

Vinod H. Nargund
Derek Raghavan
Howard M. Sandler
Editors

Urological Oncology

Second Edition

 Springer

Vinod H. Nargund • Derek Raghavan
Howard M. Sandler
Editors

Urological Oncology

Second Edition



 Springer

Editors

Vinod H. Nargund, PhD, FRCSED,
FRCSUrol, FEBU
Department of Urology
Homerton University Hospital &
Formerly St. Bartholomew's Hospital
London
UK

Howard M. Sandler, MD, MS, FASTRO
Radiation Oncology
Cedars Sinai Cancer Center
Los Angeles, CA
USA

Derek Raghavan, MD, PhD, FRACP,
FACP, FASCO
Levine Cancer Institute
Carolinas HealthCare System
Charlotte, NC
USA

ISBN 978-0-85729-481-4

ISBN 978-0-85729-482-1 (eBook)

DOI 10.1007/978-0-85729-482-1

Springer London Heidelberg New York Dordrecht

Library of Congress Control Number: 2014960231

© Springer-Verlag London 2015

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed. Exempted from this legal reservation are brief excerpts in connection with reviews or scholarly analysis or material supplied specifically for the purpose of being entered and executed on a computer system, for exclusive use by the purchaser of the work. Duplication of this publication or parts thereof is permitted only under the provisions of the Copyright Law of the Publisher's location, in its current version, and permission for use must always be obtained from Springer. Permissions for use may be obtained through RightsLink at the Copyright Clearance Center. Violations are liable to prosecution under the respective Copyright Law.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

While the advice and information in this book are believed to be true and accurate at the date of publication, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface to Second Edition

We are delighted to present the second edition of *Urological Oncology* for our readership. When we collaborated with our fine team of authors initially, we felt that there was a need for a simple handbook focused on the interface between science and practical management that would allow the less experienced clinician or one with less specific knowledge of urological malignancies to understand clinical management practices and the basis for their implementation. We were gratified by the impact of the first edition of *Urological Oncology* and by the high level of feedback from readers requesting an update.

With this second edition, we have sought to maintain the didactic and easy-to-assimilate format and at the same time improve domains that might have been covered in more detail and include data from recent practice-changing clinical trials, innovations in laboratory diagnostics, surgery, radiation oncology, systemic therapy, and palliative/supportive care.

Medicine is changing at an ever-increasing pace, with a shifting focus on value rather than volume and an astounding amount of complex molecular and biostatistical information, daunting even to the most experienced clinician. We hope that our second edition will enable all to place these advances in the context of existing practices, so as to encourage more tailored management of patients. The second edition remains again compact, concise, and comprehensive.

We thank our contributors, staff at Springer, and, most of all, our readers, who have made this new edition possible.

September 2014

Vinod H. Nargund
Derek Raghavan
Howard M. Sandler

Preface to First Edition

*I keep six honest serving men
(They taught me all I knew);
Their names are What and Why and When
And How and Where and Who.*

Rudyard Kipling ("The Elephant's Child," in The Just-So Stories, 1902)

Clinical knowledge is based on three components: meticulous observation, detailed recording, and an understanding of basic science relevant to the clinical situation. The first two come with apprenticeship and the last one with personal research or inquisitive reading. It is the last component that is the basis for this book. Although most general urology books contain a fair amount of urological oncology, most of them are written by urologists for urologists. There is an increasing realization, however, that a multidisciplinary approach is required for the management of all cancers, including urological cancers. In particular, there is a need for surgeons and oncologists to have an integrated strategy for the management of complex cancer cases. A multidisciplinary team will include anesthetists, radiologists, minimally invasive surgeons, intensivists, nutritionists, and support and social work staff in addition to the cancer clinicians. We aim, in this book, to provide this integrated approach as it has contributions from specialists from these different disciplines. All these specialists should have a role in the management of patients to provide them with optimal chances of recovery. They have also a key role in counseling patients in a coordinated way, for otherwise, patients would gain piecemeal information of variable quality from a number of sources, including the Internet. The media and the Internet have increased cancer awareness among patients, who demand more and more answers to questions such as: What caused my cancer? How can I prevent a recurrence? Will my children get it? How do I get the best up-to-date treatment for my cancer?

