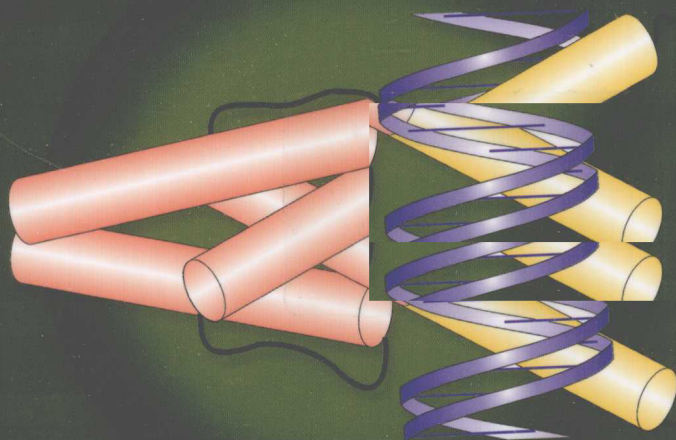


郑杰·编著

CELLULAR AND
MOLECULAR
BIOLOGY OF CANCER

肿瘤的 细胞和分子生物学

系统介绍肿瘤的一般生物学特点，同时兼顾介绍近年出现的一些新的概念和研究方向。主要内容包括肿瘤的病因学、发病学、肿瘤防治及相关知识等。



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内容提要

本书比较系统地介绍了肿瘤的一般生物学特点,同时兼顾介绍近年出现的一些新的概念和研究方向。主要内容包括肿瘤的病因学、发病学、肿瘤的防治及相关知识等。编写思路是先介绍正常细胞活动的机制,然后介绍肿瘤细胞的结构性改变以及由此产生的功能改变。由于采用了大量图表,使内容显得生动活泼,一些难懂的内容变得通俗易懂和容易记忆,读者通过本书的阅读能对肿瘤生物学的基本概念和研究现状有一个基本了解。

本书适合作为综合性大学生命科学专业、医学院校本科生和研究生的教材或参考书。由于该书内容涉及生命科学的不同领域,比较好地反映了当今国际上该领域的前沿水平。因此,对从事生物学、医学研究的人员和临床医务工作者来讲,也是一本有价值的参考书。

前言

生物学是研究生命现象的一门科学。生物体的基本构成单位是细胞,生物学的每一个问题,最终必须由细胞来解答。随着 20 世纪中后期分子生物学的兴起,人们又在分子水平层面对生命活动的各种现象予以解释。细胞和分子生物学是当今自然科学非常活跃的研究领域,知识更新速度很快,新概念、新方法和新内容层出不穷。肿瘤作为生命过程中出现的一种现象,与其他生命过程有着密不可分的联系。用研究生命活动过程的理念和方法来研究肿瘤的病因、发病机制及潜在的临床应用,就演化出肿瘤生物学这门学科。

肿瘤是严重威胁人类生命和健康的疾病。统计数据显示,在过去的 30 年间,我国恶性肿瘤死亡率呈明显上升趋势。到 2000 年发病和死亡人数分别为 180 万~200 万和 140 万~150 万,恶性肿瘤死亡人数占总死亡人数的 20%,仅次于心血管疾病。由于我国人口年龄结构更趋老化,以及已暴露于不良生活方式和环境的人口基数过大等原因,将导致在未来 20~30 年间,我国恶性肿瘤死亡率继续呈上升趋势。为了降低肿瘤的发病率和死亡率,各国的研究人员和临床医生都在为之进行不懈的努力。肿瘤学的研究也方兴未艾,无论是基础肿瘤学还是临床肿瘤学都在迅速进展变化。可以毫不夸张地说,目前临床肿瘤学的进步,出现的各种新的治疗方法,主要还是得益于人们对肿瘤生物学认识的提高。例如由于许多肿瘤蛋白和信号途径的被揭示,使得肿瘤分子靶向治疗成为可能。

