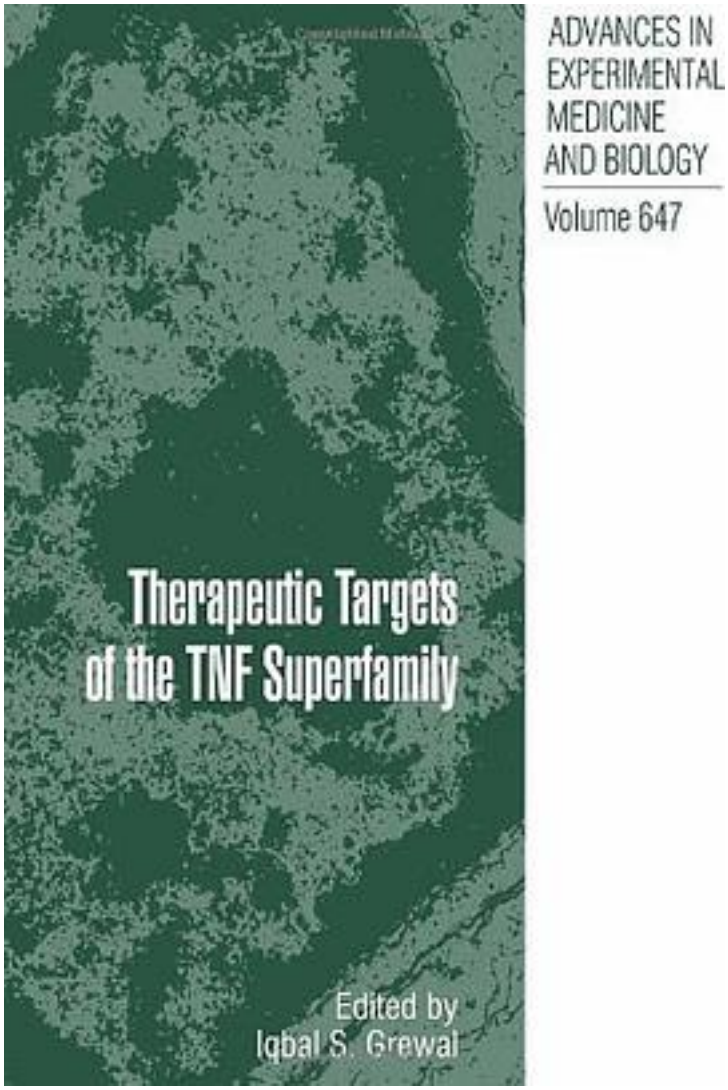
Therapeutic Targets of the TNF Superfamily



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TNF superfamily has been the most highly investigated area of basic medical research for over two decades. These investigations have benefited from the enormous growth in our understanding of the principal functions of the immune system and the explosion in the knowledge involved in regulation of normal and pathological immune response. In addition, much has been learned about the molecular mechanisms of programmed cell death and the escape of tumor cells from apoptotic demise and from discovery of the key role played by TNF ligands in this process. As the functioning of these superfamily members is very complex, understanding TNF ligands and their receptor biology requires a melange of research activities in many different disciplines including organ development, molecular biology, experimental pathology, and immunology. As a consequence of intensive studies in multiple areas over many years, much has been learned. A key role of members of this superfamily in normal functioning of the immune system, autoimmunity, and other fundamental cellular process by which tumor cells develop has been established. Many novel mechanisms involving TNF superfamily members in the disease development process have been defined, and a unified concept and new perspectives have also emerged. For example, abrasions in the innate immune system, so far not considered critical in autoimmunity, have found increasing attention, and TNF-directed and not antigen directed therapy has emerged as the most impressive therapeutic advance in managing autoimmunity in humans. These findings provide a foundation for novel drug design efforts that are poised to utilize newly acquired knowledge. Several of these strategies have already materialized into successful therapeutics such as use of TNF for cancers and anti-TNFa antibodies and TNFR-Fc for autoimmune diseases, and many have advanced to human clinical trials, while many more are still being tested in preclinical settings. As in other rapidly evolving fields, these advances are not necessarily congruent and are often difficult to organize into a cogent whole. The aim of Therapeutic Targets of the TNF Superfamily is to make readily available the major research important in the exploitation of this family for developing therapeutic strategies for human diseases, in a single volume. In this volume, a number of leading scientists in the field cover many aspects of biology of TNF superfamily members, ranging from the cloning and characterization of TNF ligands and their receptors, through the use of animal models to study their functions in vivo and their exploitation for human therapeutic use. Each chapter also includes relevant background information and provides useful bibliography for a more detailed analysis, making the study of TNF ligands/receptors accessible at all levels of expertise. This volume presents the state-of-the art account on the role of TNF superfamily members in the pathogenesis and their use in current intervention of cancers and autoimmune disease. This text will be highly valuable for investigators to understand the disease processes regulated by TNF superfamily members and to develop effective therapeutics. A view into the future, inspired by the comprehensive work presented in this volume, predicts that researchers studying TNF superfamily members will continue to make rapid progress in identifying relevant components to the disease process and new therapeutic strategies to target many human diseases including cancers, autoimmune disease and others.

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