RESEARCH COLLECTION ON

# IMMUNOLOGY

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# RESEARCH COLLECTION ON IMMUNOLOGY

**Research Collection on Immunology**

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Chapters from books edited by: **Spaska Stanilova, James Chan, Jagat Kanwar, Suman Kapur, Fang-Ping Huang** and **Clio Mavragani**

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Research Collection on Immunology

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# Preface

In recent decades researchers have greatly improved their understanding of immunological processes at the cellular and molecular level. While this knowledge is already being used to develop vaccines and drugs for the prevention and treatment of a range of disorders including infection, inflammatory diseases and cancer, there are still areas requiring further study/development, such as the etiology of autoimmune disease, the mechanistic pathways that govern the immune response, and the development of vaccines and novel stem cell and antibody therapies.

Concentrating mainly on autoimmune disorders, this book presents a selection of chapters outlining some of the latest advances, key trends and current concepts. Specific disorders discussed include type 1 diabetes, human papillomavirus infection, leishmaniasis, Hashimoto's thyroiditis, Sweet syndrome and vitiligo, while other chapters will focus on general topics such as the role played by regulatory B cells in various autoimmune disorders, the mechanisms governing immunosuppression, and the immunosuppressant antibody therapies that are currently available.

This book is intended for all clinicians, students and researchers who are working on, or have an interest in, immunology-related topics, and who want to gain an insight into current thinking and advances in this fascinating topic.

# GENES AND AUTOIMMUNITY - INTRACELLULAR SIGNALING AND MICROBIOME CONTRIBUTION

Edited by **Spaska Angelova Stanilova**

# Chronic Fatigue Syndrome/Myalgic Encephalomyelitis and Parallels with Autoimmune Disorders

Ekua W. Brenu, Lotti Tajouri, Kevin J. Ashton,
Donald R. Staines and Sonya M. Marshall-Gradisnik

Additional information is available at the end of the chapter

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## 1. Introduction

Autoimmune disorders are known to affect a substantial number of people worldwide and in some cases may be fatal. They occur in the presence of unregulated inflammatory responses including failure in self-tolerance. Some unexplained disorders with immune compromises may demonstrate certain characteristics that suggest an autoimmune disorder including Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME). CFS/ME remains an unsolved disorder with multiple symptoms and no single causative factor. These symptoms may include but are not limited to incapacitating fatigue, weakened short term memory or attentiveness, sore throat, tender cervical or axillary lymph nodes, muscle pain, severe headaches, impaired sleep and postexertional malaise. To date succinct and concise mechanisms that underlie this disorder have not yet being identified although, many hypotheses have been put forward. CFS/ME often occurs as a consequence of a post-infectious episode accompanied by compromises in the immune, endocrine and nervous systems. The sequences of these events have not being clearly identified. Importantly, immune deterioration in CFS/ME is related to heightened or suppressed cell function, differential gene expression, equivocal levels of immune cell numbers and protein secretion promoting adverse inflammatory activation. Both innate and adaptive immune system perturbations persist in CFS/ME. These characteristics are in many respects similar to mechanisms of disease in autoimmune disorders suggesting that the changes in immune response may develop from cellular and molecular changes in immune cells and proteins. We propose here that as the mechanism of CFS/ME may involve certain immunological factors that have been shown to be compromised in other autoimmune diseases, CFS/ME may in some cases have an autoim-

mune component or perhaps the symptoms of CFS/ME are hallmarks of a novel autoimmune disorder yet to be identified.

## 2. Characteristics of CFS/ME

CFS/ME belongs to a class of unexplained disorders whose causal factor(s) remains to be proven. The prevalence rate of CFS/ME worldwide is 0.4-4% with a female to male ratio of 6:1 (Lorusso et al., 2009). A predominant characteristic of patients with this disorder is persistent debilitating fatigue. Apart from the debilitating and unrelenting fatigue, patients may also experience other symptoms which may include sore throat, headaches, post exertional malaise etc (Fukuda et al., 1994). A diagnosis of CFS/ME is affirmed if these symptoms have persisted for at least 6 months. To assist with correct diagnosis of CFS/ME patients, various diagnostic tools have been developed. Currently, most researchers prefer to use two definition criteria, the CDC and the Canadian definition, for assessing their patients.

Occurrences of disparities in immunological, neurological, endocrinological, cardiac and metabolic function have been reported among CFS/ME patients (Klimas et al., 2012). Although, these observations highlight the extent of physiological damage associated with CFS/ME, the findings are most often not consistent across studies thus posing doubt as to whether these reported disparities are associated with CFS/ME. Nonetheless, alterations in immunological function are the most consistent data associated with CFS/ME (Klimas et al., 2012). Important among them is the observation that CFS/ME patients have a significant decrease in cytotoxic activity (Brenu et al., 2010; Brenu et al., 2011; Fletcher et al., 2010; Klimas et al., 1990; Maher et al., 2005). Other factors such as cytokines also vary in CFS/ME patients in comparison to non-CFS individuals (Patarca, 2001). Thus considerable evidence exists to suggest that CFS/ME is an immune dysfunction disorder and therefore it may share homology with some autoimmune disorders.

Autoimmune disorders arise as a consequence of increased creation of pathological antibodies against self-antigens, in other words the body assumes a diseased state and therefore generates antibodies to attack self-cells and molecules. The result of this over active immune system is tissue damage and inflammation. Tissue damage may develop from elevations in antibody or cellular processes. Autoimmune disorders can either be systemic or organ specific, exemplified by the presence of autoantibodies, autoreactivity to autoantigens, loss in B cell tolerance, alterations in regulatory T cells (Treg) function, changes in T cell repertoire, genetic abnormalities or environmental agents (Davidson and Diamond, 2001). In most autoimmune diseases including Multiple Sclerosis (MS), autoimmune Rheumatoid Arthritis (RA) Systemic Lupus Erythematosus (SLE), and Autoimmune Diabetes (AID), disparities in immune cells such as neutrophils, Natural Killer (NK), T and B cells have been reported. Perturbations in the normal function of these cells are contributory factors to the mechanism of these diseases. Incidentally, these cells have also being described in CFS/ME. Hence, the purpose of this chapter is to describe the findings related to the above mentioned cells in