist has got to be an artist as well, he has to have a sense and taste for intellectual perfection, perfection of form. The hypothesis he develops has to be beautiful, but it also has to be true.”

### **10.11.28**

*ITW Massimo Zeviani, Neurologist, Director of the Mitochondrial Diseases Centre, Milan, Italy*

“We’re still profoundly ignorant, there are many things we don’t know about physiopathologies, molecular mechanisms, the way everything works as a whole. We expect surprises every month, every year. From that point of view I can see a very strong link with artistic experience. Artistic experience, like scientific experience, is a fundamental element in the human adventure, so it’s a journey.”

### **10.12.08**

*ITW Axel Kahn, Geneticist, Director of the Cochin Institute, Paris, France*

“I’ve often thought that science and art are two areas where it’s possible, even essential, to be creative in an atmosphere of freedom, although naturally the two areas have different limitations.”

### **10.12.30**

#### *COMMENTARY*

European scientists work together because they are concerned that their work should bear fruit, though it’s also about reducing the extraordinary costs involved. This morning four nations have been brought together around the table by the magic of video-conferencing. French, Italian, Dutch and British researchers are working together in direct and real time, forging solutions that will help them find tomorrow’s remedies for these notorious mitochondrial diseases. It’s a major first, both technologically and linguistically.

### **10.13.02**

*IN THE TELECONFERENCE - Arnold Munnich, Director, Genetics Department, Necker Hospital*

Scientist from Newcastle: “At least to begin with, if you wouldn’t mind...”

Arnold Munnich: “We’re not quite getting you. If you could sum up in a few words, we don’t fully understand...”

Scientist from Newcastle: “I’m not sending you to sleep, am I, Arnold?”

Arnold Munnich: “Not at all – I just had coffee, because unfortunately we didn’t have the chance to have one together this morning!”

Scientist from Newcastle: “I thought I could smell French coffee! Arnold, I think the best thing for this little bit of research would be to keep it as simple as possible. If you could provide us with a sample and determine whether a person would go blind or not, it would be a lot more useful for us than having nothing at all.”

Arnold Munnich: “OK, but being paediatric geneticists we have very few samples of Leber’s disease. Still, we have no problem about sharing what we have. Can you send us someone to do the research at our place?”

Scientist from Newcastle: “Probably.”

Arnold Munnich: Agnès says: “Someone who can read”...

Jean-Paul Bonnefont: “In French!”

### **10.14.00**

*ITW Jean-Paul Bonnefont, Doctor, Genetics Department, Necker Hospital*

“The current problem in genetic research is that one country is swamping all the others, the USA, which means that if we want to remain competitive we have to join forces. This is why we’ve set up a project funded by Europe.”

### **10.14.01**

*IMAGE*

<i>Jean-Paul Bonnefont</i>
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*Doctor, Genetics Department  
Necker Hospital*

#### **10.14.22**

ITW Axel Kahn, Geneticist, Director of the Cochin Institute, Paris, France

“The competitive element is important for researchers, all the more because as a doctor the usefulness of my profession doesn’t need to be spelled out – I cure people, I help them to cope with pain, just like you could say an architect wants to build houses that aren’t going to collapse. But just imagine, a researcher who’s always the second or third person to find something out, when he comes to the end of his life or maybe he’s still in the middle of it, looking back over the course of his life would feel hopeless because he’d have the feeling that no-one had benefited from his work, which might be considerable. So competition is an essential part of the drive to carry out research, it’s what makes you tick!”

#### **10.15.11**

*IN THE TELECONFERENCE (continued)*

Agnès Rötig: “Valeria, when you’ve just launched the “transfer microset” and as soon as you’ve got a gene for a patient, you do the sequencing for all the patients. But I’m not sure that’s the best way forward. Is there a better way?”

Valéria: “I’m afraid I’ve no idea!”

#### **10.15.27**

ITW Valeria Tiranti, Biologist, Mitochondrial Diseases Centre, Milan, Italy

Our aim is to find a common way to proceed, to treat and study the patients so that we can move our research forward in such a way that will help the patients and families.

