Transcript

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PROFESSOR AXEL ULLRICH, DIRECTOR, MOLECULAR BIOLOGY AT MAX PLANCK INSTITUTE IN GERMANY

CHAIR: Ladies and Gentlemen welcome to the National Press Club and this National Australia Bank Address. It's a great pleasure to welcome Professor Axel Ullrich here today. He's one of the most distinguished Molecular Biologists in the world and has been responsible for some major discoveries and some major commercialisations of discoveries and he'll talk about that process a little later. He's also been awarded the Medal, the Annual Medal of the Australian Society for Medical Research this year and he's about to be presented with it by Professor Warwick Anderson, the Chief Executive Officer of the National Health and Medical Research Council and that's one of the reasons that he's in the country - he's - the Medalists don't get it easy. I mean they do a pretty tough tour to accompany their presentation of the Medal, but Professor Anderson will present the Medal to start off. ... anyway. And after that Professor Ullrich will go on to talk about his views about current

levels of research and where they might lead. Professor Anderson, would you like to start.

[Applause]

PROFESSOR ANDERSON: Well thank you Ken and I must say it gives me a great deal of pleasure to be able to present the 2007 Australian Society of Medical Research Medal to really one of the truly outstanding international health and medical research leaders.

For those that don't know, the Australian Society of Medical Research is one of those organisations that if it didn't exist, we'd have to invent it. They do tremendous work throughout the year making sure that the message of the importance of research to the benefit of the health of Australians is there at the forefront of Australians' consciousness and it's an organisation that's always been led by young researchers and people only stay in the [indistinct] one year so Maria, six months to go or something like that and Maria Kavallaris has been doing a wonderful job.

Dr Axel Ullrich is internationally recognised by citations which we scientists use as the ultimate recognition of the value of their work, amongst the top few in the entire world.

Added to that he has been involved in three discoveries which have led to products that have direct benefit to human health. Initially Humulin

which is human insulin for the treatment of Diabetes from gene technology. Then Herceptin which has been much in the news here in Australia over recent years. This last year and a very pivotal discovery there too that led to the drug. And recently, he has been involved in the development of another cancer drug, a protein kinase inhibitor, for the scientists in the audience, which is making its way also through the process.

He's recently been named as one of the top twenty-five European tech leaders changing the way we live, work and play and I think that's what research does. It's live, work and play. He's currently the Director of the Department of Molecular Biology at one of the Max Planck Institutes in Germany.

He's here for all the medical research work as Ken said, about three-fifths of the way through, it's a gruelling - is a gruelling schedule but we very appreciate your willingness to do this on behalf of ASMR.

Professor Ullrich it gives me great pleasure to present you with the 2007 ASMR Medal.

[Applause]

PROFESSOR ULLRICH: Ladies and gentlemen. It's a great pleasure and a particular honour that I'm now standing here in front of you after I've already given a few talks in difference places in Australia, and finally here it is,

the Medal. This makes me very happy and I really am grateful to the Australian Society for Medical Research for selecting me this year to be the recipient of this honour. I hope you, you think - you will think also after my presentation that I deserve it and I will talk about work that I have done essentially over the past thirty years and for that I have about twenty-five minutes, so I guess I will rush a little bit through it and concentrate on the subject of cancer.

Will there be a magic bullet for the treatment of cancer?

Well you would like of course me to answer this question with yes and right here at the beginning I would like to say that there are very good signs now that this, that developments that we have now brought underway are going to lead to fundamental changes in the treatment of cancer.

Cancer is still one of the biggest problems of mankind. Every fourth person that dies, dies of cancer. This is frustrating because we have, we scientists have realised and recognised this problem many years ago actually in the nineteenth century already this problem was realised and scientists, famous scientists like Robert Koch would [indistinct] in Europe - they discussed the problem whether it will ever be possible to treat cancer.

At that time there were not many possibilities but one imminent mind named Polieshi designed at that time already a new concept, a so-called magic bullet concept which was not named that way in the late 1800s but it was essentially what we are calling today targetted therapy. Not only for cancer but also for other diseases.

