
Preface

Immunotoxins represent a new class of human therapeutics that have widespread applications and a potential that has not yet been fully recognized since they were first conceived of by Paul Ehrlich in 1906. The majority of advances in the development and implementation of immunotoxins has occurred over the last 20 years. The reasons for this use of immunotoxins in basic science and clinical research are the powerful concurrent advances in genetic engineering and receptor physiology. Recombinant technology has allowed investigators to produce sufficient quantities of a homogeneous compound that allows clinical trials to be performed. The identification of specific receptors on malignant cell types has enabled scientists to generate immunotoxins that have had positive results in clinical trials. As more cellular targets are identified in coming years, additional trials will be conducted in different disease states affecting still larger patient populations. Modulation of the immune system to decrease the humoral response to immunotoxins may improve their overall efficacy. As increasingly more effective compounds are generated, it will be necessary to decrease the local and systemic toxicity associated with these agents, and methods for doing so are presently being developed.

The work presented in *Immunotoxin Methods and Protocols* focuses on three specific areas of immunotoxin investigation that are being conducted by experts throughout the world. The first section describes the construction and development of a variety of immunotoxins. The conjugates that have been created by these investigators contain entire monoclonal antibodies, single-chain antibody fragments, and cytokines as their carrier ligands. The toxic portion of these agents can include such conventional chemotherapeutics as doxorubicin or such ribosome-inactivating proteins as ricin A chain or saporin. Additional considerations that must be addressed when developing immunotoxins, and are included in this section, are the use of such potentiating agents as the carboxylic ionophore monensin for plant-derived toxins, receptor expression modulation for immunotoxin targeting using such modalities as irradiation, and the quantification of the number of immunotoxin molecules that are necessary for a complete therapeutic response. The section ends with an evaluation of the very important potential side effect, vascular leak syndrome, which can occur with any of these molecules.

Because of the unparalleled toxicity of these compounds, it is no surprise that the area of their greatest application has been in the field of oncology, which supports the focus of the second section of this work on these investigations. The central nervous system provides an ideal environment for the administration of immunotoxins because of the relative impermeability of the blood–brain barrier. Circumventing the blood–brain barrier by directly infusing these compounds into primary malignant brain tumors, makes it possible to achieve high local concentrations; these have resulted in complete therapeutic responses in some cases. The central nervous system is also of considerable clinical interest for bacterial-based immunotoxins because of the encouraging therapeutic responses that are described in this section.

The last section of *Immunotoxin Methods and Protocols* investigates alternative applications of immunotoxins for generating selective lesions within the brain by targeting neural antigens and their receptors. By creating lesions in specific areas, investigators hope to better understand and localize such critical functions as memory and learning. Since the onset of the acquired immunodeficiency syndrome epidemic, there has been little progress toward finding a cure, although the overall survival for patients has been extended. Targeting the virus with immunotoxins represents a reasonable concept, provided that a unique receptor can be identified on the human immunodeficiency virus. In reflecting on the present state of the wide variety of immunotoxin research compiled in this text, it is hoped that the present contributors and other investigators who read *Immunotoxin Methods and Protocols* will be stimulated to consider and to create new applications for this exciting class of compounds.

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