



## THE CHARLIE ROSE SHOW

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### DISCUSSION WITH SIR PAUL NURSE

**CHARLIE ROSE, HOST:** Welcome to the broadcast. Tonight, all about science with Sir Paul Nurse. He is a Nobel laureate for study of how cells change. He is president of Rockefeller University.

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**PAUL NURSE, PRESIDENT, ROCKEFELLER UNIVERSITY:** Working out how these tens of thousands of gene products work together to produce the extraordinary activity that generates a human life, the beauty of it, everything about it, is going to be a fantastic challenge.

Now, why am I saying that in the context of medicine? I'm saying it because I do not think we really, truly understand very well many, many clinical conditions. I think we begin to understand them, but understanding how they work physiologically in the body, how they generate these disease functions, requires a lot of understanding. And I like these theoretical ways of thinking that I think are going to pop out really new ways that we can think about disease.

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**CHARLIE ROSE:** Paul Nurse for the hour, next.

(COMMERCIAL BREAK)

**CHARLIE ROSE:** Sir Paul Nurse is here. In 2001, he received the Nobel Prize in medicine for his work on the cell cycle of yeast. The research was conducted in the 1970s and 1980s, but since then has had serious implications for the study of cancer in humans. Until recently, Paul Nurse was the director general of Cancer Research U.K., United Kingdom's leading cancer research charity. In 2003, he joined Rockefeller University in Manhattan as its president. I am pleased to have him here for the first time in what I hope will be a series of

conversations as he and I together explore science and medicine and the future. Welcome.

**PAUL NURSE:** Thank you very much, Charlie. It's a pleasure to be here.

**CHARLIE ROSE:** Great to see you. Let's start with cancer where you won the Nobel -- received the Nobel Prize.

Where are we? Are we winning this war? Where are the important developments taking place, and what remains as the challenging difficulty?

**PAUL NURSE:** Let me start with talking about what cancer is, because if we can understand better what cancer is, we can talk more straightforwardly about the treatments and what we can do about it.

We're all made up of billions of cells. You and me and everybody else. And these cells grow and divide from one to two to four to eight to 16 and so on. So you go from a single-celled egg to an embryo to a baby to adults like you and me.

Now that's good. Growth and cell division is a very good thing. But when it occurs in the wrong place at the wrong time, that's when you get cancer. That's when you get a mass of dividing cells that are not in the normal place. They are going to occur somewhere where they shouldn't be dividing. They'll form a mass. And that will prevent normal function of the body happening.

That's when we get cancer. That's when it gets dangerous. And it gets very dangerous when those cells begin to slip away from the initial tumor, travel through the body, and then what we call metastasize, that is spread throughout the body and interfere with how we work properly. And that's, of course, the killer that we know as cancer.

So cancer itself is not just one disease. It's actually maybe as many as 200 different diseases, where, what happens is that cancer cells undergo certain genetic changes, changes in the genes that control what all cells do. And those lead to uncontrolled growth, uncontrolled division.

And there's different ways you can generate cancerous cells, which is why there's so many different cancers.

So the key, the real key here in cracking cancer is to get rid of those cancerous cells, by either cutting them out and getting rid of them by the conventional methods, or by finding new ways of blocking those genetic changes that cause cells to behave in a different sort of way. And that's what all the new drugs and new treatments really are about.

**CHARLIE ROSE:** I'm going to get to some of those. But it's my understanding that the body's immune system cannot tell the difference between a cancerous cell and a normal cell.

**PAUL NURSE:** It's not quite true, but it is almost true. Because the cancerous cell is so closely related to our normal cells -- there's very few differences between a cancerous cell and our normal cell -- this is what makes cancer so difficult, because it's not like a bacterium, which is so different, and we can just make an antibiotic that can kill it. A cancerous cell is very similar. That means the immune system has great trouble telling any differences between a cancerous cell and a normal cell.

But you can get it to work. And one of the ways of treating cancer that's being investigated at the moment is to try and promote the immune system, so it can recognize those very tiny differences between a cancerous cell and a normal cell, so the whole energy of the immune system can be directed against the cancerous cell. And that is one of the more exciting possibilities I see in the future.

**CHARLIE ROSE:** And what's exciting to me in terms of what I understand, you received the Nobel Prize in 2001. Because you had studied over years how cells -- the cell cycle, how cells divide. And you looked at yeast.

**PAUL NURSE:** I looked at yeast. It doesn't sound very...

**CHARLIE ROSE:** Not many cells.

**PAUL NURSE:** No. Not very many cells.

**CHARLIE ROSE:** And humans have 100 billion cells.

**PAUL NURSE:** At least.

**CHARLIE ROSE:** At least. But the mechanism?

**PAUL NURSE:** Let's talk about yeast, because it doesn't sound very promising, does it?

**CHARLIE ROSE:** Not much.

**PAUL NURSE:** This very simple organism. It makes, you know, makes beer, makes wine, make bread. But how on earth can a yeast tell us anything about cancer?

The strange thing is that all life is inter-related. So a yeast cell in some real sense is not so dissimilar to one of the billions of cells in our bodies. And studying basic processes, like cell division in yeast, tells us a great deal about how similar processes work in a human cell.

**CHARLIE ROSE:** Go ahead.

**PAUL NURSE:** And those -- because yeast is so much easier to work with, you know, we can grow it in a test tube. It's fast. We can do fantastic genetics, we can play with the genes, and nobody gets excited or worried about us working with them, like they would do with mice or rats or other animals. It means we can do fantastically good experiments really rapidly, understanding basic processes in simple organisms like yeast or flies or worms, and then translating that knowledge rapidly to the situation in human beings. And that's a part of what my work was about.

**CHARLIE ROSE:** Why has it been so difficult? I mean, what is it about cancer that has made it so difficult -- I want to talk a bit about the drugs and some of the interesting things that's happened, especially with leukemia and some other areas. But why is it so hard?