### **10.15.33**

#### *IMAGE*

*Valeria Tiranti*  
*Biologist, Mitochondrial Diseases Centre,*  
*Milan, Italy*

### **10.15.48**

#### *IN THE TELECONFERENCE*

Arnold Munnich: “Are the Dutch as happy as we are to exchange knowledge?”

### **10.15.52**

*ITW Bert Smeets, Director of the Genome Centre, Maastricht, Netherlands*

“Scientists have to work in teams. They all have an interest in making use of each other. In our team we all know each other, we know each other’s work, we share privileged relationships. It’s a good mixture, not too difficult to manage. We understand each other very well and everyone is highly skilled. The basis of this teamwork is an intelligent blend of personal affinity, scientific skill and a good understanding of our discipline.”

### **10.15.59**

#### *IMAGE*

*Bert Smeets*  
*Director of the Genome Centre*  
*Maastricht, Netherlands*

### **10.16.18**

*IN THE MEETING - Arnold Munnich, Director of the Genetics Department, Necker Hospital*

Arnold Munnich: “Good, thanks very much. Thank you, my friend. Goodbye for now. That worked quite well in the end. When you already know each other, it’s not so bad.”

### **10.16.28**

*IMAGE*

<p><i>Maastricht University</i> <i>Netherlands</i></p>
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### **10.16.40**

*COMMENTARY*

Here in Maastricht, Bert Smeets’ Dutch team are working on other diseases, those linked to the working of enzymes. Enzymes are like hormones, small chemical reactions which take place within our bodies. If they’re not there they can damage the organism to quite a considerable extent.

### **10.17.03**

*ITW Bert Smeets, Director of the Genome Centre, Maastricht, Netherlands*

“This type of research requires a very labour-intensive infrastructure and also needs very expensive equipment to carry out research on a grand scale. Since we have around 300,000 genes, if you want to examine them all it will generate a monumental amount of computer data that you then have to interpret.”

“Look at all this equipment. This is a PCR machine (maximum cell throughput). This is one of the very refined and very simple techniques which is, however, so

essential that now you can't imagine how nobody ever thought of it before. You can't do without it."

#### **10.17.49**

##### *COMMENTARY*

Some Dutch researchers have recently discovered the mechanisms of a disease, duly connected to an enzyme which is not working correctly.

It may be this new discovery which might finally make it possible to do something for Sofiane. This young patient is under the care of Pascale De Lonlay at the Arnold Munnich facility. He's a doctor who specialises in diseases which involve serious behavioural problems.

#### **10.17.58**

##### *IMAGE*

*Necker Hospital*

*Paris, France*

#### **10.18.00**

*IN THE CONSULTING ROOM Pascale De Lonlay – Metabolism expert, Genetics Department, Necker Hospital*

Pascale de Lonlay: "How's it going?"

Mrs. Saou: "OK. OK. He's taken his medicine."

Pascale de Lonlay: "He was completely out of it on Monday. He was very emotional. I couldn't examine him. What did the doctor say to you?"

Mrs. Saou: "That they'd discovered a deficit, that some cells weren't there, they weren't secreting..."

Pascale de Lonlay: "Right. This investigation is important because you've been trying for years to find out what your children have got. There you are. With the mental retardation and behavioural problems... and yet there are kids who are

doing well, developing well. That's important. And it turns out that what's missing is creatin. And that's why you keep at it, trying to carry out this kind of treatment for children like this, because it's treatable. In theory. Because you can give creatin. That's the stuff that these great sportsmen take. Creatin is important for the nervous system. They seem to be lacking in an enzyme which assists in the manufacture of creatin. And it goes without saying that there are no side effects. So you don't have to worry. There you go. So now for the MRI."

#### **10.19.40**

Nurses: "Hello, hello there, Sofiane. So they brought you in ? Everything going OK, then, Sofiane?"

#### **10.19.59**

##### *COMMENTARY*

Before treatment Sofiane must have an MRI. This is an x-ray examination that should make it possible to actually observe some brain malfunction.

#### **10.20.38**

*AFTER THE MRI, Francis Brunelle, Department Head, Paediatric Radiology, Necker Hospital*

"Actually, the way you work with Arnold is like a kind of loop which contains the clinic, genetics and now we've got computer imaging. In reality none of the approaches takes priority, you can come in at any of the three doors. You know, the first 3-D models anyone ever made were created by Leonardo da Vinci, who made a copy of a cow's brain from wax..."

