



3rd EDITION

癌症的 分子基础 The Molecular Basis of Cancer

(原书第三版)

(美) John Mendelsohn
Joe W. Gray

Peter M. Howley
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Mark A. Israel
等 原著

许兴智 佟伟民 李静 杨跃 丛羽生 等 译



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内 容 简 介

癌症作为重大非传染性疾病，其防治在国家中长期科技规划中得到了重要支持，本书全面系统地阐述了癌症的分子基础和最新进展，为癌症的研究提供理论支持。全书共分5篇59章，包括癌变和癌症遗传学、癌症生物学、分子病理和诊断、癌症的分子病理过程、癌症治疗的分子基础等内容。

本书内容丰富，兼顾基础研究与临床，可供从事癌症研究的科研人员、临床肿瘤科与放射治疗科的医护人员参考使用。也可作为肿瘤专业研究生的教材使用。

The Molecular Basis of Cancer, 3rd Edition

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丛羽生博士,教授,博士生导师。中国老年学学会衰老与抗衰老科学委员会理事,中国生物物理学会膜与细胞生物物理专业委员会委员,北京细胞学学会理事。1994 年获法国巴黎南大学和居里研究所博士学位。先后在加拿大 McMaster 大学、美国西南医学中心、美国路易斯维尔大学医学院做博士后和助理教授。2005 年 8 月受聘北京师范大学京师特聘教授。2006~2009 年受教育部聘任担任细胞增殖及调控生物学教育部重点实验室主任,细胞生物学研究所所长。长期从事细胞衰老及无限增殖化分子机制研究,对端粒酶活性调节机制及其新功能进行了系统研究,发表 SCI 论文 20 余篇。主持国家自然基金 3 项,作为骨干参与 863、973 课题等多个国家及省部级项目。

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杨晓博士,军事医学科学院生物与工程研究所发育和疾病遗传学研究室主任,研究员、博士生导师、中国遗传学会常务理事。一直从事发育和分子遗传学研究,利用转基因和基因剔除小鼠研究基因在发育和相关疾病发生中的功能和机理。

王荣福博士,教授,博士生导师,北京大学医学部核医学系主任,北大医院核医学科主任,中华医学会和医学分会常委、肿瘤和医学专业主任委员,中国肿瘤影像专业委员会常委兼秘书长,中国和医学同位素分会常务理事。1982 年毕业于福建医科大学医疗系后留校从事核医学医疗、教学和科研工作。1990 年国家公派法国留学,并于 1992 年、1995 年分别毕业于法国巴黎五大和图卢兹三大获医学(MD)和药学(PhD)双博士学位。主要从事分子核医学包括放射性药物研发、单克隆抗体放射免疫显像和治疗、受体研究、基因显像和治疗等,临床核医学包括甲亢、肿瘤核素诊治、符合探测正电子成像应用研究等。

何琪杨博士,研究员,博士生导师。2006 年至今在中国医学科学院北京协和医学院医药生物技术研究所工作,研究方向为分子药理学。中国老年学学会衰老与抗衰老科学委员会主任委员,中国抗癌协会抗癌药物专业委员会委员,北京市抗癌药物专业委员会委员。硕士毕业于北京师范大学,博士毕业于中国协和医科大学,曾在美国从事博士后工作近 5 年。主持和参加过 NIH、973、国家重大新药专项和国家自然科学基金等多个项目的研究,共发表研究论文 47 篇,其中 SCI 收录论文 26 篇,研究结果发表在 *Science*、*Genes Dev*、*PNAS*、*EMBO J*、*J Biol Chem* 等重要杂志上,申请发明专利 3 项。

曹胜利博士,教授,硕士生导师。1997 年毕业于北京大学药学院,获药物化学专业理学博士学位,1997~1999 年在清华大学化学系从事博士后研究。1999 年到首都师范大学化学系任教,现任化学系副主任。主要从事抗肿瘤药物的设计、合成与活性评价研究。主持国家自然科学基金、北京市自然科学基金等科研项目。在国内外学术刊物上发表论文 60 余篇,获得授权的发明专利 5 项。

张玮玮博士,副教授,硕士生导师。2002 年本科毕业于北京大学医学部,2008 年博士毕业于新加坡国立大学,2008 年 12 月至今就职于首都师范大学生命科学学院。

杨志伟博士,副教授,硕士生导师。2003 年毕业于中国科学院微生物研究所,获遗传学博士学位。长期从事本科生“生物化学”和研究生“微生物分子生物学”的教学工作,2004 年获北京市青年教师教学基本功比赛二等奖,2008 年获北京市教育教学成果奖(高等教育)二等奖。曾主持国家自然科学基金及北京教委科研项目各 1 项,目前主要研究胁迫条件下微生物应答响应及适应突变。

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序

分子生物学已经使我们对癌症发病机制的认知发生了改变,而对恶性肿瘤的研究则改变了我们对控制正常细胞生长与增殖的分子和遗传过程的认知。

至1995年,知识的扩增呈现大爆炸之势,让我们觉得有必要为研究人员、学生以及各领域的临床护理人员编写一本教科书——《癌症的分子基础》。如今本书已出版至第三版,目标仍然是解释癌症而不仅仅是描述癌症。在过去的十年里,我们对于癌症的发现和观察手段极速地发展,形成了现在理解癌症的基础,而在此之前,直到20世纪90年代,我们对癌症的了解还仅仅停留在纯粹的描述阶段。