Patients have a greater understanding that there may be choices in the management of their condition, and oncologists, both surgical and medical, have to listen to and include the patient's views in the decision-making process. We hope this book will assist in both the management and the counseling of patients with urological cancer. The book also includes chapters on basic science, research, and trials related to urological cancers, which will help those students with an interest in research. Relevant surgical anatomy and other details of basic science are included wherever necessary.

Initially, this book was intended to be a pocket guide on adult urological cancer, but it quickly metamorphosed into a minitextbook. The authorship is truly international and therefore reflects a consensus approach to investigation and treatment across the world. The text is didactic and should provide the basis for further reading from journals or more detailed review papers. The book is aimed at residents and urological specialists at all levels of training in urology and oncology.

London, UK
Cleveland, OH
Ann Arbor, MI

Vinod H. Nargund
Derek Raghavan
Howard M. Sandler

Contributors

Adam Alleemudder, MBChB, BSc, MRCS (Ed) Department of Urology,
Barts and The Royal London Hospital, London, UK

Ravishankar Rao Baikady, FRCA Department of Anaesthesia,
The Royal Marsden Hospital, London, UK

Sohail Ibrahim Baithun, MB, FRCP Department of Histopathology,
King Hospital, Busaiteen, Bahrain

Eric Barret, MD Department of Urology, Institut Montsouris- Universite
Paris Descartes, Paris, France

Yakup Bostanci, MD Department of Urology, New York University Hospital,
NYU, New York, NY, USA

Ronald M. Bukowski, MD Department of Solid Tumor Oncology, Cleveland
Clinic Foundation Taussig Cancer Center, Cleveland, OH, USA

John Buscombe, MD, FRCP Department of Nuclear Medicine,
Addenbrookes Hospital, Cambridge, UK

R.S.K. Chaganti, PhD Department of Medicine and Cell Biology Program,
Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Seungjean Chai, MD Department of Solid Tumor Oncology and Investigational
Therapeutics, Levine Cancer Institute, Carolinas HealthCare System,
Charlotte, NC, USA

Lewis Chan, FRACS, DDU Department of Urology, Concord Repatriation
General Hospital, Concord, Australia

Shern L. Chew, BSc, MB, BChir, MD, FRCP Department of Endocrinology,
The London Clinic, London, UK

Bob Djavan, MD, PhD Department of Urology, VA University Hospital,
New York, NY, USA

Tanya Barauskas Dorff, MD Department of Medicine, USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA

Albert A. Edwards, FRCR Department of Oncology, St. Luke's Cancer Centre, Royal Surrey County Hospital, Guildford, UK

Darren R. Feldman, MD Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

David J. Feuer, FRCP Department of Palliative Medicine, Barts Health NHS Trust and Homerton Hospital NHS Foundation Trust, West Smithfield, London, UK

Sophie D. Fossa, MD, PhD Department of Surgery, Oslo University Hospital, Montebello, Oslo, Norway

Nicos Fotiadis, MD, FRCR, EBIR Department of Interventional Oncology, The Royal Marsden NHS Foundation Trust, London, UK

Gary Frenette, MD, PhD Department of Solid Tumor Oncology, Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC, USA

Matthew D. Galsky, MD Department of Medicine/Oncology, Tisch Cancer Institute/Mount Sinai School of Medicine, New York, NY, USA

L. Michael Glodé, MD Division of Medical Oncology, Department of Medicine, University of Colorado, Aurora, CO, USA

Veronica Greener, BSc, MBBS, MRCP, MD Department of Endocrinology, Chelsea and Westminster Hospital, London, UK

T.R. Leyshon Griffiths, BSc, MD, FRCSEd Department of Cancer Studies and Molecular Medicine, University of Leicester, Leicester, UK

Sounak Gupta, MBBS, PhD Department of Anatomic Pathology, The Cleveland Clinic, Cleveland, OH, USA

Donna E. Hansel, MD, PhD Department of Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH, USA

Axel Heidenreich, MD, PhD Department of Urology, University Hospital Aachen, Aachen, Germany

Thomas Hermanns, MD Division of Urology, Department of Surgical Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada

Simon Horenblas, MD, PhD, FEBU Department of Urology, Netherlands Cancer Institute, Amsterdam, Netherlands

Bo Hu, PhD Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, USA

Ray K. Iles, PhD, CBiol, FSB, FRSC The Eric Leonard Kruse Foundation for Health Research, An Scoil, Monzievairst, CRIEFF, Perth and Kinross, Scotland, UK

Benjamin L. Jackson, MBChB (hons), FRCS (urol) Department of Urology, University Hospitals Leicester, Leicester, UK

