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Inquiry on

REGENERATIVE MEDICINE

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Witnesses: Professor Peng Tee Khaw, Professor Roger Barker and Professor Michael Schneider

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Lord O’Neill of Clackmannan
Lord Patel
Baroness Perry of Southwark
Lord Rees of Ludlow
The Earl of Selborne
Baroness Sharp of Guildford
Lord Turnberg
Lord Wade of Chorlton
Lord Willis of Knaresborough
Lord Winston

Examination of Witnesses

Professor Peng Tee Khaw, Moorfields Eye Hospital, UCL, Professor Roger Barker, University of Cambridge, and Professor Michael Schneider, National Heart and Lung Institute, Imperial College London, gave evidence.

Q21 The Chairman: I would like to welcome our second witness panel and to repeat what I said at the beginning of the previous session. Members of the Select Committee are urged to declare any relevant interests before they speak for the first time in this inquiry. This is an inquiry into the topic of regenerative medicine. The focus of this session is going to be around the public understanding, in part, of what is available through regenerative medicine, so we will ask you about certain articles that have appeared in the press. We are trying to understand what actually it is in reality, as opposed to the hype there is in presenting to the public what is going on in the field.

What I would like to do is invite you to introduce yourselves for the record. If you wish to say anything in addition to introducing yourself, please feel free to do so but keep your comments brief because we have a limited amount of time. I would also like to remind you that in the second part of the session, say the last 20 minutes or so, we have a number of
questions that were submitted by the public through Twitter and we want to put some of those questions to you, so that those who have submitted the questions—who we hope will be watching the webcast of this session—will have the chance see their question being put before top experts and hear your responses to them. We will not be able to cover all of the questions because of time, but we will cover a number of them. So without further ado, could I ask you to introduce yourselves, starting with Professor Khaw?

Professor Khaw: I am Professor Peng Tee Khaw. I am a clinician scientist, working in an area called glaucoma, but I have an interest in regenerative medicine and also drug therapeutics to enable that and to prevent scarring. I also direct the NIHR Biomedical Research Centre for Ophthalmology at Moorfields Eye Hospital and the UCL Institute, which has the express purpose of fast-tracking translation, hence the infrastructure behind that.

Professor Barker: I am Professor Roger Barker. I am a Professor of Clinical Neuroscience at Cambridge University. I am a clinician and a neurologist who sees patients. For the last 20 years I have been involved in regenerative medicine around Parkinson’s and Huntington’s diseases. I coordinate the European consortium on a foetal transplant trial in Parkinson’s disease.

Professor Schneider: I am Michael Schneider, the British Heart Foundation Chair in Regenerative Cardiology at Imperial College London. As a member of the MRC council I was a participant in the research council’s Technology Strategy Board working group that crafted the UK’s strategy in regenerative medicine, which was alluded to in the earlier session.

Q22 The Chairman: Perhaps I could kick off with the first question, which relates to the press articles that were sent to you. There were three articles, one from The Guardian, one from the Daily Mail and one from the BBC. What we would like to ask you is whether you
could comment on the treatments discussed in each of the articles and, particularly, when they might be available to patients on the NHS and whether the articles portray a realistic view of the efficacy of the treatments. The one from The Guardian talked about improved vision for a man with Stargardt’s disease; the Daily Mail one talked about Parkinson’s disease; and the BBC one talked about heart attack scars. Perhaps on the question of treating diseases of the eye I could turn to Professor Khaw and invite you to talk about the report from The Guardian by Sarah Boseley.

**Professor Khaw:** I think Sarah Boseley’s article was a good one. It reflected some of the clinical issues facing us—and our patients’ desires—and it reflects very well how passionate our patients feel about wanting stem cell treatments. There is not a week that goes past that I do not get asked about this. It also reflected quite nicely some of the difficulties facing the translation of stem-cell research.

On this particular issue, though, going back to the public’s desire, we meet the public. The board of Moorfields Eye Hospital meets the public every year and this year an elderly gentleman stood up and said, “I have age-related macular degeneration; is there any help for me? Will there be stem cell treatment in the public forum?” I answered that. I said, “Unusually, I am not going to tell you, ‘Five to 10 years’ time’. I am going to tell you that within 18 months we are going to have the first clinical trial.” I was wrong, because we actually started the first clinical trial six months after I made that statement. That is a very unusual situation for us, but it is a reflection of the rapidity at which—at least certainly within regenerative medicine for the eye; in gene therapy we did the world’s first patient a few years ago—this is moving forward. It is moving forward rapidly.

Going back to the articles, I think the public is inevitably very hopeful about this. Early reports of the first two patients for a particular treatment were published in The Lancet which was done by a former alumnus of ours in Los Angeles. The ACT (Advanced Cell
Technology) people came across to our biomedical centre, because obviously we are very big and have much expertise in this area, to carry out the first trial in Europe. These trials are obviously for safety; they are not for therapy. Inevitably, however, in these very front-line treatments—and I include gene therapy in that—we begin to see some very interesting results. That naturally raises the hopes of the public a lot, because in many ways a safety trial also accelerates expectation, because some of the patients have experienced quite interesting improvements in their vision. They have been very helpful in some ways because they have shown that, going back to stem cell therapy, it is possible to do it; secondarily, they have not been overtly rejected, which is always a major concern; thirdly, at the moment, there do not appear to be any tumours or other issues that we have seen so far. That is very helpful, but obviously there are still significant challenges moving forward to the future. Of course, there are issues about whether we can really get this through to full clinical use within the NHS. That will depend on the whole licensing issue and other issues of funding for both researchers and Government.

