肿瘤导论

---

throw your SIGHT into the MODULARS

-- A Guide to the oncology

Zheng Yanhua
2022-05-20

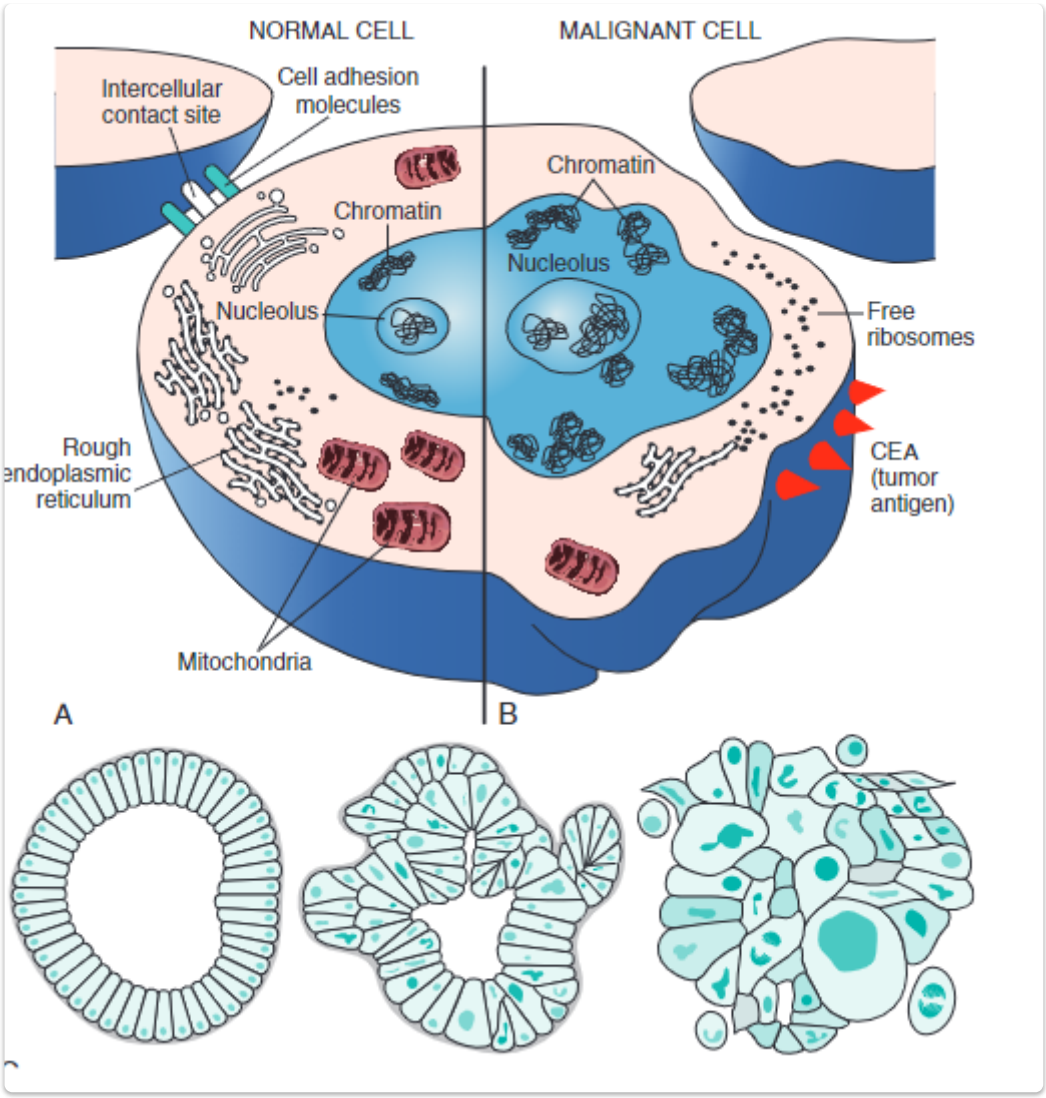
#定义与流行病学

- 黑白之间：瘤、肉瘤、癌，良性与恶性，分级与分期
- 非我族类？单克隆与多克隆

#neo-plasia unregulated，irresversible，monoclonal proliferation of cells

- Benign tumors
  - epithelial or connective tissue
  - do not invade or spread
- Malignant tumors (cancer)
  - #Carcinomas pithelial tissue—squamous, glandular, or transitional
  - #Sarcomas connective tissue (mesoderm origin)
  - invade and spread
- Tumor-like conditions 类癌
  - 错构瘤 & 迷离瘤

