Gene Therapy for Renal Diseases and Transplantation
Contributions to Nephrology

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Gene Therapy for Renal Diseases and Transplantation

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Gene therapy holds promise for treatment of renal pathologies and for preventing renal allograft rejection. Initially conceived as a strategy to correct inherited genetic disorders, in the last decade gene therapy has been successfully applied to ameliorate the renal function compromised by progressive renal diseases and to prevent kidney allograft rejection in experimental animals.

The success of transferring a gene into target renal cells essentially depends on the delivery system used. In the present book, a group of world experts in the field have provided new insights into viral and nonviral systems currently used to perform gene delivery. A chapter has been dedicated to the new field of RNA interference (RNAi). The potential of RNAi in research and therapeutics has been honoured by awarding the 2006 Nobel Prize in Medicine to Craig C. Mello and Andrew Z. Fire. Despite several obstacles still to overcome, RNAi-mediated gene transfer has already reached the clinics especially to treat age-related macular degeneration, preeclampsia and chronic myeloid leukemia. Renal ischemia-reperfusion injury, which is the leading cause of acute renal failure after surgery, trauma and transplantation could be a possible area of application. Thanks to the progressive understanding of the cellular and molecular mechanisms, gene therapy might represent in the near future a new strategy to target molecules involved in tissue damage and in inflammation processes at the basis of ARF. Progressive renal diseases are characterized by chronic deterioration of the renal function and by renal fibrosis. Experimental glomerulonephritis and interstitial fibrosis have been successfully treated by gene transfer. However, before entering into the clinic, studies in larger animals are needed. Transplantation is the therapy of choice for many end-stage organ failure. Recipients of an organ
transplant take immunosuppressive drugs all their lives which exposes them to a great risk of developing opportunistic infections and cancer. Furthermore, current antirejection drugs are still inadequate to protect the graft from developing chronic rejection. Transfer of genes whose protein products have immunomodulatory properties proved to be beneficial in treating acute and chronic graft rejection. These studies represent the proof of principle that gene therapy may become a reality in clinical transplantation after demonstrating its efficacy in larger animals. Treatment of renal cancer and HIV-associated nephropathy could also benefit from a gene therapy strategy targeted to destroy cancer or infected cells. These aspects will be also discussed in the book.

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