#### WELCOME TO THE NANOWORLD EPISODE 3 ... NANOS ON THE INSIDE... ENGLISH SCRIPT

#### TC IN 10 00 00 OPENING TITLES - NANOWORLD

# LA COMPAGNIE DES TAXI BROUSSE PRESENTS

#### WITH THE PARTICIPATION OF FRANCE TELEVISIONS

IN PARTNERSHIP WITH EUROVISION SCIENCE AND THE EUROPEAN COMMISSION, DG RESEARCH

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# 10 :00 : 00

COMM

All around us, around you, and me... the worlds of media, science and economy are resounding with the prefix « nano ». All I hear is references to this invisible scale, a billionth of a metre, just a few atoms wide...

The frenzy is global. Thanks to nanos, science and technology foresee a fascinating new world, infinite new research fields, and miraculous new possibilities.

From materials to energy, the environment to medicine, via electronics and agriculture... nanos should make everything more efficient, more resistant, cheaper and less polluting...

Nothing in our world will be free from nanos... a prospect which sometimes appears quite alarming...

Welcome to the Nanoworld.. to the Nanoworlds...

### TITLE :

# WELCOME TO THE NANOWORLD

... NANOS ON THE INSIDE ...

#### 01 02

#### COMM

Welcome to our journey of discovery, into the world of nano-medicine...

#### 01 15 MAURO FERRARI DIRECTOR OF THE DIVISION OF NANOMEDICINE UNIVERSITY OF TEXAS

My wife, my first wife, Margaret Louise got sick with cancer and she died, she was thirty two at the age when she died, we had three small children, Jack, Kimi and Kiara and when I was asking the doctors, they were telling me there was nothing we could do, that she was gonna die soon even though if you had looked at her she didn't even look sick.

the problems that the doctors were talking to me about are technological problems are engineering problems, how do you find it early, how do you vector the

drugs to the right place, and I was sitting in the middle of a ton of great technology at Berkeley and Stanford and around the country, all of these new chip making technology that were being made and that is when I started asking myself, can we use any of these technologies to help with the challenges that I hear about from the medical front.

#### 02 17

#### COMM

Technology serving health-care. Apparently, there's nothing new there...

Except that this technology is on a nanometric scale.

And bio-medical research has been working on this scale – a molecular scale – for more than a decade.

Nanoscience is promising new solutions. The main areas of research are clearly defined. Earlier and more precise diagnosis, more effective treatment, using smaller doses, repairing what has been damaged or destroyed more efficiently; skin, muscles, bones, and why not organs too.

#### 02 47

A brief reminder... The prefix 'nano' signifies a scale of ten to the minus nine metres -a billionth of a metre. And thus everything else is on the same scale. A few main principles give nano-sciences and technologies their particular characteristics.

#### 03:03

First of all, working with matter on a nano scale rather than a macro scale, (our « normal » world) means working directly on the very components of matter, and no longer on a mass that's already been composed. Since the end of the 20th century, scientists in every discipline – physics, chemistry, biology - have been using their shared knowledge to manipulate atoms individually and to assemble them like simple building-blocks.

#### 03 27

You no longer need a tree to make a tooth-pick. In theory, one can assemble the atoms making up the tooth-pick to reach the same result.

# 03:40

# COMM

Acting directly on the constituents of matter also enables different properties to be exploited. Because the size is different, the materials react differently... (In this way, on a macro scale, gold is a conductor ; on a nano scale ; it's an insulator.)

Another particularity : the ratio of surface to volume changes. By changing the scale, for an equal volume, we gain in surface area. It's like Comparing the surface area of a ball, with the potential area of all the smaller balls it could contain, which is much larger.

### 04 10

# COMM

Other characteristics and properties are also revealed on the nano scale, such as the effects of quantum physics.

Our reality, defined by classic physics, is no longer valid in the nano-world.

For example, if I take a ball, and throw it against a wall, it will bounce off it. But if I am very small, and the ball is of nano-metric size, when it hits the wall, it will bounce, but it will also pass through it... it will be here, there and nowhere.

If you're a little lost, don't worry... so am I. And the leading scientists are still wondering...

# 04 50

### COMM

The consultancy, Lux Research, estimates that by 2014, up to 16% of the turnover generated by health-care products will come from nanotechnologies.

And there is the same priority around the world : the battle against cancer. The means available are impressive, as are the results... Here, in Europe, for example...

I have an appointment in Germany with Professor Andreas Jordan in a small building close to the gardens at an institution called the Charité Clinic.

### **SYNTHE :** BERLIN

# 05 16 JOURNALIST Hello... hello...

### ANDREAS JORDAN

We can start here...

