

The promises and challenges of biomodifying technologies for the UK

Michael Morrison, Senior Researcher in Social Science at the Centre for Health, Law and Emerging Technologies (HeLEX), University of Oxford, sheds light on the promises, as well as the challenges when it comes to biomodifying technologies for the UK

One of the most promising areas of medical innovation is the idea of using our own cells and genes to treat disease. Scientists have been studying these possibilities under a variety of labels including 'gene therapy', 'tissue engineering' and 'regenerative medicine' for several decades. Despite this work, only a limited number of cell or gene-based therapies are currently available, with the most common procedure being the use of stem cells from bone marrow or umbilical cord blood to replenish the body's immune system after chemotherapy.

The UK has a well-established life sciences sector, with world-class academic research, a commercial sector that ranges from pharmaceuticals to data analysis and contract manufacturing, a National Health Service with multiple research-intensive hospitals and an established system of regulatory oversight. It is in many respects an advantageous location for developing new regenerative medicines.

However, there are a number of challenges in bringing innovative science to the clinic, a process known as 'translation', especially in a sector still largely designed around conventional drugs, medical devices or surgical procedures¹. Therapies based on living tissues are more difficult to manufacture and standardise than

traditional drugs. They change in response to their environment and often vary from batch to batch making it harder to establish quality and safety. They may require new clinical skills and working arrangements to deliver and there is a lack of proven models for balancing viable commercial production with sustainable healthcare costs.

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In this context, robust, innovative science is clearly important but it is not sufficient by itself to deliver workable new therapies that deliver tangible patient benefit. The process of translating knowledge into novel medical products and services is necessarily a collaborative endeavour. It requires academics, companies, healthcare professionals, regulators, funding agencies, hospital managers and health economists working together to develop solutions.

Infrastructure is important, as recent investment by the UK Government in the Cell and Gene Therapy Catapult centre and the three Advanced Therapy Treatment Centres (ATTCs)

acknowledges. This investment is further complemented and on occasion informed, by social science studies of innovation and clinical translation which can clarify points of alignment or tension between the priorities of different stakeholders, identify organisational factors that support or inhibit the uptake of new medical technologies and help to understand how regulations impact academic, commercial and clinical activity^{1,2,3}.

A number of recent discoveries have enabled researchers to modify living biological tissue in novel ways that raise the prospect of increasingly customised, patient-orientated treatments. Three contemporary examples of such 'biomodifying technologies' are; 'gene-editing' using tools like CRISPR-Cas9* to modify DNA, induced pluripotent stem cell technology that allows an ordinary skin or blood cell to be turned into a stem cell capable of producing any tissue type in the human body, and the emergence of bioprinting which can produce three dimensional structures made from living tissues. Each of these are 'gateway' technologies: versatile, comparatively easy to use, with advantages in speed or precision over existing tools and having a broad range of potential applications. Translating these technologies into new medicines holds promise for addressing significant unmet medical need; potential cures

for genetic diseases, tissue-based therapies for degenerative conditions and replacement organs to ease the pressure on transplant waiting lists. 3D bioprinting, gene editing and induced pluripotent stem cells (iPSC) also represent potential 'personalised' medicines, tailored to match the biology of an individual patient or made from a patient's own modified cells.

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Two projects, 'Biomodifying technologies and experimental space', funded by the Economic and Social Research Council and 'BIOGOV: Governing Biomodification in Life Sciences Research' (Leverhulme Trust), are building on previous social and legal research^{2,3} to identify critical issues for the development of customised cell and gene therapies in the UK. While it is difficult to predict exactly what new applications of each technology will emerge and bioprinting, gene editing and iPSC are at different stages of maturity, reimbursement, data collection and regulation are likely to be significant challenges. Biomodifying therapies are expensive and often target rare disease or the most severely affected patients with more common conditions. In the U.S., the recently-approved gene therapy for muscular atrophy Zolgensma™ is the world's most expensive drug at \$2.125 million per treatment. Personalised or

customised therapies only exacerbate these tendencies.

The prospect of a spate of ultra-expensive biomodifying therapies coming to market is likely to threaten fair access provisions for any healthcare system based on social justice and need rather than the ability to pay. There is, therefore, a tension between the state's role in promoting the UK as a supportive environment for innovative life sciences research and its need to ensure a sustainable National Health Service by controlling healthcare expenditure. The UK's National Institute for Health and Care Excellence (NICE) 'highly specialised technologies' pathway allows significantly higher costs for complex treatments for rare conditions. However, current assessments are based on several years of data from clinical trials, which struggle to capture potentially life-long effects of cell and gene therapies. Small patient populations also means the trials often involve relatively small numbers of participants. Making biomodifying therapies a reality may require complementary innovations in healthcare reimbursement models, new forms of evidence such as large-scale open access studies of the long-term impacts of cell and gene therapies that allow safety and efficacy to be evaluated and reviewed over lifetimes, and evolving regulation whose impact can be assessed and, if appropriate, revised in a timely fashion⁴.

** CRISPR stands for Clustered Regularly Interspersed Short Palindromic Repeats. It is a molecule that can be designed to identify and bind a particular stretch of*

DNA, which is then cut by the 'molecular scissors' of the Cas9 protein.

References

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