This was established in the beginning of the twentieth century when Paul Ehrlich received the Nobel Prize for developing a drug for the treatment of syphilis salvasan. He received the Nobel Prize in 1908 and he wrote a book about applying the same concept, namely sythesising small molecules, small chemicals for the treatment of diseases. Chemicals that will no harm to the healthy issue but will destroy, optimally destroy the sick and infected or abnormal cells in the body.

Well for infectious disease he was successful, but for cancer this was much too early. Had to take a few more years and scientific breakthroughs in order to prepare the ground work for the application of this magic bullet concept.

Now this, as I said, it took a few years, it essentially until now, until recent history that we were not really able to treat cancer in this - with this magic bullet concept, just targetted therapeutic because we didn't understand enough about cancer. Cancer is an incredibly complex disease and understanding the molecular basis, molecular defects in cancer cells is

absolutely essential to apply this targetted therapy to the treatment of this disease.

There in one break through was in - that I will tell you about in more detail - is represented by the treatment by the, by the therapeutic Herceptin.

Herceptin is a so-called anti-body, a protein that has the ability to recognise a specific molecule in the body, another mocecule and bind it and thereby bock its function. The way Herceptin was developed - it took many years and it began essentially in 1984 with a project that I did in collaboration with European and American scientists that led to the discovery of a genetic defect in breast cancer.

Genetic defect only in the tumour cells. One gene that we had isolated and identified called HER2 was found to be over-produced in breast cancer cells. Not in all breast cancers but in 30% of all tumors and that the extent of over-production due to gene amplification in these cells was directly correlated with the progression of disease. So the more amplified the more of this molecule was produced, the more aggressive the tumor was.

So at that time in 1984 a very important field that we call signal transduction research, that essentially includes the, the analysis of mechanisms of communication between cells and our body. Our body is made up of one hundred trillion cells, ten to

the fourteen cells. And these cells have to function properly, communicate with each other properly, perfectly, otherwise we cannot live healthily.

Defects in this communication mechanism on various levels cause disease. One very well known disease like that is diabetes. When there is not enough insulin which is a messenger molecule that will send messages from one cell to - to many other cells essentially also in the body. When there is not enough insulin and no more insulin, people get sick and get diabetes. But the porta typical signal transductional communication disease is cancer. Because many genes that make up our, our signal transduction network that is present in every cell and in our body to make it possible for cells to communicate with each other so every cell, the body knows what to do. When this mechanism fails and in cancer there are many possibilities for failure and all these, the genes that are involved in this - in these failures are call oncle genes or cancer genes.

So the - back to the dream of Paul Ehrlich developing targetted therapies is finding the right target to interfere with so that the cancer cell preferentially over healthy cells will be negatively effected, will be destroyed or in its function impaired.

So this is the concept. So now back to Herceptin. So we identified in the year - in 1985, a molecule that plays an important role in this communication

mechanism. Cells have to communicate with molecules that are secreted and produced by some cells and the message of this molecule will be received by other cells through receptors that are on the surface of that cell, like an antenna, and receive the message of this molecule by binding to this receptor. This interaction is translated into a signal inside the salvage ultimately will define the response of the cell.

So this receptor HER2 was identified to be over produced in cancer cells and in many experiments that took years we demonstrated that the [indistinct] gene amplification and over production is absolutely critical for the progression of the disease and therefore, and we demonstrated that, in vitro, therefore blocking the function of this molecule promised to be beneficial to patients.

So we generated this antibody that I mentioned already that is known as Herceptin or Trastuzumab and this antibody was tested in clinical trials between 1992 and 1998 when it was approved for the treatement of Metastatic cancer.

So this was the first example of such a targetted therapy for a major type of cancer. Breast cancer is, after lung cancer, the most frequent disease that effects women and every tenth woman in her lifetime will be effected by this terrible disease.

So Herceptin, an antibody, that only specifically targets this molecule, this oncle gene product in cancer cells. It has some side effects, very mild side effects for, for most patients, but we must realise that all these targets play also normal roles, also normal functions in healthy cells, so one has to expect some side effects. But in the case of Herceptin they are very mild and very well tolerated by patients.