#### 05 32 COMM

Andreas Jordan created his start-up almost ten years ago, to develop nano-technology based therapy for treating certain brain tumours. The nano dimension has rendered effective a process which didn't work on the micro scale.

#### 05 48 ANDREAS JORDAN BIOCHEMIST FOUNDER OF MAGFORCE NANOTECHNOLOGIES

*Heat treatment so a thermotherapy against cancer was* (*a*?) *well-known.* 

But the conventional systems are not able to only heat up the tumor. They normally heat up a side from the tumor also the normal environment a normal tissue. So we looked for particles that might be able to absorb energy from an energy field coming from outside the body just to focus, just to absorb and deposit energy within the tumor.

# 06 19

### COMM

I learn that, like every cell in our bodies, tumours won't survive a brutal increase in temperature. In order to heat the tumour, and only the tumour, Andreas Jordan uses nanometrically sized particles.

### 06 30

### COMM

As I prepare to enter Professor Jordan's lab, where the nanoparticles are developed, I imagine a futuristic, high-tech universe... But no...

#### 06 38

# **ANDREAS JORDAN**

*Our technical departement*' where (inaudible) our nanoparticles are produced and manufactured. The basic principle of our new cancer therapy here is that we have these iron oxide nanoparticles which have a size of 15 nanometers, it's a very tiny particle. If I take this magnet they respond to such a magnetic field.

### 07 00

### COMM

A magnetic field ? Why ? And how ? Andreas Jordan answers my questions with a little experiment... demonstration time...

### 07 09

# ANDREAS JORDAN

*I put on a magnetic field then I take my hand here and one feels nothing although the magnetic field is on maximum power.* 

07 20 **JOURNALIST** Can I try with my hand?

07 23 ANDREAS JORDAN

Yeah, put it. Do you feel any warmth or any sensation?

#### JOURNALIST

No, no

# 07 31

### COMM

On my hand, there's no metal, and no iron oxide, so no heat... but elsewhere...

#### 07 36 ANDREAS JORDAN

And now, I put this cent here and you will see, just a few seconds and the cent is...look !

### 07 45

#### JOURNALIST

It was like exactly the process that you're using after you inject...

#### 08 30

# ANDREAS JORDAN

*Exactly, after we inject the particles into the tumor, the particles get excited by the magnetic field and only the particles.* 

#### 08 10

### COMM

When nanoparticles are subjected to an oscillating magnetic field, they vibrate, some 100,000 times a second, which means that they will heat up. The temperature inside the cancer cells will climb by 43 degrees, and destroy them.

#### 08 23

### JOURNALIST

Why this idea doesn't work with macro particles? Why do you have to go to nanoparticles?

08 30

#### ANDREAS JORDAN

I tested hundreds of different larger particles with different **shells?** And it was really frustrating to see that, always with the magnetic fields and frequencies possible to apply to humans, one needs gram of iron oxyde per gram of tumor tissue, it's a really huge amount which we wouldn't apply at anytime to humans.

The second point is that the surface structure can be really exactly modified so that the particles remain in the tumor, that they are taken up by tumor cells but not by normal cells, that they migrate through the tumor tissue, not into the normal tissue, all these things are features of the coding of these nanoparticles. And this can only be done in nanoscale, but not in bigger particles.

09 23

#### COMM

And the results are there. Patients have recovered and there were even some exemplary remissions.

#### 09 44 JOURNALIST

Do you understand that you make people hope a lot?

#### 09 48

# **ANDREAS JORDAN**

Since the clinical trial is still in progress statistically significant a confirmation of efficacy (?) is not possible but what I can say is that we have several patients in our brain tumor study which have survived much longer than it was expected from their pronosis.

#### 10 09

#### COMM

Why are things not moving more quickly?

Subjecting the nanoparticles to a magnetic field is easily done, but injecting them into the tumour is a complicated business.

Professor Jordan's teams today have to simulate the intervention using artificial images before operating in vivo. The injection must be perfectly controlled so that the content is equally distributed and no tissue is damaged during the process.

#### 10 33

# **ANDREAS JORDAN**

Certainly, we have limitations that is access to the tumor tissue. If the tumor tissue cannot be injected by a needle under image control, then we have the problem that we cannot inject at all sides or at different injection points into the tumor.

#### 10 52

#### COMM

Andreas Jordan's work is in phase 2 of clinical tests. The final stage before general application. Is this a revolution ? Not exactly... But it's progress, a real step forward, brought about through working on the nano scale. The progress heralds further developments too, both in terms of treatment, and in health care economy. The two are now indissociable. Gaining six months or ten years in life expectancy is evaluated in terms of a cost-benefit ratio. In modern medicine, you and I are patients, but also clients... consumers.

