
Cancer Biology


Carsten Carlberg • Eunike Velleuer

Cancer Biology

How Science Works

Second Edition

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Carsten Carlberg 
InLife, Institute of Animal Reproduction
Polish Academy of Sciences
Olsztyn, Poland

Eunike Velleuer 
Department for Cytopathology
Heinrich-Heine University Düsseldorf
Düsseldorf, Germany

School of Medicine, Institute of
Biomedicine
University of Eastern Finland
Kuopio, Finland

Department for Pediatric Hemato-Oncology
Helios Children's Hospital
Krefeld, Germany

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Preface

This book begins with sobering news: *approximately one in two individuals in high-income countries will receive a cancer diagnosis during their lifetime*, meaning a malignant tumor will be detected in their body. Yet there is encouraging news as well: *fewer than half of all cancer patients die from the disease, and every second cancer-related death is preventable*. Cancer is not a single disease but a heterogeneous group of disorders that can arise in virtually any organ. What they all share is uncontrolled cellular growth.

Every newly diagnosed malignant tumor in adulthood reflects an individual history of *two or more decades of tumorigenesis*. Cancer is traditionally viewed as a disease of the genome, driven by accumulated DNA point mutations, as well as chromosomal translocations, deletions, and amplifications. Tumorigenesis also involves profound alterations in cellular identity, responsiveness to internal and external signals, and major shifts in the transcriptome. These changes are rooted in *epigenomic dysregulation*. In fact, most cancers harbor mutations and alterations not only in their genomes but also in their epigenomes.

Cells in our body have the capacity to grow when needed: during wound healing or in the continuous renewal of blood, skin, and intestinal tissues. Because malignant transformation is typically slow, *cancer is largely an age-related disease*, one that seems inevitable as we grow older. Yet tumorigenesis depends on numerous environmental influences, including the ability of the immune system to detect and eliminate cancer cells. Many environmental factors that either promote or protect against cancer lie within our own control: *avoiding smoking, choosing a healthy diet, and staying physically active* are key examples. Thus, *cancer prevention through lifestyle choices* remains the most powerful strategy for reducing cancer risk.

Understanding cancer requires insight into ourselves, both in detail and within a broader context. Basic biology explains the cellular mechanisms of growth, differentiation, and cell death that make life possible. Every human being represents an intricate interplay of hundreds of cell types, each forming specialized tissues and organs. These processes must be precisely coordinated during embryonic development and maintained throughout adult life to preserve homeostasis. Studying the cellular and molecular foundations of these processes is deeply fascinating, yet also demanding. Much of what we know about normal biology has arisen from investigating what happens when these mechanisms go awry in disease.

Accordingly, this book not only describes the *fundamental mechanisms underlying cancer* but also aims to offer a more holistic perspective placing molecular insights into the wider context of the personal and societal implications of lifestyle choices.

The content of this book is linked to the lecture course “*Cancer Biology*,” taught by one of us (C. Carlberg) at the University of Eastern Finland in Kuopio since 2005, alongside related courses in *Molecular Medicine and Genetics*, *Molecular Immunology*, and *Nutrigenomics*. The biological concepts introduced here are complemented by clinical insights drawn from daily oncology practice, contributed by one of us (E. Velleuer). This book also relates to the books *Gene Regulation and Epigenetics: How Science Works* (ISBN 978-3-031-68729-7), *Aging: How Science Works* (ISBN 978-3-031-61256-5), *Molecular Immunology: How Science Works* (ISBN 978-3-031-04024-5), and *Nutrigenomics: How Science Works* (ISBN 978-3-031-85880-2), which may interest readers seeking more detailed information.

Chapters 1, 2, and 3 provide a general overview of cancer. Chapters 4, 5, 6, 7, and 8 examine the molecular basis of the disease, Chaps. 9, 10, and 11 discuss its cellular aspects, and Chaps. 12 and 13 present the principles of effective cancer therapy. By integrating fundamental biological mechanisms with clinical examples, we aim to make this book not only informative but also personally engaging. A glossary in the appendix defines key specialized terms; gene and protein name abbreviations are explained in the abbreviations list.

We hope readers will enjoy this visually rich book and become as enthusiastic as we are about understanding life, and its malfunctioning counterpart, cancer biology.

Kuopio, Finland
Düsseldorf, Germany
December 2025

Carsten Carlberg
Eunike Velleuer

Acknowledgments

The authors dedicate this book to all those affected by cancer whom we have known personally. Some have survived and continue to enrich the world with their presence. Others are no longer with us, yet they remain unforgettable and forever cherished.