So this was really a breakthrough and triggered many medical research developments on - various approaches, many targetted strategies have been designed and I would like to tell you now, a new step into a new sort of approach that is even more effective than the specific targetted therapy and this is the development of so-called multi targetted drugs and this pays tribute to the fact that over the past fifteen to twenty years we have learned that cancer is not a monogenic disease, a disease that is caused by a defect in only one gene, but by many genes are involved in this.

So many defects can lead to the same result and over the development the evolution of cancer, new defects accumulate and the cell becomes - the cancer cell becomes very flexible and difficult to attack because it can always so - sort of evade an attack by one target, which means by one drug which means it becomes resistant to that therapy.

So therefore this concept of either combination therapy, combining different kinds of drugs that different - that have different mechanisms of action or so-called multi targetted drugs is absolutely critical.

In 2001 one announcement actually in *Time Magazine* on the cover of *Time Magazine* was made that said 'New ammunition in the war against cancer'. The drug Glebic that was announced at that time to be approved by the FTA. So new ammunition against cancer in the war against cancer which was declared twenty years ago.

Thirty years ago, in 1971 by Richard Nixon, President of the United States. Well this was for a change a good war, or a good declaration of war but it cost also a lot of money. Since - I mean - Richard Nixon did this in order to get more money out of Congress to support cancer research, and actually since 1971 in the USA alone 250 Billion dollars have been raised to fight cancer. The war against cancer. But if one is honest, you know, below the line, there are not many drugs, new drugs. We have learned a tremendous amount about the mechanisms of cancer which are now becoming extremely important to develop new drugs, but over a long period of time there was no progress. Chemotherapy that was - had been used since the '50s with molecules which were essentially toxic, you know, poisons for the cells, especially the cells that were in the process of divisions, cell division and all organs where tissue regeneration is

necessary and the gastro intestinal tract and so on like the hair has to grow, this includes cell division and [indistinct] such processes in every second of our life, several million such cell divisions take place. So all these cells that divide are being killed by this chemotherapeutics. This causes these major side effects so now we want to find drugs that are really side effect poor and more efficacious than chemotherapy because chemotherapy in most cancer types, there are some that are actually cured by chemotherapy, but most especially the major cancers are not.

So, now the new developments started really in my laboratory in Europe at the Max Planck Institute of Biochemistry with one graduate student and she discovered a new of these - a new molecule, a receptor like this HER2 receptor and this - she could show that this receptor called Flk1 or VEGF receptor 2, VEGF R2, is critical for the process of new blood vessel formation. The process that's caused angigenesis.

In various situations we need to form new blood vessels for example in the process of wound healing. When you cut your finger in order to make it possible that the tissue heals and closes again, new blood vessels have to be formed. This includes the receptor VEGFR and the lingand, the growth factor that binds to the receptor called VEGF vascular endothelial growth factor.

So she demonstrated in a model experiment in a mouse model that in a - that a tumor that is implanted in mouse requires angigenesis new blood vessel at that one - when one blocks the function of this receptor that she has discovered, this process did not take place. There was no angigenesis. And this was the step, was the basis then for further development and in this case we didn't use an antibody but small chemicals - like predicted one hundred years earlier by Paul Ehrlich that one could develop such small molecules that can be taken like aspirin in form of a pill, swallowed and the patient has not to go into the stressful situation of a hospital but can take these pills at home.

So, this was the basis and the company that I had started just two years before that, together with a colleague Josef Schlessinger, the company was called Sugen, started to develop the screen for small molecules that inhibit the function, this angigenetic function of this receptor and the result was a drug that is called today Sutent or Sunitinib.

Now in the process of development, this drug or many different chemical drugs developed from a very specific, according - modelled after Herceptin because we wanted to be absolutely sure that there is no side effect or few side effects. It developed into something that we originally feared, we don't - didn't want the drug to be too unspecific because this could lead to side effects and we don't want new drugs that are as bad as the old chemotherapeutics. But surprisingly this drug that

came out now Sunitinib or Sutent is not unspecific but multi-specific. That means it blocks the function of many different such target molecules and nevertheless has a very low side effect profile.