本书比较系统地介绍肿瘤的一般生物学特点,同时兼顾介绍近年出现的一些新的概念和研究方向。主要内容包括肿瘤的病因学、发病学、肿瘤防治及相关知识等。编写思路是先介绍正常细胞活动的机制,然后介绍肿瘤细胞的结构性改变以及由此产生的功能改变。

全书内容新颖,语言精练,采用了大量图表使内容显得比较活泼,让一些难懂的内容变得通俗易懂和容易记忆,读者通过本书的阅读能对肿瘤生物学的基本概念和研究现状

有一基本了解。全书共十九章,章节的目次是按逻辑顺序安排,一环扣一环,尽量做到前面章节的内容对理解后面的内容有帮助。除了第七章(沈传陆,郑杰)和第十二章(洪泽辉,郑杰)外,其他章节由郑杰撰写。全书内容交叉引证,这样既减少了内容重复,又增加了信息的使用效率。最后增加了英文索引,以便于读者查阅有关内容。本书适于作为综合性大学生命科学专业、医学院校本科生和研究生的教材或参考书。由于该书内容涉及生命科学的不同领域,较好地反映了当今国际上该领域的前沿水平,因此,对从事生物学、医学研究的人员和临床医务工作者来讲,也是一本有价值的参考书。

由于全书内容广泛,错误在所难免,敬请读者予以指正。

本书在编写过程中得到东南大学优秀研究生教材的资助,在此谨表感谢。最后我要衷心感谢博士研究生高鹏出色的绘图工作及其他多方面的协助。

郑 杰

2010年8月于东南大学医学院

缩略词

0~9		APC	adenomatous polyposis coli, antigen presenting cell
4EBP1	4E binding protein 1	APC	anaphase promoting complex/cyclosome
4-HPR	N-4-hydroxyphenyl retinoid	APL	acute promyelocytic leukaemia
5-AZAC	5-aza-2'-deoxycytidine	AR	androgen receptor
5-LOX	5-lipoxygenase	ARE	androgen response element
7TM receptor	7- α helices transmembrane segment receptor	ARF	alternative reading frame
8-oxoG	8-oxoguanine	ASI	allele-specific inhibition
15-PGDH	15-hydroxyprostaglandin dehydrogenase	ASO	antisense oligonucleotide
aa	amino acid	AT	ataxia telangiectasia syndrome
AAF	N-2-acetyl-2-aminofluorene	Atg	autophagy-related genes
ABC	ATP-binding cassette	ATL	adult T-cell leukemia
Abl	Abelson leukemia virus oncoprotein	ATM	ataxia-telangiectasia mutated gene
ADAM	a disintegrin and metalloproteinase	ATR	ATM-related kinase
ADCC	antibody-dependent cellular cytotoxicity	ATRA	all-trans-retinoic acid
AFB1	aflatoxin B1	BAFF	B cell-activating factor
AFP	alpha-fetoprotein	BAX	Bcl2-associated X
AIs	aromatase inhibitors	BCC	basal cell carcinoma
AIF	apoptosis inducing factor	Bcl-2	B cell lymphoma-2
AIG	anchorage-independent growth	BCR	breakpoint cluster region
AIPC	androgen independent prostate cancer	BER	base excision repair
ALDH	aldehyde dehydrogenase	BFB	breakage-fusion-bridge
ALL	acute lymphocytic/lymphoblastic leukaemia	BH	Bcl-2 homologous domain
ALT	alternative lengthening of telomeres	bHLH	basic helix-loop-helix transcription factors
AMF	autocrine motility factor	BIR	baculovirus IAP repeats
AML	acute myeloid leukaemia	BITC	benzyl isothiocyanate
AMPK	5'AMP-activated protein kinase	BLM	Bloom's helicase
Ang	angiopoietin	BMP	bone morphogenetic protein
AOM	azoxymethane	bp	base pair
AP	apurinic/aprimidinic	BrdU	bromodeoxyuridine
AP-1	activator protein 1	BS	Bloom syndrome
Apaf-1	apoptotic protease-activating factor 1		
APBs	ALT-associated PML bodies	CAFs	carcinoma-associated fibroblasts

