Preface

Skin gene therapy has recently generated a high level of interest due to the ease of accessibility and several successful attempts to treat blistering skin diseases. Gene therapy represents a novel concept of treating diseases at the molecular level by introducing corrective genes. This is made possible through the elucidation of the genetic background of many diseases, monogenic and polygenic, that has provided the necessary knowledge to correct inborn genetic mutations. On the other hand, the skin can be used as a 'bioreactor' for the production of proteins for use in the body. Furthermore, necessary enzymes for detoxification of metabolic products can also be synthesized in the skin ('metabolic sink'). Finally, the concept of DNA vaccination or genetic immunization against cancer and infectious diseases exploits the skin-derived immune system for the elicitation of potent cellular and humoral immune responses. DNA vaccination through the skin or the muscle is about to revolutionize traditional vaccinology. In this regard, clinical phase I/II studies in advanced tumor patients have shown good tolerability of these cancer vaccines. These trials have demonstrated proof of concept in eliciting tumor-directed cellular immune responses. In an interdisciplinary effort based on the expertise of basic biology, biochemistry, immunology, microbiology, virology, clinical medicine, biotechnology and ethics the power of a novel concept of treating human disease will unambiguously change the way of clinical practice. However, only a team effort will resolve the many problems that were identified in the early days of gene therapy. For example, it is paramount to direct and control expression to the entire organ and to increase the public acceptance of this therapy in the years to come.

The present special issue of *Cells Tissues Organs* gives an overview of the achievements in the field of skin gene therapy touching upon basic biology and describing initial preclinical applications. The potential to generate epidermal equivalents from hair follicle cells that can be manipulated in culture and transplanted back onto the host represents a convenient method to harvest and grow autologous keratinocytes not only for skin gene therapy, but also for the treatment of chronic ulcers. This outstanding development in biotechnology paves the way for ex vivo gene transfer and provides a good model system to study and refine the various aspects of gene transfer into the skin. Along these lines, the reaction of keratinocytes to the addition of exogenous DNA has been carefully analyzed using DNA arrays that led to the identification of an acute phase-like response as seen following trauma or in the early stage of infection.

Some of the identified proteins regulated by exogenous DNA (e.g. follistatin) have stimulated further analysis in cell biology.

Potential applications of skin gene therapy include the utilization of skin as a metabolic sink for treating metabolic disorders. From these studies, it appears that systemic deficiencies can be corrected through introducing intact enzymes by gene expression from the skin. As the currently studied diseases are rare, the expansion towards more common diseases such as hyperlipoproteinemia and hypercholesterinemia would have a high socioeconomic impact. Along the same lines, the treatment of chronic wounds by stimulating growth and regeneration of wound tissue could result in a convenient therapy of long-standing disease, especially in the elderly. Current concepts of modern wound treatment are highlighted in this special issue. Not only in dermatology, but also in plastic surgery, gene therapy has stimulated outstanding research. This special issue also touches on the treatment of hypertrophic scars, keloids and other applications in plastic surgery that serve as a powerful addition to surgical operations. The use of gene transfer to muscle, tendon, nerves and bone is discussed. The recent achievement of the regulation of gene expression by using common antibiotics is also discussed in this volume. These drugs are amenable to topical in vivo application.

This special issue also includes an overview of genes and strategies used to treat cancer in animal models and human beings, which could serve as an approach to the treatment of bulk tumors or metastatic disease. Currently, many research laboratories aim to target these apoptotic genes to the different tumor sites in the body. Gene therapy also makes progress in the treatment of sarcoma using adeno-associated virus, which is detailed in one chapter of this issue.

This issue of *Cells Tissues Organs* represents a state of the art summary of skin gene therapy in its second decade. The articles are meant to generate interest among basic researchers and clinical physicians interested in both innovative treatment strategies and improvement of the standard of care. Some of the presentations were given as part of the First International Symposium on Gene Technology and Skin Gene Therapy in 2000 that attracted more than 300 researchers from all over the world. Given the rapid progress in this field, the next meeting is scheduled for spring 2003 (www.isgt-congress.org).

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