#RegenMed

Regenerative medicine: the ground-breaking opportunities it offers for improving patient healthcare 8.11.16

Professor Andrew Webster, Director SATSU, University of York

Professor Webster began by explaining that his talk would focus on examining the opportunities which regenerative medicine affords to patients, and how these opportunities can be translated into practice. He went to on to highlight the timely nature of the event, given the ongoing Science and Technology Select Committee enquiry into the subject. Professor Webster concluded the introductory section of his talk by providing a brief explanation of the nature of regenerative medicine and its importance to society as a whole. Regenerative medicine is about regenerating cells, tissue and organs to establish normal functionality. This establishment of normal functionality is crucial as it creates the possibility of curative rather than simply therapeutic treatment. As such, in 2013, the House of Lords Science and Technology select committee produced a report which identified regenerative medicine as "one of the eight great technologies" which the UK government should strongly support.

Professor Webster went on to identify nine key challenges (see slide four) which create barriers to the implementation of regenerative medicines into the clinical setting. Of course there have been attempts to bridge this gap which have been manifested in a series of initiatives in the UK which are displayed on slide five. He showed how, within this context, there are five typical pathways (slide 6) to the clinic driving most company activity, each having quite different profiles in regard to the likelihood of clinical adoption. Identifying where these pinch points are in the clinic (slide 9) helps key actors to target the most effective policy responses, beyond the wider initiatives we see today.

Contact

Judith Abel
Manager, APHG
T: 020 7202 8580
E: judith.abel@healthinparliament.org.uk

#RegenMed

Slide six of the presentation focused on challenges which the field of regenerative medicine face which are specific to this discipline of medicine. The three specific problems identified were:

- Safety and efficacy challenges deriving from the perceived complexity and fragility of live material.
- The classification of therapies poses specific challenges to developers and regulators.
- Scale up and quality assurances are particularly challenging for regenerative medicine products since they are based on living tissues and cells.

With this in mind, the project identified five paradigmatic pathways which regenerative medicine products and therapies take to the clinical setting as well as examples of companies that are currently located in these areas. The pathways, displayed on slide seven, are:

- Enabling, gateway innovation such as immunotherapy.
- Automated cell processing 'point-of-care' device/technique.
- Surgeon-led innovation.
- Implantation/infusion therapy innovation.
- Bioprocessing innovation.

The project then analysed these pathways to assess their implications at the clinical level. Slide 9 maps three of these pathways against deliberations which clinicians and others involved in adoption undertake when they're deciding whether or not to take on board a particular type of innovative technology. The resulting chart allows one to think about pathways to the clinic, and then within that context the sorts of adoption processes that are at work, where there is contestation, where there is approval, and focus attention and resources appropriately.

Once the most effective clinical adoption strategy has been identified, it is important to assess if scaling up of cells can be completed to a level which allows sufficient levels of patients to be treated. The scaling up of cells in relation to regenerative medicine products is particularly difficult given the fact that cells are live tissue. Slide 10 identifies the challenges in this respect.

Contact

Judith Abel
Manager, APHG
T: 020 7202 8580
E: judith.abel@healthinparliament.org.uk

#RegenMed

• The growing environment of cells can affect the safety and potency of the material.

• Inherent variability within cell lines means that the 'chemicals' based concept of 100% 'product purity' and reproducibility may not be possible.
• Manufacturing of most RM products must take place within a clinical-grade Good Manufacturing Practice (GMP)-licensed facility. These are costly.
• The 'shelf life' of this material is very limited, meaning that decentralised, distributed 'bed-side' closed system manufacturing models will be likely, using automated, modular, closed-system manufacturing platforms. Currently 16 such (commercial) systems being used in the UK for cell cultivation, separation and expansion.

Professor Webster finished by sharing some overall conclusions from his presentation. Whilst there are distinct routes to the clinic, it is possible to identify sites or domains where one can target resources to foster clinical adoption. Furthermore, effective structures for Regenerative Medicine Centres of Excellence need to be put into place. What organisational features do these centres have? How do they map on to existing types of arrangements within the NHS? It can also be argued that scenarios for the likely size and profiles of clinical populations, treatable through different manufacturing modalities and scales, should be developed to support national planning. Lastly, the development of product, process and manufacturing standards and guidelines need to be encouraged.

