Regenerative Medicine

Response by the Wellcome Trust - May 2016

KEY POINTS

- Funding for regenerative medicine must cover all parts of the innovation chain, from basic research through to manufacture of clinical products, if the UK is to deliver on the potential of these therapies.

- Early stage research for regenerative medicine requires input from diverse disciplines, and more support is needed to encourage interdisciplinary work. To develop viable products, there are gaps in both the understanding of the fundamental biology and technical skills that must be addressed.

- Much better engagement with industry is needed at an early stage of development, to share experience and knowledge — particularly on regulatory and technical issues — in order to facilitate translation.

- It is difficult both to manufacture and to scale up regenerative medicines. The challenge of moving from one-off uses to routine delivery is compounded by personalised or individual approaches, such as cell therapies.

- Regulators must take a pragmatic approach, and ensure that they do not inappropriately apply criteria from small molecule regulation to regenerative medicine. Although the Advance Therapy Medicinal Products legislation is complex and not perfect, significant improvements can be made through improving implementation without revising the legislation.

Introduction

1. The Wellcome Trust is a global charitable foundation dedicated to improving health. This year, we are planning to invest up to £1 billion in biomedical research and the humanities. Through our Innovation funding we have invested over £49.5 million into “Advanced Therapy Medicinal Products”(ATMPs), including somatic cell therapies, gene therapies and tissue engineering. We continue to support projects in this exciting field, where the aspiration of seeing new therapies in clinical use is starting to be realised.

2. The Regenerative Medicine Expert Group (RMEG) was formed to advise on the development and delivery of regenerative medicines to the NHS. The Government should take action based on RMEG’s recent report, ‘Building on our own potential: a UK pathway for regenerative medicine’¹, which has provided a comprehensive review of this issue.

3. The public must be engaged in the discourse about regenerative medicine, and ethical considerations should be taken into account throughout the research and regulatory processes.

Allowing researchers to innovate

4. It is critical that regenerative medicine research is funded across all parts of the innovation chain, from basic research through to clinical products. The focus on treatment outputs as a key indicator of success should not lead to a funding shift towards later-stage research, particularly as incomplete knowledge of the basic biology is one of the primary barriers in the field.

¹ Building on our own potential: a UK pathway for regenerative medicine:
5. There are some skills gaps amongst basic researchers in the UK, for example the knowledge of how to produce vectors, scaffolds and homogenous cell cultures, which are needed to ensure the development of viable products. This has been made worse by a “brain drain” to the more favourable culture in the US. To counteract this, the UK should initiate training programmes, including specific regenerative medicine PhD programmes, to train researchers and develop the field.

6. The development of regenerative medicines requires input from wide-ranging fields, from mathematics to medicine, as well as expertise from outside academic research, in order to be successful. There are limited schemes and funding available that encompass the interdisciplinary nature of regenerative medicine projects.

7. There is currently a lack of disease models in which to test regenerative medicine therapies, for example the immunosuppression required in animal studies limits their ability to demonstrate safety and efficacy. This makes phase 1 trials particularly important for the development of regenerative medicines, but there are limited resources available to fund these trials.

Funding and support for innovation

8. Cultural, financial and logistical issues that impede the translation of research are compounded by difficulties specific to regenerative medicine. For example, the complexity of the regulatory framework and the technical challenges of manufacturing and scale up must be considered from a particularly early stage to develop a successful product. This requires much better collaboration and knowledge sharing with industry. Academics should be incentivised to work with industry, to encourage a ‘revolving door’ between universities and businesses.

9. We welcome the protection of Innovate UK within the proposed structure of UK Research and Innovation (UKRI). Innovate UK is well placed to fund research in this space, with strong relationships with industry and good governance structures. We hope the integration of Innovate UK into UKRI will bring more focus on commercialisation to early stage funding, and aid collaboration between academia and industry. However, we are concerned that a switch from a grant-funding model to loans would not sufficiently de-risk projects to attract follow-on investors.

10. The Cell Therapy Catapult is at an early stage of development. However, there are still mixed opinions about its effectiveness as an advisor and convener. The impact of the Catapult should continue to be evaluated but a commitment to ongoing funding will provide reassurance and resource so the Catapult is able to adapt to the needs of the community.

Manufacturing and scale-up of advanced therapies

11. Manufacturing regenerative medicine products is technically difficult and requires specialist knowledge and equipment. We welcome the Government’s decision to fund the new Cell and Gene Manufacturing Centre. This will provide early stage companies with easier access to the expertise and specialist facilities necessary to develop their products. It will therefore increase their viability and appeal to investors, while also delivering economies of scale for production.

12. Some regenerative medicines, such as cell therapies, are tailored or personalised, which makes it more difficult to scale-up production and treat large numbers of patients. This not only limits how widely the therapy can be used but also impacts the costs of treatments.
Regulation

13. There are currently only a small number of licensed ATMPs. Patient access to these therapies is therefore often provided through exemption schemes that allow these products to be used in specific circumstances, such as ‘specials’ and hospital exemptions. However, these schemes are used inconsistently across the EU and do not promote wider access to, and uptake of, these products. The European Medicines Agency (EMA) should encourage and facilitate licencing to enable the widest possible benefit to patients.

14. The regulation of regenerative medicine in the EU is complex and not perfect. Significant improvements can be made through implementation without revising the Advance Therapy Medicinal Products legislation. Instead, regulators should take a pragmatic and proportionate approach to working within the current legislation.

15. There is perceived to be a failure within the EMA to take into account the specific requirements of this field and a tendency to apply inappropriate criteria from small molecule regulation to new regenerative medicinal products. The United States Food and Drug Administration is seen to be more willing than the EMA to engage with scientists at early stages in their research and to approve new therapies. Dialogue between researchers and regulators should be fostered to promote an open, flexible and iterative approach.

16. The UK Medicines and Healthcare products Regulatory Agency (MHRA) takes an informed and pragmatic approach to the field. Recent development of the ‘regenerative medicine one-stop shop’ has improved access to advice on the regulatory process.

17. The US has banned therapeutic use of blood cell products that come from donors that have lived or received a transfusion in the UK, based on concerns about the potential transmission of classic and variant Creutzfeldt-Jakob disease. This could impact the acceptance of human embryonic stem cells from the UK, even when they fully comply with UK and EU standards. The UK government should encourage the US government to review the rationale for the continued ban.

Conclusion

18. It is important that the Government takes action to tackle the issues across all the stages of regenerative medicine development. This will be vital to reap the full benefits of these new therapies for patients.

The Wellcome Trust is a global charitable foundation dedicated to improving health. We support bright minds in science, the humanities and the social sciences, as well as education, public engagement and the application of research to medicine. Our investment portfolio gives us the independence to support such transformative work as the sequencing and understanding of the human genome, research that established front-line drugs for malaria, and Wellcome Collection, our free venue for the incurably curious that explores medicine, life and art.

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2 The road to providing human embryo stem cells for therapeutic use: the UK experience: http://www.reproduction-online.org/content/132/5/681.full.pdf