There is no question that the desire is there. That gentleman’s question reflects the desires of literally millions of people around the world for this treatment to work; therefore, I suppose, it is within our scope to try to see how we can make that a reality. I think it is not just hype. Going back to your initial question, there is real hope. We are proceeding; we are right at the front line. There is a lot more to do, and a lot of the problems have been identified here, but certainly we are moving fast and moving forward.

**Q23 The Chairman:** In terms of a specific answer to the question of when might the treatments be available to patients on the NHS, you have said you hope that in the future they would be, but you have not hazarded at whether that would be five, 10 or however many years off?
Professor Khaw: The trials are moving quickly. One of the interesting things about stem-cell therapy is that, unlike pharmaceuticals, because you are going for regeneration, you need perhaps less patients. It is still very difficult to do these trials because you need very sophisticated analysis techniques to look at efficacy, but you do not need so many patients. This is important in relation to your question, Chairman, because if the safety trial goes well—these will hopefully complete in perhaps the next year or so—then companies will hopefully move forward to later-phase trials. Clearly, if they do show efficacy—and that depends on regulatory issues both here and around the world—then potentially the treatment will go through the normal licensing process. Given the speed at which you can go, given the small number of patients, it is possible that treatments like this will be available within the next five years, or at least be licensed. There are other issues, of course, governing availability of treatments such as cost etc, but there is a distinct possibility that they could be available within the next five years. That is an exciting possibility for all of us.

Q24 The Chairman: Now I would like to move on to the second article and ask Professor Barker to comment. This is the article from the Daily Mail by Sadie Whitelocks: “Hope for Parkinson’s treatment breakthrough as human stem cells successfully used to treat disease”.

Professor Barker: This refers to this very influential and important paper that Lorenz Studer’s group published last year in Nature. As is often the case with newspaper articles, the headline is somewhat distorting what the article was saying. In this field of Parkinson’s disease, the use of cell-based therapies to repair the damage of Parkinson’s has been going on for 25 years. In Parkinson’s disease there is a specific loss of a cell that produces a specific chemical, so any cell that could produce that chemical could, in theory, repair the brain. For 15 years up to the turn of this century, foetal dopamine cells were being used with mixed efficacy. Many people have got confused with the idea that foetal
tissue is the same as stem cell-based therapies. In the public’s mind there is confusion between when you talk about foetal-based cell-based and stem-cell therapies. Are the two one and the same? Have stem cells not been around for a long time with Parkinson’s disease?

The big problem in the field of Parkinson’s disease has been two-fold, I would say. One side is this: do foetal dopamine cells actually work in Parkinson’s disease? I would say the answer is yes but it is not consistent, and that is the reason for our trial. Secondly, in the field of stem-cell therapies, are those stem cells which you are producing truly of the right character to produce the same efficacy as you might see with a foetal dopamine cell? The problem with stem cells is obviously to do with tumours and things of that nature. In Parkinson’s disease, the critical question has been this: have you been able to make a dopamine cell which is of the right type to treat Parkinson’s? It is not just any dopamine cell, but an appropriate dopamine cell.

This paper by Lorenz Studer took a new approach, which was to take a developmental-biology approach and say, “How do dopamine cells normally develop? We should recapitulate that.” They did that successfully using human embryonic stem cells, transplanted them into immunodeficient rats, mice and immunosuppressed monkeys for a short period of time and showed that the transplants that survived made dopamine and restored deficits in those animal models, which are a crude approximation of what you see in the clinic. This paper was important because it demonstrated that and this paper makes that quite clear. The problem then is about when that will translate to the clinic. I think there are a couple of issues there. One is that we do not know whether dopamine-cell therapies truly work, which is the purpose of our trial. Secondly, the dopamine cells as produced from these stem cells still do not have all of the hallmarks of normal dopamine cells. There are still issues to do with that.
When will these treatments come into the clinic? It is envisaged that there will be early trials using this technology in patients at some point in the next five to 10 years, but they will be trials. Lorenz Studer himself has applied for funding to do that through the New York Stem Cell Foundation. We have just received a grant from the MRC to take Roslin GMP-grade cells, human embryonic stem cells, through to dopamine cells to transplant into animal models. We have a cell that is of clinical grade that could go to the clinic. If that all goes according to plan and those cells work, then the fundamental question which will face the NHS is this: is that treatment any better that any other dopamine therapy that is out there? In my mind there is clearly an issue here. You can get something to work, but is it then competitive?

In Parkinson’s disease, as you may know, whilst the loss of dopamine can be remedied with these type of approaches the disease is much more diffuse than that. Dementia is quite common in Parkinson’s disease and that is independent of that. All therapies for Parkinson’s disease which are currently available in the clinic work on the principle of replacing dopamine. Fundamentally, will a stem cell-based therapy be any better than a Duodopa infusion or an apomorphine pump? Are there better oral therapies for dopamine?