Audrey E.T. Jacques, MDDS, BSc, MRCP, FRCR Department of Radiology, Guy's and St. Thomas Hospital, London, UK

Günter Janetschek, MD Department of Urology and Andrology, Paracelsus Medical University, Salzburg, Austria

Jana Jeyakumar, MRCP, MBBS Department of Medicine, Barts and The London NHS Trust, London, UK

Prashanth Kanagarajah, MD Department of Urology, University of Miami-Miller School of Medicine, Miami, FL, USA

Michael W. Kattan, PhD Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, USA

Amir Kazzazi, MD Department of Urology, New York University Hospital, NYU, New York, NY, USA

Bridget F. Koontz, MD Department of Radiation Oncology, Duke University Medical Center, Durham, NC, USA

Cynthia Kuk, MSc Division of Urology, Department of Surgery, Mount Sinai Hospital, University Health Network, Toronto, ON, Canada

Priyadarshi Kumar, MB, BS, MRCS, MD, FRCS Department of Urology, Lancashire Teaching Hospitals, NHS Foundation Trust, Lancashire, UK

Robert W. Laing, FRCP Department of Oncology, St. Luke's Cancer Centre, Royal Surrey County Hospital, Guildford, UK

Elaine T. Lam, MD Division of Medical Oncology, Department of Medicine, University of Colorado, Aurora, CO, USA

Stephen E.M. Langley, FRCS Department of Urology, Royal Surrey County Hospital, Guildford, UK

Abigail Lee Department of Morbid Anatomy, The Royal London Hospital, Barts Health NHS Trust, London, UK

Irwin H. Lee, MD, PhD Kaiser Permanente, Rohnert Park, CA, USA

W. Robert Lee, MD Department of Radiation Oncology, Duke University Medical Center, Durham, NC, USA

Hing Yip Leung, MBChB, PhD, FRCS(Urol.) Department of Urology, Beatson Institute for Cancer Research, Institute for Cancer Sciences, University of Glasgow, Glasgow, Strathclyde, UK

Karen W.E. Lord, PhD Department of Palliative Care, University Hospital of Leicester NHS Trust, Leicester, UK

Lukas Lusuardi, MD, FEBU Department of Urology and Andrology, Paracelsus Medical University, Salzburg, Austria

Eamonn R. Maher, BSc, MD, FRCP, FMedSci Department of Medical Genetics, University of Cambridge, Cambridge, UK

John Mahoney, MD Department of Solid Tumor Oncology and Investigational Therapeutics, Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC, USA

Kim Mammen, MS, MCh, FRCS, FACS Department of Urology, Christian Medical College and Hospital, Ludhiana, India

Murugesan Manoharan, MD Department of Urology, University of Miami-Miller School of Medicine, Miami, FL, USA

Rajesh Mehta, MBBS, BSc, FRCA Department of Anesthesia, The Royal London Hospital, Barts Health NHS Trust, London, UK

J. Killian Mellon, MD, FRCS Department of Cancer Studies and Molecular Medicine, University of Leicester, Leicester, UK

Maria Carmen Mir, MD Department of Urology, Cleveland Clinic, Cleveland, OH, USA

Alex J. Mitchell, MBBS, BMedSci, MSc Department of Cancer Studies and Molecular Medicine, University of Leicester, Leicester, UK

Mark R. Morris, PhD, BSc Department of Biology, Chemistry and Forensic Science, University of Wolverhampton, Wolverhampton, UK

Ghulam Nabi, MS, MD, MCh, FRCS (Urol) Department of Urology, Ninewells Hospital, University of Dundee, Dundee, Scotland, UK

Vinod H. Nargund, PhD, FRCSEd, FRCSUrol, FEBU Department of Urology, Homerton University Hospital, London, UK

Jan Oldenburg, MD, PhD Department of Oncology, Oslo University Hospital, Oslo, Norway

Ali Panah, MRCS Department of Urology, Homerton University Hospital NHS Trust, London, UK

Gilles Pasticier, MD Department of Urology, Service d'urologie A-Hopital Pellegrin Place, University Hospital Pellegrin, Bordeaux, France

Jacek Pinski, MD, PhD Department of Medicine, USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA

Melanie Powell, MB, BS, MD, FRCP, FRCR Department of Clinical Oncology, Barts Health NHS Trust, St. Bartholomew's Hospital, London, UK