### **10.20.45**

#### *IMAGE*

Francis Brunelle Department head, Paediological Radiology Necker Hospital
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### **10.21.17**

#### *IMAGE*

Leonardo Da Vinci's drawings
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### **10.21.36**

*AFTER THE MRI, Francis Brunelle, Department Head, Paediatric Radiology, Necker Hospital*

“It’s interesting because the terms used in the software are the terms a sculptor would use. What’s happening is that from the moment I saw it, I could feel it in my hands.”

### **10.21.52**

*ITW Massimo Zeviani, Neurologist, Director of the Centre for Mitochondrial Diseases, Milan, Italy*

“We work with our minds and our hands. I’m thinking about the Italian artists of the Renaissance. At that time the idea was to apply intellectual rigour to the artistic process. Mathematical criteria were used for painting or sculpture. In a way it’s comparable to what we’re doing.”

### **10.22.26**

*ITW Axel Kahn, Geneticist, Director of the Cochin Institute, Paris, France*

“The act of grasping all the influences of the period, all the influences of the past and rearranging them according to their own creativity, emotion, originality is completely shared by artistic creativity and scientific creativity.”

### **10.23.01**

*IMAGE*

Francis Brunelle Department Head, Paediatric Radiology, Necker Hospital
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### **10.23.01**

*ITW Francis Brunelle, Department Head, Paediatric Radiology, Necker Hospital*

“The common point is the emotion. Artistic creation means translating an emotion. Scientific research means translating an emotion. And, paradoxically, you know that science has a very Cartesian phrase. You have to define a hypothesis, define a technique, define the equipment, the methods, analyse the statistics, analyse the results, and finally draw conclusions. But before all of that there has to be something that nobody talks about, which is intuition. And before intuition comes emotion.”

### **10.23.48**

*COMMENTARY*

While Sofiane is in the recovery room after the MRI, his mother talks to Professor Arnold Munnich. He's going to explain to her what can be expected of this new treatment for her son, which exists only thanks to inter-continental collaboration.

### **10.24.13**

*IN THE CONSULTING ROOM WITH Mrs. SAOU - Arnold Munnich, Director of the Genetics Department, Necker Hospital*

Arnold Munnich: "I don't want to take up too much of your time this morning. But there are a couple of things you have to know. Sofiane and Miriem are the first two cases of this condition we've ever seen. We know about it because of the work we've done with our Dutch colleagues, but personally we have no direct experience. So we're very pleased to have this first case ourselves. For a number of reasons. First of all, because a success from time to time in our profession means a lot to us."

Mrs Saou: "Yes."

Arnold Munnich: "Above all, when there's a treatment we can use. And that's another important thing, this is a condition we can improve by adding the substance that the brain doesn't have. Secondly, we can now diagnose the condition before birth. Well, you knew all that already. Pretty soon we'll have found the mutation. The gene has been identified. What you have to tell me, if you're interested in this side of the subject, is whether you want to have another child who will certainly be unaffected. If you do, you must let me know so that we can prepare. This is something we can offer you as a certainty."

### **10.25.24**

*ITW Bert Smeets, Director of the Genome Centre, Maastricht, Netherlands*

“We know all the genes of the human organism and now we can study them and identify the faulty ones. In particular, in the case of a genetic disease or dysfunction, we can deduce a link with a genetic fault or activity.”

### **10.25.43**

#### *COMMENTARY*

Science is moving forward, and as it does the hopes of patients – waiting for a treatment to provide solutions that have so far been unthinkable – are growing.

### **10.25.57**

*IN THE MEETING – Bert Smeets, Director of the Genome Centre, Maastricht, Netherlands*

Woman: I wanted to talk to you today because we were wondering about prenatal diagnosis of mitochondrial diseases.

Bert Smeets: “From a technical point of view I don’t foresee any major problems. It’s simply a test you do using a cell, and then you do it using copies. The actual test is quite simple. What is complicated is interpreting the results and working out if the discoveries made over a given period of time will stay valid as the baby develops.”

Woman: “Would it be possible for a prenatal diagnosis expert to email us the results?”

Bert Smeets: “In Paris, France, during our last meeting some data was shown to us, but it was still at the experimental stage.”