Q25 The Chairman: Professor Schneider, would you like to comment on the BBC news article “Stem cells used to ‘heal’ heart attack scars”?

Q26 Professor Schneider: Yes, the trial being discussed is the CADUCEUS (CArdiosphere-Derived aUtologous Stem CElls to Reverse ventricUlar dysfunction) trial led by Eduardo Marbán at UCLA. To put its importance into perspective, I would say that over the past decade there have been more than 1,000 patients treated worldwide with stem cells of different kinds for heart repair—typically bone-marrow cells or their circulating derivatives in the blood stream. The consensus from those trials is that small benefits are seen and overall they are safe, but the benefits might be less than the enthusiasts would have
wished, partly because the bone-marrow cells probably do not turn into beating cardiac muscle cells and therefore do not achieve myocyte replacement as might be necessary for the optimal restitution of heart function after a heart attack.

This particular trial was one of two reported in *The Lancet* this past year that used, instead, dormant stem cells from adult heart muscle along with other cells grown from a cardiac biopsy, which have a very well proven potential to form new beating heart muscle, both in tissue culture experiments and in experimental animals. The point to which the title of the BBC report made reference was the shrinking of the scar by advanced magnetic resonance imaging technologies. I agree very much with the caveats Professor Khaw raised. These are Phase 1 trials that are designed and powered chiefly to prove safety and gain the approval to go ahead from a few dozen patients to a few hundred patients in the Phase 2 study. It is really only in the Phase 3 study involving thousands—and sometimes tens of thousands—of patients that we get genuine proof of clinical effectiveness.

Piggy-backed on the safety trial, however, are studies which are designed to provide a preliminary indication of effectiveness, such as the imaging that was done in the case of this trial. The problem is partly that the media do not always make it clear to the public what a trial is and is not. A Phase 1 safety trial is not proof of effectiveness; it can contain a preliminary indication of effectiveness, but those are not the same thing.

**Q27 Lord Winston**: I have two brief questions, Lord Chairman, if I might.

**The Chairman**: Keep the questions brief and the answers brief, please.

**Lord Winston**: One is the paper by Kim published over 10 years ago in *Nature* on tyrosine hydroxylase activity in dopamine. You will remember this paper, which showed clear efficacy in rats for the treatment for Parkinson’s disease. One of the issues is that this was over 10 years ago. It takes a hell of a long time; I wonder if you could address that.
To Michael Schneider, very briefly, one of the issues, as we have discussed in the past together, is the fact that the early trials with stem cells—whatever kind of stem cells were injected—all looked rather good. There were all sorts of parameters which showed an improvement, but actually once randomised controlled trials were done the improvements, if at all, were extremely small.

**Professor Barker:** Yes, there are always reports. This paper was from Ron McKay’s lab. The ability to turn a stem cell into a TH+, which is the enzyme which makes dopamine cells, has been shown many times. They do have efficacy in these animal models. In order to reverse the behaviour in an animal, you only need 160 TH+ cells to effect that. In order to have a successful transplant in a patient based on foetal material, you need 100,000 TH+ cells. Extrapolating from animal models to patients is always very difficult. It is a starting point, but the issue is the reproducibility of that technique or protocol in other people’s hands. In those particular cells, what the cells looked like was not the same as what Lorenz Studer has managed to do with his cells, but his cells still do not look like normal nigral dopamine cells.

**Professor Schneider:** Turning to the small effect of bone marrow in the early clinical cells for heart repair, I would agree with your point that even preliminary indications of efficacy are more convincing if randomised rather than not. However, I would say that a lot is learned even from the early trials that affect the design of later trials. For instance, although the overall effect of bone marrow was just a small improvement in the ability of the heart to eject blood each time it contracts, other kinds of improvements can be detected more readily in trials, such as protecting the heart from progressive dilatation and wall-thinning. That effect is a big one, not a small one. Those early trials also helped pinpoint those patients who might be most likely to have a big improvement. If you inject bone-marrow cells in someone who has a small, uncomplicated heart attack, whose heart is pumping well
already, there is not much benefit. Those patients in turn diluted out the benefit that is seen in patients who have a big heart attack whose hearts are pumping worst, in whom the benefit was largest. In talking about the early bone-marrow trials, I think a lot was learned that affects the design of the trials we see today.

_Q28 Baroness Sharp of Guildford:_ These sorts of articles are leading to a lot of interest, obviously, in stem-cell therapies of one sort or another. The question I want to put to you is whether there are dangers for the public travelling overseas. There are quite a number of places overseas that have been setting up clinics of one sort or another. We have seen this happening. Are there dangers to the public if they travel overseas to have regenerative treatments of this sort and, if so, to some extent, what can be done about this?