# 11 23

#### COMM

Money is, more than ever, the key to the war against disease. In the United States, where I continue my journey, 55% of the funds allocated to nanosciences and nanotechnologies are devoted to bio-technologies alone. The National Cancer Institute initiated a programme in 2004, investing 144 million dollars over five years into nano research against cancer. The competition for controlling the infinitely small is fierce, from one continent to another, between countries, and between laboratories.

**SYNTHE :** HOUSTON

# 11 50

#### COMM

The next challenge for nano-bio-technology, is bypassing the need to inject the treatment directly into the affected areas. Thanks to nanotechnology, medicines are becoming intelligent. In other words, once they're in the blood, these nanoparticles can identify and reach their target, by themselves and more quickly, accurately and effectively.

# 12 16

### COMM

In Texas, I meet two new pioneers. Scientific institutes and hospitals cover one third of the city's area here.

Professor Ferrari's team is one of the leaders in developing intelligent nano-particles.

### 12 35 MAURO FERRARI DIRECTOR OF THE DIVISION OF NANOMEDICINE UNIVERSITY OF TEXAS

Even the best anti cancer drugs that we have such as Heraseptin the drugs that we use it against breast cancer, for some sub set of patients it's a miracle drug only one part in a hundred thousand or one part in a million will go to the tumour the rest will do damage in the rest of the body, that is the problem of cancer therapy making sure that the drugs go to the place where they are intended to go

The body's full of biological barriers, the body's set up with all sorts of defensive system that the body has to keep foreign invaders away so to speak, so we need to be able to make it across them, it's like barbed wire, they got landmines, you got trenches, you got all sorts of different things, you cannot do that with a single particle, you need to be able to orchestrate a system

### 13 34

### **MAURO FERRARI**

our strategy and the strategy of other laboratories around the world is taking advantage of design parameters that were impossible to play with just a few years ago

### 13 54

#### COMM

Today, Ferrari has tools that enable him to formulate nanoscopic treatment doses – for example, integrating a medical molecule in a nanometric tube – and combine the nano-doses with a probe.

### 14 09

### **MAURO FERRARI**

We have defined that the best possible design, that we can find, if you know a better one tell me about it, but the best one that we could find after all these years of math, is this size and shape that you see right here half a coconut. now all of a sudden we can build very many different functionalities on to the particles and we do that by design 14 35 JOURNALIST

And just, what is it made of?

### **MAURO FERRARI**

L'interviewé 1 - Ha. Tell him.
L'interviewé - Ho, we didn't mention that ...
L'interviewé 1 - Tell him.
L'interviewé - That's porous silicon.

14 44

#### MAURO FERRARI

It's a material used for making computer chips, but if you make it, there is a beauty to it, if you make it so porous it desintegrates, it is fully degradable and the degradation product is extremely benine.

So we can load inside of the particles, different payloads, different Nano particles and get them to different sub cellular addresses, some to the nuclear, some to the cytoplasm at different moments.

# 15 10

# COMM

The nanoparticle transporters can be injected anywhere, and once in the body, are able to reach the most inaccessible areas, to cross natural barriers, locate their targets, attach themselves, and release the active agents.

#### 15 39

#### **MAURO FERRARI**

Kind a like a rocket going to the moon, it took three stages and we are doing the same, we are driven by theory with the validation in biology and the implementation is a collaborative effort of physics of chemistry and molecular biology, so the teams that are required for something like this are extraordinarily inter disciplinary.

15 59 **JOURNALIST** But theoritically it works this technic ?

MAURO FERRARI Yeah.

16 06 **JOURNALIST** You've tested already ?

MAURO FERRARI Yeah. It works. 16 08 **JOURNALIST** So why it's not in use ?

### MAURO FERRARI

It takes time to validate. It is no way you can do this without years worth of testing.

#### 16 28 COMM

Once again, I'm tempted to tell them to go faster... As fast as possible in the fight against cancer. I would wager that with the energy and conviction Ferrari is capable of, theory and practice will soon coincide. But for him there is still one imperative : diagnosing the disease in time, before it's too late.

### 16 46 MAURO FERRARI

in the vast majority of cases we diagnose cancer very late and we have to intervene in very heavy ways with a knife or with radiation which is very damaging drugs to try to keep it from spreading and metastasising or to bring back the metastasis and extend life a little bit.

Now the question is : « how can we find cancer early ? We have screening techniques that we have all over the world, things like X rays, MRI or cut scans and those are very good techniques; however anytime you have to do imaging, you have a radiologistical problem, you have the problem of the burden of radiation, you have the problem with the fact that we can not find the smallest tumors through radiological imaging.

# 17 32

# COMM

How can we see better, and more precisely, and diagnose earlier, without harming the patient ? Nano-technologies are here contributing decisive progress.

The idea is to build another probe, this time a nano-marker, whose mission is to reveal the diseased cells in the body.

