IN THE LAST OF A FOUR-PART SERIES, **DR JONATHAN DANDO** ARGUES THAT THE FOCUS MUST SHIFT FROM FINANCIAL GAINS TO HEALTH GAINS IN THE FIELD OF REGENERATIVE MEDICINE

Socioeconomic needs

With the shortage of effective therapies on the market, the even shorter list of real therapies in development and the potential benefits that regenerative medicine therapeutics provide, in this final editorial in a four-part series, we reflect on the challenges the field is now facing to provide patient therapies and how the risks of focusing too much on commercialisation can result in poor ethical decision making and can irreversibly damage the generation of these much needed therapies.

Networks such as Endostem and Biodesign offer brilliant environments for sharing knowledge and advancing that knowledge into a potential therapy, but with the ever prevalent onus on generating inventions with financial value as opposed to patient value, the potential benefits of such networks is at risk of being diluted.

Strategy

For virtually every researcher working in the life science field attempting to obtain funding for their projects, a direct link to an exploitable product has to be indicated with a clear strategy to develop that product. This has been a staple of the grant application system for quite some time, based primarily on the historical anomaly of the financial returns obtained from the recombinant DNA patent, which has been used as a benchmark for what can be obtained, rather than the exceptionally clever licensing that was performed for a broad acting platform technology.

While understandable in the context of justifying the engagement of taxpayers' or donors' money, the emphasis on exploitation has created a complex scenario for the implementation of research itself.

In the field of regenerative medicine, which can result in the lifelong correction of the disorder when no other therapy exists, there is the added risk that the motivation to obtain funds can additionally result in questionable ethical decision making.

Cost

Trying to overenthusiastically link early research in this field with economically viable therapies in the present economic climate, where there is a significant shortage of funding anywhere for research and development, is nonsensical.

The cost of developing a new therapeutic, from concept to market release, is between €800m and €1.7bn; if developed for a widespread disease or disorder when released onto the market and purchased by the healthcare systems, revenues can reach upwards of €1bn per year. This is termed the 'blockbuster' model, and has served as a key constituent of the large pharmaceutical/medtech companies' strategies.

Successful development of such therapeutics is rare, and the strategy has been altered to try and repurpose (i.e. to use a therapeutic designed for one disease for another) less lucrative therapeutics to increase the revenue potential.

At face value, this appears to be a great opportunity for the development of regenerative therapeutics as many of the technologies can arguably be tailored for many different tissues or several different diseases that impact the same tissue. However, for this to be applicable and for effort to be engaged in repurposing, some demonstration of the efficacy of the therapeutic in a human has to be achieved.

In the critical path of therapy development, this first occurs in a phase II clinical trial, yet the costs to get there are significant (www.forbes.com/sites/matthewherper/2012/02/10/the-truly-staggering-cost-of-inventing-new-drugs and www.manhattan-institute.org/html/fda_05.htm and www.lehigh.edu/~inbios21/PDF/Fall2009/Simon09042009.pdf).

Inventions

It is now publicly known that large companies looking to license inventions (the process of bringing in and owning an invention that has not been invented in the company so that it can be developed into a product) are mainly looking for those inventions that have been validated in phase II. The implications here are clear: any entity must have engaged at least €10m (the minimum for rare diseases in which there are no failures in research and development).

However, in reality, this could be significantly more – before they can potentially expect to see any revenue or a hint of a licensing deal that is proportionate to the further risks and market sizes. The development of treatments for rare diseases costs significantly less, and the potential revenues are relative; and, because licensing revenues are not as high, the 'deal' can therefore be difficult to obtain.

Some small companies find it difficult to identify and engage such funds that facilitate a deal being agreed, whereas public research institutions have no possibility whatsoever of identifying and dedicating that amount of funding for a single project. Nevertheless, these same institutions have been given the added mission as purveyors of innovation and supposed high value invention validation while simultaneously knowing they do not have the capacities to reveal that value.

Values and ethics

It is therefore impossible to prove that early stage research (read, public research) has a commercial value, and, as the institutions themselves do not have the funds to prove the value, there is little or none in the private sector for such high risk work. This means that, by default, the whole research community is being encouraged to not tell the truth simply as a means of survival, to be somewhat self-delusionary and, in rarer circumstances, to behave unethically.

This is on the verge of being devastating for patients and their families. In the recent Mesenchymal Stem Cell scandal in Italy, where one institute aimed to use these cells as a panacea for many diseases (www.eurostemcell.org/story/scientists-raise-alarm-italian-government-rules-unproven-stem-cell-therapy), evidence-based approaches to therapeutic development were ignored, the perceptions and feelings of the public (and, more worryingly, sufferers and supporters of sufferers) were shamelessly played on and the only entity to obtain any benefit, likely both financial and publicity, was the one claiming the applicability of the unproven therapy.

Other examples have been the increasing prevalence of scientific fraud or misrepresentation, resulting in the retraction of articles and removal of fake therapies, in some cases, those that had already been applied to humans.

Policing the retraction of fake data is undoubtedly a benefit (www.independent.co.uk/news/science/the-bad-science-scandal-how-factfabrication-is-damaging-uks-global-name-for-research-8660929.html). However, even this endeavour has been exploited by unscrupulous actors to prevent beneficial research from occurring, through anonymous allegation and a new form of McCarthyism.

Once accused, even anonymously, the researcher has great difficulty having new grants approved and publications accepted. We can, of course, speculate on the plethora of motivations behind such actions. If your competitors are applying for the same grant, generating a competing invention, or are disproving their invention validity, one can simply submit an anonymous accusation about some of their work and make their life extremely difficult. Fraud is a 'staining' accusation, because even if you are proven innocent, the stain of the allegation remains.

Potential

To realise the potential of regenerative medicine, the whole field needs to step back from the installed commercial need, draw breath, and focus more on generating groundbreaking high impact knowledge with an onus on patient functional restoration and less focus on ownership.

There is little room for compromise models, and they should not be considered if humans are to benefit. The knowledge 'coffers' have to be significantly refilled before exploitation should be considered.

Fundamentally, we simply have to remove the 'imaginary' goal of long-term financial rewards from developing exploratory and underdeveloped concepts. At some later point, more illuminated debate should be performed when the correct focus has been re-obtained.

If we are going to reach our original and idyllic scenario of treatments for all (see the first editorial in the series in Pan European Networks: Science & Technology, issue 6), based on highly efficacious, reproducible and affordable therapies for all, which expands the possibilities of tissue function restoration, it cannot be on a foundation of financial return.

Companies, governments, charities, patient associations and the scientific community must become more enlightened, as they all have a significant and positive role to play from taking an altruistic approach while still standing to benefit. In the context of regenerative medicine, this field has the potential to alleviate many of the diseases and disorders that impact the socioeconomic balance of the world we all inhabit and provide sustainable healthcare management.

The long-term benefits to a global population of sufferers must be emphasised over financial gains for a much smaller population. This will help to ensure that hope for the greater good prevails.

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