CAK	CDK-activating kinase	DNA-PK	DNA-dependent protein kinase
CAMs	cell adhesion molecules	DNA-PKcs	the catalytic subunit of the DNA-dependent protein kinase
CARD	caspase activation and recruitment domain	DNMT	DNA methylases
CASP8	caspase 8	DNMTi	DNA methylase inhibitor
CCK	cholecystokinin	DP	dimerization protein transcription factors
CD	cluster of differentiation	DPC4	deleted in pancreatic cancer 4/Smad4
Cdc gene	cell-division-cycle gene	DR	death receptor
CDK	cyclin dependent kinase	DSBs	DNA double-strand breaks
CDKI	CDK inhibitor	DSBR	DNA double-strand breaks repair
CE-3,4-Q	catechol estrogen-3,4-quinones	dsRNA	double-stranded RNA
CEA	carcinoembryonic antigen	EBV	Epstein-Barr virus
Chk	checkpoint kinase	EBNA	EB nuclear antigen
CIP/KIP	cell cycle inhibitory protein/kinase inhibitory protein	ECM	extracellular matrix
CIS	chromosome instability syndrome; cytokine inducible SH2-containing protein	EGCG	epigallocatechin-3-gallate
CLL	chronic lymphocytic leukemia	EGF	epidermal growth factor
CMA	chaperone-mediated autophagy	EGFR	EGF receptor
CML	chronic myeloid leukemia	eIF4F	eukaryotic initiation factor 4F
CNL	chronic neutrophilic leukemia	ELR	glutamic acid-leucine-arginine motif
CoA	Co-activators	EMT	epithelial-mesenchymal transition
CoR	Co-repressors	eNOS	endothelial nitric oxide synthase
COX-2	cyclooxygenase 2	EPC	endothelial progenitor cells
CR	complete response; conserved region; calorie restriction	EPO	erythropoietin
CRC	colorectal cancer	EPOR	EPO receptor
CRE	cAMP response element	EphA2	epithelial cell kinase
CREB	CRE binding protein	ER	estrogen receptor; endoplasmic reticulum
CRPC	castration resistant prostate cancer	ERE	estrogen response element
CSC	cancer stem cells	ERK	extracellular signal-regulated kinase
CSF1	colony stimulating factor 1	ES	embryonic stem cells
CTAR	C terminal activation region	ESA	epithelial specific antigen
CTLs	cytotoxic T lymphocytes	ET	endocrine therapy
CUP	metastatic cancer of unknown primary	ETS	environmental tobacco smoke
CYP	cytochrome P450-dependent enzymes	Ezh2	enhancer of zeste homolog 2
DAG	diacylglycerol	FA	Fanconi anemia
DAPK1	death-associated protein kinase 1	FADD	fas-associated death domain
DBD	DNA binding domain	FACs	focal adhesion complex
DC	dendritic cell	FAK	focal adhesion kinase
DCC	deleted in colorectal carcinoma gene	FAP	familial adenomatous polyposis
DeR	decoy receptor	FasL	Fas-ligand
DD	death domain	FDA	U. S. Food and Drug Administration
DED	death effector domain	FGF	fibroblast growth factor
DES	diethylstilbestrol	FGFR	FGF receptor
DFMO	difluoromethylornithine	FHIT	fragile histidine triad
DFSP	dermatofibrosarcoma protuberans	FISH	fluorescence in situ hybridization
DHT	5 α -dihydrosterone	FPR	formylpeptide receptor
DISC	death-inducing signal complex	FSH	follicle-stimulating hormone
Dll4	Delta-like ligand 4	FTI	farnesyltransferase inhibitor
DM	double minute chromosome	G6PD	glucose-6-phosphate dehydrogenase

