Foreword

The writing is on the wall: cancer's long and terrible reign as "The Emperor of All Maladies" is soon coming to an end. The disease that kills more than eight million people a year worldwide has met a new foe capable of outsmarting and defeating it, and it's been right under our noses the entire time: our own immune system.

Though still in its early days, cancer immunotherapy—also called immuno-oncology—has been hailed as a revolutionary treatment approach that is disrupting the status quo in cancer care. Mobilizing the immune system to recognize and attack cancer has been a dream that has long eluded the field, and it is only recently that unprecedented recoveries of patients with very advanced disease have effectively demonstrated immunotherapy's power to save lives.

Although such complete responses are yet the exception to the rule, they give new hope to patients and fuel the passion of the scientists, clinicians, and drug manufacturers who are working to realize immunotherapy's full potential.

How did we get here? Why is the world only now hearing about immunotherapy? The recent flurry of headlines about clinical successes and FDA approvals seems to have come from nowhere. This is hardly the case.

Cancer immunotherapy's story stretches all the way back to the late 1890s, and it has taken decades of basic research and billions of dollars of investment to build the foundation upon which today's lifesaving treatments are based. This book offers a uniquely entertaining yet inspiring glimpse into the lives and minds of the academic and industry pioneers who forged this new field. It is a story of how an obscure and oft-derided field of cancer research—and the tenacious few scientists who refused to abandon it—came from behind to become the new "darling of oncology."

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As the CEO of the Cancer Research Institute (CRI), the first and, up until recently, the only nonprofit organization dedicated exclusively to advancing immuno-oncology, I have had a front-row seat to the exciting developments

as this field has grown from the earliest laboratory discoveries into today's headline-making breakthroughs. I also am very proud of the fact that nearly all of the individuals featured in this book are in some way connected to CRI, whether as members of our scientific leadership and/or as recipients of funding from our research programs. Many consider CRI's support a lifeline that enabled them to continue pursuing their important research.

Throughout this book, a name appears of another pioneer who not only contributed seminal discoveries to the field in his own right, but who also touched so many others, guiding them and supporting their research and encouraging them to press forward. That man was Lloyd J. Old, M.D., whose long and distinguished career as a scientist, mentor, and visionary leader earned him the title "Father of Modern Tumor Immunology." His many contributions to the field include the discovery of the first link between the major histocompatibility complex (MHC) and disease (leukemia); discovery of the role of Epstein–Barr virus (EBV) in the development of nasopharyngeal cancer; the discovery of tumor necrosis factor (TNF); and his definition of the concept of cell-surface differentiation antigens, a key to our understanding of how the immune system and its various cellular components function. These are but a few of his many notable accomplishments.

Lloyd was a wise mentor to me, as he was to so many others. But he was also a friend and confidant and was always a gentleman and scholar. As the director of the Cancer Research Institute Scientific Advisory Council, he played a pivotal role in guiding CRI's programs and future directions. When he assumed this role in 1970, his first action was to persuade the world's leading immunologists, including Nobel Prize winners and members of the National Academy of Sciences, to join CRI as advisors. Together, they established the primacy of basic immunology research as the first and most important step toward the eventual immunological control of cancer. By association with these scientific luminaries, CRI's reputation in the field rocketed, enabling us to attract the finest minds to this work.

In 1971, Lloyd established CRI's Postdoctoral Fellowship Program, as he devoutly believed in young scientists and the need to train a generation of immunologists. This program has supported more than 1300 scientists since then, many of whom have gone on to achieve prominence in the field and who have, in turn, trained generations of other young minds. More importantly, their work has produced fundamental knowledge that provides a scientific rationale for human trials of experimental immunotherapies.

Lloyd's prescience and vision would lead to other CRI programs, each designed to fill a critical need in the spectrum of scientific discovery and drug development. The one he was most proud of, however, was the Cancer Vaccine Collaborative. Through this initiative, he forged a partnership

between CRI and the Ludwig Institute for Cancer Research, an organization he led as director and chief executive for nearly 20 years. This partnership enabled a global network of expert tumor immunologists to carry out coordinated, multicenter, single-variable, parallel, academic clinical trials that employed standardized correlative immunological monitoring designed to extract the most meaningful data from first-in-human studies. It was the first network of its kind in the cancer immunotherapy space.

Tragically, in 2011, Lloyd died from prostate cancer at the age of 78. It's a cruel irony not only that the disease he'd dedicated his life to defeating ultimately took him from us, but also that it should happen just as immunotherapy was beginning to prove itself and take its first steps toward the limelight.

No one person can be credited with the successes of an entire field. Lloyd would certainly never say so, as he often cast credit aside, but I think his indelible imprint is evident across the careers and lives of many in this field, whether directly or indirectly. I do not believe the field would be where it is today if it were not for his vision, leadership, and pursuit of scientific excellence.

It is gratifying that the field is now rich with other distinguished scientists whose own seminal work has helped us to come closer to immunologically based cures for all cancers. I trust that you will enjoy learning about them, their work, and this powerful new way to treat cancer as you explore the chapters ahead.

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