Competing Interests The authors have no competing interests to declare that are relevant to the content of this manuscript.

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Abbreviations

3C	Chromosome conformation capture
3D	Three-dimensional
5hmC	5-Hydroxymethylcytosine
5hmU	5-Hydroxyuracil
5mC	5-Methylcytosine
β-hCG	Beta-human chorionic gonadotropin
A	Adenine
ABL1	ABL proto-oncogene 1, non-receptor tyrosine kinase
AFP	α-fetoprotein
AI	Artificial intelligence
AIDS	Acquired immune deficiency syndrome
AKT	Akt murine thymoma viral oncogene homolog
ALK	Anaplastic lymphoma kinase
ALL	Acute lymphoid leukemia
ALOX12	Arachidonate 12-lipoxygenase
AML	Acute myeloid leukemia
AMPK	AMP-activated protein kinase
AP1	Activating protein 1
APAF	Apoptotic peptidase activating factor
APC	APC regulator of WNT signaling pathway
APL	Acute promyelocytic leukemia
APOBEC	Apolipoprotein B mRNA editing catalytic subunit
AR	Androgen receptor
ARID	AT-rich interaction domain
ARTR	Atypical teratoid/rhabdoid tumor
ASC	Apoptosis-associated speck-like protein containing a CARD
ASNS	Asparagine synthetase (glutamine-hydrolyzing)
ATAC-seq	Assay for transposase-accessible chromatin using sequencing
ATM	ATM serine/threonine kinase
ATR	ATR serine/threonine kinase
ATRX	ATRX chromatin remodeler
BCL2	BCL2 apoptosis regulator
BCR	B cell receptor
BER	Base excision repair

BH3	BCL2 homology 3 domain
BID	BH3 interacting domain death agonist
bp	Base pair
BRAF	B-Raf proto-oncogene, serine/threonine kinase
BRCA	BRCA DNA repair-associated
BRD	Bromodomain containing
BRIP1	BRCA1 interacting protein C-terminal helicase 1
C	Cytosine
CAR	Chimeric antigen receptor
CASP	Caspase
CCL	Chemokine (C-C motif) ligand
CCN	Cyclin
CCR	C-C chemokine receptor
CD	Cluster of differentiation
CDH	Cadherin
CDK	Cyclin-dependent kinase
CDKI	Cyclin-dependent kinase inhibitor
CDR	Complementarity-determining region
CEBPA	CCAAT enhancer binding protein alpha
cGAS	Cyclic GMP-AMP synthase
CHEK	Checkpoint kinase
ChIP-seq	Chromatin immunoprecipitation sequencing
CIITA	Class II major histocompatibility complex transactivator
CIMP	CpG island methylator phenotype
CIN	Cervical intraepithelial neoplasia
CIS/TIS	Carcinoma in situ
CLEC12A	C-type lectin domain family 12 member A
CLL	Chronic lymphoid leukemia
CML	Chronic myeloid leukemia
CMMRD	Constitutional mismatch repair deficiency
CNS	Central nervous system
CNV	Copy number variation
COVID-19	Coronavirus disease 2019
CREBBP	CREB-binding protein, also called KAT3A
CRP	C-reactive protein
CSF	Cerebrospinal fluid
CSNK2A	Casein kinase 2 alpha
CT	Computed tomography
CTCF	CCCTC binding factor
ctDNA	Circulating tumor DNA
CTLA4	Cytotoxic T-lymphocyte-associated protein 4
CXCL	Chemokine (C-X-C motif) ligand
CYP	Cytochrome P450
DAMP	Damage-associated molecular pattern
DAXX	Death domain-associated protein

