Foreword

The discovery and development of completely new therapeutic platforms in medicine has provided enormous benefits in the past by improving the efficacy and widening the utility of therapeutic products to improve outcomes in patients. This was certainly true with the revolution in antibodies and biologics, which now dominate the list of the most successful medicines used in healthcare systems, but the journey from Kohler and Milstein's discovery of hybridomas to antibody products approved and used in man took over 25 years. It is now clear that we are on the verge of a new revolution driven by the ability to manipulate genetic material in cells using gene therapy and also to use cells themselves as an effective therapeutic modality. Again, of course, this journey has taken decades. In many ways, it began with the characterisation of the human genome and the role that gene defects play in human disease as well as the role that gene products play in the modulation of cell function. From this fundamental understanding, it has taken decades to prepare the tools and strategies to apply this new knowledge to human disease. It is now clear, however, that we are on the verge of a wave of new therapeutics opportunities underpinned by these tools. The safe and effective introduction of genetic material into cells has now been achieved and is clearly having an impact on our ability to treat a range of monogenic disorders. These tools, however, will also have a potentially more important role in altering the function of cellular populations, allowing cells introduced into patients to be the therapeutic modality that produces benefit. Recent clinical data and regulatory approval of both cell therapy and gene therapy demonstrate that safe and effective ways in administering these interventions have now been thoroughly established, and it is now likely that a cascade of these new interventions will become available to healthcare systems and patients in the coming years.

The discovery and development of these new medicines, however, requires much more than simply discovery science. The journey from the original discovery of stem cell populations, the genetics of Mendelian disease or the first experimental observations that one could manipulate T cell activation with engineered cell surface recognition elements has had to involve novel manufacturing processes, new approaches to regulation, new clinical trial methodology and the management of a whole set of new and important safety issues. As with biologics in a previous generation, their adoption will require significant alterations in the way healthcare systems are structured to deliver such therapies and also improvements and efficiencies in the way these products are generated and administered to make them truly affordable to already hard-pressed healthcare systems. These innovations will also require a significant shift in the way health economists and funders consider the value of potentially curative therapies when the system has become

accustomed to therapeutic interventions that are time-limited and incomplete in their efficacy. It is already clear that health economic models utilised by Health Technology Assessment functions are not fit for purpose in this new world.

The pace at which exciting results are reported for both gene therapy and cellular interventions has increased enormously in the past 12 months. The manipulation of immune cells is particularly suited to this approach, and the striking efficacy signals seen in cancer accompanied by the large range of new cell and gene therapy and modalities being developed in this area suggest that there will be enormous potential for patient benefit. Cost, however, remains a significant issue, particularly if these therapies are to be used for wide patient benefit. It is likely – as with antibodies – that processing improvements will improve the efficiency of manufacturing cells and that allogenic cell solutions may ultimately become available. Similarly, with the ability to manipulate genomes with considerable precision using gene editing technology, there may be further enhancement of the methodology used to deliver these therapies. Healthcare systems will need to prepare themselves to using cells and gene therapy interventions much more routinely, and this also requires a significant shift in their infrastructure and capabilities. Now that the benefit for patients seems unambiguously proven, this is likely to follow at speed.

These new interventions also take precision medicine to a new level, targeting very specific cellular functions or gene targets in human disease biology. Ultimately, some of these therapies may be necessary for very small patient subpopulations and for very rare indications and this will create its own challenges in healthcare systems.

Despite all the important challenges that remain, it is critical to acknowledge the enormous progress the field has made over the past 20 years in delivering novel forms of therapeutics that have very significant efficacy signals. As with all new therapeutics, we will inevitably get better at designing the tools and administering them effectively. Ultimately, though, success needs to be defined by our ability to use these across wider populations in a cost-effective way. Although this will take time, the weight of current clinical data and the steady creation of new innovations suggest that this is an inevitable outcome and patients with multiple different diseases across all therapeutic areas will ultimately be the beneficiaries of this new therapeutic revolution.

This book provides an extremely timely review of many of the key methodologies and platforms. It is a very welcome addition to our understanding of this transformational field.

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