**PAUL NURSE:** It's hard for the reason that you pointed out, really. The immune system can't easily tell the difference between a cancerous cell and a normal cell. Because a cancer cell is almost identical to a normal cell. We have maybe 25,000 genes making different gene products. And that's sort of what makes the cells work. A cancerous cell may only differ from a normal cell in five, 10 genes, maybe even less. So by far the majority, 25,900 and whatever it is, 90, of those genes are exactly the same.

So when you try and find a drug or a treatment that will kill the cancerous cell but leave the normal cell alive, that's fantastically difficult. That's why conventional treatments that we're all aware of have so many side effects, because the truth is, these treatments kill normal cells almost as much as they kill the cancerous cells. That's why our hair falls out when we have chemotherapy.

**CHARLIE ROSE:** Because it kills the cells that grow the hair?

**PAUL NURSE:** Exactly. You know, we have hairs coming out of the head. At the base of each of these hairs is a little growth of cells that generates the hair. And those growing cells get killed by the drug that is used also to kill the cancer. And that's why our hair falls out when we have chemotherapy.

**CHARLIE ROSE:** What's the likely next breakthrough? What's the big...

**PAUL NURSE:** I don't like talking about big breakthroughs. You know, I'm a scientist, I'm cautious and all of that. I prefer a different metaphor, if you don't mind. I prefer bricks

in the wall. What I see is gradual progress over the coming decades, one brick after another, making progress.

Now, if you ask me where do I think the general direction will be, well, there's a number of things. I'd like to talk a bit about prevention, because that's crucial. But let's just talk about, just for a moment, about if you have cancer, where are the new treatments going to come from?

Where they're going to come from is identifying those tiny differences that I've already mentioned, those specific -- those few genes that differ between a cancerous cell and a normal cell, finding out what is different about those genes, what different sorts of products are made that change the cell so it grows and divides out of control. And then directing drugs or treatments that specifically will go for those altered processes.

Let me give you an example. Many cells have what we call growth factor receptors on their surface. Growth factors are, as you could imagine, factors that promote growth. And the receptors are the elements on the surface of the cell that can detect those growth factors.

Now, when a cell grows and divides out of control, it often can be because you activate a signaling pathway which is normally activated by those growth factors or the growth factor receptors.

So one way we can actually get at a cancerous cell is to block that pathway that is activated by the growth factors. It sounds simple, but it is horrendously difficult to do. But the good thing is, we now know what targets to aim at. We now know what is going wrong in cancer so we can devise the new treatments to do. I think that's where the key for the future is going to be.

**CHARLIE ROSE:** Breast cancer.

**PAUL NURSE:** Breast cancer.

**CHARLIE ROSE:** Any interesting -- I just talked to on this program, Elizabeth Edwards, the wife of Senator John Edwards, the vice presidential nominee for the Democratic Party. She's getting the best treatment possible. And was telling me some of the interesting things that are taking place there. Is there hope there? I mean, what is going on that makes it -- I realize you're not a medical doctor. In fact, you're research. You came out of the research end of this. But you have a Ph.D. and you understand molecular structure.

**PAUL NURSE:** I do, yes.

Well, breast cancer is an interesting disease. First of all, we are seeing improvement. You know, I use this brick in the wall metaphor. And in the last 10 years, survival rates have improved. I mean, actually quite significantly. So it's better getting breast cancer now than even just 15 years ago.

**CHARLIE ROSE:** There's more hope now.

**PAUL NURSE:** Absolutely more hope. And I think it's worth emphasizing that, because simply fine-tuning present

treatments can do a lot. Working out, you know, exactly where you have the radio therapy, exactly the dosage you need with convention treatment, better surgery, that can do really a great deal.

But what are the sorts of things that are being talked about in breast cancer? First of all, we're getting much better at predicting those women who will get breast cancer, because of genetic factors, predisposition. Because we're beginning to know better those genes that can influence the onset of breast cancer. And indeed, there's been one new gene published in the last couple of months which adds to the three that were previously known before.

So that means we're going to be able to describe the cancer better.

Now, why is that important? I'll give you an example. Often chemotherapy is given to women after the surgery and after radio therapy. But some women do well, and others don't do so well. And chemotherapy is a nasty, nasty treatment.

We now know, by taking what we call a signature of the tumor, we can now identify which women will do better and which women will do worse with chemotherapy. And what we do is we take a sort of fingerprint of the activities of all those thousands of genes that are found in cells. And a number of them, 21 in a recent study, have been identified as the sort of signature of a tumor, which will be treated best by chemotherapy, and tumors that won't. (r)MDNM\_ And that means that when a physician is treating this disease, they can make a decision as to whether they give a woman chemotherapy or not, because they can already predict five years down the line which ones will do better.

Now, that's real progress. And that's happening now, and it's based on that basic knowledge.

**CHARLIE ROSE:** You have mentioned genes several times. How significant in terms of taking the knowledge and employing it in a significant and beneficial way has been mapping the human genome?

**PAUL NURSE:** Right. The human genome is really, really important, but it is only the first step. And sometimes our scientists and maybe our media people hype this stuff up just too much. Because this is a fantastic advance, but it is the first step.

Why do I say that? I use sometimes a metaphor to help explain this. It's like understanding a play. Before you can understand a play, you first have to have a list of the parts, a list of the actors. The parts that they're going to play in that play. That is the list of the human genome. Then you have to write the text. Now, you can't write the text unless you know who is going to play in it, but I tell you, you've only taken the first step by identifying the list of the characters that will be in that play.

I sometimes think of the human genome project as providing the list of the genes that we now have to work out, how does

all those 25,000 genes work together to produce the wonderful thing like you sitting there, the phenomenon of life?

**CHARLIE ROSE:** What is it -- there's also work being done by people like Lee Hood in Washington about process. What is the emphasis there, and how is it different?

**PAUL NURSE:** What people like Lee Hood and others are doing are recognizing that the many thousands of genes that I've been talking about that are all there, that have to operate to produce the functioning of a cell, the function of a tissue, the function of an organ, the function of a whole organism, that what we have to be able to do is to provide descriptions of how all those genes and what they produce are working. It's no good just understanding five or 10 or 20 of them, which is what classically most of us have done in the last 30 years or so.