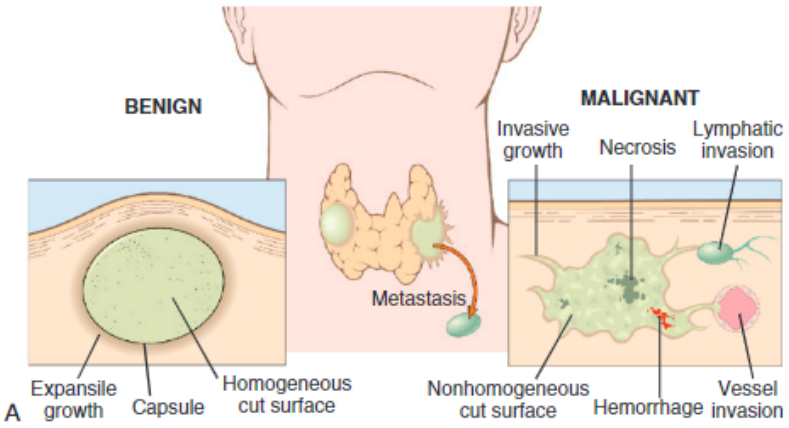
#肿瘤的组成成分及其分化



- 肿瘤实质 肿瘤细胞的分化指其停留的形态
- 基质/微环境

单克隆?

- Nonneoplastic tumors derive from multiple cells (polyclonal)
- Benign and most malignant tumors derive from a single precursor cell.
  G6PDa,G6PDb,G6PDc
  Ig kappa/lambda



B

Comparison of benign and malignant tumors		
Feature	**Benign**	**Malignant**
Growth	Slow Expansive	Fast Invasive
Metastases	No	Yes
Gross appearance		
External surface	Smooth	Irregular
Capsule	Yes	No
Necrosis	No	Yes
Hemorrhage	No	Yes
Microscopic appearance		
Architecture	Resembles that of tissues of origin	Does not resemble that of tissues of origin
Cells	Well differentiated	Poorly differentiated
Nuclei	Normal size and shape	Pleomorphic
Mitoses	Few	Many irregular

9-8: Comparison of a benign and a malignant tumor using thyroid neoplasms as an example. *(From my friend Ivan Damjanov, MD, PhD: Pathology for the Health Professions, 4th ed, Saunders Elsevier, 2012, pp 69, 71, Fig. 4-1, Table 4-1, respectively.)*

B. Grading and staging of cancer

1. Degree of differentiation (e.g., low, intermediate, or high grade)
2. TNM system for staging cancer
   T：肿瘤大小及原位侵犯的深度
   N：淋巴结转移
   M：远端器官侵犯

#临床表现

- Cachexia (wasting disease)
  (a) Proteolysis-inducing factor (PIF) ubiquitin-proteasome pathway myosin
  (b) Lipolysis-mobilizing factor (LMF) hormone-sensitive lipase (HSL) body fat
  TNF loss appetite
- Anemia
- Hemostasis abnormalities
- Fever in malignancy
- Paraneoplastic syndromes

#病理组织

- 大体最后的荣光：病理组织与金标准
- 肿瘤标志物
  diagnose cancer, estimate tumor burden, detect recurrences, and predict the tumor response to treatment
- 分子与免疫的曙光：免疫组化及免疫治疗

起源与基本原则

- 干细胞暴露在致癌物、病毒、射线中，导致DNA损伤（甲基化、双键形成...）
- 源于干细胞DNA突变，克服DNA修复机制

#突变大爆炸：中心法则的全链失衡
基因突变的多重打击的不可逆

- 原癌基因（生长因子、cyclin/CDKs）、
- 抑癌基因(RB 细胞周期检查点；P53 DNA损伤修复)
- 自噬相关机制失调（bcl2）
- 其他肿瘤生长必要基因（端粒酶、血管生成FGF VEGF）