Woman: “So nothing has been published yet?”

Bert Smeets: “No, nothing so far.”

### **10.26.40**

## COMMENTARY

In Maastricht as in Paris, the first thing the teams have to do is to approach the ethical questions raised by the improvements in screening techniques for mitochondrial disease.

### 10.26.50

*IN THE MEETING, Arnold Munnich, Director, Medical Genetics Department, Necker Hospital*

Arnold Munnich: “I’m going to tell you about a request that has been made by a woman who is five weeks pregnant. This lady would like to know if a foetal sex test would be acceptable because male children are seriously affected in her family. Girls less so. We can make a suggestion: it’s better than aborting all the boys. And I’m completely in agreement.”

Agnès Rötig: “Can you guarantee that for her?”

### 10.27.40

*ARRIVING, Gavin Hudson, Biologist, Newcastle University*

Jean-Paul Bonnefont: “Did you have a good journey from Newcastle?”

Gavin Hudson: “Yes.”

### 10.27.45

## COMMENTARY

As agreed at the videoconference three months before, some English researchers have come to Necker to use the genetics department DNA bank.

### 10.27.58

*RESEARCH LIBRARY Gavin Hudson, Biologist, Newcastle, England*

Woman: “...I can’t find...”

Gavin Hudson: “I think that means...”

## 10.28.02

### COMMENTARY

They're starting off a new research programme on a mitochondrial condition that above all affects males.

## 10.28.12

*ITW Axel Kahn, Généticist, Director of the Cochin Institute, Paris, France*

“Very often cooperation is the best way to win the contest. Subject areas have become so complex that it's very unusual for one person to have the clout to get a chance to bring it home, with this degree of competition.”

## 10.28.32

*ITW Gavin Hudson, Biologist, Newcastle, England*

“What we're actually looking for is a gene, or a polymorphic gene inside a gene which could be the source of mitochondrial mutation. We're trying to find a treatment by attempting to discover where this gene could be. This might help us to decide why these people go blind, which could mean that in the future we could eradicate this condition.”

## 10.28.36

### IMAGE

Gavin Hudson Biologist Newcastle, England
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### **10.28.56**

*ITW Arnold Munnich, Director, Genetics Department, Necker Hospital*

“When new knowledge or innovation is no longer at stake, then we’re very willing to share biological resources, but while there are still discoveries to be made, new concepts, well, then you get competition.”

### **10.28.57**

*IMAGE*

Arnold Munnich Director, Genetics Department, Necker Hospital, Paris, France
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### **10.29.16**

*COMMENTARY*

Being in competition... with the Italians, for example. Massimo’s team, our partners from way back, have just discovered a gene responsible for some mitochondrial diseases. They could never have made this discovery without the DNA samples sent by Necker a few months previously. Professor Munnich’s team are delighted to know this.

### **10.29.39**

*IN THE MEETING*

Agnès Rötig: “Massimo has found a mutation for Rabailu, for its gene.”

Arnold Munnich: “Never!”

Agnès Rötig: “He has, he really has!”

Arnold Munnich: “Good for him!”

Agnès Rötig: “But he hasn’t said what it is. He said that he had a gene on chromosome 2 with part-linkage and he’s just told me that he’s found the continuation.”

Arnold Munnich: “You’re kidding!”

Agnès Rötig: “No, it’s true.”

Arnold Munnich: “That’s fantastic! That’s really great news!”

*(Laughter)*

Arnold Munnich: “As François Jacob used to say, the hardest thing about science is putting up with other people’s discoveries!”

Arnold Munnich: “Anyway, there you go.”

### **10.30.23**

#### *IMAGE*

Bert Smeets

Director of the Genome Centre

Maastricht, Netherlands

### **10.30.46**

*ITW Bert Smeets, Director of the Genome, Maastricht, Netherlands*

“You know yourself, you have a justifiably high opinion of yourself, but you still want to be the first. It can be a blow when someone else gets there first. That’s the case as regards the European project. The diseases we’re working on can be pretty rare, so it’s a much better idea to share the patients, to be able to approach all of them, and work as a unit. But that means you’re taking the risk that some other researcher will make the discovery using the patients you feel are yours.”