What we have to be able to do is to describe the whole orchestra. We can't just listen to a couple of the first violins. We have to describe the whole orchestra.

Now, the real problem with this, I have to say, is will we be overwhelmed with description and not get the understanding that we need? Now, what do I mean by that sort of statement? What I mean is that describing how 25,000 things may be behaving going up and down or whatever is one thing. Trying to take that data and turn it into hypotheses and knowledge and understanding of the processes requires a lot of intellectual leg work, which I'm not sure we're so well prepared to do yet.

But there's many very good brains working on that problem. And I'm sure we'll gradually make progress in the coming years.

**CHARLIE ROSE:** In the most recent political campaign, we were still talking about molecular biology and cells, where you made your reputation. There was much discussion of stem cell. Without the political dimension, which we can go back to, because some people -- there is things happening in California, they had an initiative that passed and \$3.5 billion will be spent on stem cell. It's tied up in some battles out there. But that's a place where research will be taking place, because of state's money coming from a referendum.

Leaving aside the politics for a second, is the -- tell us about what you believe is the promise of stem cells and the reality of it, and what you think over the next 25 years might be possible?

**PAUL NURSE:** Let's start with just explaining what stem cells are. And then a little bit about what it might mean. What stem cells are, are cells which are capable of turning into many different types of cells, of constantly regenerating themselves, and then turning into blood cells, liver cells, kidney cells, and so on. This is embryonic stem cells.

So what you have there is a cell which can have many different fates.

Now, that is an embryonic stem cell. Later in the development of a human being, there will be what are called adult stem

cells, with have a much more limited potential, but can still self-rejuvenate and can produce cells of a particular tissue, like the skin or the liver or whatever. So there's two different sort of types, and then there's sort of range in between.

Now, why are these important? These are important because these cells can rejuvenate and regenerate and replace damaged tissue. If you cut yourself, then it will be stem cells that will actually produce the new cells that can heal that particular scar. Thinking about that, you can then imagine, if we have degeneration of the brain, because we have a neurodegenerative disease...

**CHARLIE ROSE:** Like Alzheimer's.

**PAUL NURSE:** For example. If we have the analogy of the cut, what you can imagine is, that damaged brain, if we can now put back into that brain stem cells that could turn into brain cells, we have the possibility of reforming and replacing those damaged tissues.

**CHARLIE ROSE:** Let me ask this one question there. Is it -- are most scientists who focus on this, those that are making this their life's work, whether it's Doug Melton at Harvard and Irv Weissman at Stanford and people at Rockefeller and other places, wherever they may be, are they relatively convinced that it's going to happen, that they will have the capacity to regenerate cells that through degeneration or whatever happens leads to Alzheimer's or leads to other kinds of degenerative diseases, and it's only a matter of time?

**PAUL NURSE:** Well, you've mentioned a list of excellent research workers. And I think there are very optimistic. I can give my own opinion, which, of course, I'm very happy to do.

**CHARLIE ROSE:** Go ahead.

**PAUL NURSE:** I think the answer will be yes. I can't be certain of that.

**CHARLIE ROSE:** Now, why might it not be true? What could go wrong?

**PAUL NURSE:** Well, it's a question of getting these things to work properly in the clinical setting, without any risks associated with it. You've got to go through that risk -- the science of it looks really good. The practice of it may turn out to be more difficult. We just have to be realistic about it.

But not to do would be really a disgrace. I mean, not to take it on and to try and deal and cure people who are suffering so much through these diseases.

**CHARLIE ROSE:** OK, but people -- the political question, people raise the fact that there's real questions about how many stem cell lines there were in the end in terms of when the president made his decision and how many are left, and whether we are going to be behind, and where there are scientists in the United Kingdom...

**PAUL NURSE:** For example.

**CHARLIE ROSE:** For example, are going to step forward and the United States might lose some of its scientific leadership. I mean, is that counterbalanced by what's happening at the Harvard Institute or not?

**PAUL NURSE:** Well, this is complex. Let's talk about this, because I think there's real...

**CHARLIE ROSE:** Because you're in the role of your leadership of a great institution.

**PAUL NURSE:** Yes, and we have stem cell research going on in Rockefeller University. The stem cell has real promise. We have to understand the biology better. We have to understand the clinical applications. I think in some years, we will start seeing clinical application. Can't be certain of that, but I think we should try it, so that's my starting position. Now...

**CHARLIE ROSE:** Is that 10 years or 15 years or what's your...

**PAUL NURSE:** It will certainly be 10 years. It always is, you know? One of the things that you ought to be careful of is people peddling cures in three years. It isn't like that. It will be 10 years.

**CHARLIE ROSE:** And another thing you have to be careful about is journalists looking for easy answers.

**PAUL NURSE:** Well, journalists, you know, they want a story. You know, they always push you. You know, is it three years, is it four years? But it will be 10, I think.

**CHARLIE ROSE:** It's certainly 10.

**PAUL NURSE:** Now, the politics of this is complicated. The so-called presidential or approved lines are getting smaller in number each year, because they're dying out.

**CHARLIE ROSE:** And there was some fear about they were contaminated.

**PAUL NURSE:** They're also contaminated. I mean, the problem is these have been generated in ways where you have to grow the human cells on mouse feeder cells. And then there's a risk of transferring viruses from mice to human.

Now, in fact, in my institution we have one researcher, Ali Brivanlou, who has devised a method, a chemical which will replace those mice cells. So he could make embryonic stem cells which are not contaminated by mice cells. He can do that now. But of course, he can't get federal funding for that. That's the reality of what we're doing.

**CHARLIE ROSE:** So his research...

**PAUL NURSE:** It could not be funded by the federal government, because it's banned under present regulations...

**CHARLIE ROSE:** So...

**PAUL NURSE:** ... and the present stem cells cannot be used for clinical activities because they're contaminated. That's just where we are.

