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0521811023 - Biomarkers of Disease: An Evidence-Based Approach

Edited by Andrew K. Trull, Lawrence M. Demers, David W. Holt, Atholl Johnston, J. Michael Tredger and Christopher P. Price

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Biomarkers of Disease

An Evidence-based Approach

This new publication takes a critical, evidence-based look at the efficacy of new diagnostic tests which are increasingly being used to evaluate organ damage and dysfunction. The use of biomarkers is growing, with a steady stream of new products being brought out by the diagnostics industry. Some of these assist in diagnosis, while others provide a means of monitoring the state of progression of disease and the effectiveness of therapeutic options. However, in many cases, the evidence which supports the use of these new methods as opposed to traditional biochemical tests has not yet been demonstrated, and it is intended that this volume will help clarify the strengths and weaknesses of using these biomarkers across a wide range of applications and in the various organs of the body. This approach will provide clinicians, pathologists, clinical biochemists and medical laboratory scientists with an invaluable overview of the diverse applications of biomarkers in medicine.

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PUBLISHED BY THE PRESS SYNDICATE OF THE UNIVERSITY OF CAMBRIDGE

The Pitt Building, Trumpington Street, Cambridge, United Kingdom

CAMBRIDGE UNIVERSITY PRESS

The Edinburgh Building, Cambridge CB2 2RU, UK

40 West 20th Street, New York, NY 10011-4211, USA

477 Williamstown Road, Port Melbourne, VIC 3207, Australia

Ruiz de Alarcón 13, 28014 Madrid, Spain

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<http://www.cambridge.org>

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First published 2002

Printed in the United Kingdom at the University Press, Cambridge

Typeface Minion 8.5/12pt *System* QuarkXPress™ [SE]

A catalogue record for this book is available from the British Library

ISBN 0 521 81102 3 hardback

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Cambridge University Press

0521811023 - Biomarkers of Disease: An Evidence-Based Approach

Edited by Andrew K. Trull, Lawrence M. Demers, David W. Holt, Atholl Johnston, J. Michael Tredger and Christopher P. Price

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Preface

Biological markers or 'biomarkers' of organ damage and dysfunction occupy a central position in the armamentarium of the clinician that is used for the screening, diagnosis and management of disease. Our knowledge of the pathophysiological basis of individual diseases continues to increase inexorably and the discoveries emanating from the Human Genome Project are set to enhance this knowledge immeasurably. Understanding the aetiopathogenesis of changes that take place in individual tissues, organs or compartments of the body can help in the search for markers that reflect these changes. Some of these changes may be directly related to the pathological abnormality while others might be a secondary consequence of the abnormality.

Basic research into the pathophysiology of a disease provides the foundation of knowledge that can lead to the discovery of valuable biomarkers. This foundation can also act as the starting point for the discovery of pharmaceutical interventions. Increasingly, with a more systematic approach to biomarker development and drug discovery, we are seeing the measurement of the biomarker playing a greater role in monitoring the efficacy and/or side effects of the therapeutic intervention. From a clinical standpoint, this can have a major benefit in assessing compliance with therapy, which is acknowledged to be one of the key determinants of efficacy, especially when there is no other ready means to judge the patient's response.

The discovery of a new biomarker is complemented by the development and validation of appropriate analytical technology. The appropriateness can be viewed in relation to a number of performance characteristics and the mode of delivery. Thus, the test may be delivered on an automated analytical platform from a centralized laboratory facility or by means of a point of care testing device. The ability to deliver the test at the point of care, with the immediacy of response, may be a key factor in ensuring the clinical utility of the test. The basic analytical characteristics include imprecision and inaccuracy which, together with the issues surrounding the biological variation and stability of the biomarker, constitute the core components of technical performance.

The diagnostic performance of the test must then be established by comparing biomarker measurements in appropriate populations of patients and controls in

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the relevant clinical setting. A diagnostic test is one element of a process which begins with a clinical question; the ideal test is one which provides an unequivocal answer to the question and enables a decision to be made on what action must be taken next. When effective action is then taken, a positive outcome or benefit can accrue to the patient, the healthcare system and society as a whole. Unfortunately, few tests are ideal in this respect and the medical practitioner usually has to appreciate the limited diagnostic performance of a test in order to make a balanced interpretation of the results in the context of the patient's clinical status.

The above description of the technical and clinical validation of a test applies to most research into diagnostic tests today. However, this is not the end of the process, as it is also necessary to consider the decision-making process associated with the introduction of a new test into the routine laboratory. In order to justify investment – from a clinical, operational and economic standpoint – it is not only important to prove that the test meets required standards of diagnostic performance but also that it delivers a positive clinical, operational or economic outcome – and, preferably, all three! Incorporating these outcome metrics into the evaluation of laboratory diagnostics provides a more rigorous and holistic standard of healthcare than is often embraced by laboratory medicine and illustrates the importance of integrating laboratory medicine fully into clinical practice – in terms of investment, delivery and quality management.

This book is the first attempt to review the current literature on biomarkers from an evidence-based and clinical outcomes perspective. It represents a distillation of the presentations made at the 'EMBODY 2000' conference held in Cambridge, England. It covers selected key areas – a comprehensive book would have necessitated a whole textbook! However, each of the authors, all clinical scientists of international repute, was asked to review the literature in their chosen field from the perspective of the impact of biomarkers on clinical outcome. We hope that this initiative, both the meeting and the book, represents a watershed in the literature on biomarkers, focusing more attention on clinical outcomes.

It is self-evident, but still worth stating, that a positive outcome will not be achieved unless the right test is requested in the first instance and the result acted upon with the relevant therapeutic strategy. This book, therefore, is not only relevant to professionals in laboratory medicine but also to the users of biomarkers.

Andrew K. Trull**Laurence M. Demers****David W. Holt****Atholl Johnston****J. Michael Tredger****Christopher P. Price**