Patients, the worst side effect is fatigue for patients, but this is compensated by extreme efficacy. The drug works extremely well in the treatment of kidney cancer, a cancer that until very recently was absolutely untreatable, even though doctors used in the [indistinct] for treating it but this was only expensive and not very successful.

So, Sunitinib has great effects, very strong remission effects in kidney carcinoma and a special kind of gastrointestinal cancer called GIST or gastrointestinal stromal tumors. Again, another tumor that was so far not treatable at all.

And now Sunitinib is really expanding its, its sort of field of application to breast cancer, liver cancer, again a very untreatable cancer, pancreatic carcinoma, that patients usually when they were diagnosed died within six months. [indistinct], same situation.

So here we have a drug that - that attacks tumors from many different sides including by anti angigenesis, blocking the formation of new blood vessels and attacking at the same time, vital function of cancer cells.

So, here we are, from Herceptin which is still very valuable being treated in - being used in treatments that are new and the treatment strategies are changing over and over as the more the doctors in the hospital are learning about the, the best way of using it. And I understand in Australia this antibody's also available to breast cancer patients in the pharmaceuticals benefit programme.

Now Sutent I hope, if it's not already available here in Australia, I hope it will be soon, because that together with some other drugs that are also in the pipelines of companies, there'll be a new era very soon, a new era of cancer treatment with drugs that attack tumors from various sides, molecular sides and they'll much more effective than everything that we have seen so far.

Now cancer research and medical research in general requires a few very important things. You know, dedicated scientists, a lot of money. Much of the money comes from companies that - the development of Sutent cost probably more than 1 Billion US dollars. So this has to come from somewhere but it takes also time already in the pre-clinical part of the development before it gets sort of in the hands of big pharma companies in academia, in small companies for example, in bio-tech companies, research, pre-clinical and fundamental research has to be done in order to develop these drugs and this is what ASMR is doing and I have learned now about some of these activities and already these kinds of events I think

all that is a great contribution against cancer and many other diseases.

So I wish all the best to the ASMR for the future and I hope that you, you will continue to believe that I deserve this wonderful Medal. Pretty good weight here and again, all the officials and organisers of this event here and the ASMR officials like Maria Kavallaris and Emma Parkinson-Lawrence, thanks very much and thank you for listening.

[Applause]

CHAIR: Thank you Professor. Stay there. We have a period of questions today. The first one comes from Maurice Reilly.

QUESTION: Welcome to the Press Club Professor. I've got two questions. You touched on about the level of Billions of dollars that have to go into research before - and there's long lead times before we get to, you know, drugs that work in the market place. The question I'm posing is there's a commercial interest and there's a public interest. We've seen the recent politics about drugs for Africa. The company dealing with the public relations issues of you know not providing drugs for Aids at an affordable rate that poor countries can afford. How do we strike this balance? I mean this is a, this is a common problem. We have governments who say you Mr Biotech company, your - it's too expensive, and I

mean, where do we find the balance between the legitimate public interest of these great new endeavours that we're finding and the commercial interest of a company? And you seemed like you'd worked on both sides, so I'd be really curious to see how you might analyse - the second question in a second.

PROFESSOR ULLRICH: Yeah, this question of course one could discuss for hours. You are right, I have worked on both sides. I worked for ten years for a company for Genentech. I founded four companies so, so I know that side pretty well. Making money is absolutely part of our - the nature of humans and I think it also provides a motivation, even though I honestly can say that I never did anything for money. I really had always the realisation of ideas of concepts in mind and this is still true today even in the companies that I started. But big pharma companies of course need motivation. You know, if you would take the profits away from them after they have invested a Billion dollars in the development of a drug, they will probably say next time okay let's close doors and we'll just not do this anymore. It actually is happening. I have experienced that myself. I started one company that was called [indistinct] for the development of drugs against infectious disease based on the same concept of cancer drug development. We had extreme difficulties finding money, venture capital money for that. And eventually the venture capital list closed the company because they said well the biggest - actually the infectious diseases are still

