

718. Cell Therapy Commercialization: An Assessment of Translational Barriers

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Cellular based therapies represent a platform technology within the rapidly expanding field of regenerative medicine and are distinct from conventional therapeutics - offering a unique approach to managing what were once considered untreatable diseases. Despite a significant increase in basic science activity within the cell therapy arena, alongside a growing portfolio of cell therapy trials and promising investment, the translation of cellular based therapeutics from “bench to bedside” remains challenging, and the number of industry products available for widespread clinical use remains comparatively low. This systematic review identifies unique intrinsic and extrinsic barriers in the cell based therapy domain. Key electronic databases were searched and manuscripts subjected to pre-defined inclusion and exclusion criteria. Two independent reviewers examined the retrieved publications, and performed data extraction. 3374 unique publications were identified. 138 of these qualified for full assessment and subsequent data extraction. A number of key themes were identified, enabling examination of current challenges and opportunities facing cell therapy development, including manufacturing, regulatory, reimbursement, ethical and clinical adoption issues. In addition to an up-to-date analysis of the current landscape, we discuss a number of pragmatic solutions to facilitate future development and translation.

719. Stability Could Be a Weak Point for Gene Therapy Sponsors

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So far, no gene therapy product has been approved by the Food and Drug Administration (FDA). One gene therapy for an extremely rare disease was approved in Europe in 2012, but questions about its effectiveness remain. Gene therapy refers to products that introduce genetic material into a person's DNA to replace faulty or missing genetic material, thus treating a disease or abnormal medical condition. There have been hundreds of trials of gene therapy in humans since 1990, and few gene therapies have reached advanced stages of development and have been submitted for authorization. Therefore, regulators have not yet worked out how best to assess gene therapy. While the same requirements as other medicinal products generally apply to the clinical development of gene therapies, regulators recognize that there might be cases where the principles might not apply and have issued guidance specific to gene therapy in order to facilitate product development and marketing approval. The shelf lives of gene therapy products may vary widely, depending on the nature of the product and its storage conditions. The design of stability testing should be based on a comprehensive understanding of the final product and its intended use. Testing should be based on real-time, real-temperature studies and should include a measure of product integrity, sterility, identity, purity, quality and other applicable assays. Additionally, potency assays should measure a relevant biological functionality either in vitro or in vivo. Interaction with the FDA however indicates that, beyond what is provided in the current guidelines, the regulators will likely scrutinize the results from the stability program for gene therapy during submission for marketing approval. Therefore, establishing shelf life and storage conditions of gene therapy products would most likely be a weak point for gene therapy sponsors. Even if the stability protocols follow the current

guidelines, because the gene therapy territory is new and innovative, it is difficult to gauge whether an unexpected impact on product quality can occur years after stability has been completed. Based on this feedback, the recommendation is that the stability protocol should be established conservatively, maximizing time points, lot testing and with a careful evaluation of quality parameters and critical product attribute. In conclusion, the regulatory environment for gene therapy is still being established and commonly accepted principles guiding current product development should be thoroughly evaluated and most likely reassessed. Because of the biological complexities of these products, a conservative approach should be followed with regards to the stability program.

720. Data-Driven Development to Deployment of Recombinogenic to Reprogramming Drives

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We consider an approach to addressing health and well-being disparities on large scales by the development and deployment of recombinogenic and reprogramming drives. Among these are, for example, “gene drives” which “drive” themselves and proximally involved genetic elements through space, i.e. (sub)populations of individuals, and time, i.e. successive generations of these (sub) populations. In doing so, they can be engineered to propagate through (sub)populations despite reducing individual fitness, since most all offspring harboring drives are affected through inheritance, rather than fractional numbers of progeny. Fitness costs are thus compensated by this inheritance advantage. This, too, has spatial, e.g. ecological, as well as temporal, e.g. evolutionary, consequences for the (sub) populations being driven, as well as the network of interactions among the (sub)populations and the shared living environment.

We analyze and extend the data in our research and that of others to present technically possible types of drives, and the epidemiological contexts in which they can be applied to recombine genetic components and reprogram cellular chasses. Transient behavior during these modifications can give way to new equilibria in which, for example, disease transmission is mitigated, or disease resistance is bolstered, thus ultimately benefiting human health and agricultural well-being, respectively.

We combine the aforementioned and conclude with the technological and environmentally amenable consequences of drives as applied to contexts. As a powerful synthetic technology operating in the living world as intimately and broadly as natural evolutionary drives, potential unintended and off-targeting issues as well as safeguards and optimization of the development to deployment of drives are discussed. Simultaneously, as a technology dependent on its successful interplay with the environment, natural and man-made, drives are limited in their applicability due to their own inherent requirements, e.g. suitable for mating organisms, and brief generational timespans, as well as those external to them, e.g. ethics and safety for the target for the drive and others in the ecosystem, and immediate and long-term effects on other interactions in the network.