Conceived to be autonomous, it should find its objective, fix itself, and make it visible. What's crucial, is finding the right marker...

### 18 00 **SYNTHE :** GRENOBLE

# 18 00

### COMM

In France, along with my guinea pig, I meet the NanoBio team at the Electronic and Information Technology Laboratory (LETI) where the eminently serious and competent scientists take the time to attempt to explain their work to me.

# 18 16 FABRICE NAVARRO BIOLOGIST DTBS/LETI

So we have a small capillary, which contains the fluorophore, and I'll insert it into our lizard. There... We'll put it in the optical device. We stimulate it with light, at a given wavelength for the fluorophore. This then gives off light, and we can see the fluorescent signal through the lizard. When we inject the fluorophore into a mouse, what we see appearing is an homogenous distribution of the fluorophore in the mouse. It goes into the blood vessels, and there are blood vessels in every organ, so the fluorophore and the nanoparticles will be equally distributed via the blood system.

Then, with time, the nanoparticles will go an latch onto the tumour area. If we increase the timeframe, up to 24 hours, we'll observe more fluorescence around the tumour, under the mouse's skin.

What happens with the tumour, is that there are now blood vessels which form, but these new blood vessels are imperfect, they have pores that are bigger. The nano-particles that are smaller than 100 nanometres can go through these pores in the tumour's blood vessels.

#### 19 38

#### FABRICE NAVARRO

The nanoparticles flowing in the blood-stream will gather on the tumour and stay there. And as they are giving off light, if we stimulate them, after a certain time, we can detect the tumour through fluorescent imaging.

# **SYNTHE :**

PASADENA

#### 19 59

### COMM

But here again, having to inject a fluorophore restricts the possibilities. For all our scientists, the simplest thing would be to establish a diagnosis directly from the bodily fluids. A simple sample, and bingo...

Laboratory analyses today are too expensive, and ultimately do not provide a great deal of information. Which prevents widespread early screening from being carried out.

The solution, once again, entails changing scales, moving from macro to micro, and then to nanometres.

#### 20.28

### COMM

This is being studied in California, at the California Institute of Technology. Jim Heath seems like a cool dude, but his resumé is a boffin's dream and he's not short of original ideas.

20 42 JOURNALIST Hello Hi I'm Charles...

#### ... 20 55 JAMES HEATH CHEMIST CALTECH

Unlike the old question where, is there a tumour or not, we wanna be able to answer a lot of questions, we wanna know do you have cancer? What organ is it in? Is it early, late stage or metastatic? What is the right therapy? If you're on therapies, what's the bad and good response to therapies etcetera. So that means doing a lot of measurements, you know perhaps even for a survey scan a thousand measurements

Um, and so that's been something that's driven us; number one to understand the biology to get that right and then to develop technologies that will allow us to do, in a relatively trivial fashion, you know hundreds of thousands of measurements and the way this is distributed to the patient, just a finger prick of blood but can give us real detailed information about the status of the patient, how they're responding to drugs what have you

And so it's become a challenge of not just new drugs but new measurements,

#### 22 00

### JAMES HEATH

There's a lot of, well you know, it's a working lab so it looks like a mess um and uh it turns out that these proteins are in your blood we utilise them to get the information about the health status of various organs in your body, and we do it in a timescale that's about as long as it takes the blood to clot, so just a few minutes well you see all this plumbing these are this is the um an an all this plumbing that we use to deliver the various reagents to some of the chips and if you look at one of these chips when it's wired up, you'd think it looks really really complicated and it kinda does, because it's got you know plumbing in it you think how could that possibly ever be cheap.

#### 23 04

#### COMM

Low-cost diagnosis... A simple drop of blood for thousands of analyses, in just a few seconds.

I start fantasising about a time when prevention and cure will be one and the same. And this is indeed the ultimate aim of what we call « labs on chips » : systems no bigger than a tiny chip which can carry out analyses and even deliver treatment.

Research in the field is not just limited to Professor Heath's lab in the US. Back in France, at the LETI, Christine Pepponnet's team is working on the subject with the same enthusiasm, albeit without the Hawaiian shirts...

### IN

It's the first time they've seen their boss in a lab-coat..

### 24 05 CHRISTINE PEPONNET HEAD OF THE BIOSYSTEMS ON CHIP DEPARTMENT DTBS/LETI

The « lab on a chip » is the little device we see here. With a system like this we can have a very precise analysis of just a few cells : two or three. So, in fact, it's a tool that enables us, for example, to work on nano-samples.

Here we're in the process of manipulating some drops, not with pumps, or with syringes or fluid systems, but quite simply by turning an electrode on or off. In this way we can modify the topology of a surface and move a droplet from one electrode to another, and in fact, adapt its function, so we get it to either add a reactive agent or to perform a detection function, and in this way it can carry out all the steps of a biological protocol and complete an analysis.

