Preface

The articles in this issue of *Cells Tissues Organs* report on the progress of molecular diagnostics and skin gene therapy that has been achieved since the last special issue of *Cells Tissues Organs* on this topic [Cells Tissues Organs 2002;179:78–149]. The papers are a selection of the Second International Symposium on Molecular Diagnostics and Skin Gene Therapy that was held at the University of Düsseldorf in March 2003 and attracted more than 340 researchers from many different countries. In addition to gene technology and skin gene therapy, this issue also discusses the latest developments in molecular diagnostics which has experienced tremendous progress. These findings are summarized in the section on Advances in Molecular Diagnostics. Various forms of DNA arrays allow the simultaneous analysis of up to 22,000 genes in a given tissue. Using this technology several groups have started to profile malignant melanoma on a molecular level, where important pathways and gene products can be found that are differentially expressed in comparison with normal human melanocytes and benign nevi. In addition, human clinical melanoma specimens prior to and following immunotherapy permit the identification of certain tumor subgroups that respond to immunotherapy of melanoma.

In the section entitled Progress in Molecular Technology recent advances in molecular targeting and modification of expression profiles are described. Since the genetic correction of inborn diseases including genetic blistering diseases has proven difficult due to low transfection efficiency, novel strategies such as targeting of viral vectors to certain tissues with altered tropism have been devised.

For example, retargeted adeno-associated virus-2 (AAV-2) has been shown to transduce cell populations that have previously not been infectable (e.g. from liver to leukemia cells). Moreover, initial results have shown that AAV-2 can be used to target rare cutaneous genodermatoses such as the Sjögren-Larsson syndrome.

Molecular therapies such as small inhibitory RNA (siRNA) allow the modification of sequence-specific gene expression. This technology has revolutionized the in vitro gene expression. Recently, a sequence-independent system of gene suppression induced by viral replication through Toll-like receptor-3 (TLR3) and induction of type I interferon has been discovered. In addition to sequence-specific effects, it is reported in this issue that TLR3 activated through exogenous DNA also signals to activate sequence-independent suppression of protein synthesis and enhancement of mRNA degradation.

In contrast, topical selection with the cytostatic drug colchicine has been developed to allow the preferential expansion of transduced keratinocytes permitting continued expression of desired genes from the skin.

Paramount to the progress of skin gene therapy is the development of inducible mouse models for inherited skin diseases, e.g. for autosomal dominant keratin disorders. Two valuable models for testing somatic gene therapy of dominant skin genodermatoses, i.e. epidermolytic hyperkeratosis and epidermolysis bullosa simplex, are described.

In the section Progress towards DNA Vaccination and Skin Gene Therapy genetic immunization against HIV-1

is reported that has led to protection against an HIV-1/MuLV pseudovirus challenge in a mouse model. In a different model of DNA-based HIV-1 vaccination, the concomitant experimental infection by *Leishmania major* has been shown to impair the cellular immune response, thus providing valuable information to tackle the AIDS epidemic in developing world countries, where leishmaniasis is endemic.

Finally, significant progress has been made in attempting to correct the autosomal recessive disease xeroderma

pigmentosum, where several defects in nucleotide excision repair lead to the occurrence of various skin neoplasms. Using retroviral-based gene transfer significant progress is detailed.

In summary, recent achievements in molecular diagnostics and gene therapy of several dermatologically relevant diseases are discussed in the current issue.

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