today the biggest killers of mankind - malaria, tuberculosis and Aids are really the biggest killers, you know, much bigger than cancer and cardiovascular disease. But this is poor people - so you know how can these people pay for the drugs? So that the investment comes back. This was the argument and there are some exceptions. There is the company Novartis from Switzerland which started an institute in Singapore that aims exactly at infectious disease. So there is as you say one has to find a balance between the, the cost of such development and the justified expectations of companies to get a return at least cover the cost and make some, some profit. Where it's excessive, - the profit is excessive there I think, governments have to sort of step in and have a look at that. But it will be difficult obviously. But I think, I think this is absolutely appropriate and only, only governments can sort of step in and regulate this. In the interface between companies, of course another possibility is that and which is actually starting to spread in academic institutions is that with the help of the government, of grants from the government, that sort of company like drug discover and drug development facilities are established in academic institutions. I was just in Sydney and I've heard that like at the Garvan Institute and in the Centenary Institute such efforts are being initiated. I think this is a fantastic way of counter-acting the, well the not so pleasant profit aspects and greediness of the big pharma companies if to say very bluntly. This is one way but it requires still money and I believe very firmly it does not require a Billion dollars for

one drug. One can make this, one can do this much, much cheaper. It costs 1 Billion dollar for Pfizer or for Roche because they are not - they are huge organization that are not efficient and they are wasting a lot of money. One can do the same thing also for 200 Million, but still it's a lot of money. And this is where the government has to step in as a public service in my opinion this is a very, very realistic, possible and also a good way to do.

CHAIR: Question two.

QUESTION CONT'D: Second question, on the war on cancer to use your words, how important is stem cell research and it's widely debated in this country and I imagine it's widely debated in Europe. Embryonic stem cell research and - for the non scientists who might be watching this, perhaps if you just explain the importance or the difference between embryonic and adult stem cells and how it might be important in the war against cancer and do you support it?

PROFESSOR ULLRICH: Well it, to say very briefly, at this point I don't consider it to be important at all. It has to do - I mean there is a dispute between different scientific, you know groups. One's a cancer, originally it's only from stem cells, others say they can originate from normal cells and the normal cells then [indistinct] to differentiate to look like a stem cell. This is a dispute which I think is futile because at the end, you know - at the moment when we diagnose cancer, the situation is already clear. It's

there and it doesn't really matter if it's a stem cell or another cell that became something like a stem cell that is now in place. The treatment is in both cases the same. So the stem, the stem cell issue does not only theoretically effect cancer research but not in the drug development area.

CHAIR: Professor, I'd like to remind our audience again that they're free to indicate their interest in asking a question to our colleague over here on my right, but in the meantime, let me just take you back to a point you made a moment ago. Diseases like malaria and tuberculosis still kill far more people than some of the more rarified versions of cancer. What do you think about the ethical division of resources between the two areas. I mean we've got the Gates Foundation, I've forgotten the actual figure, but they're giving a big donation now to malaria control. But in scientific terms that's relatively simple compared with what you're talking about. Why don't we do more about that?

PROFESSOR ULLRICH: Well that's a very good question and I try to do something, applying a new concept essentially using the same strategy, focusing on the same molecules that we use as targets for cancer, drug development, applying to infectious disease. We had, we had developed actually a, a - you know an early drug for the treatment of tuberculosis. We were underway to apply the same concept to malaria. But without funding you cannot really do that and it's very difficult to get this funding.

CHAIR: So you're suggesting the funding can only come from public sources?

PROFESSOR ULLRICH: Well from public - from the public, you cannot - at least in Germany it was impossible when we started doing this to get enough funding from public sources you can get. But usually these grants are relatively small. And, you know, malaria drug development is rather difficult because for clinical trials of course one has to go to Africa and so on so one has for that kind of thing - one needs really a company - small company at least that is well funded. It can be done but there's not much support for it. This is really terrible. I mean one example that is well known is Aids - Aids in Africa. That was solved by the sort of revolutionary step of some countries in Africa that say okay we make, we develop our own drug or we copy the drugs that are - have been developed by big pharma companies and we treat our people and I think this is absolutely justified and fair. This will happen with other - if there is a - if Sutent becomes really a magic bullet that destroys many cancers, I'm sure it will be copied and I would have absolutely no problems with that. So it's fair to do that but the profit aspect is at least a cost recovery aspect [indistinct].