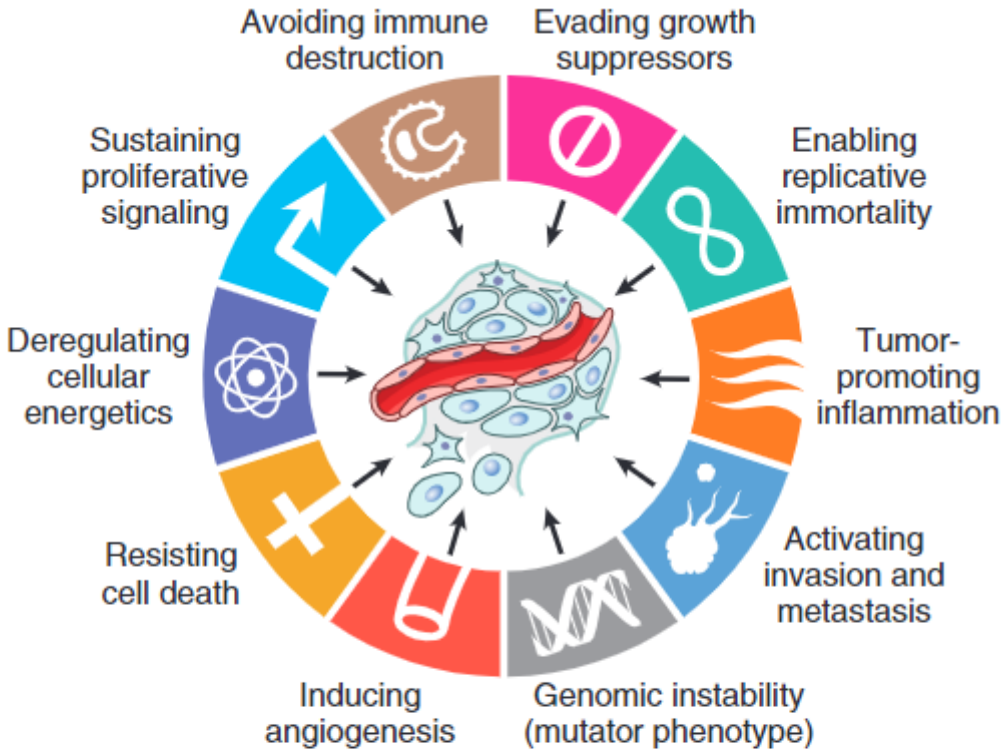
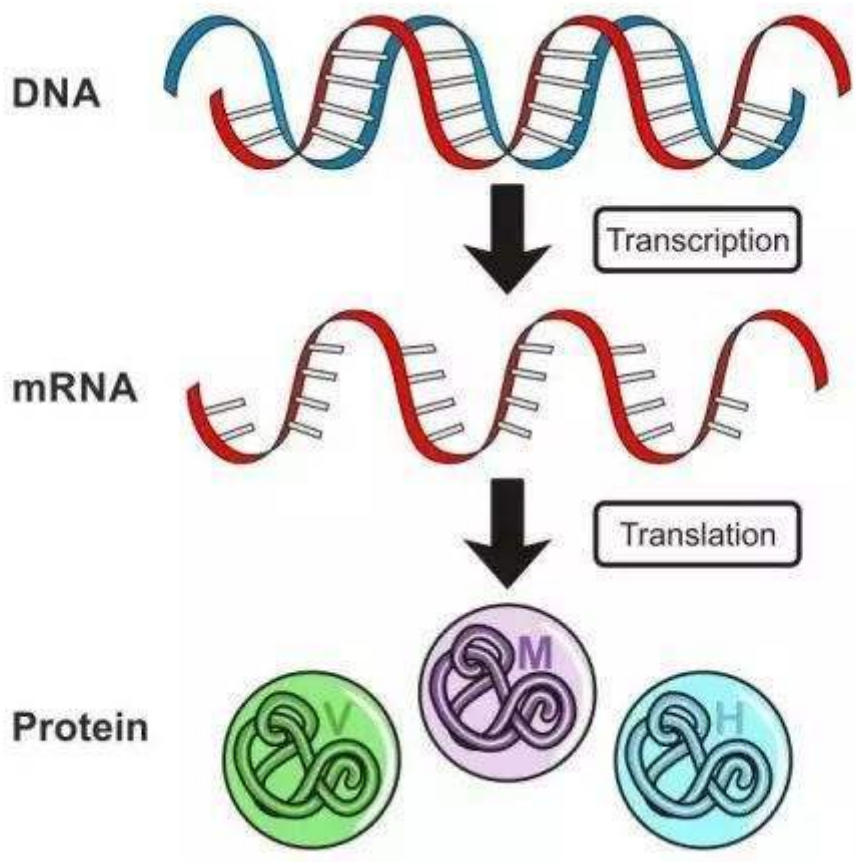