Shirish G. Prabhudesai, MBBS, MS, MRCS Department of Radiology, St Bartholomew's and The Royal London Hospital, London, UK

Derek Raghavan, MD, PhD, FRACP, FACP, FASCO Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC, USA

Bhavan Prasad Rai, MBBS, MRCSEd Department of Urology, Medical Research Institute, Ninewells Hospital and Medical School, Dundee, Scotland, UK

Prabhakar Rajan, MA, MBBChir, PhD, MRCS Department of Cancer Research, University of Glasgow, Glasgow, Strathclyde, UK

Andrew J. Richards, MBBS, FRACS Department of Urology, Prince of Wales University, Randwick, Australia

Christopher Ricketts, PhD Medical and Molecular Genetics, IBR, University of Birmingham, Birmingham, UK

Brian I. Rini, MD Department of Solid Tumor Oncology, Cleveland Clinic Foundation Taussig Cancer Center, Cleveland, OH, USA

Anju Sahdev, MBBS, MRCP, FRCR Department of Imaging King George V Block, St. Bartholomew's Hospital, London, UK

Howard M. Sandler, MD, MS, FASTRO Department of Radiation Oncology, Cedars Sinai Cancer Center, Los Angeles, CA, USA

Amlesh Seth, MBBS, MS, DNB, MCh(Urol) Department of Urology, All India Institute of Medical Sciences, New Delhi, India

Jonathan Shamash, MD, FRCP Medical Oncology, St. Bartholomew's Hospital, London, UK

Andrew J. Stephenson, MD, FACS, FRCS Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, OH, USA

Clare Sweeney, MBBS MRCSEd, FRCS (Urol) Department of Urology, Medical Research Institute, Ninewells Hospital and Medical School, Dundee, Scotland, UK

Paul Symonds, MD, FRCP Department of Cancer Studies and Molecular Medicine, University of Leicester, Leicester, UK

Chandran Tanabalan, MRCS Department of Urology, Homerton University Hospital NHS Trust, London, UK

Raj Thuraingham, MD, FRCP Department of Renal Medicine and Transplantation, Royal London Hospital, London, UK

Alexandre Zlotta, MD, PhD, FRCSC Division of Urology, Department of Surgery, Mount Sinai Hospital, University Health Network, Toronto, ON, Canada

Contents

1	Normal Cell	1
	Ray K. Iles	
2	Experimental Urological Oncology: Cellular, Molecular, and Animal	39
	Prabhakar Rajan and Hing Yip Leung	
3	Genetics and Genito-Urinary Cancer	51
	Mark R. Morris and Eamonn R. Maher	
4	Principles and Design Considerations of Clinical Trials	71
	Bo Hu and Michael W. Kattan	
5	Non-Interventional Imaging in Genitourinary Cancer	85
	Shirish G. Prabhudesai, Audrey E.T. Jacques, and Anju Sahdev	
6	Nuclear Medicine in Urological Cancer	135
	John Buscombe	
7	Clinical Emergencies in Genito-Urinary Cancers	157
	Lewis Chan and Andrew J. Richards	
8	Clinical Aspects of Urological Cancers Including Haematuria and Haematospermia	171
	Kim Mammen	
9	Renal Failure, Dialysis and Transplantation: In the Management of Renal Cell Carcinoma (Solitary Kidney and Bilateral Renal Tumours)	193
	Raj Thuraisingham	
10	Diet and GU Cancers	209
	Ali Panah and Chandran Tanabalan	