**CHARLIE ROSE:** So science is made more difficult.

**PAUL NURSE:** It's made more difficult.

Now, Rockefeller is a highly distinguished institution. We have the muscle, the intellectual muscle to raise money from donors who are very generous to us, who recognize that there is real potential benefit here. So we do have private money, which will support that basic research.

Not all institutions are in that position. They can't do it. The Harvards of the world can do that. We can do that. California has now, of course, put in place major state funding which allows it.

But, you know, it doesn't seem to quite make sense to me, as not having been long in the U.S., that we seem to be sort of approaching this problem with one arm tied behind our back. I just really hope this is looked at again. I get a sense that it might be.

**CHARLIE ROSE:** I do too.

**PAUL NURSE:** I get a sense, a little sort of crack opening up there.

**CHARLIE ROSE:** I think I saw some statements coming out of the White House, I think by some of the scientific advisers, saying maybe we can look at this this way.

**PAUL NURSE:** And you know, we've got to help them -- we've got to help them move along graciously along that track.

**CHARLIE ROSE:** And you have Mrs. Reagan and others...

**PAUL NURSE:** Exactly.

**CHARLIE ROSE:** ... who have had personal tragedy out there, out front saying this is not about politics, and the political divide, you know, should stop here on that.

**PAUL NURSE:** Yes.

**CHARLIE ROSE:** But stem cell. What -- is there an -- what else like stem cell that we may not know about offers the kind of promise in the future as a dramatic scientific path to changing the fight against disease?

**PAUL NURSE:** Yes. Well...

**CHARLIE ROSE:** Is genetic engineering and genetic...

**PAUL NURSE:** I'm going to identify something that won't be immediately obvious, but I think it is important. And it's back to my distinction I was making a little while ago between description and understanding. I said a little while ago is that you're extraordinary. Not you as an individual, but

you as a living thing. The phenomena of life, of what we can do is just truly amazing. I mean, we're just a set of, you know, chemical reactions, you know, and we -- look what we can do.

Now, understanding that is not easy. This is very, very difficult. I mean, I work on yeast. It couldn't be simpler. And it is fantastically complicated, fantastically difficult. We have not solved the problem by sequencing the genome and identifying the genes. Working out how these tens of thousands of gene products work together to produce the extraordinary activity that generates a human life, the beauty of it, everything about it, is going to be a fantastic challenge.

Now, why am I saying that in the context of medicine? I'm saying it because I do not think we really, truly understand very well many, many clinical conditions. I think we begin to understand them. But understanding how they work physiologically in the body, how they generate these disease functions, requires a lot of understanding which will come out of these new ways. You mentioned Leroy Hood, for example. And I like these theoretical ways of thinking that I think are going to pop out really new ways that we can think about disease. It's not like it's sort of magic stem cells, it's a different type of answer. What I'm saying is out of understanding, which I think we're on the brink of, we're really going to see rapid progress.

**CHARLIE ROSE:** And my understanding is technology has added to the velocity of understanding in an extraordinary way.

**PAUL NURSE:** Let's think about it. We've got technology, as you mentioned. Fantastic microscopes, fantastic ways of identifying the shapes of molecules, ways of looking at how things work in living cells. We can make proteins colored, so we look down a microscope and we see red proteins, yellow proteins, green proteins buzzing around a cell in realtime. Not only is it beautiful, not only is it fantastic, but it puts a whole dimension of time and space into these studies that we've never had before.

This is going to lead to new understanding, those technologies. We have new thinking. New ways of thinking. Leroy Hood, putting everything together. The way of thinking of so-called systems biology. You may have heard some of the -- it's a bit of a buzz word, but how does a living system work? How does it all work together? This is an intellectual contribution, which goes with the technology.

And the third part is we are building on fantastically firm foundations. The last 50 years have seen enormous advances in molecular biology, cell biology and medicine. You know, really starting with the discovery of DNA, I have to say in my institute, Rockefeller, the structure of DNA, Watson and Crick, and the 50 years since then has put a fantastically firm foundation to understand how living things and disease works.

**CHARLIE ROSE:** Did you and Jim Watson get involved in something having to do with -- was it Gregor Mendel who did all the early stuff?

**PAUL NURSE:** Yeah. Well, Jim and myself are trustees for Mendel's monastery in Bruno. You know, Mendel was this monk, Gregor Mendel, in the 1860s.

**CHARLIE ROSE:** Who helped us dramatically understand genetics.

**PAUL NURSE:** He started genetics. Some monasteries were really intellectual. And they encouraged certain activities. This one encouraged science. He had a gigantic greenhouse -- I've seen the space where it is -- and he did lots of breeding of different plants, including peas. He discovered the concept of genes. He published it. And there was a huge silence. He published it in 1865, 1868. And it took until about 1904 until anybody took any notice of it.

He gave up science. He was an interesting character. Let me say something more about him. He was a meteorologist, a physicist. And he turned to biology, and he applied to biology the rigor that you see normally in the physical sciences. He counted what happened, he looked and found if you crossed two sorts of peas, you know, with red flowers or white flowers -- I'm inventing that, I can't remember quite what it was -- and then he looked what was in the first generation, and he counted how many different plants there were, what came in the second generation.

And this allowed him to identify nice ratios. And he realized that actually, what was determining whether you had a red flower or a white flower were particles, which were sort of inherited in an undivided sort of a way, from one generation to the next. These were genes, just abstract. Abstract thinking.

And then 30 years it took before anybody really fully understood it. And the word genetics was not invented until 40 years later. But he was the guy who did the first stuff. Fantastic, that.

**CHARLIE ROSE:** Yeah, what are you and Watson doing, though? Are you and Watson doing something to...

**PAUL NURSE:** Oh, yeah, I forgot, that's right. OK. What are Jim and I and a couple of others doing...

**CHARLIE ROSE:** Are you restoring the monastery or something like that?

**PAUL NURSE:** We're helping it. There are people locally in Austria -- and this is in, of course, the Czech Republic, in Bruno. And we both volunteered to help, put our names to it, and to do a little bit of work.