#### 25 08

### JAMES HEATH

Well now we've been able to remove all of this **plumbing** and we're just, the whole thing is just a piece of glass and plastic and it runs by itself, we have a little chemical reaction that drives the whole powers, the whole system so we can just bring you the chip, no wires nothing, **take a finger prick**, **a little button** on the chip starts a chemical reaction, the whole thing works.

#### 25 43

**JOURNALIST** Then you will have the result at the end? **JAMES HEATH** *Yeh* 

# 25 46 JOURNALIST

the chip is not doing only one operation, it's doing ...

### JAMES HEATH

Yeh, yeh, doing many operations

# 25 54

### JAMES HEATH

You know I want this to happen while I'm still young or at least middle aged, and um and I I I wanna do it for a small amount of money, and so we need, if we integrate all these technologies we believe that we can have a much more efficient and rapid, um, protocol for taking a therapeutic with these diagnostic measurements, getting them through patients all the way to a drug that can be uh, you know on the market and help people.

#### 26 19

### **CHRISTINE PEPONNET**

The boundary between diagnosis and therapy is becoming increasingly more vague, so, for example, adding fairly continual doses of a medicine in the blood can be an intelligent way of treating people. In fact, there's a two-way relation between diagnosis and treatment : I measure a dose, I apply the medicine, another dose, I apply the medicine and soon we'll have almost

continual monitoring, or every hour or so, notably with assisted delivery to maintain the doses at a constant level, and avoid surges and peaks and everything that's undesirable in administering medicines.

#### 26 59

### JOURNALIST

What are the prospects for this?

#### 27 02

### **CHRISTINE PEPPONNET**

The aim is to get as close to the patients as possible. In general, it could be for analysis systems that are in an ambulance, or close to the patient, or even in his pocket ... why not... for certain pathologies it can be important to be able to perform tests once or twice a day. It could also be in under-developed countries, where they don't have laboratory infrastructures. In the same way as we've gone from no phones at all to mobile phones, we could go from very few laboratory analyses to something completely delocalised, using these new systems where we don't require a technical expert to make the analysis.

27 43

### COMM

But we're not there yet... The first miniature integrated delivery systems are still of a size comparable to large capsules. The information gathered and interpreted by the lab-on-chip diagnosis systems is not yet reliable and reproducible.

But progress is being made at a staggering speed. The first laboratories integrated on chips – but devoted to a single analysis, H5N1 - have been perfected. They can rapidly confirm a suspicion. Perhaps one day they will replace an unreliable system such as the one I was subjected to as I was passing through Hong Kong airport. As part of the battle against bird flu, I passed through a filter that checked my body temperature. No temperature, means no disease. The process is simplistic, but at least it exists.

After labs on chips, some are looking far ahead... They are already dreaming of nano-robots that will intervene directly in our bodies. But today, this notion is still in the realm of science fiction.

#### 29 15

#### JAMES HEATH

I think all cases especially in science truth is better than fiction and so, let me tell you about a drug my colleague here Mark Davis has designed, so there is a cancer chemotherapeutic called "Camptothism" that was removed from the market because it was too toxic. And so Mark designed a little package that looks like a sugar to your body, but it looks like a sugar that you can't eat, so your body neither metabolises it but it also doesn't attack it like it's a foreign ah ah ah a foreign beast, and so he puts this drug inside this this uh little sugar capsule, most drugs when you take them, they um they clear out of your body in just a few hours and they're small molecules and so they'll also leak out of your blood vessels and the tissues and kill tissues, not his. His stays in your body for uh a week, waits until it finds a tumour and tumours have a different blood vessel system than the rest of your body that's how it finds them, and still nothing happens and then a particle gets ingested by cells in the tumour and, if it's a cancerous cell it's more acidic than other cells that causes the particle to burst open and release the drug.

So the result is he takes this drug that's removed from uh the market because it's too toxic, he's able to lower the dose down twenty fold, give it to patients, he gave it to one guy he had pancreatic cancer, it was metastatic, meaning that it had spread around his body, he had about a month or two to live, it sent the cancer **backwards**, the guy is still alive today two years later and uh, uh and didn't even have hair loss, **no toxicology associated with it, ok**? So that to me is just a well engineered through chemistry and material science, a way to deliver drugs, it's not a Nano but damn! Ha ha ha, it's truth, much better than fiction !

# **SYNTHE :**

ABANO TERME

# 31 20

#### COMM

Reality is perhaps ahead of fiction when nanotechnologies manage to imitate, encourage or control certain properties of living beings. For certain mechanisms that indispensable for life occur on a nanometric scale. If we can understand them, and reproduce, or even improve them, then why not dream of being able to re-grow a member or an organ, such as a lizard's tail. The medicine of the future, or a dream of Creation...