CHAIR: Our next question's down here. I invite people to identify themselves if they think it's appropriate.

QUESTION: Congratulations Professor on your fantastic work and winning the ASMR Medal. I'm Mark Hewitt

from the John Curtin School of Medical Research. Just following on from the successful sequencing of the human genome, it's now financially viable to sequence an individual's entire genome. Can you comment on the potential for future applications of this technology in screening for cancer and also tailor making treatments for cancer?

PROFESSOR ULLRICH: Well this is of course also a very key issue in the diagnosis of pre-disposition of cancer for example but also in the treatment of cancer. Because a drug will not work the same way in every individual, in every cancer patient, even if they have the same cancer. First of all every cancer tumor is probably different from the other. Because of the great combination possibilities of genetic defects, probably all cancers are very different. Therefore, one development goes into individualised therapy. Individualised means [indistinct] I mean has to be a new drug developed for every cancer patient but different combination of drugs will be used in the future without any doubt. Different combinations of drugs for different individuals and into this information it is necessary to make the decision which treatment should be applied comes the genome, the genetic makeup of every individual. We are all humans, our genetic information, I mean our genome is probably almost identical. 99.9%. And we differ, you know, men differ from women pretty dramatically but among men and among women, you know the genetic sequences are very similar, but we differ from each other by so called polymorphisms, SNPs, Single Nucleotide

Polymorphisms. These Single Nucleotide Polymorphisms of which there are a few million probably, they're sort of sequence different as in our genomes. They make in percent not very much of a difference but the consequences are clear when I look round here, people look different. This is our individuality comes from SNPs. These little, tiny little differences. We have identified one of these SNPs in one again, one of these receptors, just one Nucleotide, one building block in three billion Nucleotides that make up our entire genetic information. And this one difference predisposes when a human being, one person, one individual gets cancer and has this abnormal or this SNP then it will develop cancer much faster than other people. So, taken together, this - these SNPs provide a tremendous amount of information and therefore I started a project that I'm carrying on in Singapore with a group - the Singapore OnOnco Genome project. There are many other projects ongoing in the same direction. So in the future, pathologists in the hospital when their patient comes in they will not only look at the tumor but also at the DNA characteristics of every individual. They will put all that together and decide then how to treat this patient and this is probably in twenty years or so we'll have this technology to do so and tailor made drugs together with a combination with other drugs, will definitely be the future.

CHAIR: Professor, could I just ask you on the other side of that question, how far would you take that process? I mean if you get down to individual gene

identification, what are the implications for individuals in terms of insurance, future medical treatment, privacy in the community? All of these things that are associated with it.

PROFESSOR ULLRICH: Yeah. This is obviously a very justified concern but it can be handled very easily I believe. This information - genetic information should not be available to insurance companies before some person gets sick. This would be bad. I mean this would definitely be - even though there is in the United States there are efforts underway to make exactly that possible. For insurance companies to be able to predict if somebody will get a certain disease or not and so on and thereby adjust you know cost of insurance policies also. I hope most companies will resist that but at the moment for cancer patients - at the moment you know, you have cancer and the doctor asks you would you like us to include your genetic data in the diagnosis and design of your treatment? I'm sure every cancer patient will agree. As long as the use of information became - remain confidential and every other - I mean, it's already today when you go to the doctor, what the doctor finds out is confidential, so doctors are obligated to be, to treat all the information secretly and confidentially so I think it can be handled. I cannot really see any circumstance at least in normal countries with democratic governments and so on that there's an abuse of this information.

CHAIR: Next question's down there ...

QUESTION: Maria Kavallaris, the Australian Society for Medical Rsearch. Professor I'd like to congratulate you on a great talk and also to tell you yes you are definitely deserving of the Medal. I just, I'd just like to ask you a question. I mean the multi targetted anti-cancer agents obviously are looking incredibly exciting. As someone who works in children's cancer research, I'd like to know whether you think there's some potential for these agents and the treatment of childhood cancer? There are as you know some specific childhood cancers like certain brain tumors, neuroblastoma and a few other aggressive childhood cancers that don't respond very well to current therapies. Do you think there's some promise for these agents given that they inhibit blood vessel formation and you've got growing children?

