
Preface

The process of metastasis formation is hugely complex, as described in the introductory chapter of this book, and this complexity has led us to compile two volumes of methods, from a vastly divergent background that attempts to encompass the whole spectrum of cancer biology. This first volume, *Metastasis Research Protocols: Analysis of Cells and Tissues*, concentrates on analysis and mapping of molecules produced by cells and tissues and analysis of the molecular biology underlying their expression, whereas the second volume, *Metastasis Research Protocols: Cell Behavior In Vitro and In Vivo*, focuses sharply on the determination of cell behavior in vitro and in vivo. We have deliberately included chapters describing well-established and familiar techniques (for example, SDS-PAGE and Western blotting [Chapter 11], and immunocytochemistry [Chapter 2]) in addition to the newer and more specialized approaches and specific examples of their application, because—although the methodology is readily available in the published literature and established in many laboratories—we wished these volumes to “stand alone” and to make accessible here the standard techniques that underpin much metastasis research for both the newcomer to the field and the seasoned researcher. Undoubtedly, owing to the complexity of the metastatic cascade and the wealth of research techniques involved in scientific approaches to its unraveling, and despite our best efforts to make these volumes as comprehensive as seems feasible, this is a tall order, and there will inevitably be omissions. For these we apologize.

Part I of the present volume, *Detection Methods for Cellular Markers of Metastatic Potential*, begins with a chapter on the evaluation of the presence or absence of metastatic spread by “traditional” histopathological assessment. It seemed to us that this topic was the best way to launch a book of metastasis research protocols because it is essential to so much of clinically based metastasis research. Old fashioned histology and its ramifications, such as immunocytochemistry, remain the gold standard for the diagnosis of the metastatic spread of a tumor. The methodology for basic immunocytochemistry is described, as are variations such as multiple labeling and lectin cytochemistry, and some examples of clinically relevant applications of immunocytochemistry to metastasis research are given. Several approaches to the assessment of cellular proliferation, including immunocytochemistry, calculation of mitotic index,

and flow cytometry, are described. Another classical method of enormously wide applicability in metastasis research, SDS-PAGE and Western blotting, is detailed. This technique allows at least initial analysis of protein extracts from cells and tissues and is inevitably referred to in numerous other protocols in this and the following volume. The last chapter in this section describes enzyme zymography for assessment of levels of gelatinases.

Having outlined techniques for mapping cellular expression of gene products of potential significance in the metastatic cascade, Part II extends the level of analysis further with a range of techniques for analysis of *Genetic Aspects of Metastasis*. A range of molecular biological methods applied to metastasis research are presented, facilitating a focused and specific single gene approach. They include *in situ* hybridization to localize mRNAs, a variation on this approach, fluorescence *in situ* hybridization (FISH), and comparative genomic hybridization (CGH). RNA purification and quantification methods are also presented. The classical approaches of Northern and Southern blotting and PCR are described. Methylation analysis of CpG islands is covered, as is detection of metastatic tumor cells in blood by the classical technique of reverse transcriptase polymerase chain reaction (RT-PCR). The final chapter in this section presents the technique of differential display.

The last section of the book deals with the *Mathematical Modeling of Metastasis*. This aspect might seem unfamiliar to many cancer scientists, but it may well be that mathematical models will help to direct further research efforts in metastasis research or may help to evaluate whether a particular strategy in the treatment of metastases will have any influence on the overall outcome of the disease. Complex and nonlinear biological systems will need the help of mathematicians to adequately model their effects.

Cancer mortality will only drop if metastases can be treated successfully. To do so, it is probably necessary to understand the metastatic cascade first at the cellular and molecular level, then at the tissue level, and finally—the subject of Volume II—to appreciate the subtleties of cellular behavior in both *in vitro* assays and at the level of the whole organism. Based on this comprehensive knowledge, rational strategies to combat metastatic disease might be developed. We hope that this collection of protocols will help to work toward this goal.

Susan A. Brooks
Udo Schumacher



<http://www.springer.com/978-0-89603-610-9>

Metastasis Research Protocols

Brooks, S.A.; Schumacher, U. (Eds.)

2001, 344 p., Hardcover

ISBN: 978-0-89603-610-9

A product of Humana Press