# 32 02

#### COMM

In Italy, close to Venice, I meet Alessandra Pavesio. She is interested in the regrowth of skin and cartilage, one of the first steps towards regenerative medicine.

# 32 21

### ALESSANDRA PAVESIO DIRECTOR MEDICAL DEVICE R&D FIDIA ADVANCED BIOPOLYMERS

Our technology, is tissue engineering. We take cells from a patient, for example who has suffered a trauma, or who has a cartilage problem. We take the cells, and we cultivate them in a quite classic manner to multiply them. When we have a sufficient number, we implant them on the material we've developed thanks to our technology, and which will guide their growth.

The cells feel at home on this structure, and can proliferate in the laboratory in every direction, as they would naturally.

### 33 07

### COMM

Alessandra shows me the manufacturing process. It is developed from a polysaccharide, a form of carbohydrate, which is present in the organism, and which enables supports to develop, on which the skin and cartilage will be rebuilt.

The supports act like lures.

The support-cell combination is perfectly bio-compatible, as the material itself is bio-compatible, and the cells come from the patients themselves.

#### 33 40 ALESSANDRA PAVESIO

This takes place on a nanometric level. The communication between the cells and the bio-matter takes place on a nano scale. Gaining a better understanding of how communication is established between the cells and the bio-matter, and how information is exchanged on a nano scale, should enable us to intervene, and so to make this material more intelligent... which will allow us to control the growth of the tissue cells more effectively.

The potential for this technology goes far beyond the simple reconstruction of cell tissue... it could lead to veritable cellular therapies.

That's why an essential part of our research focuses on learning about the information exchange between cells on the nano scale, be it of a chemical or structural nature. This activity is still new, it will be several years before we see a clinical application. But it's certainly one of the most interesting applications in nano-medicine.

# 34 58

СОМ

How can one intervene in the process of regeneration ? And control it ?

# **SYNTHE :**

HONG KONG

# СОМ

We head for China, where we shall perhaps find the beginning of an answer. I have been told that certain mice are regaining their sight !

China is investing massively in nanotechnology. The government, as in many emerging countries, is counting on such disciplines to bridge the technological gap vis-à-vis the western countries.

# 35 26

The University of Hong Kong is backing the work of Rutledge Ellis-Benhke, a scientist who divides his time between the prestigious Brain and Cognitive Science department at MIT and Chinese laboratories.

35 47

# JOURNALIST

« Hello, Hi... How are you... »

### 35 51

# COMM

To start with, Rutledge introduces me to Professor Soe, his boss, an eminent member of the Chinese Science Academy, and a great Francophile.

# IN

« I was in Provence once, very nice beautiful place, we were driving and... » **JOURNALIST** "for a vacation ?"

# IN

# *"for a vacation."* **RUTLEDGE ELLIS-BEHNKE**

In southern France as well, the food is unbelievable.

# 36 15

# COMM

Above and beyond polite chit-chat, Rutledge Ellis-Benhke and Kwok-Fai Soe have a taste for the spectacular. At least in the way they present their work. The manner in which they promote their research and results is so impressive, that I could perhaps for the first time, feel that the nanoworld is the result of magic.

#### 36 49

# RUTLEDGE ELLIS BEHKE ASSOCIATE PROFESSOR DEPARTMENT OF ANATOMY UNIVERSITY OF HONG KONG

Well, imagine a medical device that looks like a glass of water, and the liquid inside that's a medical device, this is going in to you you're gonna pour it in or inject it, it's gonna go to a specific place in your body and it's going to repair a blood vessel, or it's going to create an environment that allows a repair of the brain or the liver, or the leg. Or you can take the same medical device and pour it on the back of someone who has just had a severe burn and it allows cells to migrate back in and reconstitute or re-grow skin, the full thickness, and not just skin, I'm working on hair, but we haven't gotten that far yet, I'm when, next time you see me if I have a full set head of hair...

37 38

# JOURNALIST

It will be the same with me

# 37 39 RUTLEDGE ELLIS-BEHNKE

we were successful ha ha ha.

#### 37 42 COMM

One can always dream... but what's the reality ?

### 37 44

### **RUTLEDGE ELLIS-BEHNKE**

we build structure with molecules and those structures allow the body to repair itself that's what we're doing. It sounds fantastic but that's what we're doing

the way I look at it is, we're self assembled organisms, the human is, we start with a few molecules, we then become an egg, and a sperm they come together, we become cells, organs, hair, eyes, ah small hair follicles, small skin cells, moles, lungs and all sorts of different types of tissue; that all was assembled exquisitely at the Nano, it started at the Nano scale and then became the micro scale and then the macro scale which is what we see now.