GADD45	growth arrest and DNA damage-inducible protein 45	HP1	heterochromatin protein 1
GAP	GTPase activating protein	HPV	human papilloma virus
G-CSF	granulocyte-colony stimulating factor	HR	homologous recombination
GCV	Ganciclovir	HSCs	hematopoietic stem cells
GDI _s	guanine nucleotide dissociation inhibitors	HSP	heat shock protein
GDNF	glial cell-derived neurotrophic factor	HSR	homogeneously staining region
GEF	guanine nucleotide exchange factor	HSV-TK	herpes simplex virus-thymidine kinase
GF	growth factor	hTEP1	human telomerase protein 1
GFR	growth factor receptor	hTERT	human telomerase reverse transcriptase
GIST	gastrointestinal stromal tumor	HTLV-1	human T-cell leukemia virus-1
GM-CSF	granulocyte macrophage-colony stimulating factor	hTR	human telomere RNA
GOF	gain of function	IAP	inhibitor of apoptosis protein
GPCR	G protein coupled receptor	ICAM	intercellular adhesion molecule
GPx	glutathione peroxidases	ICR	imprinting control region
Grb2	growth factor receptor-binding protein 2	Id	inhibitor of differentiation
GR	gastrin receptor	IFN	interferon
GRK	GPCR kinase	IGF-1	insulin-like growth factor-1
GRP	gastrin-releasing peptide	IGF-2	insulin-like growth factor-2
GRPR	gastrin releasing peptide receptor	IGF-2/M6PR	IGF-2/Mannose-6-phosphate receptor
GSH	glutathione	IGFBPs	IGF-binding proteins
GSK3 β	glycogen synthase kinase 3 β	IGFR	IGF receptor
GSTs	glutathione-S-transferases	I κ B	inhibitor of NF- κ B
HAT	histone acetyl transferase	IKK	I κ B kinase
HBV	hepatitis B virus	IL	interleukin
HBZ	HTLV-1 basic leucine zipper factor	ILK	integrin linked kinase
HCC	hepatocellular carcinoma	ING	inhibitor of growth
hCG	human chorionic gonadotropin	INI1	integrase interactor 1
HCV	hepatitis C virus	INK4	inhibitor of kinase 4
HDAC	histone deacetylase	INK4a/ARF	inhibitor of cyclin-dependent kinase 4a/ alternative reading frame
HDAC _s	histone deacetylase inhibitors	IP3	inositol (1, 4, 5) triphosphate
HDM2	human homolog of MDM2	ITCs	isothiocyanates
HECT	homologous to E6-AP C terminus	JAK	Janus kinase
Hes	hairy/enhancer of split	JH	jak homology
HGF/SF	hepatocyte growth factor/scatter factor	JHDM	jumonji C (JmJc) - domain-containing histone demethylase
Hh	Hedgehog	JM	juxtamembrane
HHV-8	human herpesviruses - 8/KSHV Kaposi sarcoma herpesvirus	K	lysine
HIF-1	hypoxia inducible factor-1	Kb	kilobase pair
HIV	human immunodeficiency virus	KGF	keratinocyte growth factor
HKMT _s	histone lysine methyltransferases	KIR	killer inhibitory receptor
HL	Hodgkin lymphoma	KS	Kaposi sarcoma
HLA	human leukocyte antigen	KSHV	kaposi sarcoma herpesvirus/HHV-8
HLH	helix-loop-helix	LAK	lymphokine-activated killer cell
HMGA2	high mobility group A2	LANA	latency-associated nuclear antigen
HMT _s	histone methyltransferases	LATS	large tumor suppressor homolog
HNPCC	hereditary nonpolyposis colorectal carcinoma	LEF	lymphoid enhancing factor
HNSCC	head and neck squamous cell carcinoma		
HP	Helicobacter pylori		