### **10.30 .46**

*ITW Massimo Zeviani, Neurologist, Director of the Centre for Mitochondrial Diseases, Milan, Italy*

“Most of the time it’s just a matter of luck. Luck is a basic factor, really important. In this actual case we had good families, had located the gene. Collaboration was good – and then along comes a bit of luck.”

### **10.30 .47**

*IMAGE*

Massimo Zeviani Neurologist, Director of the Centre for Mitochondrial Diseases Milan, Italy
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### **10.31.10**

*ITW Antonella Spinazzola, Neurologist, Centre for Mitochondrial Diseases, Milan, Italy*

“I was extremely pleased, because I’d worked really hard on this project. I might be small, but in one leap I’d reached the ceiling! I went to see Massimo and I said to him: I’ve found the mutation! Massimo was delighted, but as usual he said, ‘OK, good, but stay cool – don’t get carried away!’”

### **10.31.19**

*IMAGE*

Antonella Spinazzola Neurologist, Centre for Mitochondrial Diseases, Milan, Italy
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### **10.31.36**

*ITW Massimo Zeviani, Neurologist, Director of the Centre for Mitochondrial Diseases, Milan, Italy*

“Some 80-90% of experimental research gets nowhere. When you start a project you know that you’ll get frustrated, there’ll be plenty of setbacks, experiments that tell you nothing. But the pleasure of making a discovery makes it all worth while.”

### **10.32.06**

*ITW Axel Kahn, Geneticist, Director of the Cochin Institute, Paris, France*

“When you set your heart on a scientific goal that’s hard to reach, and you get there, you make a discovery, straight away you can see all kinds of new openings, you get the feeling everything’s falling into place. It starts with everything out of place, you can’t understand anything, there’s hardly any data, nothing to bring it together.”

“And then – harmony! Everything connects, the jigsaw pieces fit, it’s very beautiful.”

### **10.32.12**

*IMAGE*

<p>Axel Kahn Geneticist, Director of the Cochin Institute, Paris, France</p>
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### **10.32.47**

*ITW Gavin Hudson, Biologist, Newcastle, England*

“I’m going to put them in the fridge.”

### **10.32.52**

## COMMENTARY

The British researchers have finished taking their DNA samples from Necker. Now they have to go back to the UK to analyse them.

### 10.33.01

*ITW Gavin Hudson, Biologist, Newcastle, England*

Jean-Paul Bonnefont: “OK, have you finished?”

Gavin Hudson: “Yes, yes, we’ve finished and we’ve got around 130 samples. That’s quite a lot and some of them have really good pedigrees which should really help.”

Jean-Paul Bonnefont: “Are you going to Paris tomorrow?”

Gavin Hudson: “We’re going to be tourists for a while. So thanks for everything.”

Jean-Paul Bonnefont: “You’re very welcome!”

### 10.33.25

*ITW Arnold Munnich, Director, Genetics Department, Necker Hospital*

“There’s that feeling you get, that you can free yourself by listening to music, or perhaps by composing or improvising it – maybe that has something to do with the way scientists see solutions in their dreams. It comes from sleep, it comes from, from, I don’t know where, but anyway, these ideas just bubble up when all the problems of the day have melted away.”

### 10.34.05

*ITW Massimo Zeviani, Neurologist, Director of the Centre for Mitochondrial Diseases, Milan, Italy*

“You have to look outside of the evidence if you want to discover something. From that point of view there’s a strong link between artistic experience and scientific experience. The pleasure of discovering something and of making

progress, or of setting up a project, or trying to find new ideas is an intense personal experience.”

### **10.34.50**

#### *COMMENTARY*

Today it's the turn of the morphology team led by Professor Stanislas Lyonnet. He works with Arnold Munnich in the Genetics Department. Nearly every day there is a meeting where doctors and researchers talk in an atmosphere of non-stop excitement where observation, the association of ideas and innovation blend together.

### **10.35.12**

*IN THE MEETING, Stanislas Lyonnet, Geneticist, Genetics Department, Necker Hospital:* “Sylvain shows very unusual symptoms. He looks as though he's about to fall over. His hands are like that. He's very unsteady.”