Professor Alex Faulkner, Centre for Global Health Policy, University of Sussex

Professor Faulkner began by explaining that his talk would outline the regulatory bodies which regenerative medicines currently sit in and where they may appear in the future as well as providing an overview of the debates surrounding the payments and reimbursements of the products.

The body of the talk began by highlighting the current range of regulations which sit in the pharmaceutical and Advanced Therapy Medicinal Products regime and how this relates to the flexibility of the regimes themselves given their connectedness to European Union regulations and directives.

Contact

Judith Abel
Manager, APHG
T: 020 7202 8580
E: judith.abel@healthinparliament.org.uk

#RegenMed

The three flexibilities within the pharmaceutical area within the EU and these are generally unmet need or public health emergencies which have been brought into a programme called MAPPS. Many of these products are used to treat diseases which affect very small proportions of the population but for which there's generally no current treatment. Continually exemptions for hospital based pathways into the NHS are also in effect. Within the Advanced Therapy Medicinal Products regulations is a so-called hospital exemption, whereby if a medical practitioner prescribes a particular treatment for a single patient, they can be given locally-based dispensation – which will be overseen by the regulatory body, the MHRA – and treatment will be allowed on an experimental basis. Similar such exemptions exist with regards to the regulation of regenerative based medical devices.

Professor Faulkner then went on to examine the adaption, reimbursement and repayment of regenerative products. There are a number of initiatives which are moving towards bringing flexibility to modes of access for patients. These are:

- 'Promising innovative medicine'/ 'Early access to medicines' (MHRA)
- NICE valuation methodology and assessment decisions
- NHS Executive commissioner schemes (Commissioning through Evaluation scheme; Risk sharing schemes are being explored and we know are already being used in some of parts of the NHS for some applications, where risk is shared between the company producing the product and the NHS commissioning the service or the product.)
- Individual patient funding.

Continually, there are various initiatives to bring NICE and NHS England closer together to coordinate their activities, and also NICE and the regulator, MHRA, around these kinds of innovative therapies.

Professor Tony Pagliuca, National Clinical Lead Regenerative Medicine, Kings College Hospital, London

Contact

Judith Abel
Manager, APHG
T: 020 7202 8580
E: judith.abel@healthinparliament.org.uk

#RegenMed

Professor Pagliuca described the rapid growth in funding across the broad area of regenerative medicine in the past five years and identified the main actors driving the field today, including the Cell and Gee Therapy Catapult, the NHS Blood and Transplant Units, universities, spin-out firms and small and large pharmaceutical companies. He pointed to the translational gap which has prevailed for a number of years and how the Catapult in particular has been designed to address this, especially in regard to clinical trials of new treatments as they reach Phase 3 and beyond, where manufacturing and scale-up is underway. The importance of providing bespoke innovation pathways for regenerative medicine reflects its very different route to the clinic compared with the conventional pharmaceutical one.

He went on to illustrate this through describing three cases where new challenges in translation needed to be considered: the cases related to CAR T-cell therapy, gene therapy for patients with sickle cell disease, and a trial relating to cell therapy treatment for 'acute respiratory stress syndrome'.

Professor Pagliuca concluded by arguing that such cases suggest the need to consider the following factors when developing policy and resourcing for the field:

- Understanding the clinical complexity
- Skills and training
- Logistics of managing ATMP's – speed, access and storage
- Appropriate infrastructure funding in clinical delivery facilities
- Managing expectations - patients already travelling abroad to access novel therapies eg autologous CAR-T in the USA or travelling to single EU centre for Strimvelis
- Defining the scope and specifications for possible Centres of Excellence via the Regenerative Medicine Clinical Reference Group

Q&A Session

The Medicines and Healthcare Products Regulatory Agency (MHRA) is very influential in the UK medicines and technology regulatory system, but the situation post-Brexit depends on what kind of agreement is reached between the UK and the EU. We need to be careful to focus on the UK's scientific excellence and achievement, not just on the politics of Brexit.

Contact

Judith Abel
Manager, APHG
T: 020 7202 8580
E: judith.abel@healthinparliament.org.uk

#RegenMed

At the moment the UK has a very productive relationship with the European Medicines Agency. The MHRA carried much of the regulatory burden within the EMA to set early standards for regenerative medicines. Manufacturers need this reassurance to proceed to the clinical trial stage for their products. Moreover, the UK Stem Cell Bank is an example of an excellent resource we have developed that ensures the quality of cell lines for both research and clinical applications. (Note: funded by the MRC and Biotechnology and Biological Sciences Research Council, the UK Stem Cell Bank was established to provide an ethically approved, quality controlled and assured repository of human embryonic, fetal and adult stem cell lines to underpin research and healthcare developments).