DBD	DNA-binding domain
DCIS	Ductal carcinoma in situ
DDR	DNA damage response
DFS	Disease-free survival
DLBCL	Diffuse large B cell lymphoma
DNMT	DNA methyltransferase
DOT1L	DOT1 like histone lysine methyltransferase
E2F	E2 promoter-binding factor
EBV	Epstein-Barr virus
ECM	Extracellular matrix
EFS	Event-free survival
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
EHMT	Euchromatic histone lysine methyltransferase
EMA	European Medicines Agency
EMT	Epithelial-mesenchymal transition
ENCODE	Encyclopedia of DNA elements
EP300	E1A binding protein p300, also called KAT3B
EPN	Ependymoma
ERBB2	Erb-B2 receptor tyrosine kinase 2, also called HER2
ERCC3	ERCC excision repair 3, TFIIH core complex helicase subunit
eRNA	Enhancer RNA
ES	Embryonic stem
ESCAT	ESMO Scale for Clinical Actionability of molecular Targets
ESR1	Estrogen receptor
ETMR	Embryonal tumor with multilayer rosettes
EZH	Enhancer of zeste homolog
FACS	Fluorescence-activated cell sorting
FAD	Flavin adenine dinucleotide
FBXO32	F-box protein 32
Fc	Fragment crystallizable
FDA	US Food & Drug Administration
FGF	Fibroblast growth factor
FGFR	Fibroblast growth factor receptor
FLT	Fms-related receptor tyrosine kinase
FOS	Fos proto-oncogene, AP1 transcription factor subunit
FOXO	Forkhead box O
G	Guanine
G-CSF	Granulocyte colony-stimulating factor
GART	Phosphoribosylglycinamide formyltransferase
GBM	Glioblastoma
GD2	Disialoganglioside 2
GDF	Growth differentiation factor
GDP	Guanosine diphosphate
GH	Growth hormone

GLS	Glutaminase
GM-CSF	Granulocyte–macrophage colony-stimulating factor
GTE _x	Genotype–Tissue Expression
GTP	Guanosine triphosphate
GVHD	Graft-versus-host disease
GWAS	Genome-wide association study
HAT	Histone acetyltransferase
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HDAC	Histone deacetylase
HGF	Hepatocyte growth factor
Hi-C	High-throughput chromosome capture
HIF1A	Hypoxia inducible factor 1 subunit alpha
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
HP1	Heterochromatin protein 1, official name CBX5
HPV	Human papilloma virus
HR	Homologous recombination
HSP	Heat shock protein
ICAM	Intercellular adhesion molecule
ICGC	International Cancer Genome Consortium
IDH	Isocitrate dehydrogenase
IDO	Indoleamine 2,3-dioxygenase
Ig	Immunoglobulin
IGF	Insulin-like growth factor
IGFBP3	Insulin-like growth factor binding protein 3
IGH	Immunoglobulin heavy locus
IL	Interleukin
IL3RA	Interleukin 3 receptor subunit alpha
IL6R	IL6 receptor
ILC	Innate lymphoid cell
indel	Short insertion or deletion
INF γ	Interferon γ
iPS	Induced pluripotent stem
ITAM	Immunoreceptor tyrosine-based activation motif
JAK	Janus kinase
JUN	Jun proto-oncogene, AP1 transcription factor subunit
kb	Kilo base pairs (1000 bp)
KDM	Lysine demethylase
KDR	Kinase insert domain receptor, also called VEGFR2
KIT	KIT proto-oncogene, receptor tyrosine kinase
KLF	Krüppel-like factor
KMT	Lysine methyltransferase
KRAS	Kirsten RAt Sarcoma viral oncogene homolog
LAD	Lamin-associated domain

LDHA	Lactate dehydrogenase A
LIN28A	Lin-28 homolog A
LINE	Long interspersed element
lncRNA	Long ncRNA
LOCK	Large organized chromatin K9-modification
LSD1	Lysine specific demethylase 1, also called KDM1A
LTR	Long terminal repeat
MAF	Minor allele frequency
MAPK	Mitogen-activated protein kinase
MAX	MYC-associated factor X
MB	Medulloblastoma
Mb	Mega base pairs (1,000,000 bp)
MBD	Methyl-DNA binding domain
MBP	Methyl-binding proteins
MDM2	MDM2 proto-oncogene, E3 ubiquitin protein ligase
MDSC	Myeloid-derived suppressor cell
MECP2	Methyl-CpG binding protein 2
MET	Mesenchymal-epithelial transition
MGMT	O-6-methylguanine-DNA methyltransferase
MHC	Major histocompatibility complex
miRNA	Micro RNA
MIS-C	Multisystem inflammatory syndrome in children
MLH	MutL homolog
MMP	Matrix metalloproteinase
MMR	Mismatch repair
MNT	MAX network transcriptional repressor
NPV	Negative predictive value
MRI	Magnetic resonance imaging
MS	Myeloid sarcoma
MSI	Microsatellite instability
MSS	Microsatellite stable
mTOR	Mechanistic target of rapamycin
mTORC1	mTOR complex 1
MYC	MYC proto-oncogene, BHLH transcription factor
NAD	Nicotinamide adenine dinucleotide
NADPH	Nicotinamide adenine dinucleotide phosphate
NANOG	Nanog homeobox
NBN	Nibrin
ncRNA	Non-coding RNA
NER	Nucleotide excision repair
NFκB	Nuclear factor κB
NGS	Next-generation sequencing
NHEJ	Non-homologous end-joining
NK	Natural killer
NLR	NOD-like receptor