LMP	latent membrane protein	NEC	Notch extracellular domain
LMVD	lymphatic microvessel density	NEMO	NF- κ B essential modifier/IKK β
LNA	locked nucleic acid	NER	nucleotide-excision repair
LOH	loss of heterozygosity	NES	nuclear export signal
LOI	loss of imprinting	NF- κ B	nuclear factor κ B
LPS	lipopolysaccharide	NGF	nerve growth factor
LSD1	lysine-specific demethylase 1	NGFR	NGF receptor
LSCs	leukemia stem cells	NHEJ	non-homologous end joining
LTA	lipoteichoic acid	NHL	non-Hodgkin lymphoma
LTB4	leukotriene B4	NICD	Notch intra cellular domain
LTR	long terminal repeat	NIK	NF- κ B-inducing kinase
Mab	monoclonal antibody	NK	natural killer cell
MAGE	melanoma antigen-encoding gene	NKT	natural killer T cells
MAP	mitogen-activated protein	NLS	nuclear localization sequence
MAPK	MAP kinase	nm23	non-metastatic 23
MBDs	methyl CpG binding domain proteins	NO	nitric oxide
MCA	3'-methylcholanthrene	NPC	nasopharyngeal carcinoma
MCM	mini chromosome maintenance	NQO1	NAD(P)H: quinone oxidoreductase 1
MCP-1	monocyte chemotactic protein-1	NRP1/NRP2	neuropilin
M-CSF	macrophage-colony stimulating factor	NSAIDs	nonsteroidal anti-inflammatory drugs
MDM2	mouse double minute chromosome 2	NSCLC	non small cell lung carcinoma
MDR	multidrug resistance	NTM	Notch transmembrane fragment
MDS	myelodysplastic syndromes	NuRD	nucleosome remodeling histone deacetylase
MDSCs	myeloid derived suppressor cells	NURF	nucleosome-remodeling factor
MeCP	methyl CpG binding protein	ODC	ornithine decarboxylase
MEK	MAPK/Erk kinase	OGG1	8-oxoguanine DNA glycosylase 1
MEN	multiple endocrine neoplasia	OIS	oncogene induced senescence
mER	membrane estrogen receptor	OPN	osteopontin
MET	mesenchymal-epithelial transition	OR	odds ratio
MGMT	O6-methylguanine DNA methyltransferase	ORC	origin recognition complex
MH	mad homology region	ORF	open reading frame
MHC	major histocompatibility complex	PA	plasminogen activator
miRNA	microRNAs	PAF	platelet activating factor
MIN	microsatellite instability	PAHs	polycyclic aromatic hydrocarbons
MLL1	mixed linkage leukemia 1	PAI	plasminogen activator inhibitor
MM	multiple myeloma	Pak	p21-activated protein kinases, Paks
MMP	matrix metalloproteinase	PAMPs	pathogen-associated molecular patterns
MMR	mismatch repair	PARs	protease-activated receptors
MOMP	mitochondrial outer membrane permeabilization	PARP1	poly ADP ribose polymerase 1
MPTP	mitochondrial permeability transition pore	Pax2	paired box 2
MRN	Mre11, Rad50, Nbs1	PCD	programmed cell death
MTA	metastasis associated gene	PcG	polycomb group
mTOR	mammalian target of rapamycin	PCNA	proliferating cell nuclear antigen
MVD	microvessel density	PCR	polymerase chain reaction
MyD88	myeloid differentiation factor 88	PDGF	platelet-derived growth factor
NAC	N-acetyl-L-cysteine	PDGFR	PDGF receptor
NAT	N-acetyltransferase	PDK	phosphoinositide-dependent kinase
N-CoA	nuclear receptor coactivator	PEDF	pigment epithelium derived factor
N-CoR	nuclear receptor corepressor	PEST	praline glutamate serine threonine rich

