The Academy of Medical Sciences

Response to the House of Commons Science and Technology Committee inquiry into regenerative medicine

May 2016

Summary

- The Academy welcomes the opportunity to respond to the House of Commons Science and Technology Committee's inquiry into regenerative medicine (RM). We support the efforts of the Government and other organisations to maximise the benefits of RM in the UK.
- Now is a time of great opportunity for RM in the UK. We are supportive of the establishment of a number of UK initiatives and the various translational and innovation funding streams to support the development of this area. It would be helpful if further clarity was provided on the scope of these initiatives and how they interact with one another, to help users navigate the RM landscape. It is also important to maintain a balance of funding for basic scientific research and translational medicine, as preserving this balance will help to support evidence generation throughout the development process to ensure the most effective and safe treatments reach patients.
- There are generally positive experiences of the UK regulatory structure and it is essential to maintain the balance between flexibility and rigour in the evaluation of these new approaches. Criteria for cost-effectiveness evaluation for RMs will need to be reviewed.
- There is a need to address the gaps in infrastructure for manufacture of RMs, and it may be useful to consider dedicated facilities to respond to this need. We welcome the role of the Advanced Therapies Manufacturing Taskforce in helping to support and anchor increased manufacturing and supply-chain facilities in the UK.
- It is important to consider the preparedness of the UK healthcare system for RM, which will need both technical and clinical capacity and capability for such complex therapies.
- The term 'regenerative medicine' is used broadly to encompass a diverse range of different approaches within the fields of cellular, genetic, pharmacological and bioengineering science. Therefore it is important to consider whether a national strategy should, in the short term, focus on a subset of RM approaches aligned with the UK's research strengths.
- We would support the development of a UK RM strategy developed jointly by government, academia, industry, regulators and healthcare bodies, amongst others.

Introduction

The Academy of Medical Sciences promotes advances in medical science, and campaigns to ensure that these are translated into healthcare benefits for society. Our elected Fellowship comprises some of the UK's foremost experts in medical science, drawn from a diverse range of research areas.

The Academy welcomes the opportunity to respond to the House of Commons Science and Technology Committee's inquiry into regenerative medicine (RM). Our response is formed based on the views of the Academy's Fellows, many of whom have extensive experience of RM – from early-stage laboratory research, through clinical translation, to commercialisation and healthcare delivery. Our responses to the four key areas outlined within the inquiry can be found below.

Opportunities for regenerative medicine and the UK's ability to reap those advantages

The UK has a reputation as an international leader in RM. The desire for a new generation of more 'personalised' medicines targeting particular disease subgroups, and potentially enabling treatment or cure of currently untreatable diseases, means that RM is an area of great opportunity and likely to expand rapidly. To reap the rewards of this expansion – for patients and the economy – it is important that the UK stays at the forefront of this increasingly competitive field.

In terms of seizing opportunities in RM, there is an important role for academia in discovery, translational and clinical research. Increasingly, this depends on national and international collaborations for pooling expertise, resources and patient cohorts, and industry collaborations for scientific and manufacturing expertise and resources. UK higher education institutions (HEIs) are continuing to coordinate activities in RM, with several leading UK universities establishing RM centres to pool expertise. Industry also plays a critical role in developing and embracing new opportunities in RM, with increasing activity and investment in RM both at SME and 'large pharma' levels, as well as involvement in a number of collaborations and innovation initiatives.

UK regenerative medicine initiatives

The UK is well placed to capitalise on the potential of RM through a number of recent initiatives supporting HEIs and industry, including the UK Cell and Gene Therapy Catapult (CGTC) and the UK Regenerative Medicine Platform (UKRMP). The CGTC offers support to translate early research into commercially viable opportunities, and provides helpful guidance on the regulation in this area. However, it has been noted that on occasion, the cost implications and limitations in capacity for the CGTC to provide this guidance can mean that further advice needs to be sought elsewhere. Similarly, the UKRMP has had positive impact through bringing together interdisciplinary experts and providing key infrastructural support. Now the UKRMP and the CGTC are fully established, it would be helpful to further clarify the scope of these initiatives and how they interact and work with each other, to help users to understand when to approach and interact with these organisations in the development process.