### **10.35.23**

*IN THE CONSULTING ROOM Stanislas Lyonnet, Geneticist, Genetics Department, Necker Hospital*

“There now, you're going to walk a bit. Look, that's great. OK, off you go, back to your Mum.”

### **10.35.31**

*IN THE MEETING Stanislas Lyonnet, Geneticist, Genetics Department, Necker Hospital*

Stanislas Lyonnet: “The second thing you notice when you examine him is that his extremities are almost oedematous, his fingers are stubby, short, pointed, a bit like a cofilnori.”

Woman: “Yes, they're very noticeable.”

Stanislas Lyonnet: “They really do remind you of the thick hands of a child with a cofilnori. But I agree, the rest of the case is not very convincing. And then again, there are some dysmorphic elements, the very narrow face, narrow from the front, facial hypotonicity, strabismus.”

### 10.35.56

*ITW Jeanne Amiel, Geneticist, Genetics Department, Necker Hospital*

“We all have our own view of things, the ideas we put on the table, and bit by bit we work out a hypothesis, several different versions and the idea becomes clear. Look, this is how it works!”

### 10.36.01

*IMAGE*

Jeanne Amiel Geneticist, Genetics Department Necker Hospital
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### 10.36.11

*IN THE MEETING, Stanislas Lyonnet, Geneticist, Genetics Department, Necker Hospital*

“Let me tell you something, something that I thought of. As you know, you get mental retardation with thyroid hormone transport anomalies. That made me think of these photos, and it looks a little bit like adenoma. This family, you know, have been afflicted by adenoma over six generations. And these are older people. However, in his case you can at least perhaps dose the T3 . See what I mean, establish a thyroid balance?”

Stanislas Lyonnet: “Go on, I’m listening, because I really have no idea.”

Woman: “X-rays”.

Stanislas Lyonnet: “X-rays of the skeleton, naturally.”

#### **10.36.44**

*ITW Stanislas Lyonnet, Geneticist, Genetics Department, Necker Hospital*

“A file can really come to life in one of these meetings, in the sense that even if the best doctor at this or any centre just reads the file it’s still nothing like the opportunity of comparing viewpoints. That’s what creates ideas. And that certainly has a lot in common with certain kinds of artistic creativity.”

#### **10.36.46**

*IMAGE*

Stanislas Lyonnet Geneticist, Genetics Department Necker Hospital
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#### **10.37.05**

*ITW Jeanne Amiel, Geneticist, Genetics Department, Necker Hospital*

“When you’re doing research, I think you need to create, and you have to do it on the basis of medicine, which is a moving, slippery, very ill-defined surface.”

#### **10.37.18**

*ITW Arnold Munnich, Director of the Genetics Department, Necker Hospital*

“Some people think that researchers are very sure of themselves – but the truth is, they’re plagued by doubts! They edge forward by trial and error. They make up a hypothesis, they test it... In any case, the discoveries we’ve made, we’ve made them by luck, or by comparison, between two patients, between two situations, and often the further apart the situations are, the more fruitful the association is. These are chance associations – links you tease out as the days of good ideas go by.”

### **10.37.53**

*IN THE CONSULTING ROOM – Pascale de Lonlay, Metabolism Expert, Genetics Department, Necker Hospital*

Pascale de Lonlay: “Two children were being monitored by the department for hyper-insulinism. Both have a Visigoth mutation of the gene on one chromosome. They display intra-ventricular signals, which are quite significant, with dilated spaces and abnormal myelin as well, yes, there’s a myelinisation fault, too.”

### **10.38.15**

*ITW– Pascale de Lonlay, Metabolism Expert, Genetics Department, Necker Hospital*

“We have to interpret each speciality in our way, we have our specialist’s way of looking at things, and we have all been trained differently. So the radiologist is there to interpret this MRI, the neurologist to interpret his clinical examination for us, and all together, it’s quite a miracle.”

### **10.38.30**

*IN THE MEETING - Pascale de Lonlay, Metabolism Expert, Genetics Department, Necker Hospital*

Woman: “Just one question – which chromosome is your Visigoth mutation on?”

Woman 2: “Chromosome 11.”

Woman: “P?”

Woman 2: “Yes.”

Woman: “That’s the same location as.... Yes, it’s just to the side.”

Pascale de Lonlay: “I have a Visigoth mutation, too.”