11 The Anaesthetic Management of Patients with Genitourinary Cancer	223
Rajesh Mehta and Ravishankar Rao Baikady	
12 Laparoscopy and Robotic-Assisted Laparoscopy in Uro-oncological Surgery	253
Lukas Lusuardi and Günter Janetschek	
13 Principles of Chemotherapy for Genitourinary Cancer	277
Gary Frenette and Derek Raghavan	
14 Principles of Radiotherapy in Urologic Tumors	299
Irwin H. Lee and Howard M. Sandler	
15 Palliative Care in Urological Cancer	311
Jana Jeyakumar and David J. Feuer	
16 Life After Urological Cancer – Psychological Issues	323
Paul Symonds, Karen W.E. Lord, and Alex J. Mitchell	
17 Renal Cell Carcinoma: Overview	337
Christopher J. Ricketts and Eamonn R. Maher	
18 Renal Cancer – Epidemiology and Aetiology	345
Adam Alleemudder, Amlesh Seth, and Vinod H. Nargund	
19 Pathology of Renal Cancer	353
Abigail Lee and Sohail Ibrahim Baithun	
20 Renal Cancer: Clinical Features	367
Adam Alleemudder, Vinod H. Nargund, and Amlesh Seth	
21 Renal Cancer: Investigations and Staging	373
Adam Alleemudder and Amlesh Seth	
22 Renal Cancer: Surgical Management	383
Adam Alleemudder and Vinod H. Nargund	
23 Nephron-Saving Procedures: Ablative Techniques (Non-surgical) Radiofrequency Ablation (RFA), High-Intensity Focused Ultrasound (HIFU), Cryotherapy	395
Nicos Fotiadis	
24 Medical Management of Metastatic Renal Cell Carcinoma	401
Brian I. Rini and Ronald M. Bukowski	
25 Tumours of the Adrenal Gland	413
Veronica Greener and Shern L. Chew	
26 Epidemiology, Biology, and Genetics of Adult Male Germ Cell Tumors	431
Darren R. Feldman and R.S.K. Chaganti	

27 Pathology of Testicular Tumors	451
Sohail Ibrahim Baithun and Abigail Lee	
28 Testicular Cancer- Clinical Features, Staging and Surgical Management.	463
Axel Heidenreich	
29 Chemotherapy for Testicular Cancer.	493
Jonathan Shamash	
30 The Role of Radiotherapy in Testicular Cancer	513
Sophie D. Fossa and Jan Oldenburg	
31 Superficial Bladder Cancer.	519
Benjamin L. Jackson, T.R. Leyshon Griffiths, and J. Killian Mellon	
32 Intravesical Therapy for Bladder Cancer	541
Benjamin L. Jackson, T.R. Leyshon Griffiths, and J. Killian Mellon	
33 Molecular Biology of Urothelial Cancer	563
Sounak Gupta and Donna E. Hansel	
34 Invasive Bladder Cancer: Combined Modality Treatment.	591
Derek Raghavan and Howard M. Sandler	
35 Surgical Management of Bladder Cancer	609
Murugesan Manoharan and Prashanth Kanagarajah	
36 Management of Metastatic Bladder Tumours.	627
Matthew D. Galsky	
37 Surgical and Minimally Invasive Management of Upper Urinary Tract Tumours.	647
Bhavan Prasad Rai, Clare Sweeney, and Ghulam Nabi	
38 Urachal and Urethral Cancer (Excluding Penile Cancer).	663
Priyadarshi Kumar and Vinod H. Nargund	
39 Epidemiology, Screening, Pathology and Pathogenesis	677
Bob Djavan, Yakup Bostanci, and Amir Kazzazi	
40 Clinical Presentation, Diagnosis and Staging	697
Thomas Hermanns, Cynthia Kuk, and Alexandre R. Zlotta	
41 Expectant Management of Localized Prostate Cancer	719
Maria Carmen Mir and Andrew J. Stephenson	

42 External Beam Radiation Therapy for Clinically Localized Prostate Cancer	731
Bridget F. Koontz and W. Robert Lee	
43 Brachytherapy for Prostate Cancer	743
Albert A. Edwards, Robert W. Laing, and Stephen E.M. Langley	
44 Cryotherapy for Prostate Cancer	773
Eric Barret	
45 High Intensity Focused Ultrasound (Hifu) in Prostate Cancer	783
Gilles Pasticier	
46 Surgical Aspects of Prostate Cancer Management	799
Vinod H. Nargund	
47 Management of Locally Advanced Prostate Cancer	807
Elaine T. Lam and L. Michael Glodé	
48 The Hormonal Management of Metastatic Prostate Cancer	817
Tanya Barauskas Dorff and Jacek Pinski	
49 Castrate Resistant Prostate Cancer: Systemic Chemotherapy and a System Problem	835
Derek Raghavan, Seungjean Chai, and John Mahoney	
50 Cancer Penis and Scrotum	847
Simon Horenblas	
51 Non-Urological Cancers Affecting the Urinary Tract	857
Melanie Powell	
Index	879

Chapter 1

Normal Cell

Ray K. Iles

Knowledge of normal cell biology is crucial for understanding the function of a normal cell and its deregulation in cancer. This chapter describes briefly the cellular and molecular features of a normal and malignant human cell with particular reference to genitourinary cancers.