	sequence	RLF	replication licensing factors
PF4	platelet factor 4	RNAi	RNA interference
PGE2	prostaglandin E2	RNS	reactive nitrogen species
PGF	placental growth factor	ROCK	Rho associated coiled coil forming protein kinase
PGN	peptidoglycans	ROS	reactive oxygen species
Ph	Philadelphia chromosome	R point	restriction point
PH	pleckstrin homology domains	RR	relative risk
PI3K	phosphatidylinositol 3-kinase	RTK	receptor tyrosine kinase
PIP2	phosphatidylinositol (4,5) diphosphate	RT-PCR	reverse transcriptase polymerase chain reaction
PIP3	phosphatidylinositol (3,4,5) triphosphate		
PKA	protein kinase A		
PKB	protein kinase B/AKT		
PKC	protein kinase C	S6K	S6 kinase
PLC	phospholipase C	SA- β -Gal	senescence-associated β -Galactosidase
PMA	phorbol-12-myristate-13-acetate = TPA	SAC	spindle assembly checkpoint
PML	promyelocytic leukaemia	SAHFs	senescence associated heterochromatin foci
POT 1	protection of telomeres 1	SARMs	selective androgen receptor modulators
PPAR γ	peroxisome proliferator-activated receptor γ	SCE	sister chromatid exchange
PR	partial response; progesterone receptor	SCF	stem cell factor, Skpl - Cullin - F - box ligases
PRAK	p38-regulated/activated protein kinase		
pRb	retinoblastoma protein	SCLC	small cell lung carcinoma
PRC	polycomb repressor complexes	SDF-1	stromal cell-derived factor 1
PS	phosphatidylserine	SERDs	selective estrogen receptor down regulators
PSA	prostate-specific antigen	SERMs	selective estrogen receptor modulators
PTB	phosphotyrosine binding	SF	scatter factor
Ptc	patched	SFRP	secreted frizzled-related proteins
PTEN	gene for phosphatase and tensin homolog deleted on chromosome ten	SH1	Src homology domain 1, tyrosine kinase
		SH2	Src homology domain 2, phosphotyrosine binding
PTGS	post-transcription gene silence		
PTK	protein tyrosine kinase	SH3	Src homology domain 3, proline rich binding
PTP	phosphotyrosine phosphatase, permeability transition pore	SH-PTPs	the SH2 - containing phosphotyrosine phosphatases
PUMA	p53-upregulated modulator of apoptosis		
		sir	silent information regulator
RA	retinoic acid	siRNAs	short interfering RNAs
RAM	RBP J κ associated molecule sequence	siRNP	small interfering ribonucleoprotein complex
RANK	receptor activator of NF- κ B	SKp2	S-phase kinase-associated protein 2
Rap1	repressor activator protein 1	Smad	mothers against decapentaplegic
RAR	retinoic acid receptor	Smo	Smoothened
RAR β 2	retinoic acid receptor β 2	SMRT	silencing mediator for retinoid thyroid-hormone receptor
RASSF1A	Ras association domain family member 1		
Rb	retinoblastoma protein	SNCG/BSCG1	human γ -synuclein/breast cancer specific gene 1
RdRp	RNA-dependent RNA polymerase		
RER	replication error	SNP	single nucleotide polymorphism
RFLP	restriction fragment length polymorphism	SOCS	suppressors of cytokine signaling
RGD	Arg-Gly-Asp	SOD	superoxide dismutase
Rheb	Ras homolog enriched in brain	Sos	son of sevenless
RhoGDI2	Rho GDP dissociation inhibitor 2	SRC1	steroid receptor coactivator 1
RING	really interesting new gene	SSBs repair	DNA single-strand breaks repair
RIP	receptor interacting protein	STK11	serine-threonine kinase 11/LKB1
RISC	RNA-induced silencing complex	STAT	signal transducer and activator of