Preparedness of the healthcare system

It is important to consider the preparedness of the UK healthcare system for RM, both in terms of technical and clinical capacity and capability for the complexity of such therapies, (including when running clinical trials) and also with regard to the cost implications. The required technologies are not currently available through NHS laboratories and there will be significant training needs for all healthcare staff. With RM therapies, the cost per patient is likely, at least initially, to be relatively high and this could prohibit access through the NHS system. To maximise cost-effectiveness and appropriately manage demand in the shorter term, there may be a case for accreditation of centres that wish to deliver RM therapies, so that the appropriate infrastructure is in place.

The regulatory systems involved, their effectiveness and ease of use

UK regulatory landscape

In general, the UK and EU regulatory systems for RM are felt to be effective with many positive interactions to date. We also welcome access schemes such as the EMA's adaptive licensing and MHRA's Early Access to Medicines Scheme to facilitate uptake of medical innovation. It is important that the regulatory environment remains flexible for RM to accommodate new and diverse

approaches alongside maintaining robust review processes to ensure that the most promising, effective and safe therapies are made available to patients. Where RM technologies require review by multiple regulatory bodies, such as those involving human tissue, it is important that the review processes are coordinated between the different regulators.

Furthermore, the UK has guidance available to help navigate the RM regulatory framework, including the Department of Health's UK Stem Cell Tool Kit as well as advice available from the various regulatory bodies and others. Some of those contributing to the Academy's response noted that the MHRA's often quick turnaround times, and its increasing communication and involvement with external groups, have enabled the RM community to remain agile. We also welcome the establishment of the MHRA's 'One Stop Shop' RM regulatory advice service. In future, the complexity and increasing volume of RM-related enquiries may stretch the resources of the regulatory bodies, potentially requiring additional capacity to address this.

Given that RMs can be potentially transformative for disease management, there is some concern that there may be a premature 'rush' to clinical translation of these therapies, potentially allowing through some therapies with relatively low effectiveness in the clinic. Therefore it is essential that alongside safety data, there is a strong scientific evidence base for RMs with robust proof of efficacy, to ensure that only those therapies likely to succeed enter the clinic. This is particularly important for RMs where there are high levels of emotional investment for patients in such transformative (and even curative) approaches, as well as their significant cost. The complexity of Good Manufacturing Practice (GMP), safety and tolerability for RMs, amongst other factors, further complicates the generation of this scientific evidence. Animal models also remain critical for this translational research and it is therefore important that this area is supported.

Challenges in the regulation of regenerative medicine

The RM sector has some unique regulatory issues which it is useful to consider. There are significant challenges to standardisation and reducing batch-to-batch variability, such as in cell differentiation. This makes requisite standard operating procedures for GMP difficult. Traditional evidence criteria are also sometimes difficult to apply to RM studies. For example, there are significant challenges with running satisfactorily randomised and placebo-controlled trials of RMs due to the complex and 'personalised' nature of many of the therapies, particularly when surgery is required. These challenges in the regulation and manufacturing of RMs were explored in detail during the MHRA's 'regenerative medicine regulatory workshop' sponsored by the Academy and others.[1]

Historically, difficulties have been encountered with Research Ethics Committee approval and variability in efficiency between R&D departments of NHS Trusts, which impact on the delivery of studies in areas such as RM. Therefore we welcome the establishment of the Health Research Authority (HRA) and the recent launch of the HRA's centralised single approval system which will hopefully address these challenges.[2,3]

[1] Academy of Medical Sciences *et al* (2012). Regenerative medicine regulatory workshop. http://www.acmedsci.ac.uk/viewFile/51d179911937d.pdf

[2] The Academy's 2011 report on the *'Regulation and governance of health research'* highlighted the challenges and inefficiencies encountered with NHS site approval, and recommended the establishment of the Health Research Authority to overcome these problems: http://www.acmedsci.ac.uk/download.php?f=file&i=13646

[3] HRA Approval: http://www.hra.nhs.uk/about-the-hra/our-plans-and-projects/assessment-approval/

Evaluation of cost-effectiveness

We welcome the increased engagement of the National Institute for Health and Care Excellence around RM technology and its continued dialogue with the CGTC. The applicability of current assessment models to RMs needs to be reviewed, so that they are sufficiently flexible to accommodate the unique cost and benefit profiles of RM. The relatively high costs of RMs need to be considered alongside their potential to treat, and even cure, diseases such as degenerative conditions that would otherwise be progressively disabling. Therefore in addition to patient benefit, any wider advantages for society and the economy need to be taken into account. This debate feeds into a wider concern that a lag in NHS adoption of RM may disincentivise companies and others from investing in this technology.