Cell Structure and Function

Cell (plasma) membrane is a bilayer consisting of amphipathic phospholipids, a polar hydrophilic head (phosphatidyl choline) and a lipid hydrophobic tail (commonly two long chain fatty acids). The phospholipids spontaneously form an effective bilayer barrier impermeable to most water-soluble molecules; the barrier also defines cellular internal environment. The membrane exchanges are regulated by proteins embedded within the lipid bilayer. *Cytoskeleton* is a complex network of structural proteins that regulates not only the shape of the cell but its ability to traffic internal cell organelles. The major components are microtubules, intermediate filaments, and microfilaments. *Cytoplasm* contains organelles and defines the interior of the cell. Although a fluid compartment, the organelles are held within a scaffolding or cytoskeleton that regulates the passage and direction in which the interior solutes and storage granules flow.

Basement membrane (BM) is a specialized form of extracellular matrix (ECM) that has been recognized as a key regulator of cell behaviour. In addition to structural support and cell compartmentalization, BM sends a signal to the cells about the extracellular microenvironment, thereby regulating cell behaviours [1]. The role of BM in

R.K. Iles, PhD, CBiol, FSB, FRSC
The Eric Leonard Kruse Foundation for Health Research, An Scoil,
Monzievairst, CRIEFF, Perth and Kinross, Scotland, UK
e-mail: ray.iles@anglia.ac.uk

angiogenesis is described later. The *nucleus* is an organelle containing the human genome and it is bound by two bilayer lipid membranes. The outer of the two is continuous with the endoplasmic reticulum (ER). Nuclear pores are present in the membranes, allowing the passage of nucleotides and DNA interacting proteins in and messenger RNA (mRNA) out. *Nucleoli* are dense areas within the nucleus rich in proteins and RNA chiefly concerned with the synthesis of ribosomal RNA (rRNA) and ribosomes.

The *endoplasmic reticulum* (ER) is interconnecting branching tubules or flattened sacs (cisternae) of lipid membrane bilayer. It may contain ribosomes on the surface [rough endoplasmic reticulum (RER) when present, or smooth endoplasmic reticulum (SER) when absent]. ER is the site of production of transmembrane proteins and lipid and proteins for secretion or for other organelles. *Ribosomes* are complexes of protein and RNA that translate mRNA into a primary sequence of amino acids of a protein peptide chain. This chain is synthesized into the ER where it is first folded and modified into mature peptides.

The *Golgi apparatus* is characterized as a stack of flattened cisternae from which, vesicles bud off from the thickened ends. The primary processed peptides of the ER are exported to the Golgi for maturation into functional proteins (e.g. glycosylation of proteins, which are to be excreted, occurs here) before packaging into secretory granules and cellular vesicles, which bud off the end. *Lysosomes* are dense cellular vesicles containing acidic digestive enzymes.

Mitochondria are semiautonomous organelles responsible for cellular energy metabolism, free radical generation, and apoptosis [2]. They have two lipid bilayer membranes and a central matrix. The *outer membrane* contains gated receptors for the import of raw materials [pyruvate and adenosine diphosphate (ADP)] and the export of precursor of amino acids and sugars (oxaloacetate) and adenosine triphosphate (ATP). Proteins of the Bcl-2-Bax family are incorporated in this membrane and can release cytochrome C that triggers apoptosis [3]. The *inner membrane* is infolded (cristae) to increase its effective surface area, and it contains transmembrane enzyme complexes of the electron transport chain, generating an H^+ ion gradient. The *inner matrix* contains the enzymes of the Krebs' cycle. Mitochondria also possess several copies of their own DNA in a circular genome and thereby maintain genomic independence from the nucleus [4].

Mutations in mitochondrial DNA (mtDNA) have been identified in renal cell carcinoma (RCC) and prostate cancer. In RCC there is evidence to suggest alterations of mtDNA (mutation of the *ND1* gene) and mRNA coding for the subunit *ND3* gene [5, 6]. In prostate cancer there is evidence of mtDNA deletions that increase with advanced age [7]. The knowledge of cancer related mitochondrial abnormalities may help in devising novel anticancer therapies.

Cell Dynamics

The cell component proteins and organelles are continually being formed and degraded. Old cellular proteins are mopped up by a small cofactor molecule called ubiquitin. Ubiquitination acts as a signal for destruction, and a complex containing more than three ubiquitin molecules is rapidly degraded by a macromolecule called