What we would like to see is the monastery restored, Mendel's museum maintained. There is a small museum there. Maybe have a conference center. But basically, this was one of the great intellectual discoveries of all time. And yet the place where it was -- and it's actually a beautiful little monastery, baroque monastery too -- yet we're not taking care of it. Now, if you took a painting, you know, Cezanne, you know, everybody would want to keep it, quite rightly. Yet here we have one of the places where a great scientific

discovery was made, and it was going into decay. That isn't right, you know?

**CHARLIE ROSE:** So you've stopped that, or you're in the process of stopping that.

**PAUL NURSE:** We are in the process of stopping it, we're in the process of ensuring that it becomes a proper homage to a great scientist.

**CHARLIE ROSE:** Before I go to other sciences, a couple of things about, one, I forgot to talk a little bit about Gleevec, and -- which is, you know, cancer. It's a means of treating...

**PAUL NURSE:** Gleevec is -- I explained a little earlier about how the key with cancer was to get at the specific differences between normal cells and cancerous cells. And I mentioned signaling pathways. Signaling pathways that promote cancerous growth. Gleevec is a drug that's been designed to specifically inhibit a gene that's become rearranged in cancerous cells to inhibit the product, the protein that's made by that rearranged gene. It's something call a protein kinase. It doesn't matter quite what it does, but the drug precisely fits that particular altered protein. Just like in one of these children's toys, you know, where you put sort of different colored objects of different shapes through holes. And it precisely fits the cancerous type of protein that is made in those cells, so it stops it working.

**CHARLIE ROSE:** So you can target.

**PAUL NURSE:** Absolutely specifically target the changed gene product that is causing the cancer in these sorts of leukemias.

**CHARLIE ROSE:** And if they can do with that Gleevec and leukemia, they can do it...

**PAUL NURSE:** It's a paradigm shift. Do it there, in principle you can do it everywhere. And it's just a question of getting the knowledge and learning how to apply it.

**CHARLIE ROSE:** There's some other interesting ideas about being able to shrink vessels. How does that work?

**PAUL NURSE:** Right. This works a bit in a slightly different sort of a way. It's the same principle, in the sense of trying to get specific chemicals that will alter or change the situation in the vicinity of a tumor. But what this is doing is the following. When you have a tumor, it will grow for a while without much supporting blood vessels. But then once it gets beyond a certain size, you need blood vessels to invest into the tumors to provide the oxygen and the nutrients it needs, for the tumor to grow. Otherwise, it will just stop as a small sort of mass of cells.

If you can block those blood vessels being formed, then you will block the growth of that tumor. And because we know now through molecular biology and genetics what the factors are that promote blood vessel growth, then this allows us to identify targets that if we can block and inhibit, then we can prevent the tumor getting very large.

Now, there was a lot of excitement about this a year or two ago. It's a good approach. It's still in sort of clinical testing. It's not yet there. But I think there's real promise in that approach as well.

**CHARLIE ROSE:** OK. There is finally this: Vaccines. All of us know of what the Salk polio vaccine did. And there has been forever a great desire, even Jonas Salk worked on this, to no success, I think, a vaccine for AIDS, for HIV virus. Is that an area of research in cancer?

**PAUL NURSE:** Yes, it is. It is. And people are approaching it in two different ways. As a way of preventing the disease, and then as a way of treating, a therapeutic vaccine.

So let's talk about prevention. There are some cancers where infectious agents are important. For example, cervical cancer, there is a virus. I think it counts for about two-thirds of cervical cancers. And if that virus can be stopped, then you dramatically reduce the onset of cervical cancer, which is a very nasty disease.

And there are now vaccines that have been developed that will knock out, prevent infections from the two commonest HPV, which is this type of virus, that are there.

So these two HPV viruses can be stopped. And those women will not get cervical cancer, or it's much, much reduced. So the notion here is that if you vaccinate young women, before sexual contact, then you will prevent them getting cervical cancer. And this can have a dramatic effect. So that's the preventive type of vaccine.

But vaccines are also being developed to treat cancers. And the way they work is to actually promote the immune system to attack cancerous cells. And so what you do is you introduce a vaccine to encourage the immune system to attack those cancerous cells.

Now, as well as vaccines, we shouldn't forget just straightforward prevention, you know, because we can often get very excited by this high-tech and science stuff, which is really good, but it's also really important to understand the causal factors of cancer that ordinary Joe and Joanna Public can just avoid. And the big success story there...

**CHARLIE ROSE:** Smoking.

**PAUL NURSE:** ... (UNINTELLIGIBLE) is tobacco. And that will have -- if we could just stop tobacco, this would have a huge effect on the number...

**CHARLIE ROSE:** What is it that tobacco does?

**PAUL NURSE:** Tobacco -- people often get the nicotine in tobacco confused with the cancer-forming components. Tobacco...

**CHARLIE ROSE:** Smoking is carcinogenic in...

**PAUL NURSE:** Exactly. Tobacco has got nicotine, which is highly addictive. Really, really addictive. So that is what keeps you sort of smoking. And then there are other chemicals in the tobacco which causes cancer, so you have a sort of double whammy. You can't stop, and all the time you're taking in these carcinogens and making cancerous cells. So stop smoking, fantastic reduction in lung cancer.

The other causal factor that is easy to avoid is the sun. If you go to Australia, for example, on the gold coast, in those regions, skin cancer is now I believe after car accidents the second biggest killer of young people under the age of 30. And that's because of the sort of sun culture, sun worship culture that's there.

Avoiding exposure to sun will avoid much of skin cancer. Not all, but much of it.

Now, when we get to other causes of cancer, it gets very complicated, both difficult to do the research and difficult to fight off those that are convinced that they have discovered the cause. And this is really difficult territory. There's lots of cranks about who are convinced that this causes cancer or that causes cancer. There's a lot of research which isn't that great, which says this causes cancer and that doesn't.