我们选了五位编者,他们都是在癌症分子研究领域极富专长与名望的教育家,由他们共同设计了章节的顺序,引导读者了解癌变的基础遗传和分子机制、癌细胞生长和转移的分子和生物学特性、个性化风险评估和早期检测的新技术、常见癌症分子异常的描述,以及治疗新手段的分子基础。

编写本书的目的不是详细描述癌症的临床表现或特定治疗的诊断和管理,而是为临床医生和看护癌症病人的专业人员更好地理解和治疗疾病提供科学支撑。虽然本书的章节次序安排是从发病机制到治疗设计,但每一个章节都独立成章。因此对生物医学领域的实验室工作人员和临床研究人员,以及需要理解控制恶性肿瘤细胞的获得功能和失去功能的分子机制的高年级学生和实习生来说,这本教科书也有同等的,甚至更大的益处。

癌症源于遗传学与表观遗传学上的改变,这些改变或加强,或消减了介导正常细胞活动的信号通路的活性。一旦修复遗传改变的能力受损就可能促使细胞累积遗传变异,导致恶化。因此,癌细胞周围的分子对一个变异细胞变成肿瘤有重要影响。

我们从癌症研究中得到了一个惊人的发现:尽管细胞谱系极其多样化,但它们调节生长与分化采用的是共同的分子通路。在多种肿瘤中反复观察到的是,控制这些分子通路的关键是基因累积突变或基因表达改变。显然肿瘤会这种遗传异常是因为这让肿瘤在特定微环境中最有利地逃避正常的调节机制。

癌症不仅仅是个体转化细胞的紊乱,而是这些紊乱的细胞增殖成肿块,同时吸纳血液供应,侵入周边组织并转移。

这些复杂过程的分子基础对了解此类恶性疾病的自然历史和治疗设计是非常重要的。

在本书的第三版中,我们增加了全新的章节来介绍实验室新技术,使研究人员能鉴定癌症的遗传和分子异常,发现能预测患癌风险和治疗结果及治疗选择的生物标记物。

本书最后一章探讨了临床研究程序和还处在探索阶段的新治疗制剂,我们希望这些制剂能针对特定遗传、分子和抗原靶点。

现今最激动人心的消息是临床医生和实验室科学家之间已开始积极合作,他们的共同目标是将遗传学和分子生物学的新知识应用于疾病诊断、治疗和预防。可以预计,在未来10年中我们将有机会从数以百计的、针对恶性细胞特定异常的新生物和化学制剂中,选择部分用于临床治疗的研究。本书介绍的知识将为那些对生物技术革命的新产物感兴趣的人们,对这些产物的理解和评估,以及评价新治疗手段提供理论基础。

本书所有的编者都为自己能与其他优秀的研究人员一起参编本书感到高兴。他们对于能将自己的专业知识按教科书的形式来表述感到兴奋。而这要求他们花费更多的时间和精力,在此我们对他们的奉献表示感激。我们希望至少正向我们设定的目标前进。本书的出版同时也得到了爱思唯尔出版社专业人员的帮助和鼓励,对一如既往帮助我们的耐心的办公室秘书们一并致以我们的谢意。

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癌症已经成为威胁我们生命的最大元凶之一。美国癌症协会(www.cancer.org)在2010年6月公布的《Cancer Facts & Figures》中预计美国在2010年约有150万例的癌症新病例、57万例的癌症死亡病例,其中30%的病例与吸烟直接相关,35%的病例与营养、运动和肥胖或者说我们个体的生活习性直接相关。其实,仅有不足15%的致癌因素是遗传性的(或者说来源于我们的父母),超过85%的致癌因素是可以预防的,其中戒烟、运动及健康均衡的饮食是最容易做到,也是最有效的防癌手段。因此,临床医生掌握癌症生物学知识,民众熟悉癌症基本知识都是十分必要的。

自从1971年美国总统尼克松向癌症宣战以来,在全世界科学家的共同努力下,我们在分子水平上对致癌机制有了相当充分的阐述,并将这些致癌的分子机理应用于癌症的分子诊断、抗癌新药的开发和治疗。《癌症的分子基础》一书对各种癌症(生物学、诊断和治疗)的分子基础做了全面系统的介绍,而不是简单描述癌症的临床表现或特定治疗的诊断和管理。因此,本书对临床医生、生物医学领域的实验室工作人员和临床研究人员、高年级生物医学及生物学学生来说是本不可多得的教科书;对广大民众熟悉癌症基础知识来说具有同等的,甚至更大的益处。

《癌症的分子基础》英文版由五位著名的生物医学家、临床医生及教育家负责召集上百位的相关学者编写的,全面覆盖癌症生物学、诊断及治疗的分子基础。同样的,本书第三版的中文版由资深的癌症基础研究专家和临床专家精心翻译,尽管如此,不当或错误之处在所难免,请不吝指正。

许兴智

2011年2月于德国耶拿

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