PROFESSOR ULLRICH: Well childhood cancer is of course a particular problem....also being treated as a very special problem by the regulatory agencies. That in order to get the drug approved for use in children you need to fulfill many more requirements and when you apply it to people that are eighty years old or sixty years old then and have cancer. So this is a big problem but it will be overcome I think because these new drugs are rather side effect free, there will be approvals for the treatment of also the childhood cancers. Fortunately as you know many of the childhood cancers, Leukemia, [indistinct] are treatable already today respond to chemotherapy, but not all as you say. So definitely this will be although I haven't really said anything yet about,

about side effects, long term side effects. We obviously don't know. I mean the most experience we have with [indistinct] which was introduced in the clinic in 19 - in 2001, there is obviously formation of resistance to this drug because of accumulated mutations in the target of, of the drug. Now this will happen, most likely, also with Sutent because there are many drugs, may be it takes a little longer - but one should, one also has to realise that many of these targetted molecules have important functions in many different, and many of them are not understood, in many organs and there could be in long term treatment, there could be side effects that do not occur right away, but in five years or in ten years. For example neuro degenerative effects could happen. So what - we have to be very, very watchful and, and I've spoken with many doctors about this and they are, they have not seen anything yet but it could happen. So, not only children, also adults have to deal with this problem and we will see but, but this is the good thing and of course then of companies that they - they are aware of this and they constantly develop second, third generation, fourth generation drugs and the same is happening for [indistinct] now in [indistinct].

CHAIR: Next question...

QUESTION: Peter Eastwood from the University of Western Australia. A continuation of the side effect theme. My question concerns the side effects and you described the, the nasty side effects of the original

chemotherapeutic drugs and then you went on to talk about the targetted, the mono-targetted approach, Herceptin being an example but there still are side effects of Herceptin and you proposed a future of, of therapy for cancer being multi-targetted approaches and I would have thought that with a multi-targetted approach you'd have more opportunities for side effects given you've got multiple approaches there. I just wonder if you'd comment on, on where we're going with side effects and mono versus multi - are we headed back towards the chemotherapeutic approach?

PROFESSOR ULLRICH: Well this is justified argument but I'd tell you right now if we knew better, we would do better things. We would use better strategies. The biggest hindrance in finding the optimal treatment is that we don't understand yet everything. So science is not far enough to really understand every function of every molecule even in the single transduction network. So we interfere with this and it's being done on an experimental basis. We have to be sometimes like to believe that we know a tremendous amount but I think we know only sort of the, the big picture maybe, but the details, especially in a human being. I mean we scientists, we do our experiments in vitro with cells and culture and so on. This is not representative. Even when you go into a mouse, it's not represented if you cannot measure side effects within the mouse even if the mouse you know drops dead. It doesn't mean that it's - that the drug is no good. So you're absolutely right. We have - every drug

development - once it goes into patients, into human beings, is in a completely different - it's out of science almost - it's in an empirical scenario. And you have to try it and find out and see and hope for the best. I mean this is - I'm very honest about this. I don't see any near term improvement of that situation. One area of research that is sort of becoming more and more popular is called systems biology or systems medicine. That term tries to describe that one tries to by computational methods but also by normal scientific method to understand the complete picture of a complex organism. I am personally very sceptical about that approach because it will by definition, it will have mistakes in it and computational methods make me very suspicious because you hide behind this illusion that a computer knows everything and algorithm is also only made by humans. So, you may even run into more problems when you use these approaches. I think today we have absolutely no choice but making sure that the drug is safe in animals, then go into phase one trials with humans, see if the drug is toxic, and then do regular clinical trials and with the development, even after approval, drug development continues. Like with Herceptin, there's still today so many clinical trials going on where doctors find out you know how to use the drug best. What the possible side effects are and so on and so on. So this is something that I don't see changed in the next ten years or so.

CHAIR: Maurice Reilly.