But if we could understand the factors in diet that are important for cancer and other factors about our lifestyles, that's very important.

Let's take breast cancer, which is so important. Oriental women in China, for example, have very low incidence of breast cancer. Take them here to the U.S., their granddaughters, breast cancer incidence will be much increased. This has nothing to do with...

**CHARLIE ROSE:** And the only difference is the diet.

**PAUL NURSE:** Something to do with the lifestyle. It may be diet.

**CHARLIE ROSE:** Maybe stress or something.

**PAUL NURSE:** People think it could be fat content, but it's probably correlated with mobile phones as well. What I mean is, it's very difficult with epidemiological studies, as these are called, population-based studies, because there's so many differences between a woman living in rural China and a woman living in San Francisco. And trying to work out what the causal factors are is really tough.

**CHARLIE ROSE:** There have been some articles in national magazines, "Time," "Newsweek," whichever, and "U.S. News and World Report" and others about stress, and how is it that stress affects your health?

**PAUL NURSE:** Yes....

**CHARLIE ROSE:** Does it affect cells? Does it?

**PAUL NURSE:** You know, this is quite difficult. I sit a little bit on the fence over this one. I think the traditional scientific

response to that would be that there's really very little evidence in favor of stress. And it's certainly difficult to sort out. But I could imagine stress influencing cells a bit. I wouldn't rule it totally out, but I think we need rather -- in fact, a lot better evidence than what we have there. It could affect, but I'm not convinced one way or the other just at the moment.

**CHARLIE ROSE:** Because in some cases, we don't know why cells go bad.

**PAUL NURSE:** No, we don't. We don't. Well, you know, cells -- why do cells go bad in cancer? Let's just think about that. Most people think there has to be a cause, like sort of exposure to sun or you ate something. The fact is, it could be just the natural changes that occur in cells. You know, our billions of cells are growing and dividing all the time in our body. Sometimes they make mistakes. If they make the mistakes, they can make a cancer cell.

**CHARLIE ROSE:** Then they become abnormal, then they become...

**PAUL NURSE:** And there's nothing we can do to avoid that. You know, we could eat the most perfect food, avoid the sun, never smoke. We'll still have cancer. We can't avoid it altogether.

**CHARLIE ROSE:** All right. Let me move -- I'm often accused by my friends in the world of science of being too focused on molecular biology, which is your area. And that's what stem cells are about, that's what genomics is about, and that's what genetics is about, you know. I also know that over at the Rockefeller University on the roof there, you have -- you look at the sky.

**PAUL NURSE:** It's true. Yes.

**CHARLIE ROSE:** And you are a kind of amateur astronomer.

**PAUL NURSE:** It's true. Yes.

**CHARLIE ROSE:** What's going on with respect to the universe that's of note in recent times?

**PAUL NURSE:** Yes. I am an amateur astronomer. But let's first of all put that -- I just like looking at these things because they're beautiful. I'm not involved in serious studies. I like looking up and seeing the rings around Saturn. And what I know is that any kid in New York City, you know, if they could persuade their parents, a couple of hundreds of dollars...

**CHARLIE ROSE:** A little telescope.

**PAUL NURSE:** ... a little telescope, they will see the rings around Saturn.

**CHARLIE ROSE:** Now, what would they see?

**PAUL NURSE:** They will see -- if you look at it, it's magical. You go look up there, and you've got this black sky, and there will be a star up there, that looks just like any of the other stars. You get a telescope on it, and you'll see this little creamy ball, and then these rings around it.

Now they don't look like NASA photographs, of course. It's not the sort of gigantic orb with these rings, but you can see it with this couple of hundred dollar telescope, and your son or daughter could look up there and see this. And it's a revelation to them. They can look at Jupiter. Jupiter, the moons, there's four moons you can see going around Jupiter. And that led to Galileo being shown the instruments of torture, because it led him to really push the fact that the sun wasn't the center of the Solar System. Any 10-year-old kid can look from New York City and see it.

**CHARLIE ROSE:** And see it. Yeah. Anything going on in the universe? Are we making any discoveries?

**PAUL NURSE:** No, I'm interested in that too. And I mean, I'm not an expert about this, but I mean, one thing I read about recently, which I think completely fantastic, because anything that has to do with cosmology and so on is so interesting, sort of into the origins of the universe and all those mysteries. And as you know, if you look further...

**CHARLIE ROSE:** Wait, let me interrupt you. And you find out, for example, that Stephen Hawking just changed his ideas.

**PAUL NURSE:** He did. He did.

**CHARLIE ROSE:** About some -- but go ahead.

**PAUL NURSE:** He had some idea and he had some...

**CHARLIE ROSE:** About black holes and...

**PAUL NURSE:** (UNINTELLIGIBLE) 25 years ago. It's a bit arcane for me, I have to say, but there was something in there, and...

**CHARLIE ROSE:** It just shows you...

**PAUL NURSE:** ... he bought a pint of beer or something for somebody.

**CHARLIE ROSE:** ... that great ideas and great minds change.

**PAUL NURSE:** Of course they do. We'll get back to the -- science is, you know, the way we're taught science in school, it's like it's chiseled in stone. At the level of research -- I always use the word it's tentative knowledge. You know, you're reaching out there, and you don't quite know. It isn't -- it isn't shameful to get things wrong when you're at the edge of knowledge. And you do get things wrong.

And one of the problems we have is that scientists, research scientists know this all the time. But the politicians and maybe the public look for certainties from science, because,

you know, Newton's laws of physics are certain. That's because they've been tested for 300 years. My discovery of last year is highly tentative. So if somebody wants to come out and know whether -- what a disease agent is, and, whether you know, mad cow disease can be controlled in a certain way, scientists often will only say, well, it could be like this, or like this, I don't really know. But the policy makers have to say, it's like this. You know?

**CHARLIE ROSE:** Right, right.

**PAUL NURSE:** And this is some of the tensions that you see between science and society, which are very interesting, and maybe things we can talk about.

