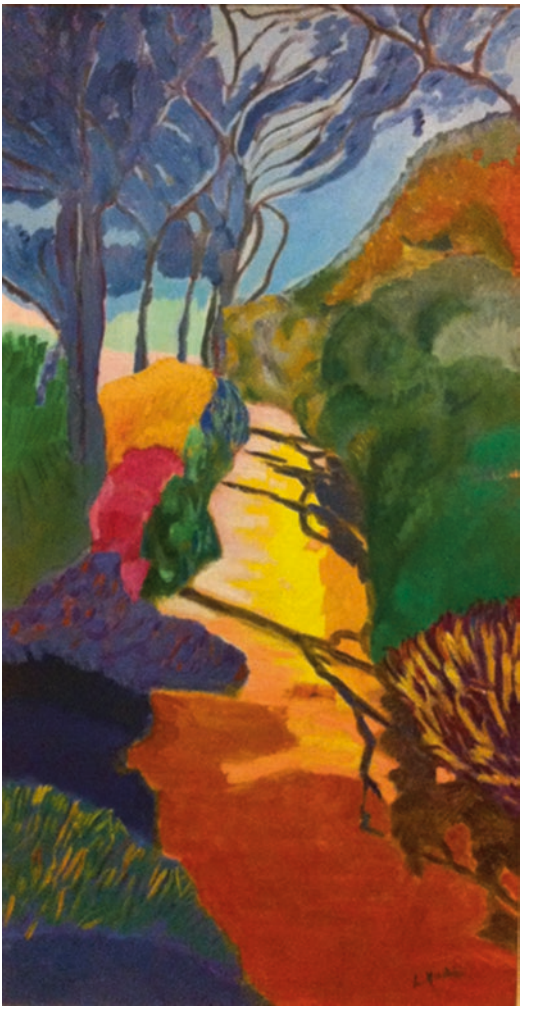
Rare Diseases of the Immune System



Sentiero al mattino Laura Maddii Emmi (Private collection)

Mario Milco D'Elios • Marta Rizzi
Editors

Humoral Primary Immunodeficiencies

Springer

Editors
Mario Milco D'Elios
Careggi Hospital
Department of Clinical and Experimental Medicine, University of Florence
Firenze
Italy

Marta Rizzi
University Medical Centre Freiburg
Department of Rheumatology and Clinical Immunology and Center for Chronic Immunodeficiency
Freiburg
Germany

ISSN 2282-6505 ISSN 2283-6403 (electronic)
Rare Diseases of the Immune System
ISBN 978-3-319-91784-9 ISBN 978-3-319-91785-6 (eBook)
https://doi.org/10.1007/978-3-319-91785-6

Library of Congress Control Number: 2018962559

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Dedicated with love to our children
Emilia, Carlo, and Flavia
and
Sofia, Emanuele, Alessandro, and Bernardo;
to all of our patients with primary
immunodeficiencies and their families;
to our nurses;
and to all of our students.

Preface

Primary immunodeficiencies are rare diseases. Nevertheless, the study of patients with primary immunodeficiencies has provided the chance to understand how the immune system really works. This journey into the pathogenetic mechanisms behind primary immunodeficiencies started many years ago, inspired by several giants in the field of immunology. One of them, Charles Janeway, Jr., spent his life discussing how the immune system functions and the importance of the pioneering discoveries made by his father, Charles Janeway, Sr., the first person to use gammaglobulin to treat patients with humoral immunodeficiencies.

When we think about antibodies, our minds drift immediately to vaccination responses (with the question as to whether or not they are protective), to the power of our antibody repertoire to defend ourselves from reinfection with specific viruses (e.g., rubella or measles), or to the pathogenic potential of self-reactive antibodies and their contributions to disease manifestation in autoimmune diseases. We live in a time of controversy in which public opinion against vaccination is very strong, thanks to fake, only half-true, or distorted information, spread via the media and via social media. Thanks to this discussion, there is public awareness of the rare group of patients who benefit greatly from herd immunity against common infections that are harmless for most people but possibly deadly for weak individuals. Those weak individuals carry some sort of fault in their immune system. In the great majority of cases this may be acquired (secondary) because of severe illnesses (e.g., cancer), treatment (e.g., immune suppression in cases of autoimmunity), or transplantation; or it may simply be due to age (in newborn or elderly patients). In more rare situations, subjects with a weak immune system carry a primary immune defect. The prevalence of such patients in western countries is around 40–50 patients per 100,000 inhabitants, with more than half of them having B cell immunodeficiencies. Hence, the awareness of primary immunodeficiency has increased in the community, and this has occurred in parallel with the creation of national and supranational registries (e.g., the European Society for Immunodeficiencies (ESID) registry), patient advocacy, research, and discovery.

Indeed, we have witnessed a blossoming of research into primary immunodeficiency in the past 25 years; many genetic defects related to immunodeficiency have been discovered, and since the advent of high-throughput sequencing a new genetic defect is discovered almost monthly. This is especially true for the group of patients who carry humoral immunodeficiency or common variable immunodeficiency

disorders. In this group of patients the main clinical features are a reduced level of immunoglobulin in the serum and inability to mount vaccination responses. Infection is not the only feature in these patients, who may present with a complicated course of disease, with lymphoproliferation, autoimmunity, cancer, lung involvement, or gastrointestinal involvement.

The perception of humoral immune diseases as a complex entity and the identification of specific defects leading to that phenotype represent major contributions to the understanding of the human immune system in past years. The discovery of genetic defects has also aided the identification of new therapeutic targets and the forecasting of adverse events that may occur with targeted therapies.

Nevertheless, many molecular, cellular, and clinical aspects of primary immunodeficiencies (e.g., the roles of epigenetics, the microbiome, and gene therapy) are yet to be disclosed, making primary immunodeficiency one of the most exciting fields to work in. Indeed, we hope that this book will boost the curiosity of young students approaching immunology for the first time, as well as being of interest to specialists and researchers in clinical immunology.

Firenze, Italy — Mario Milco D'Elios
Freiburg, Germany — Marta Rizzi

Contents