Woman 2: “So, it’s a Visigoth mutation. By the way, are they blood relations?”

Pascale de Lonlay: “Yes.”

Woman: “Hey, great, that’s exactly what it is!”

Woman 2: “If it’s on 11P, it’s just to the side.”

Woman: “Incredible!”

### **10.38.58**

*ITW Stanislas Lyonnet, Geneticist, Genetics Department, Necker Hospital*

“When those who have seen patients meet those who see them less (or maybe see them as a file, pictures, blood samples, DNA fragments), something creative happens. In my opinion there are two neat ways to assess the meeting of these two partitions.”

### **10.39.34**

*COMMENTARY*

Two months have passed. And something which is becoming more and more rare in medical research: progress has been seen in the behaviour of Sofiane and his sister Myriem, thanks to the treatment developed by the European collaboration project..

### **10.39.49**

*CONSULTATION WITH THE SAOU FAMILY - Pascale de Lonlay, Metabolism Expert, Genetics Department, Necker Hospital*

Pascale de Lonlay: “How are things?”

Mrs. Saou: “He’s shown some progress. He hasn’t blanked out. It’s a miracle, because we thought he’d put up with everything.”

Pascale de Lonlay: “And he hasn’t blanked out for some time, or is this really the first time?”

Mrs. Saou: “It’s the first time.”

Pascale de Lonlay: “That must be a real change for you.”

Mme Saou: “Yes, he’s always agitated. He always sleeps at night. Yeah, but it’s just this blanking out.”

Pascale de Lonlay: “So you started with very little doses of creatin.”

Mrs. Saou: “Four grams.”

Pascale de Lonlay: “Lots of teams see changes at the end of a few weeks, so you have to be patient. It’s true that you can slightly increase the dosage.”

### **10.40.36**

*ITW Arnold Munnich, Director of Genetics Department, Necker Hospital*

“There are two occasions which are terribly exciting and moving, as a musical emotion should be. It’s when you imagine an explanatory theory, you say ‘It could be that!’, and then the second occasion when you test it, and you get that echo of the positive response to the idea, to the imagination, to the theory you’ve dreamed of, well, it’s almost like a drug.”

### **10.41.09**

*IN THE MEETING, Arnold Munnich, Director of the Genetics Department, Necker Hospital*

Arnold Munnich: “First of all, Pascale, I saw the Saou family after you. Fantastic! I’ve never seen them so calm. And I know them very well. Here they’re moving the library and everything. You see.”

Pascale de Lonlay: “So it’s started well. The treatment is 410 grams per kilo of creatin, which is a standard dose. The only other thing you can do is try to lower the guanine-acetate. And maybe put them on ornithine. I’m waiting for the doses they’ve made up for me there.”

Arnold Munnich: “Do you think it’s a good idea to change the parameters now?”

Pascale de Lonlay: “You can either try everything because you want to improve these children’s lives, or you can carry on for a while longer with just the creatin treatment.”

Arnold Munnich: “Who is it who does that the most?”

Pascale de Lonlay: “The Dutch.”

Arnold Munnich: “And what do they say?”

Pascale de Lonlay: “They recommend bringing over their file and reducing the insulin.”

Woman: “And if you do it separately, they say it doesn’t work.”

Arnold Munnich: “But we’ve already seen that it does work.”

Femme: “Yes, it’s satisfying with epilepsy. They’ve already discovered creatin. But the others... because that was with smaller children. You see, there were psychomotor development stages that could be evaluated and they found that the children were significantly backward. Particularly as regards walking, etc. While when they administered both there was real progress. Children who could walk, whose language was improving

Arnold Munnich: “That would be my kid, I’d say, you’re doing it right away, right?”

Pascale de Lonlay: “That’s why. I was thinking you wouldn’t want to wait a second before administering the creatin. So you have a choice – either you see improvement for a year and after a year... or, you do everything, all at once. That’s the choice.”

Arnold Munnich: “It’s the children’s health that matters.”

## **10.42.50**

### *COMMENTARY*

Sofiane and his elder sister are improving. This heartening news in an environment where successes are still rare has to be shared with the scientific

community. That's why today Pascale de Lonlay is talking at this international conference of specialists in diseases of the metabolism.

