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## Preface

In the early nineties, the induction of a specific immune response by injecting a eukaryotic expression vector into the skin or muscle appeared somewhat “magic”. However, the basic mechanisms underlying “genetic immunization” could be explained by simple rules of text book immunology, i.e. transcription of the gene, translation of the gene product, processing and presentation on MHC, and induction of the immune reaction. The simplicity of using a genetic “sentence” and thus talk to the immune system inspired the imagination of scientists, and the approach was appraised as a revolution in modern vaccine design. Obviously, a dialog with the immune system was possible – you talk, using the genetic code, and the system responds. This analogy still holds true, and from my point of view, is the major cause of fascination for gene vaccines. As scientists gained a deeper understanding of the language of the immune system, they were able to extend their vocabulary and improved the dialog with the system. Elucidation of the manifold regulatory pathways and mechanisms of activating or inhibitory immune mediators enabled to command the immune system and to trigger desired immune responses.

Another intriguing aspect of genetic immunization is the quick and easy implementation of the latest knowledge into application. Within several days, a novel gene of interest can be inserted into vectors, or any steering sequence can be added to the basic vaccine constructs, and within weeks, the resulting effects can be evaluated in animal models. Logically, the vast potential of this novel approach stimulated the creativity of researchers worldwide, with the result of a “DNA vaccine hype” in the late nineties.

As often happens with highly praised new developments, the peak of popularity and excessive hopes was followed by disillusion, which in the case of gene vaccines was triggered by the results of the first clinical trials. Yet again, their outcome confirmed the well-known and dreaded “mice to men” barrier, and seemed to prove the common proverb “mice lie and monkeys exaggerate”. Barely any of the striking successes observed in animal models could be validated in humans. The consequence was a drastic drop of acceptance, the so-called “gene vaccine hangover” (as termed by David Weiner) during the first years of the new century.

Fortunately, many scientists distinguish themselves by thirst for knowledge paired with a certain stubbornness. The authors of the present book belong to this category and their work reversed the disparaging attitude towards gene vaccines. In the past years, they elucidated hitherto unknown mechanisms underlying genetic

immunization and improved existing, or developed novel application modes and techniques. Thus, they could overcome the hurdles of impaired immunogenicity in humans and initiated a new era of gene vaccines.

Many of the chapters of this book focus on human vaccine approaches and describe recent progress and current strategies. Leading companies in the field were invited to present their vaccine platforms and clinical research. This application-oriented view is complemented with up-to-date scientific knowledge of the mechanisms underlying gene-based vaccines.

I hope, “gene vaccines” will both, provide insight into a still young and exciting field of immunological research and its applications, as well as transfer a portion of our enthusiasm and curiosity to the reader.

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Josef Thalhamer



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Thalhamer, J.; Weiss, R.; Scheiblhofer, S. (Eds.)

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