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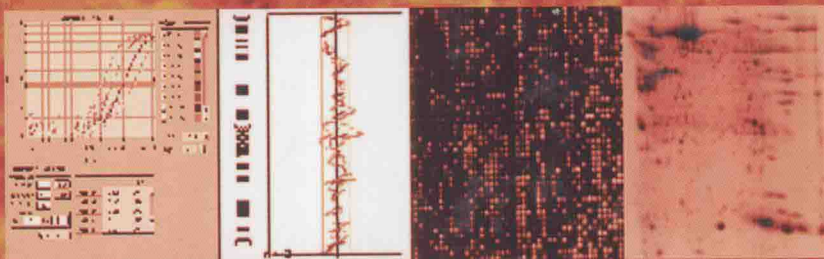
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# Laser Capture Microdissection

*Methods and Protocols*

*Edited by*

Graeme I. Murray  
Stephanie Curran



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# Laser Capture Microdissection

*Methods and Protocols*


Edited by

**Graeme I. Murray**

and

**Stephanie Curran**

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## Preface

Laser microdissection techniques have revolutionized the ability of researchers, generally, and pathologists in particular, to carry out molecular analysis on specific normal and diseased cells and fully utilize the power of current molecular technologies, including polymerase chain reaction (PCR), microarrays, and proteomics. The primary purpose of *Laser Capture Microdissection: Methods and Protocols* is to provide readers with practical advice on how to carry out tissue-based laser microdissection successfully in their own laboratories using the microdissection systems available and how best to apply a wide range of molecular technologies. The individual chapters encompass detailed descriptions of each of the laser-based microdissection systems. Applications of the laser microdissected tissue described in the book include PCR in its many different forms and gene expression analysis involving microarrays and proteomics.

The editors are especially grateful to all the contributing authors for the time and effort they have put into writing their chapters.

The series editor, John Walker, has expertly guided us through the editorial process, while Craig Adams of Humana Press has been very helpful in dealing with all the publication related issues.

We are particularly pleased to acknowledge the excellent secretarial support of Ms. Anne McMillan of the Department of Pathology, University of Aberdeen who helped us deal efficiently with all the correspondence relating to this book. We hope the readers will find this volume valuable.

**Graeme I. Murray**  
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# I ---

## INTRODUCTION



# An Introduction to Laser-Based Tissue Microdissection Techniques

Stephanie Curran and Graeme I. Murray

## Summary

The development and application of laser-based tissue microdissection techniques has provided a major impetus to the sensitive and specific molecular analysis of solid tissues and tumors. This chapter provides an overview of the different laser-based microdissection systems and an introduction to the principles involved in the function and applications of these individual systems.

**Key Words:** Laser capture microdissection; laser microbeam microdissection; molecular analysis.

## 1. Introduction

Tissues, especially diseased tissues, are complex three-dimensional structures composed of heterogeneous mixtures of morphologically and phenotypically distinct cell types. The meaningful molecular analysis of morphologically and/or phenotypically distinct cell types from such tissues requires rapid, efficient, and accurate methods for obtaining specific population of cells.

The molecular investigation of solid tissues, especially tumors, has been revolutionized over the past decade by the development of accurate, rapid, and effective laser-based methods of tissue microdissection (1,2). This has provided an extremely valuable and sophisticated tool to fully utilize the power and sensitivity of modern molecular analytical technologies in the detailed investigation of many different diseases and provided significant new insights into the pathogenesis of these diseases. Many of the investigations using laser microdissected cells have focused on specific types of cancers, where the morphological and phenotypic heterogeneity and complexity of tissues is often the greatest (1-3).

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Individual studies have usually based cell selection on specific morphological criteria of stained histological sections, but phenotypic characteristics as defined by immunohistochemistry of antigen expression (4) or genotypic features as demonstrated by *in situ* hybridization have also been used as selection criteria (5) and demonstrate the power of laser-based microdissection techniques. One of the major advantages of using laser microdissection methods to obtain specific cells for molecular analysis, especially from the viewpoint of the pathologist, is that the procedure is carried out under direct-light microscopic visualization of the cells. Whereas other technologies used to isolate specific cell populations for molecular analysis—e.g., fluorescent-activated cell sorting or magnetic bead-based cell separation—are indirect techniques with no microscopic visualization of the cells and require the availability of suitable antibodies to aid cell selection. Moreover, the methods used to prepare single cell suspensions (e.g., proteolytic enzyme digestion) that are necessary for antibody-based cell separation techniques from solid tissues may result in alteration or modification of cellular constituents. There is no doubt that the availability of laser-based microdissection technologies has provided a major impetus to molecular pathology research and this technology is now found in many laboratories worldwide (as represented in the diverse geographic locations of contributors to this volume). The wide availability of this easy-to-use technology has allowed many questions in a range of research disciplines to be answered that previously could not be asked or answered using manual methods of tissue microdissection because of the imprecise nature of manual methods of microdissection or the time required to obtain tissue.

There are two major systems that have been developed for performing laser-assisted tissue microdissection—namely, laser capture microdissection and laser microbeam microdissection. Both types of systems have now been commercially available for several years. An overview of the principles, advantages, and potential disadvantages of each of the systems will be provided in this introductory chapter, detailed descriptions and applications of the individual systems are given in the relevant chapters in this volume.

## **2. Overview of Laser Microdissection Systems**

### **2.1. Laser Capture Microdissection**

The laser capture microdissection system was developed in the mid-1990s at the National Institutes of Health by Emmert-Buck and colleagues (6,7), who recognized the need to develop a microscope-based microdissection system for accurately and efficiently microdissecting cells from histological tissue sections to fully exploit emerging molecular analytical technologies. They developed this system primarily to facilitate the molecular analysis of solid tumors.