_Professor Barker:_ I think you are absolutely right. There is a danger to patients; there is a danger to the whole field. If something goes wrong in one of these clinics, it will impinge on everything who is working on stem-cell therapies across the globe regardless of the origin of that transplant. This is a very big problem and I have been involved with it on two levels. I have been to China twice, where there are a lot of these clinics, to talk to the clinicians out there to see if I can persuade them to try and adopt a slightly different strategy—without success. The other way in which I have done this is through the international stem-cell organisations. We have tried to set up guidelines to help patients decide whether something advertised on the web is worth pursuing. It is very difficult, because I have one patient, for example, who has young-onset motor neurone disease and she came to see me and said, “I want to go and have an umbilical-cord stem-cell transplant. Would you support that?” I said, “No, there is absolutely no scientific evidence that that works at all.” She said, “Is there any possibility that it could work?” I said, “Of course there is a possibility it could
work.” She said, “And you are offering me nothing.” Some possibility against no possibility seems quite good odds to a lot of people, even if it costs £20,000 to £25,000.

This is very difficult, because within those clinics there may be something useful coming out which we cannot detect. The way in which the trials are done—certainly in the clinics I have been to—has no scientific or clinical basis, the follow-up is minimal and the results have many interpretations and not the interpretation that are necessarily put up on them. I think it sets up an expectation and linked into that, with the patients, are two issues which I have picked up on. One is that first of all you do not get it in Britain because, “The NHS does not have any money; that is why I have to go abroad to get it.” It is the cash-strapped NHS which means I have to go abroad. If we had enough money we would all have it. You have to disabuse them of that idea. Secondly, it is to do with the ethics: that we are so wrapped up in the ethics of human embryonic stem-cells and foetal tissue that actually these adult stem cells—bone marrow or whatever—that are being offered in other parts of the world circumvent that problem. Therefore they must be a better source of cells to use. That is what the clinics often play on. They play on this ethical issue to get around it; they say that these are much more ethically acceptable. There is no scientific basis, but it is ethically more acceptable to have them.

It is a big problem, this stem-cell tourism; people are travelling the globe to do it. It is vast. When I was on this Committee I said, “Send me the clinics.” It was 64 pages of listed clinics across the globe, so this is a vast industry that is out there.

Professor Khaw: Certainly, in eye diseases—and optic nerve disease, which currently is irreversible—we do have many patients writing constantly in and saying, “Should I go? Should I go?” I will not go over the comments that Professor Barker has been through, but I would absolutely reiterate that issue. It is a difficult situation for us when you have a relatively untreatable condition and a patient is desperate. I suppose my reiteration of that
would be that the way to try to go through this is the issue of information. We must provide the individual with as much information as possible about what we know about where they are going—that includes the individuals running it—and also what they know is available out there. I think that is the first thing that has been very helpful, perhaps, in informing people.

The second thing is the personal approach, actually. When they are in very desperate states, people want to know whether you would send your mother or your child. Actually, my answer is that I look at these things and I explain to them, “Although I am not in your position, my answer is I would not, and this is why.” That is actually is persuasive, to be honest. I give them information, but it is that very personal approach that is helpful. They need information; they need recourse to clinicians who are familiar with the area, familiar with the science and, actually, can give them a very frank, personal opinion also about the pros and cons of this.

Professor Schneider: I share the concern that Professor Barker raised that safety accidents in this field in unregulated clinics with poorly designed trials could have an adverse effect. I suppose, to an extent, we are fortunate there have not been more than have been reported to date. There is one instance that I am aware of: a young man went to the former Soviet Union for injections of foetal neural stem cells for a neurological disorder. He subsequently developed a tumour, which advanced pathological tests were capable of showing was donor cell derived. If one thinks back on the history of gene therapy and the recoiling of the investment and clinical community from gene therapy, this was based on a very small number of safety disasters. The same could happen here and so these kinds of activities do put an entire promising field in some jeopardy.

Q29 The Earl of Selborne: The article in The Guardian refers to a tide of suspicion to stem cell therapy and the need for practitioners to fight back. Is the tide on the ebb or the
flow at the moment and what research has been done on public perceptions and attitudes to regenerative treatments? What does that tell us?

Professor Barker: I have limited experience of this. As part of our European foetal transplant trial we have an ethical work package within it and the EU has been quite keen on collecting public opinion on regenerative medicine. My colleague, Professor Gottweis, who is a Professor of Life Sciences in Vienna, pointed me in the direction of a thing called the Eurobarometer, which looks at various different aspects of this, which I am sure many people are familiar with. Certainly, within the UK the support for stem-cell research and stem-cell therapies is very prominent. It is the highest in Europe. In this Eurobarometer, 80% of people would support the use of stem cells for research and for therapies. What would be interesting is, when you actually move it to the clinic, how many people would support it on an individual basis. For example, with the foetal transplant trial, whilst we have lots of people who have joined our trial, when you actually say, “Would you like a foetal transplant because we are about to start,” people just step back a little bit from that. I think people are generally—certainly in the world of neurology and in general with stem-cell therapies—very supportive of it. When it comes down to an individual person in a trial, it changes slightly. In general, people are supportive of it but it does vary across Europe. With a lot of funding for European-wide trials, this creates a certain tension in how you move some of this work forward.

Q30 The Earl of Selborne: Would further public engagement be helpful to meet some of these issues that you are referring to when it gets to the clinical stage?

