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BOOK REVIEW

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Hepatocyte Transplantation

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To date, orthotopic liver transplantation is the only clinically effective method of treating acute and chronic liver failure and genetic liver function defects. However, the application of liver transplantation is limited by a shortage of organ donors, and so a large number of patients die before a liver can be procured for transplantation. There are, furthermore, factors such as high cost, life-long immunosuppression, and relatively high morbidity that need to be considered before transplantation. This shows the necessity to develop alternative methods of liver support/replacement therapy. Such therapies include delivery of corrected genes directly to liver cells within the diseased organ, transplantation of autologous genetically corrected hepatocytes, and transplantation of normal allogeneic hepatocytes. Hepatocyte transplantation has several advantages. It is technically simple and less expensive than orthotopic liver transplantation. Hepatocytes can be genetically manipulated and cryopreserved and stored before transplantation, and cells from one donor can be used for several recipients.

The book begins with a historical review of hepatocyte transplantation and continues with a review of the important tools for hepatocyte transplantation, such as methods of hepatocyte preparation and preservation. One of the critical issues of hepatocyte transplantation is the optimal site for transplantation. The authors describe the advantages and disadvantages of various transplantation sites such as the liver, the spleen, the intraperitoneal cavity, and solid supports, i.e. prevascularized synthetic devices that can be used as carriers for transplanted hepatocytes. Intraportal hepatocyte transplantation seems attractive as it allows the transplanted hepatocytes to be placed in a physiological environment in contact with hepatocytes and non-parenchymal cells, where they are exposed to local mitogens and portal-born hepatotrophic factors. An other argument for intraportal transplantation is that hepatocytes are only able to secrete bile in the liver. However, the choice between the intrasplenic and the intraportal route is probably not critical, as it has been demonstrated that the majority of intrasplenically transplanted hepatocytes migrate to the liver and that the spleen retains only a small (15%) fraction. The book provides insights into different animal models of acute and chronic liver failure and congenital metabolic disorders in which hepatocyte transplantation has been used. In general, all studies of hepatocyte transplantation in acute liver failure are based on either chemically- or surgically-induced liver failure. The positive results on survival and liver function of suboptimal numbers of transplanted hepatocytes (corresponding to 2% of the liver mass) suggest that proliferation of the transplanted cells or stimulation of regeneration of the native liver play an important role. The study of chronic hepatic failure in animals is difficult, due to the lack of good animal models. CCl4-induced cirrhosis is highly variable, and in the portacaval shunt model the neurobehavioral abnormalities are transient and the period of study is limited to three months. There have been several animal models with congenital defects in hepatocytes leading to metabolic disorders. Their abnormalities such as high serum total bilirubin levels, very low serum albumin or ascorbic acid levels are partially corrected by transplantation of normal hepatocytes. Towards the end of the book, the authors describe immunological problems related to allo-and xenogeneic hepatocyte transplantation. They also provide information on general principles of gene transfer into hepatocytes and regulation of gene expression in hepatocytes. At the end of the book, the authors describe hepatocyte transplantation in large animals and humans. At present, hepatocyte transplantation has been performed on very few patients. The results reported in this book are not convincing, probably due to the small numbers of hepatocytes injected.

The authors being authorities on hepatocyte transplantation from all over the world, this book provides a comprehensive overview of the different aspects of this technique. It provides the reader with up-to-date information on laboratory studies and clinical trials of hepatocyte transplantation, and with new approaches for future research. The conclusion one arrives at after reading the book is that many issues will have to be resolved before hepatocyte transplantation can be applied clinically. As each part of the book can stand on its own, the reader can choose any chapter of personal interest. Especially well written and structured are the chapters providing insights into general principles of gene transfer into hepatocytes and regulation of gene expression in hepatocytes. They are easy to understand, even for readers not familiar with molecular biology. This knowledge is of great importance for future research. A few limitations of the book need to be pointed out, however. The book gives relatively little information about the immunological problems related to hepatocyte transplantation. It would also be interesting to learn about the mechanism of action of hepatocyte

transplantation. Today this knowledge seems to be limited, but hopefully we will find this information in a future book. Primarily, the book addresses hepatologists and liver transplantation surgeons, as well as scientists interested in gene transfer of hepatocytes and the development of cell lines with hepatocyte functions.

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