#### 38 28 RUTLEDGE ELLIS-BEHNKE

So this is the laboratory that we use to actually produce our Nano materials Now this is very high concentration, lower concentration looks exactly like water and it flows back and forth just like water, so when you inject it into the area, it flows in and then assembles, much like water running down a brook, it will flow into all the holes and imagine that water then freezing all of a sudden, well that's exactly what this does

these materials are very small; five Nanometers by one point three Nanometers high and I actually came across this from a colleague who was working with things like this, but they had never put it into an animal

so one of the things that I was looking to do is reconnect the decadent parts in the brain and uh we use a visual system to reconnect the disconnected parts because that's the only way you can ask an animal if they can see. we made the cut, we put the material in and twenty four hours later we started to look at the brains of the animals and what we saw was we saw the first healing that started in the first twenty four hours, we had never seen that before. Most of the time you see a big gap in the tissue, but actually what was happening was it was actually healing. Then the next question is do we get Axons growing through the centre of it? We thought we would have to go ahead and promote growth, we would have to do other things to make it happen faster and then reconnect better, what we found was just in the one that was treated, we saw a reconnection of the Axons and in addition we saw functional returns so we showed the animal something, the animal sees it, it turns and takes a seed.

### 40 04

### COMM

In the product used by Rutledge, the nanoparticles, in fact, have several functions. First of all, they gather around and in the wound. They begin by stopping the haemorrhage... and this works everywhere in the body, including in the liver, for example.

# 40 35

The nanoparticles assist in the regrowth by creating a kind of scaffolding. The cells migrate and multiply around the scaffold, ultimately reconstituting the sectioned nerve fibre.

#### 40 57 RUTLEDGE ELLIS BEHKE

We are at Queen Mary Hospital. I come up here to do research as well.

# 41 10

# **RUTLEDGE ELLIS-BEHNKE**

The biggest problem you have in any type of Neurosurgical procedure is you have a lot of small bleeders and you have to then quarterise everyone of those, , so not only will it allow for the regeneration in the central nervous system it can also speed up the time of surgery, it can reduce surgical time up to fifty percent. Then you get into some interesting new areas, um one of them may be **for crystal clear surgery** where you could put the material down and you can operate through it so it's sitting there as a reservoir, so every time you put **the instrument** through, the instrument is actually cleaned.

We also know that most operating rooms, we do everything we can to make them as clean as possible so we're going in and we're using different types of antibiotics, antiseptics to go ahead and clean the surface completely, maybe what you really wanna do is, you wanna just immobilise the bacteria there and create a barrier so none of that goes into the patient and you're not killing the bacteria that's there because it may be better to have a lawn that you know and can control than to have a few weeds sprout up because those weeds that may grow maybe flesh eating bacteria, now you don't have to be in a controlled environment to do operations so we've gone from ah very highly specific type of surgical procedure and neurosurgical suite all the way through to now we can actually do ah menial surgeries either in the doctor's office or if need be you could do it right there in the field

# 42 32

# COMM

Discoveries such as Rutledge's make me want to believe in a revolution. In the notion of a regenerative medicine that covers all the organs.

Soon, perhaps, the optic nerve. And why not the spinal cord. Accidental or birth-related impediments could be overcome by nano-bio-technology.

Thanks to the progress made on a nanometric scale in the fields of electronics and biology, prostheses should see their performance and biocompatibility substantially improved.

# SYNTHE :

# BOSTON

### 43 03

### COMM

At Boston's Harvard University, the richest in the world, Charles Lieber is working in this direction, on the interfaces between living tissue and electronics.

### 43 22

In this Massachusetts laboratory, one could easily get lost in the maze of corridors and rooms. Fortunately, I have Quan Quing, Professor Lieber's assistant, to guide me.

#### 43 33 **OUAN OUING**

I graduated in Beijing but my hometown is WOOHAN, in the middle of China.

### **CHARLES LIEBER**

Charles?

43 43 JOURNALIST

Charles yes... Charles, the same exactly...haha

#### 43 43 CHARLES LIEBER PROFESSOR OF CHEMISTRY HARVARD UNIVERSITY

One of the areas that I am most interested in today and in the future is trying making interfaces between nanoelectronic devices and biological systems. There's many many decades of ranging from people sticking big metal electrodes into a human brain to more sophisticated microdevices and that's really much bigger than the way that biology communicates naturally.

The inner connections within your brain are through synapses, either through channels in the cell membrane or through molecules which are really nanoscale structures. So our goal is really to make similar types of structures or synapses but now being partly one component being artificial and therefore by connecting in the same way that the biology does that you can input or output\* signals in a very natural manner.