Professor Barker: I am a huge fan of public engagement, because I think there are a lot of misconceptions about things. There are a lot of things we do not think about as scientists and clinicians; the public are very good at educating us on these and thinking about it differently. Managing expectations is the most important thing for these type of therapies,
because, as the papers tend to report—when I give a talk there is a headline from *The Guardian* which says, “Miraculous cure turns into disaster,” which was a foetal transplant in America—there are essentially two outcomes: it is either miraculous or disastrous. Therefore the public have this hyperbole: it is either going to cure everything or cure nothing. Trying to give them some sort of realistic expectation of what it could do over what period of time in what aspect of disease is important.

**Professor Khaw:** As part of the NIHR we have several very large public engagement days on different diseases; inflammation and retinal disease. Obviously, these groups of patients have a particular interest because they suffer from these diseases so you might expect them to be more engaged about wanting the treatments, but there is often a very active debate about whether we should be wanting stem-cell treatment. I can tell you that at the end of the day we often have a session where we ask them to take their Post-it and stick it on the bits of the board that they are really keen on. Of course, research comes very high, even though they are all sufferers of the disease. From the few informal surveys that we have done, certainly they are all very much in favour of stem-cell therapy. In ophthalmology, we have not done a large-scale public analysis of whether the same sentiments are held. However, I can tell you personally—and certainly through our wide exposure to the public through our public patient engagement—that there is very strong support for this because they do see it as giving them some hope, particularly in many of the conditions that are essentially untreatable. There is very strong support, certainly from the patient groups.

**Professor Schneider:** I would share your point that there is insufficient public knowledge of the nuances of clinical research of many kinds. This is something which most of us in academic medicine are resourced to do either through our NHS trusts or the NIHR biomedical research centres and units. I think back to Lord Winston’s programme of four or five years ago, *Super Doctors*, which painstakingly made the point that in a clinical trial half
the patients do not get the treatment and that, indeed, would have been a surprise to many members of the public. There are many things that the public would benefit from understanding better. We as a community would benefit from improving their knowledge.

**Q31 Lord Patel:** Because the question was put as the public attitudes to regenerative medicine, it implied that we are talking mostly about treatment; of course, we are not. We are talking about research, too. In the context of research, what engagement do research funding bodies, including the councils, have with the public before the research starts? Are you aware of that?

**Professor Barker:** I do not have a specific answer to that. To be honest, I have more to do with the disease-specific charities. For Parkinson’s UK, for example, I often go and give public lectures to people with Parkinson’s disease and interested parties about regenerative medicine and things of that nature. I do not know so much about the MRC and the Wellcome Trust and whether they have specific public outreach symposia or days, I am afraid.

**Professor Khaw:** I am not so sure about the Wellcome Trust or the MRC, but certainly through the NIHR there are very proactive PPI (Patient and Public Involvement) engagement activities through web media and other things. We have priority-setting partnerships, for instance, in which the public has been engaging very strongly by emailing in what they feel really matters to them in their lives in terms of research. That priority-setting process is underway at the moment; it will identify some key priorities, many of which hopefully will be funded by the NIHR and other sources.

**Professor Schneider:** In a small number of areas the ethical issues loom large. That kind of consultation takes place in a proactive way. The recent Academy of Medical Sciences report on animal/human hybrids would be one example. Foetal tissue research is another example and, of course, human embryonic stem cells would be a third. As several speakers have
pointed out, this field of work, more so than others, is very dependent on high-quality animal research, both for model organisms providing us cell types of different kinds, which one can study and then learn from, and the human model organisms like the salamander, the zebrafish and even the newborn mouse, which have a much greater regenerative capacity than middle-aged or aged humans. We learn from the model organisms mechanisms of repair that then might apply to the clinic.

In addition to those two streams of fundamental research requiring the animal models, I would point to the need for large animal studies to develop the technology for delivering cells safely, prudently and effectively to diseased sites in diseased organs. The kinds of treatments that we are talking about virtually could not exist without three strong streams of animal-based research leading to the first in human innovations. That is an area where increased public awareness of these needs might help to shape public opinion in the future as more tolerant of the need for animal studies.

Q32 The Chairman: I would like, now, to move to the Twitter questions that we received and I think you received copies of. We are very pleased that we had a good response to this experimental request for input on Twitter. We probably will not get through all the questions in the remaining 20 minutes or so, but we will pick out some to start with and see how we get on. I hope you will be able to give us reasonably succinct answers. Some of them reflect points that we have covered already but it would be good to recap them in the context of these questions. I am going to turn to Lord Rees to put the first one from our list.

Lord Rees of Ludlow: Is there a regenerative medicine research programme with measurable and realistic goals? Should research be focused on one condition to concentrate efforts?
Professor Schneider: I would like to respond to the second of those first. In regenerative medicine, the mechanisms of benefit vary from cell replacement to indirect effects on the host tissue including blood vessel formation and wound healing. I would argue against picking one prototype disease allowing us to solve all the problems in the area. Turning to the questioner’s first question—is there a good roadmap for working forward?— the UK strategy for regenerative medicine, which includes not only injecting a naked suspension of cells, as it were, to the diseased tissue, but also cell-three therapies based on the hormone-like proteins that stem cells make and also engineered constructs, having more of the three-dimensional configuration of the tissue. That is a very comprehensive plan that incorporates many of the elements of regenerative medicine and it is a very good roadmap if adequately resourced.