The arrangements for researchers and manufacturers in the field to be able to innovate and secure innovation funding and support

We welcome increased translational funding for RM provided through schemes such as the Wellcome Trust Translational awards, Medical Research Council Developmental Pathway Funding Schemes and Innovate UK. It is vital that a *balanced* approach to funding is maintained that continues to support funding for basic science alongside translational science, as this basic science is essential for building a strong evidence base for developing safe and effective therapies. The development of RM technologies often requires novel, innovative approaches with a higher level of risk. It is suggested that funding in this area can sometimes be limited by the risk-averse approach to more experimental therapies by some UK funding providers, who may more often favour projects likely to deliver incremental scientific gains over 'blue skies' investments. This approach may need to be reviewed, as the high risk (even 'blue skies') approaches may help to accelerate development of novel RMs. There is value in providing dedicated research support functions to optimise the quality of these funding applications within HEIs and SMEs.

The term 'regenerative medicine' is used broadly to encompass a diverse range of different approaches within the fields of cellular, genetic, pharmacological and bioengineering science. There are some concerns that covering this breadth of approaches may be challenging when allocating funding streams and therefore it may be helpful to focus funding of RM projects on those which intend to lead to replacement or repair of diseased tissues, rather than projects which move beyond this remit, such as those solely focussed on developing processes for drug screening.

There is some concern that on occasion, funding decisions for RM may be based on the perceived commercial potential of a therapy even with insufficient scientific evidence for efficacy. It is important that once a therapy enters clinical trials, the basic research remains ongoing so that the development can benefit from the iterative cycle of 'bench to bedside and back again'.

Finally, there are concerns around the intellectual property (IP) and patent framework associated with RM technologies, and the unique issues of IP protection for processes and complex therapies specific to RM need to be addressed.

Manufacturing of RM products

There are challenges with manufacture and supply of RM products, including the complexity of some manufacturing procedures and scale-up of processes. Specifically, further infrastructure (such as that for cell and vector manufacture) needs to be prioritised to enable affordable access to appropriate manufacturing facilities at GMP standards, particularly for academia and SMEs.

Currently, these facilities are not available at sufficient scale in the UK, and researchers need to source material from EU and US manufacturing centres, generating further cost and regulatory challenges. We welcome the Advanced Therapies Manufacturing Taskforce initiative which will address some of these UK manufacturing needs.

The case for a government-approved regenerative medicines strategy

We would support the development of a government-approved national strategy for RM. Healthcare innovation is a key component of the UK economy, and RM and the associated industry will contribute towards this. Moreover, it is important to ensure that patients in the UK can access the potential benefits of RM. The UK is world-leading in many areas of RM, and it is important that the strategy supports the continued attraction and retention of the best scientists from around the world. The development of such a strategy will require detailed stakeholder dialogue. It is also essential to ensure that there is appropriate representation of academic experts on any Government advisory committees. We welcome the formation of the Regenerative Medicines Expert Group (RMEG) and its input will be critical when forming the strategy.

Additionally, it is also important to consider whether a national strategy should focus on a subset of RM technologies. If some approaches are prioritised, then it will be important to consider: the approaches that the UK is already best placed to exploit; those most likely to lead to actual therapies; the approaches which can be best mapped to the future requirements and capabilities of the UK healthcare system.

In summary, a holistic but focussed UK strategy, developed jointly by government, academia, industry, regulators and healthcare bodies, will help the UK to best capture the health and economic benefits of RM. We would welcome the opportunity to provide input towards such a strategy.

This response was prepared by Thomas Hall (Policy Intern) and was informed by the Academy's Fellows. For further information, please contact Liberty Dixon, Policy Officer (Liberty.Dixon@acmedsci.ac.uk; +44(0)20 3176 2186).

Academy of Medical Sciences
41 Portland Place
London, W1B 1QH
+44(0)20 3176 2150

info@acmedsci.ac.uk
www.acmedsci.ac.uk

Registered Charity No. 1070618
Registered Company No. 35202