NLS	Nuclear localization sequence
NO	Nitric oxide
NOTCH	Neurogenic locus notch homolog protein
NPM	Nucleophosmin
NSCLC	Non-small-cell lung cancer
NSD	Nuclear receptor binding SET domain protein
OCT	Octamer-binding transcription factor
OS	Overall survival
PALB2	Partner and localizer of BRCA2
PAMP	Pathogen-associated molecular pattern
PARP	Poly(ADP-ribose) polymerase
PCAWG	PanCancer Analysis of Whole Genomes
PD-L1	Programmed cell death 1 ligand 1, also called CD274
PD1	Programmed cell death 1, also called PDCD1
PDGF	Platelet-derived growth factor
PDGFRA	Platelet-derived growth factor receptor α
PET	Positron emission tomography
PGE	Prostaglandin E
PI3K	Phosphoinositide 3-kinase
PICS	PTEN loss-induced cellular senescence
PIK3CA	Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit α
PIN	Prostatic intraepithelial neoplasia
PIP3	Phosphatidylinositol-3,4,5-triphosphate
PML	PML nuclear body scaffold
Pol II	RNA polymerase II
PRKDC	Protein kinase, DNA-activated, catalytic subunit
PSA	Prostate-specific antigen
PTEN	Phosphatase and tensin homolog
PTGS2	Prostaglandin-endoperoxide synthase 2, also called COX2
PTHrP	Parathyroid hormone-related protein
qPCR	Quantitative PCR
RAD51	RecA-like amiloride-binding protein DNA repair protein 51
RAF1	Raf-1 proto-oncogene, serine/threonine kinase
RARA	Retinoic acid receptor α
RAS	Rat sarcoma
RB1	RB transcriptional corepressor 1
RECQL4	RecQ like helicase 4
RNA-seq	RNA sequencing
RSV	Rous sarcoma virus
RT-PCR	Real-time PCR
RTK	Receptor tyrosine kinase
SAGA	Spt-Ada-Gcn5 acetyltransferase
SAM	S-adenosyl-L-methionine
SARS-CoV 2	Severe acute respiratory syndrome coronavirus 2

scFv	Single-chain variable fragment
SERPINE	Serpin peptidase inhibitor, clade E
SETD	SET domain containing
SETDB	SET domain bifurcated histone lysine methyltransferase
SINE	Short interspersed element
SIRP α	Signal regulatory protein alpha
SIRT	Sirtuin
SLAMF	SLAM family
SLC	Solute carrier family
SMAD	SMAD family member
SMARC	SWI/SNF-related matrix-associated actin-dependent regulators of chromatin
SNAI	Snail family transcriptional repressor
snoRNA	Small nucleolar RNA
SNP	Single nucleotide polymorphism
SNV	Single nucleotide variant
SOX2	SRY-box 2
SP1	Specificity protein 1
SRC	SRC proto-oncogene, non-receptor tyrosine kinase
STAB	Stabilin
STAT	Signal transducer and activator of transcription
STING	Stimulator of interferon genes
SUV39H1	Suppressor of variegation 3-9 homolog 1, also called KMT1A
SV40	Simian virus 40
SWI/SNF	Switching/sucrose non-fermenting
T	Thymine
TAD	Topologically associating domain
TAM	Tumor-associated macrophage
TCGA	The Cancer Genome Atlas
TCR	T cell receptor
TERT	Telomerase reverse transcriptase
TET	Ten-eleven translocation
TGF β	Transforming growth factor β
T _H	T helper
THBS	Thrombospondin
TLR	Toll-like receptor
TNF	Tumor necrosis factor
TNFRSF	TNF receptor superfamily member
TP53	Tumor protein p53
T _{reg}	T regulatory
TRIM	Tripartite motif containing
TSS	Transcription start site
TWIST	Twist family BHLH transcription factor
U	Uracil
UGDH	UDP-glucose 6-dehydrogenase

UICC	Union for International Cancer Control
VCAM	Vascular cell adhesion molecule
VEGF	Vascular endothelial growth factor
VHL	Von Hippel-Lindau tumor suppressor
WAT	White adipose tissue
WHO	World Health Organization
WNT	Wingless-type MMTV integration site family member
ZAP70	Zeta-chain-associated protein kinase 70
ZEB	Zinc finger E-box binding homeobox