Professor Barker: I would support those views entirely. Regarding concentrating on a few conditions within one area of medicine, in the world of neurology Parkinson’s is an obvious target because it has a specific pathology. Targeting one condition is a sensible thing to do; we have a very useful way of taking it forward. One of the key challenges of the future is how you measure whether your therapy has really worked in the time frame that we think about. If I give you a tablet for your high blood pressure, you would expect to see a result within a few weeks; if I put a cell in your brain to make it repair that bit of the brain, it may take five, 10 or 15 years before you see the real benefits. Thinking about how we can actually do trials better is a real challenge and that, I think, has been a problem in the American system, where trials have been ended prematurely based on how they see drugs working, which has had major consequences in regenerative medicine for trials across the planet.

Professor Khaw: Again, I would start with the second question first, like Professor Schneider. I think it is a mistake to say that just because a disease area is currently costing
you a lot it is more important. I am not saying that it is not an important factor; it is very important. But the issue of rare diseases is an important one. The UK has a unique ability to bring together groups of rare diseases. I will give you an example: the world’s first gene therapy in a human, done in the UK, was a very rare condition. It is only because we are able to gather, in the UK, these very rare conditions together that we are able to do these very early proofs of principle. Rare diseases are often incredibly good ways of finding a proof of principle for a new treatment because they are often very dramatic and very precise. Once you have that proof of principle, you can apply that principle to much more common diseases. Some of the things we have learned in gene therapy from these incredibly rare diseases could now be applicable in, for instance, potentially the treatment of the retinopathy of diabetes, which is a major blinding problem in young adults in this country. I would not stress that we should treat diseases because they are very common. There are paradigms of disease, particularly in the UK—due to the way the health system is set up—that could make us be able to complete very effectively.

The second question, going back to the first one, was whether there are programmes with measurable and realistic goals. I think the answer from all of us is absolutely yes. The trials you have heard about, the London projects and many of the other stem-cell projects have very clear goals for progressing and translating through to clinical use. Perhaps we will touch on that. I would like to raise one point about that. Translational research, which you have raised today in your Committee, is not an accident. It is something you do because you want to do it so much it burns in your heart and it hurts that you want it so much. I suppose the analogy of translational research is that it is a bridge of which every single rung has to be in position. That makes it different from some of the world-beating science that you have seen. Not to denigrate science—science is extraordinary—but to make things translate, if one rung of your bridge is missing, you will fail. It has to be very deliberate; it
has to be recognised; it has to be cultural. Often the people who put those rungs into place are not recognised or are not provided for. I think that to make translation research work, you have to want to do it so much that you put all of the rungs in position so that it works. That is how we have succeeded in some of the things we have been doing.

**Q33 Lord Turnberg** This question is to Professor Khaw. You may have covered some of it in your first remarks. It is about the FDA (Food and Drug Administration) granting orphan status for human embryonic stem cells for treatment of inherited macular degeneration in children’s Stargardt’s disease. Are we going to see this used in the UK on compassionate grounds?

**Professor Khaw:** Clearly, if you are a sufferer of Stargardt’s, you are reading at least good safety reports so far—albeit reasonably small numbers—and you are thinking, “Can I have this treatment now, please?” This is what our patients are asking us. Obviously, for a drug to be made available for compassionate use, many things have to be in place; first and foremost, of course, you have to have enough data, on the balance, to be sure that it is safe and that there is at least some evidence of efficacy. We are moving towards that but obviously that takes time. I suppose the answer to that question is that further analysis, completion of the current trials and perhaps one further trial are all needed before companies can provide this treatment for compassionate use. Obviously, however, it is a possibility once we reach the state of evidence where that might be possible.

**Q34 Lord Wade of Chorlton:** Can I ask what Stargardt’s disease is?

**Professor Khaw:** Stargardt’s disease is basically a form of macular degeneration that occurs in young people. It is a good model. Obviously, it is very tragic and very devastating for young people who lose their central vision, the vision we are all using now to read our papers and do everything, but it is a very specific condition and is relatively rare. It is obviously a very good condition in which to do an early-phase stem-cell trial.
Q35 **The Chairman:** Does the fact the FDA had granted this orphan status mean they have assessed the efficacy and safety of this?

**Professor Khaw:** Orphan status purely refers to a disease that is sufficiently rare. Going behind the thinking behind both the European and the FDA definition of orphan, it is that nobody would develop any treatment for rare disease if they did not make the pathway a little bit easier. The route, if you like, to licensing an orphan disease is a little bit easier. I think that is the main issue about orphan diseases.

Q36 **Lord Winston:** I have Twitter running in front of me, which is why I am asking the question, and I see that more than one person has quoted Professor Yamanaka from Japan. I hope one day to use iPS cells, rather than human embryonic stem cells. I wonder if you would like to comment on that specifically, because it relates to this particular respondent as well.