#### 44 52 **QUAN QUING**

See this grey piece of thing in the grid? They're brainslices. They come from a rat.

So basically, the devices are very small only in the center region you can only see the pattern but you can't really see the cell huh the device in there. And currently we bond the metal lines so they can be connected to the measurement system and the brainslice will be placed right in the middle region.

### 45 24

Here's the edge of the brainslice and these dark things are the *cortical* fibers that basically it's like highway of the brain, ok all kinds of information flows in this direction and there are different packs of cells here they communicate with this fiber

# 45 43

### COMM

In order to communicate with the brain, Charles Lieber attempts to connect with this fibre... to plug in, to receive and send messages.

### 45 49

### **CHARLES LIEBER**

In the short term what we're doing probably has the most immediate benefit in creating much more powerful tools for studying biological medical problems.

But in a slightly longer term goal I'm very interested in building interfaces that are much more sophisticated for prosthetic devices for treating for instance spinal or neurological diseases, for enhancing human, your quality of life. For instance. That's the hope.

#### 46 26 **COMM**

Enhancing humans, Charles Lieber's slip is quite revealing. Beyond therapy and medicine, some already imagine enhancing man's performance using nanotechnologies. They dream of a man with improved physical and mental capacities.

A cross between Steve Austin and the Terminator, whose skeleton and muscular architecture would be reinforced. A being whose neurone connections would be super-charged and perhaps interfaced with nano-computers, providing quicker reflexes, encyclopaedic knowledge, or, in the nightmare scenario, enslaving him.

A man – quite unlike myself, who would be worth several billion dollars.

#### 47 00

# **CHARLES LIEBER**

You can look at what people do today with laboratory animals that they can implant electrodes into those in a very crude sense and control a lot of the motor functions and things. A few years ago, "Robot Rat" or something, that was funded by DARPA that essentially, had a little radio transceiver and processor and some electrodes and they basically, you know, use a little controller and get this rat to move around so, by analogy you could already control someone if you implant an electrode in a crude sense and so, then again it turns back to how does one ensure proper safeguards and this being used to take some segment of the population and you know, implant at birth or something, you know, something and then take over by, you know.. It would make a great science fiction book !

### 48 13

### COMM

Is this really science fiction? The idea of a robotised man, improved or under control, exchanging his humanity for technological improvements, is something that continues to haunt me.

#### 48 34

# RUTLEDGE ELLIS BEHKE ASSOCIATE PROFESSOR DEPARTMENT OF ANATOMY UNIVERSITY OF HONG KONG

we're not trying to enhance, what we're trying to do is, we're just trying to restore. Now in twenty five or thirty years will somebody take something like this or something that someone else develops and take it in and try to re-enhance something? Probably, but we see that with Plastic Surgery now. Plastic Surgery was developed, how could we make people who have had a deformity or have had a massive accident look normal? Well, the logical extension to that is, how can I make myself look better?

#### 49 13 JAMES HEATH CHEMIST CALTECH

You know, you look, every decade, we are doing a lot to enhance human performance, through technologies and nanotechnologies is no different, you know, the kind of things we are thinking of doing now, the level of now, pretty minor, a little better than a wristwatch, a little more sophisticated than a glucose sensor in an insulin feeder but we have a ways to go before we really have give someone something that, you know, gives them the ability to lift up, you know, a 1000 kg with their left arm or something like that.

#### 49 49

# MAURO FERRARI DIRECTOR OF THE DIVISION OF NANOMEDICINE UNIVERSITY OF TEXAS

I am very optimistic about the future, in terms of the technical scientific challenges, I am very concerned about the challenges that have to do with access worldwide, because of course the the divide between the haves and the have nots in the world has gotten bigger as opposed to smaller over years and I think it takes guided efforts of the entire community and many leaders around the world and the people behind them to make sure the problems of access are dealt with, I think that's where we need the grounds'will of peoples' interest or community interest to force if you will, or to guide the leaders in the right direction, that is the gravest concern that I have.

#### 50 38

#### COMM

The ethical questions linked to nanotechnologies are not simply limited to insane stories of posthuman beings, with the abilities of science fiction movie heroes.

Universal access to new treatments, to cutting-edge technology, the development of new weapons, the emergence of new toxic risks...

The stakes are multiple, and high : social, economic, environmental, philosophical...

I can clearly see that at the same time as nanotechnologies progress, so do legitimate concerns and anxieties.

Everywhere, a certain tension is rising.

And everywhere, I have the feeling that the word nano is arousing less enthusiasm and more discomfort, even fear.

Although, everywhere again, discussions are being organised.

But are they not too late ?

It's time for me to pursue my exploration...

# TC OUT 51 25 END CREDITS ROLLING

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