**CHARLIE ROSE:** That's a whole area you're interested in, and we'll do a whole program about that later. But just give me a brief look at what it is about science and society that you are...

**PAUL NURSE:** Oh, I must go back to cosmology, because there's one thing I wanted to say. But the science and society thing is I think that our whole society and community is based on science. You know, everything, you know, we're sitting here in a studio. None of it would work without science. We take it all for granted.

I feel that democratic decisions increasingly are influenced by scientific issues, yet they're hugely complex. How do we deal in a democracy with highly complex issues, which the public have got to have a position on, or at least a process that they trust, which may be in fact the answer that will come to decisions, because we need to take on board stem cells, and we need to take on board global warming. We need to take on these big issues that often touch long established beliefs, often religious beliefs, often cultural beliefs. And if we can't deal with this, we're going to find that we can't harness science to the benefit of society, and that will drive wealth creation and health and protection of the environment. And we'll find these things slipping away. It's a really important issue.

**CHARLIE ROSE:** Any initiative you see in terms of people seriously thinking about this, either in the United Kingdom or here?

**PAUL NURSE:** I'm a bit more familiar in the U.K., just simply because I had a more important role there. What I think is very encouraging is an increasing dialogue between scientists and policy makers and the general public.

You know, we had an example. It wasn't such an issue in the United States. It was in the U.K. It's actually interesting why different things become issues in different places. This is GM crops, genetically modified crops. And this has gone -- this has been -- this is completely off the agenda now in the U.K., almost impossible to grow any GM crops.

Now, what happened is that the public didn't like them. But nobody talked to the public about what the issues were. And in some of the postmortem discussions, it emerged that the public -- one of the reasons they really were antagonistic to GM crops is that because the plants had genes in them.

Now, a scientist would never even think of that as an issue, because scientists know that all plants have thousands of genes in them. But if you were a, you know, Joe Public looking at the issue, genetically modified plants had genes added to them...

**CHARLIE ROSE:** And they don't want to be eating genes.

**PAUL NURSE:** And they don't want to be eating genes. The fact that they eat genes all the time was not made clear to them.

**CHARLIE ROSE:** So it's a public education thing.

**PAUL NURSE:** It's partly education, but it's partly the dialogue with them, to know what they need to be educated in. And just asking the eggheads, you know, people like me is no good at all.

**CHARLIE ROSE:** Yeah, exactly.

**PAUL NURSE:** You know, you got to get out there and find out what people...

**CHARLIE ROSE:** The people who talk to the people.

**PAUL NURSE:** Exactly. And we're seeing more of that, and that's a good thing.

**CHARLIE ROSE:** Cosmology before we leave.

**PAUL NURSE:** Cosmology. One of the things that I read recently was that they discovered a add black hole, a billion times the size of the sun, or mass of the sun. You know, black holes is where you have so much mass that light can't escape. It's one of these scary sort of concepts.

And this has been discovered, it's huge, absolutely gigantic. But it's been discovered 12.7 billion light years away. Now, I think as you probably know, as you look further and further away in space, you are looking back in time, because time -- light takes time to travel to you. So as you look further and further away in space, that light started traveling a long time ago.

Now, 12.7 billion light years means that the light from that facility of the -- in fact, it's not light. It's X-rays that comes from that black hole. Started their journey to Earth 12.7 billion light years ago. The origin of the universe is thought to be about 13, 13.7. We are looking almost at the origin of the universe.

That's one thing. Secondly, we've got this gigantic black hole that must have been formed right at the beginning of the origin of the universe. And so the same sort of physics that was sort of going on there as goes on now, we're looking at the beginning of time. It just -- it just blows my mind away.

**CHARLIE ROSE:** I just can't get my mind around that. I mean, just impossible.

Finally, there is archaeology, which is within the scientific discipline. I find myself never being able to keep score. There was this recent story about skeletons of a hobbit-like species of humans that grew no longer than 3-year-old modern child. You know? I realize this is not your field, but your curiosity seems to be unbounded.

**PAUL NURSE:** Oh, no, I'm really interested in this.

**CHARLIE ROSE:** What was this about?

**PAUL NURSE:** Well, this was discovered on the island of Flores in Indonesia. I think that's how it's pronounced, I've only read, I've not heard about it.

This was a human-like species, as you've said, only three feet tall.

**CHARLIE ROSE:** Yeah, right...

**PAUL NURSE:** So tiny.

**CHARLIE ROSE:** ... small modern child.

**PAUL NURSE:** This specimen, it's a female, a woman, was discovered, I mean, in the last year, completely unexpected. And it indicates -- this specimen is only 18,000 years old. And there's evidence that there's other skeletons on that island, I believe, which are only 12,000 or 13,000 years old.

This meant that this little hobbit-like humanoid was living together with humans, because humans were on that island from 50,000 years ago. So our close relatives, you know, just back a few generations, were living with hobbits. And now you think of all those myths that we have about dwarves and little people, maybe, maybe somewhere in this collective mythological history we have, there were little people like this, like the Flores hominid. And that they have persisted in our myths ever since that time. I mean, it's just so interesting.

**CHARLIE ROSE:** You talked about society and science. There is also this, that seems to be in some places have some ascendancy. It is religion and science, and religion and public policy. Whether it's in the Middle East, or whether it's in America.

**PAUL NURSE:** Yes. Religion and science have always had sort of somewhat of an uneasy relationship.

**CHARLIE ROSE:** One based on faith and one was based on...

**PAUL NURSE:** That -- we start with the fact that science is basically skeptical.

**CHARLIE ROSE:** Right. It says show me.

**PAUL NURSE:** You know, when I have my students, I say, when you have a theory, you have to be the worst enemy of your own theory. You have to have skepticism. Whereas, of course, religion, you look for certainties. And you look on

faith to -- look at declared knowledge, whereas scientists are looking for evidence of knowledge.

So this is a different way of thinking. And there is always a tension there. But in a sense, to some extent they should occupy different domains. I think where we get the problem is where they end up in the same domains, which is in part due to the stem cell issue.