**Professor Khaw:** Obviously we were very thrilled with the award of the Nobel Prize to Shinya Yamanaka for his very revolutionary work on iPS cells. Obviously, iPS cells have raised a lot of hope because of the fact that you can take adult cells and convert them into multipotent cells that can do various things. There are a lot of technical issues, some of which are probably beyond me, about iPS cells. There are a lot of technical hurdles with iPS cells at the moment. Embryonic cells are not used just because they are available. At the moment, we know a lot more about the current cells that we are using. Take, for example, those in the ACT trial in the London project, which are embryonic-derived and therefore we are able to move forward much more safely. With iPS-cell technology we are still very uncertain about where to do. There is obviously a lot of work being done on iPS cells and their potential for therapy. However, at the moment, we are not in a position to be able to move forward with iPS cells therapeutically.
Q37 Baroness Perry of Southwark: My question you touched on several times in your replies. I think, Professor Barker, you talked about the importance of managing people’s expectations and so on. The question is this: is there a need for improved patient education on the whole subject of regenerative medicine? Should there be better science communication strategies designed to provide accurate and realistic messages about such technologies to the public?

Professor Barker: I think it is a very dynamic process because this field moves forward. Five years ago, no one knew what an iPS cell was. The term did not exist. Well, perhaps not in 2006 but a few years ago it did not. People understanding what these terms mean and what they bring to the field is very important. Education is very important, especially as we live in a world where there is often a lot of commercialisation. The other thing which happens with stem cells is that obviously some of them get attached to companies and once they get attached to companies there is generally only one piece of news you will hear about those stem cells, which is good news. Again, it is this building-up of expectations: “There are lots of things out there, but if only I had access to it I would be much better treated.”

It is great when you have people like my colleagues on the panel who patients can talk to and say, “What do you think of that?” However, having a broader remit, whereby one can educate people and understand what they mean by stem cells, is important. An embryonic stem cell is different from an induced pluripotent stem cell, which is different from a neural stem cell, which is different from a bone marrow mesenchymal stem cell. These are all different stem cells; they all have the same term and people group them together. It is important to educate people on the science: what is a stem cell? What can you do with it? It is important to educate people on where you are trying to take that therapy—taking that cell into the clinic—and the realistic expectation of what that would actually mean to a patient in the short term, and in the long term, and the risks that that brings with it.
Professor Schneider: I agree very much with the point. This is the kind of activity that we do with our partners in the NHS trusts. Indeed, on this exact topic we had a so-called Café Scientifique just earlier this month. It is important to get these concepts across. The one community that we actually have not spoken about in terms of the need for education is the GPs. This is highly specialised and rapidly evolving knowledge; finding the right mechanisms to educate them as well is as much of a challenge, and sometimes more of one, than knowing how to reach the patients.

Q38 Baroness Perry of Southwark: You are not getting much help from the press, are you? I think, as Professor Barker said, it is either a disaster or a triumph, so to speak. The amount that you can do as individuals is quite limited. You talk to specific audiences. Surely the GPs are the ones who see patients over time.

Professor Schneider: That is exactly the limitation I would point to in our activity of last week. If it was 40, 50 or 60 patients it is just a drop in the bucket. It is a worthwhile activity; reaching GPs would be important.

Professor Barker: The headline writer is who you really need to educate but of course their job is to sell copy—not to sell the true nature of the story. The articles themselves are often very accurate; it is the headline that is misleading. That is, of course, what the patient takes away.

Professor Khaw: If I may say so, one of the opportunities is the modern media. I think we have already explored how certain parts of media by necessity—or however you wish to define it—have to sell stories in a much more extreme way. However, with the increasing democratisation of media through the internet and Twitter and various other things, that does become an opportunity to present a more balanced view—at least to the public—that they can accept. The issue is availability. One of the great difficulties of modern life is where do you look? You get covered in an avalanche of data and the question is what makes
somebody go to one source rather than another. I think we can resolve that. There is a beautiful section on neural stem cells; on stem cells for eyes. It is a nice, simple article that refers to all of the current technologies. The problem is how does the public get there? What leads them there? What do they trust as their source of information? If we can help with that guidance for the public—and also make them want to go there for other reasons—that could help a lot.

**Q39 Lord Patel:** My question from Twitter relates to the impact that the European Court of Justice ruling in Brüstle v Greenpeace will have, in particular on investment in research, and particularly on the huge European funds which are available for research. Would you like to comment?

**Professor Schneider:** I think it is worthwhile turning back Lord Winston’s question about iPS cells versus ES (embryonic stem) cells to put this one in perspective. Although iPS cells in principle and in substance can adopt many if not all cell fates, both as a platform for regenerative medicine and as a platform for related activities like pathway dissection, drug discovery and drug safety testing, the question is not whether the cells can become a neuron or a heart-muscle cell or a blood-forming cell. The question is just how good are their functional properties once they have made that lineage decision?

One of the most important and instructive examples that I have seen recently on the need for continued work on human embryonic stem cells was shown at a drug discovery symposium in Manchester last month, where an investigator from industry, from AstraZeneca as it happens, was doing systematic comparisons of drug toxicity in a panel of human ES cells on the one hand and human IPS cells on the other hand, using cardiac muscle made from these different sources. It was found, for reasons not yet understood in a fundamental or reductionist way, that the findings in terms of predictions of toxicity were very strong using cardiac muscle made from embryonic stem cells and much weaker using
the cardiac myocytes made from iPS cells. That is not to say that those kinds of problems will not be sorted out in future, but I just point to that as an example for now where the ES cells would clearly be out in front.