We not only need the right kind of framework for transformative regenerative medicine products, but also for transformative processes; that is almost more important. It would not be wise to depart from the regulatory framework we already have although many regenerative medicine companies are potentially looking to align their regulation with the US Food and Drug Administration rather than the European Medicines Agency post-Brexit.

If we remain in the European Economic Area, there will still be regulation in place, but the UK will lose influence in shaping the regulatory framework. If we sign up with the World Trade Association model there will be more flexibility as we can work to ICH standards (The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use [ICH]). The question is what is the best way to develop regenerative medicine products that can move freely around Europe? Regulation and standardisation do offer opportunities and we need to develop protocols around the use of therapeutics. It could take the sector 20 years to recover from a hard Brexit. The key thing will be to try to avoid short-term collateral damage.

For regenerative medicine we need regulatory strategies that make sense as the post-Brexit situation unfolds. We need to beware of over-regulation and top-down control. Research and development facilities need to be able to be creative too.

With the uncertainty over Brexit, it is already clear that some companies looking at a global market for their products now want to base themselves in mainland Europe rather than the UK. They will take the

Contact

Judith Abel
Manager, APHG
T: 020 7202 8580
E: judith.abel@healthinparliament.org.uk

pathway of least resistance in the face of potential change. However, regenerative medicine companies need to know it is business as usual in the UK. That is very important. We also need to encourage big pharma to come back from the US. We need to tap into the enthusiasm for regenerative medicine in the US; this is not just about money - it's about the research culture in the US.

On the other hand the 'critical research mass' in the US is not always the right way to go. For example there is a world-leading cluster in Yorkshire around woundcare led by Smith and Nephew. The same is true in the regenerative medicine field in the UK. We need to think at a higher level about what it is that creates a culture of success.. Indeed, some US-based companies are coming back to the EU and the seeking guidance from the MHRA on regulation.

Last year, the UK received 28% of IMI funding. (Note: the Innovative Medicines Initiative (IMI) is Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients). We didn't get that just because we are in the EU - we got that because of the quality of science in the UK. However, if regulation and processes get difficult in the UK, scientists from all over the globe simply may not come here. We mustn't allow ourselves to divorce ourselves form the EU as it's global collaboration that's important.

Regenerative medicine in the healthcare system

We need to commission new technologies in just a few specialised centres in the UK - at least to start with. There will only be the resources to focus on a small number of centres developing regenerative medicine products which can get treatment from the laboratory to clinicians and out to patients. We do need strong, rational leadership and decision-making at a systems level though. We also need new skill sets amongst doctors and nurses. We also need to recognise the limitations, i.e. that some patients develop toxicities from treatments, and that some treatments for very rare diseases will be very expensive. There are also funding implications. Who is going to pay for and deliver these new treatments? We also need to focus on scientific training more generally, including training of more engineers.

Contact

Judith Abel
Manager, APHG
T: 020 7202 8580
E: judith.abel@healthinparliament.org.uk

#RegenMed

Questions for Parliamentarians

For Parliamentarians, the key issues to bear in mind are those raised in the recent hearings of the Science and Technology Select Committee report on Regenerative Medicine, including:

First, how can we begin to develop centres of excellence/delivery for RM on an efficient, regionalised basis, and include within that support regionally for storage of tissues/cell lines: could this be part of regional industrial planning

and secondly, in light of this:
Have we enough understanding of the likely size and profiles of clinical populations treatable as a result of the different ways in which cells might be manufactured and deliverable at different scales, and if so how best to plan for this at a national level?

Moreover, in the recent hearings of the Science and Technology Select Committee report on Regenerative Medicine related issues have been raised including:

How can we get the processes right to develop regenerative medicines?
What socio-economic evaluation do we need to make of these new technologies?
Where does regenerative medicine fit into healthcare at a time of severe financial constraint?

http://www.parliament.uk/business/committees/committees-a-z/commons-select/science-and-technology-committee/inquiries/parliament-2015/regenerative-medicine-inquiry-15-16/

Contact

Judith Abel
Manager, APHG
T: 020 7202 8580
E: judith.abel@healthinparliament.org.uk