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Drugs Against Cancer: Stories of Discovery and the Quest for a Cure

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Preface and acknowledgements

First and foremost, I must express my gratitude to the United States Public Health Service and the National Cancer Institute for giving me the opportunity for a lifetime of wonderful association with biomedical researchers and to contribute a little to efforts to understand and hopefully to eventually control cancer. In a sense, this work is a tribute to those efforts, especially on the historical efforts to develop new drugs for cancer chemotherapy and the investigation of their mechanisms of action.

I owe special gratitude to Gordon Zubrod, David P. Rall, Emil (Tom) Frei, Emil J Freireich, and Ti Li Loo for acquainting me with the clinical, pharmacological, and chemical aspects of cancer research and helping me find my way to the research area to which I seemed best adapted. Several others to whom I owe debts of gratitude will appear in the narrative of the following chapters.

Any huge research and development endeavor is unlikely to be free of all shortcomings from which lessons could be learned. Although I have tried to give an accurate historical account without shying from shortcomings, I have no doubt committed errors, which might be corrected by future authors examining the available records and interviewing surviving protagonists.

Starting on this work, I felt a responsibility to make a record of the part of the cancer drug development effort with which I was associated, going back nearly 60 years, and to relate it to the global anti-cancer drug discovery and development efforts. However, I don't pretend to have written a scholarly history, which remains for others to accomplish.

This work may be viewed as a combination of science, history, medicine, and memoir, and hopefully could mostly be understood without a great deal of prerequisite knowledge. However, some technical material is included for experts

and students and for those who may have the fortitude to read some perhaps challenging parts of the text. However, I have endeavored to use non-technical language even in explaining those more complicated aspects. To that end, I have minimized the use of abbreviations. For the most part, the chapters are self-contained and can be read in any order.

I have tried to give an account of the earliest published work leading to the anticancer drug discovery stories that I will relate. My aim then was to explain how the knowledge and application of cancer chemotherapy drugs developed. It is in large part a historical account. Much of the history that I will relate will not go out of date, because it is based on published work and my own personal experience. However, I could not possibly have thoroughly covered the entire territory of cancer drug discovery in this writing. There are no doubt areas of omission or misunderstanding, and I apologize to those whose work I failed to mention or give adequate credit.

I am reminded of a remark by Vincent DaVita when he was our Division Director, who, on an occasion when we disagreed, quoted Winston Churchill to the effect that *The demand for perfection spells paralysis*. With that in mind, I proceeded despite the near certainty of significant imperfections.

These chapters will be made freely available in the website of the Laboratory of Molecular Pharmacology in the Developmental Therapeutics Branch (DTB) of the National Cancer Institute. They are being uploaded and managed under the direction of William C. Reinhold, Head of the Genomics and Bioinformatics unit in the DTB, and Yves Pommier, Director of the DTB. Comments are invited; the chapters are subject to being updated.