QUESTION: I'm just wondering how we're going to manage community expectation about the future. I mean, you're a message of hope here today. You're talking about these great potential cures, or at least treatments. How should we sort of manage that in the future? I mean are we talking - I mean do you see that cancer will no longer be life threatening in some years to come? Are we talking about - and there's been such rapid changes in technology and research and it gets better all the time and humans are getting better thinkers and so forth. I mean are we talking about a decade or are we talking about a hundred years. I just be - what's the future look like?

PROFESSOR ULLRICH: Well I always said it's very, very difficult to make predictions, especially about the future. So, - I firmly believe that these combination therapies, multi-targetted drugs, there will be more and more and better ones and we will learn to use them well and, and maybe in ten or fifteen years we will achieve for - maybe not for all cancers, but for many cancers that we can manage cancer. That we make cancer a chronic disease. There are other examples. I mean Aids, I have already mentioned. Aids was deadly - ten years ago and now people can live a normal life. If they have the money to pay for the drug obviously. Another example is Type 2 diabetes. Today there are, I mean this used to be a devastating disease where people lost limbs and still is if they don't manage the disease well but there are drugs today like Metformin and [indistinct] drugs that make it possible for patients to live a normal

life, even eat normal things and so for, for many years and there will be no drugs that allows these people to you know live their normal life span. I hope it will be like that for cancer. I'm pretty sure we can manage that. Maybe not for all cancers. Cancers are very different, but I think we can manage to get there. This is the message for the future.

Thank you very much.

CHAIR: Just take this one more question.

PROFESSOR ULLRICH: One more?

QUESTION: Jeff Farrell, ANU Medical School at the Canberra Hospital. Congratulations professor Ullrich and thank you for your marvellous lecture and a life time of achievement. It's a model for us all. Can I just change tact slightly now and talk about biomedical research as a national versus a international enterprise. You're at present in the middle of a very interesting experiment in Singapore in which there's a governmental initiative to make biomedical research and the fruits of that and the employing power of that, a national priority in Singapore. Do you think that that sort of thing is useful for smaller countries? I mean Australia, whilst it's a physical big country, has a small population like Sweden and Singapore. We probably have more bio-medical scholars working in the United States and in Europe than we do in

Australia, even though those remaining here I think are pretty powerful. So how important is it to bring these people home and what is the role of governments and national priorities in doing that?

PROFESSOR ULLRICH: Well there - this is complex issue but obviously Singapore must follow the strategy that they initiated, that to send out students and bring back the post docs and keep them in the country. This is - it's just a matter of size. Four million in Singapore versus twenty million or so in Australia, that's a big difference and eighty million in Germany so size matters and of course also the history - I mean Australia has a long history of top research in many fields so there is always a new supply of outstanding young people which was not the case in Singapore. In Singapore they started research to establish a research culture in 1995. From scratch because everything was only aimed at teaching and application of that - of the knowledge of the students in companies maybe but everything home grown. So this is completely different. But the strategy is not bad. But in - with our government systems, our social systems, it's impossible to say you have to come back you know and work here for six years. I mean this would be an intrusion, the freedom of an individual, but it can't be done in Singapore, it can be done in countries like Iran and so on that are more autocratically controlled and governed. But I'm not disputing the economic advantages of such a strategy of course and even necessity but I think, countries - many of the small European countries, can afford that very well

because of the depth of their culture, of their science culture that exists that includes you know Switzerland, Holland, Sweden, Denmark that's all countries that are between five and twenty million large and they are doing extremely well in science and their scientists frequently also migrate to United States, but they also come back so it, I think, we have it pretty well managed and I think here in Australia you have that too so much outstanding science but now coming back, money is necessary, more money, there is never enough money for science and the politicians have to be patient because science takes time. The two cases that I explained to you took twenty-five years taken together, so this is very important factor and one has to be aware of that. One could improve it - there are ways, and if the country of the government would provide enough funds to sort of establish work development facilities in academic institutions, I thing everything would get much better cheaper and faster.

CHAIR: Thank you very much Professor.

[Applause]

Stay here. Let's ... congratulations again on your Medal. Thank you for joining us for this past hour. Here's another momento for the day. I hope you've enjoyed your visit to Australia.

PROFESSOR ULLRICH: Thank you very much. Thanks again.

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