It seems reasonable to me that a company like AstraZeneca or others ought to be able to engineer human ES cells in different ways that make them particularly well-suited for the kinds of toxicology studies that they need, for the kinds of target discovery activities that they need to come up with new drugs. Currently, if they were to do that in the cell product that is best for the purpose, they would not be able to patent it. If they were to do the same manipulation in an iPS-derived heart-muscle cell, less fit for purpose, they would be able to patent it. That is one example at the drug discovery and big pharmaceutical level where the EU court decision is very destructive, putting aside all of the issues relating to human ES cell derived heart muscle as a potential therapeutic product. It would seem logical that the steps involved in bioprocessing, in ensuring genome stability in long-term processed cells, in purifying the cells to homogeneity and also to delivering them, all of that, would qualify for intellectual property protection, were it not for the latent religious objections to embryonic stem cells on the part of a small but vocal minority.

The Chairman: Are there any brief comments? I would like to come to one last question from Lord Wade in a moment.

Professor Khaw: I would comment that of course it is uncertain, but certainly the partner our centre is working with, which is Pfizer, has been surprisingly robust in moving forward despite the ruling, which is encouraging. Given that sometimes a problem is also an opportunity, going back to what we heard just now about the engineering issue, modern stem-cell technology is often a complex interplay of some of the high-level technological manufacturing issues and delivery issues. For instance, we have had to design special instrumentation to deliver some of the stem-cells that we are doing.
I think if we are clever about it—let us put it that way—and work in a multidisciplinary way, there can still be the platform for investment with some protection for the companies who invest. That belies the issue of the technological investment that the UK makes into this field. It is not just doing the cell and all of the biology behind it. There is a whole raft of technological co-patenting that occurs that makes it a unique product. If the UK were also to invest in some of the co-investment, then actually the value would still be there. I just wanted to make that point.

Q40 Lord Wade of Chorlton: The Twitter question is would possible long-term benefits to society justify increasing tax breaks for promising research for regenerative medicine? I suppose the underlying question is what are the long-term funding implications for the development of this technology?

Professor Barker: I do not know the answer. It is such a complicated area because there are so many “ifs” and “buts” in what happens, really. At the moment I happen to be involved in a group of scientists where this is a big issue, with the withdrawal of one drug for one indication because they have suddenly found it to be very successful, and it coming back at a higher price because they now know it works. There is always this issue. Once you have found something that works, how do you take it out and offer it in a favourable way to as many people as possible? I do not know the answer to that. If I speak for myself in terms of the world of neurology, I think these therapies will never become mainline therapies for a vast majority of people. I think they will always be kept for specialist centres for relatively select groups of patients. They will therefore get the funding they need in order to have that therapy, because it will be a restricted group. It becomes different when you move it out of, say, the field of Parkinson’s disease and you have a treatment that could help everyone with diabetes or prevent them getting diabetes, because suddenly you have a vast market. How you can regulate and support that I do not know.
**Professor Schneider:** The need for more funding is there but I leave it to others wiser than myself to decide whether the financial instrument should be tax breaks versus grants and other kinds of mechanisms such as support through the Technology Strategy Board.

**Professor Khaw:** I feel very strongly about this. If you look at what we have been successful with in getting through to first demand and then some success, it has been reliant on a variety of things but, if you look at the way the funding packages were put together for these highly successful first or second in the world-type initiatives that we do, it is very diverse. There has been a lot of leadership from the people who head up these programmes, who go all over the place to find the mixture of funding that you need to make this, without which I would not be sitting here talking about our centre having these first in the world things for the UK.

There is no question that the partnership with the commercial sector is essential. The London project is advancing rapidly—a British-based project we had to put huge infrastructure in, from charities, from the MRC, from a private US philanthropic donor. Pete Coffey makes the point that, so far, they have had to do 37,000 pages of documentation. No academic on the planet can do that. Even though they have all of the ideas and the science, they need support—probably from specialists in the field who tend to be located in industry. Industry needs to have some incentive to come in and work with us to write 37,000 pages of documentation. So whether it is tax breaks or other things, what is absolutely essential is support for intermediary funding, without which we simply cannot take these treatments through to clinical usage.

**Q41 Lord Wade of Chorlton:** Is this an issue which you think we should look at in this report?

**Professor Khaw:** Absolutely, because I think it is essential for success. If I look back to the things we are succeeding in, without that degree of support to fill in this huge amount of
regulation and administration that you need to do to get through this stage, we cannot possibly succeed in bringing treatments and technologies—particularly in the UK, for UK-born ideas—through to patients, in industry or elsewhere.

**The Chairman:** Thank you very much. Sorry that we have run over time, but it is partly a reflection of the very interesting answers you have given to our questions. It has been an excellent session. I would also like to thank all of those who sent in the Twitter feed questions. We did not get through all of them, but we had responses to at least some of them. Others were covered implicitly in the earlier responses. You will, in due course, receive a draft of the transcript for you to make any corrections. If there are any comments that you want to make in addition to those that you have made today, do feel free to write in and it will be included in the evidence that we publish with the report. Thank you very much indeed for your comments today.