	transcription	TR	thioredoxin reductase
SULT	sulfotransferases	TRADD	TNFR-associated death domain
SUMO	small ubiquitin-related modifier	TRAF	TNF receptor associated factor
SV40	Simian virus 40	TRAIL	TNF-related apoptosis inducing ligand
		TRF	telomerase regulatory factor; telomeric-repeat binding factor; telomeric restriction fragment
Tc	cytotoxic T cell	TSA	tumor specific antigen, trichostatin
Th	helper T cell	TSC1	tuberous sclerosis complex 1
Tregs	regulatory T cell	TSC2	tuberous sclerosis complex 2
TAA	tumor associated antigen	TSG	tumor suppressor gene
TAFs	tumor-associated fibroblasts	TSP-1	thrombospondin-1
TAM	tamoxifen	TUNEL	terminal-deoxynucleotidyl transferase mediated nick end labeling
TAMs	tumor-associated macrophages,		
tBid	truncated Bid	UGTs	UDP-glucuronosyltransferases
TBPs	telomere binding proteins	uPA	urokinase-type plasminogen activator
TCF	T cell factor	UPD	uniparental disomy
TCR	T-cell receptor	UPP	ubiquitin-proteasome pathway
TERT	telomerase reverse transcriptase	UV	ultraviolet
TGF- α	transforming growth factor- α		
TGF- β	transforming growth factor- β	VCAM	vascular cell adhesion molecule
TGF- β R	TGF- β receptor	VEGF	vascular endothelial growth factor = VPF
TF	transcription factor	VEGFR	VEGF receptor
THBS1	thrombospondin 1	VHL	von Hippel-Landau
Tiam-1 gene	T-lymphom invasion and metastasis gene	VM	vasculogenic mimicry
TIN2	TRF1-interacting nuclear protein 2	VPF	vascular permeability factor = VEGF
TIL	tumor infiltrating lymphocyte	VE-cadherin	vascular endothelial cadherin
TIMP	tissue inhibitor of metalloproteinase		
TK	tyrosine kinase	WAF1/CIP	wild-type p53-activated fragment 1/CDK-interacting protein
TKIs	tyrosine kinase inhibitors		
TLRs	Toll like receptors	XP	xeroderma pigmentosum
TLS	translesion DNA synthesis		
TM	transmembrane	AZT	Zidovudine
TNF	tumor necrosis factor		
TNFR	TNF receptor		
tPA	tissue-type plasminogen activator		
TPA	12-O-tetradecanorl phorbol-13 acetate = PMA		

目录

第一章 环境致癌因素

第一节 化学致癌物是人类肿瘤的主要致癌因素	1
一、化学致癌物的种类	1
二、化学致癌的机制	3
三、致癌物的检测方法	4
第二节 病毒致癌是人类肿瘤的次要致癌因素	5
一、病毒致癌概况	5
二、人类肿瘤病毒	6
第三节 辐射致癌与人类某些肿瘤的发生有关	14
一、辐射致癌概况	14
二、辐射致癌物的种类及致癌机制	14

第二章 细胞癌基因对肿瘤发生的影响

第一节 癌基因的基本概念	17
第二节 细胞原癌基因的激活方式	19
一、点突变	20
二、易位激活	20

三、原癌基因扩增	23
四、癌基因甲基化程度的降低	24
.....	
第三节 癌基因的产物和功能	24
一、生长因子类	25
二、生长因子受体类	26
三、Ras 致瘤蛋白	26
四、胞质激酶	27
五、转录因子	28
六、抗凋亡蛋白 Bcl - 2	32

第三章 生长因子及受体与肿瘤

第一节 生长因子与肿瘤	33
一、上皮、内皮和间叶细胞的生长因子	34
二、造血细胞生长因子(细胞因子)	37
三、肿瘤细胞能自泌生长因子,刺激肿瘤生长	38
.....	
第二节 生长因子受体与肿瘤	39
一、受体酪氨酸激酶(RTK)与肿瘤	40
二、受体丝氨酸/苏氨酸激酶与肿瘤	43
三、细胞因子受体与肿瘤	45
四、G 蛋白偶联受体与肿瘤	46

第四章 细胞信号及肿瘤细胞信号特点

第一节 生长因子信号传导的主要途径	51
一、G 蛋白偶联受体(GPCR)的信号传导	51
二、受体酪氨酸激酶(RTK)是生长因子主要的信号传导途径	54
.....	
第二节 细胞因子受体信号途径	60
一、Jak 和 STAT	60
二、Jak - STAT 信号途径	61
三、许多肿瘤存在 Jak - STAT 信号途径的异常激活	63
.....	
第三节 发育信号途径与肿瘤	64

一、Wnt - β - catenin 信号途径与肿瘤	64
二、Hedgehog (Hh)信号途径与肿瘤	67
三、Notch 信号途径与肿瘤	69
四、TGF β - Smads 信号途径与肿瘤	71
第四节 整合素信号途径与肿瘤	74
一、整合素信号途径及功能	74
二、整合素与受体酪氨酸激酶之间的合作	75
三、整合素信号途径异常与肿瘤	76