When we come to certain questions, science has some trouble. I'm going to start with, in one real key issue is origins. Science has a real problem with the origin of the universe. We can say there's a big bang that produces the matter. That's fantastically interesting, but what was there before the big bang? How did matter come out of nothing?

**CHARLIE ROSE:** Science doesn't know.

**PAUL NURSE:** What is nothing? Science can't help us there. We may do better. So origins is a real one that is I think probably largely in the domain of -- we don't do also so well in science, though we have stamped at it with sort of moral and ethical codes and so on, you can go a little bit down that route with sort of ideas of altruism and so on, but the truth is that we have different cultures with different belief systems, and these are often largely shaped by religion, and people have different beliefs. I'm all for keeping a good relationship between religion and science.

**CHARLIE ROSE:** And dialogue, or just relationship?

**PAUL NURSE:** Well, dialogue in a sense that we don't want to -- we don't -- I certainly don't want to derail science. And I don't want to challenge people who have such strong religious beliefs that they get offended by things that some scientists can say. Let's try and see whether we can work together on these issues.

**CHARLIE ROSE:** On a parallel track.

**PAUL NURSE:** And make some progress there.

**CHARLIE ROSE:** Now, when you won the -- when you received -- I always remember that it's Medal of Honor and especially they always say they didn't win it, they received it, or were awarded it. The Nobel Prize. Now, is this a true story that it was somewhere -- maybe that monastery. I've forgotten where you were. Somebody was on the phone...

(CROSSTALK)

**CHARLIE ROSE:** ... somebody was on the phone, and it's so crackling, your emotion is I may be but maybe not.

**PAUL NURSE:** No, you're right.

**CHARLIE ROSE:** Have received the Nobel Prize.

**PAUL NURSE:** This is true. It's not quite like that. Actually, I was at a meeting. I was with Jim, and we were talking about the Bruno monastery, in fact. And because I'm aged -- over 50, my mobile phone is always off. You know

you can tell the ages of people by whether their mobile phone is on or off. And I had a message from outside of the office. Is, could I turn my mobile phone on? So I went out into the corridor, switched on my phone. And I had a voice message. It wasn't a real living person. And it was crackly. And it was a Swedish accent, which is sort of a bit like sort of English with a hot potato in the mouth. You know? And I listened to this. And I heard the word Nobel Prize. I got a bit excited at that.

And I didn't quite catch it all, because then I had to replay the whole thing again, because I'm not good at this sort of stuff. And in the end, I thought, I think I've got one, but I'm not absolutely certain. I better get back to the office and make the phone call.

And I went back into this room, and I said exactly that. I'm sorry, I've got to go, because I think I've won a Nobel Prize. Then I thought as I went out the door, that was really stupid.

**CHARLIE ROSE:** Yes, exactly.

A couple more things before we go here. One is that this notion of you spent a good portion of your life in research. And what's fascinating -- and I don't want to get into this too much -- but part of your discovery was by accident. You looked at some effect that you weren't necessarily looking for, and you understood the consequences of the effect, and were able to build on that. Am I right?

**PAUL NURSE:** You're absolutely right. And I'm actually a great believer in nature taking you in the right direction. The mind is very inventive. We can invent all sorts of hypotheses and ways of thinking about things. And we need discipline. And the discipline we need is reality. In my case, nature, biology, how it works.

What I saw by accident was something under the microscope which I hadn't expected, but when I saw it, it immediately made me think, what does this mean? So it wasn't that I was imposing upon nature a way of thinking about it. What I was doing was seeing something that nature did, and then trying to understand it.

**CHARLIE ROSE:** What I like about that idea translated to my own life is that you're open to the unexpected.

**PAUL NURSE:** Absolutely, because you know, unless you do things like that, you'd just rediscover what's been discovered before. And here, nature is leading you. You know, it's saying, look, go here, and you'll discover something.

**CHARLIE ROSE:** So you spent most of your life trying to understand the cell cycle and were awarded for your efforts. What's the goal now for Paul Nurse? I mean, you know, you're one of those people who don't put the sir in front of your name. A lot of other people I know, you know, and you're as proud as they are, you know, want to do it. That's individual choice. But you spent your life there, in Britain, as a very successful research scientist.

So what's the goal now? What is it? There you had an end goal. You were trying to understand better than anyone else, for the benefit of humankind, cell cycle. With all the ramifications, for cancer and everything else.

**PAUL NURSE:** Well, I think I have two objectives now. One is still with my own science. You know, I'm not quite over the hill. I'm probably on a gentle descent, but I'm not quite over the hill. And I'm particularly interested in cell shape. How a cell organizes itself in space. I mean, how does it have an internal map of itself? How does it know what's the top, the bottom, left, the right, its middle?

And this is important not only as a basic biological problem, because all living things have characteristic shapes. You know, you can always recognize a human or a tree or a flower because of that. It's also important for cancer too, because when a cancer cell spreads, it changes its shape and escapes the tissue. So I think this is going to be a fundamental problem as well.

I want to pursue a set of problems of which this is a major one -- it's not the only one -- whilst I think I still have something important to contribute.

The second thing I do is I want to build institutions that encourage the highest quality of research, that will encourage young researchers to take on the big problems, to be bold and innovative, and come and just reach, reach for the skies. And that is the second thing I get satisfaction from. That's what I'm also trying to do at Rockefeller University. Great institution, where I can attract great minds, great people to actually work on very important problems.

**CHARLIE ROSE:** Thank you for this. I've loved the conversation.

**PAUL NURSE:** Thank you. It's been a pleasure.

**CHARLIE ROSE:** Paul Nurse is president of Rockefeller University, a distinguished career in science. Came here, what, about a year ago, wasn't it?

**PAUL NURSE:** Yes, a year ago.

**CHARLIE ROSE:** From a leading research position, was formerly a professor, had a chair at Oxford University. Is a well known glider and has many other obvious interests and curiosities, as we have seen on this program.

Thank you for joining us. See you next time.

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