

SAFETY CONCERNS

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TABLE 4.3 Risks of cell-based therapy. Tumour formation Genetic and epigenetic abnormalities Transmission of infection Poor viability and loss of function Differentiation to undesired cell types Rejection (allogeneic cells) Side effects of immunosuppression (allogeneic cells)

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Group 1 Group 2 Group 3 Intact Infection G/P (pretreatment) Day 16 Day 16 Day 16 Day 2 SMA SMA SMA DAPI DAPI DAPI DAPI (b) DAPI DAPI DAPI DAPI (c) DAPI DAPI DAPI DAPI Figure 4.10 Stained sections through a mouse cornea before (left) and after (second column) injury and subsequent treatment with standard of care (gentamicin [G] and prednisolone [P]; group 1), standard of care plus a novel /f_l uid gel carrier (FG) (group 2) and standard of care plus the carrier and decorin (Dec) (group 3). Sections are stained for markers of scarring: (c) laminin. Importantly,

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Tissue engineering and regenerative strategies hold out great hope for e ff ectively repairing or replacing tissues in a wide number of human diseases. The field is moving rapidly , under pinned by new developments in the relevant science in stem cells, materials and molecules. New emerging areas of tech nology include therapeutic signalling by wa y of extracellular vesicles (EVs) and gene editing of cells using CRISPR-Cas9, and gene therapies. All will require the use of a translational approach, wher eby the hypothesised mechanism is developed and translated to the clinic, building up robust clinical evidence of e ffi cacy , by way of well-designed and well-conducted clinical trials before widespread adoption. It is likely that patient stratification will further refine ther apy options. The ability to phenotype, genotype and profile patients at a molecular level will allow more detailed charac terisation of patient subgroups and staging of disease. In addi tion to clinical studies and evidence , the rapid pace of therapy development will need to be accompanied by the development of new regulatory frameworks, f or example in point-of-care manufacturing. SAFETY CONCERNS

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