MOLECULAR DIAGNOSTICS
The Key Driver in Personalized Cancer Medicine
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INTRODUCTION

It is now 10 years ago since Robert Langreth and Michael Walholz announced the “New Era of Personalized Medicine” in the Wall Street Journal. This article introduced the concept of personalized medicine to a broader audience, but in fact, the first step towards a more individualized drug therapy was taken already several decades before this manifesto. With the discovery of the estrogen receptor in the 1960’s and the introduction of the anti-estrogen tamoxifen in the 1970’s the road was prepared for a more individualized treatment of cancer patients – in this case patients with breast cancer. The assay for estrogen receptor (ER) status became an important stratification factor for anti-estrogen treatment. In the 1990’s another targeted drug was introduced which was also aimed at a selected group of cancer patients: women whose breast cancer tumors over-expressed the human epidermal growth factor receptor 2 (HER2). The drug was the monoclonal antibody trastuzumab (Herceptin®, Genentech, CA, USA), which was specifically targeted towards the HER2 protein of the tumor cells. Also, for trastuzumab a pharmacodiagnostic test played an important role in relation to treatment stratification. This was the immunohistochemical assay for the HER2 protein (HercepTest™, Dako, Glostrup, Denmark).

Since the turn of the century other targeted cancer drugs have been introduced which are guided by a pharmacodiagnostic test or companion diagnostics in order to identify the patients who are most likely to respond to treatment. The development of pharmacodiagnostic tests are, however, not restricted to new drugs only. As our knowledge about the cancer pathophysiology at the molecular level increases and the mechanisms of action of the drugs are explained, it has also become possible to develop pharmacodiagnostic tests for drugs that are already used in the clinic. One recent example is the predictive fluorescence
in situ hybridization (FISH) assay for anthracycline treatment of patients with primary breast cancer (TOP2A FISH pharmDx™, Dako Glostrup, Denmark). In fact, the cover of this book is embellished with a picture of breast cancer cells showing amplification of the TOP2A gene assessed by this assay.

The advancement within molecular diagnostics, especially genomics, is a very important driver of this development. In a recent report from the US; “Priorities for Personalized Medicine”, published by the President’s Council of Advisors on Science and Technology (PCAST), it is stated that molecular diagnostics is identified as a key driver of personalized medicine. In this respect pharmacodiagnostics or companion diagnostics are not only important tools used in the development of new targeted anticancer drugs, but they are just as important with respect to improvement of the quality of patient care. The PCAST report points at the potential of personalized medicine in relation to two important trends - the increasing costs of healthcare and the decreasing rate of new medical products being developed. For the quality of patient care the use of diagnostics will enable the treating physician to distinguish in advance those patients who will benefit from a given treatment and those who are likely to suffer the adverse effects only. The use of pharmacodiagnostics or companion diagnostics will lead to a more rational treatment of cancer that could also result in cost savings for the healthcare system. Moreover, with respect to drug development, diagnostics can be used to stratify patients according to their likelihood of response to the drug under development. Such approach could result in reduced size, duration, and costs of clinical trials, thus facilitating the development of more new drugs.

Drug-diagnostic co-development will be the future development model in stratified and personalized cancer medicine. We will see more and more drugs and diagnostics being developed in parallel in order to increase the effectiveness and safety of new anticancer drugs, and it is our hope that this book will contribute to this development and be an inspiration to those who are engaged in this important work.
Working with this book has been a pleasure and has convinced us even more that molecular diagnostics will be a decisive factor with respect to further improvement of cancer treatment.

We would like to express our gratitude to all the authors who have contributed so positively to this book.

Jan Trøst Jørgensen and Henrik Winther

Copenhagen, November 2009
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