第五章 细胞周期调控与肿瘤

第一节 细胞周期概述	79
第二节 细胞周期的自身调节	80
一、CDK 是细胞周期运行的引擎	80
二、Cyclin 与 CDK 结合是细胞周期的正调控机制	81
三、CDK 抑制剂是细胞周期的负调控机制	82
四、泛素-蛋白酶体对细胞周期的调节	84
第三节 细胞周期运行的调控	87
一、细胞外信号对细胞周期的启动机制	87
二、细胞周期检查点调控	88
三、肿瘤相关基因对细胞周期的调节	90
第四节 细胞周期紊乱与肿瘤	91
一、细胞周期监控机制破坏	91
二、细胞周期正调控机制上调	92
三、丧失对生长抑制信号的敏感性	93
第五节 CDK 作为肿瘤治疗的靶点	95

第六章 肿瘤抑制基因对肿瘤的影响

第一节 肿瘤抑制基因的概念	97
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第二节 肿瘤抑制基因失活的方式	99
第三节 肿瘤抑制基因的种类和功能	100
一、Rb 是细胞周期负调节剂	101
二、p53 是基因组卫士	104
三、PTEN 是 PI3K - Akt 信号途径的负调控因子	109
四、APC 是使 β -catenin 不稳定的因素	111
五、NF1 是 Ras 的负调节剂	113
第四节 癌基因和肿瘤抑制基因产物的相互作用	114
第五节 看门基因和看护基因	114

第七章 细胞程序性死亡与肿瘤

第一节 凋亡的概念	117
第二节 凋亡的基本特征	118
第三节 触发凋亡的信号途径	119
一、细胞膜死亡受体介导的凋亡途径	119
二、线粒体介导的凋亡途径	121
第四节 凋亡的基因调控	122
一、caspase 的级联反应是凋亡基本过程	122
二、Bcl-2 家族是调节凋亡的线粒体相关蛋白	123
三、IAP 是细胞内天然存在的 caspase 抑制物	124
四、p53 引导凋亡程序	124
五、E2F1 既能诱导细胞增生又能诱导凋亡	125
第五节 肿瘤细胞的凋亡过程受到不同程度的阻断	125
第六节 自噬	127
一、自噬的形态特点及分类	127
二、自噬相关基因 (<i>Atg</i>) 及诱导途径	129
三、自噬与凋亡既有区别又有联系	129
四、自噬对肿瘤生长是一把双刃剑	130

第七节 坏死在某些情况下也是受调控的·····	131
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第八章 端粒长度调节与肿瘤

第一节 端粒与端粒相关蛋白·····	133
一、端粒的一般结构和功能·····	133
二、端粒相关蛋白是调节端粒长度的重要成分·····	134
三、人端粒结合蛋白与肿瘤·····	136
第二节 端粒酶·····	136
一、末端复制问题·····	136
二、端粒酶是细胞维持端粒稳定的主要机制·····	137
三、细胞衰老是人体防癌机制之一·····	138
四、细胞永生是细胞恶性转化过程的第一步·····	142
第三节 端粒长度控制异常与肿瘤·····	143
一、端粒酶激活在恶性肿瘤是非常常见的·····	144
二、端粒的替代性延长(ALT)是维持端粒长度的另一种选择·····	145
第四节 端粒酶作为肿瘤治疗靶点·····	146
一、基因治疗·····	147
二、以 hTERT 为基础的免疫治疗·····	147
三、小分子寡核苷酸治疗·····	148
四、以鸟嘌呤四链体为靶点的治疗·····	148

第九章 肿瘤细胞的起源和进化

第一节 肿瘤细胞可能起源于体内干细胞突变·····	150
一、干细胞和肿瘤干细胞的概念·····	150
二、肿瘤干细胞与干细胞相似和不同之处·····	151
三、肿瘤细胞可能起源于体内干细胞或祖细胞突变·····	153
四、微环境影响干细胞的走向·····	155
五、许多肿瘤组织已发现含有肿瘤干细胞·····	156
六、肿瘤干细胞的临床含意·····	159
第二节 肿瘤是单克隆性生长,但过程是多克隆的·····	160