### **10.43.07**

*AT THE CONFERENCE – Pascale de Lonlay, Metabolism Expert, Genetics Department, Necker Hospital*

#### *SUBTITLES*

“So, thank you very much for having invited us to talk about secondary creatin deficiency in gyrate atrophy. We have seven patients afflicted by gyrate atrophy, most with mental retardation. We have tried to examine creatin deficiency in the patients’ brains and to establish a correlation between the lack of creatin, mental retardation and hyperornithine.”

### **10.43.32**

*ITW Arnold Munnich, Director of the Genetics Department, Necker Hospital*

“Clinical trials are currently in progress. When you start to experience some satisfaction, not merely intellectual, but because you have children involved in the process who are responding as you hoped they would, that is total happiness. You say to yourself ‘I might just be changing the fate of this child in some tiny way’.”

### **10.43.54**

*CORRIDOR CONVERSATION – Pascale de Lonlay, Metabolism Expert, Necker Hospital*

Woman: “As far as supplements are concerned, would the percentage be 20 rather than 50, or somewhere between the two?”

Pascale de Lonlay: “Somewhere between the two, 20, 50. Naturally, it depends on the patient and that’s without arginine.”

#### **10.44.17**

##### *COMMENTARY*

It’s what all laboratory Directors know – pushing research forward nowadays isn’t a question of just creating and inventing, it’s also increasingly a question of finding more funding to carry on the good work.

#### **10.44.31**

*ITW Bert Smeets, Director of the Genome Centre, Maastricht, Netherlands*

“In the world of scientific research we also have to chase money, just as artists do. You have to prove that what you do is worthwhile. We have to ensure that people invest in our work. That’s as true for us as it is for artists.

#### **10.44.45**

*ITW Axel Kahn, Geneticist, Director de l’Institut Cochin, Paris, France*

“The vast majority of artists and scientists for the greater part of their lives are more likely to be living from hand to mouth than enjoying a life of luxury. So devoting your life to something or other is never because you want money – it’s more like a sacred fire, a fire in your soul. Both cases involve passion, there can be no argument about it.”

#### **10.45.11**

*LEAVING FOR THE CONCERT, Arnold Munnich, Director of the Genetics Department, Necker Hospital*

“I’ll be back at half past one for the consultation.”

#### **10.45.14**

##### *COMMENTARY*

1 million, 1 gene, 2 million, 2 genes, Arnold Munnich repeats again and again tirelessly.

It is for that very reason, raising funds for the genetics laboratory of the Necker Hospital, that the opera *Philemon and Baucis* is being performed today.

#### **10.45.30**

##### *IN THE TAXI - Arnold Munnich, Director of the Genetics Department, Necker Hospital*

“Do you know where we’re going? We’re off to the dream. The opera has been reborn after 200 years. It reminds me of a story about coping with mourning. Yesterday I was with a mother who had lost two of her three children...

What I was really saying to myself as I listened to her, heard all about her grief, was that I had the impression that as long as I didn’t give exact answers to the question she asked us, the grieving would go on. And to bring this grieving to an end, to find a grave for that child, we had to find a genetic solution. Parents confuse research and care. As long as the research continues, it’s as though someone were taking care of the child. Once again you can see how the search for causes and simple scientific research are both part of the therapeutic project. Keeping on searching is in some ways like continuing the caring.

And *Philemon and Baucis*, that’s just part of the superhuman effort to help researchers with their funding problems. The means of getting answers to the questions which are still being asked.

#### **10.46.49**

##### *ARRIVING AT THE CONCERT – Arnold Munnich, Director of the Genetics Department, Necker Hospital*

“Good afternoon, gentlemen... Wonderful! Have you started already?”

**10.47.04**

*ARRIVING AT THE CONCERT – Arnold Munnich, Director of the Genetics Department, Necker Hospital*

“Wonderful!”

**10.47.27**

*ITW Axel Kahn, Geneticist, Director of the Cochin Institute*

“There are very strong links between scientific emotion and musical emotion. I always have the idea that if I were to draw a brain I’d want to ensure these two areas could flirt with each other, the one sensitive to the beauty of music and the other to the emotions of science. It is chief among the emotions.

**10.49.27**

(opening titles)

**10.50.06**

(closing credits)