Fig. 6.17 Eight cancer hallmarks and two enabling factors (genomic instability and tumor-promoting inflammation). Most cancer cells acquire these properties during their development, typically due to mutations in critical genes. *(From Hanahan D, Weinberg RA: Hallmarks of cancer: the next generation. Cell 144:646, 2011.)*



代谢紊乱及糖氧剥夺

- high levels of glucose uptake and increased conversion of glucose to lactose (fermentation) via the glycolytic pathway.

#自然选择：达尔文的终极魔力

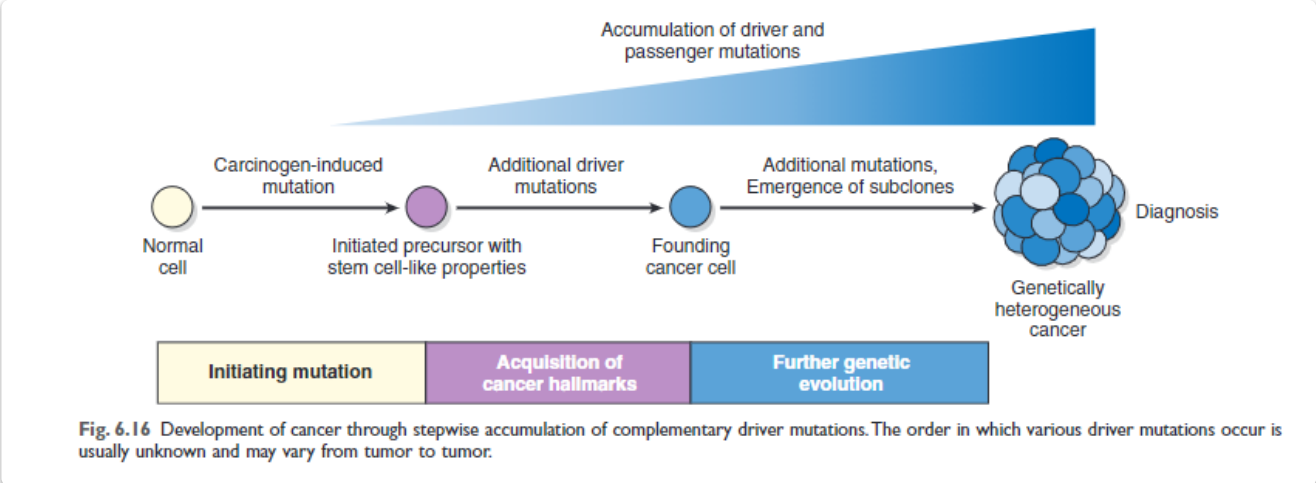


Fig. 6.16 Development of cancer through stepwise accumulation of complementary driver mutations. The order in which various driver mutations occur is usually unknown and may vary from tumor to tumor.

A.免疫系统：体液、细胞免疫、NK细胞、巨噬细胞
B.营养与血供
#自噬:细胞的自我救赎

#生化危机：肿瘤细胞的胜利大逃亡

- 肿瘤侵犯与转移
  - 解黏附：低细胞黏附素表达（eg. E-cadherin）
  - 与基底膜作用：层粘连蛋白连接，降解胶原纤维
  - 连接在外基质的纤维连接蛋白上，本地侵犯
  - 进入淋巴/血管：远端播散

#生化危机：肿瘤细胞的胜利大逃亡

- 肿瘤血管生成
  - Early in their development, most human tumors do not induce angiogenesis. Starved of nutrients, until an angiogenic switch
  - increased production of angiogenic factors and/ or loss of angiogenic inhibitors.

#生化危机：肿瘤细胞的胜利大逃亡

- 耐药与免疫抑制
  - 低MHC-1表达
  - 免疫检测点 PD-L1

- response and resistance to immune checkpoint inhibitors are unpredictable
- new biomarkers are needed to better tailor therapies for individual patients.
- new diagnostic tests to gauge both the host immune response and the likely means of immune evasion in individual cancers.

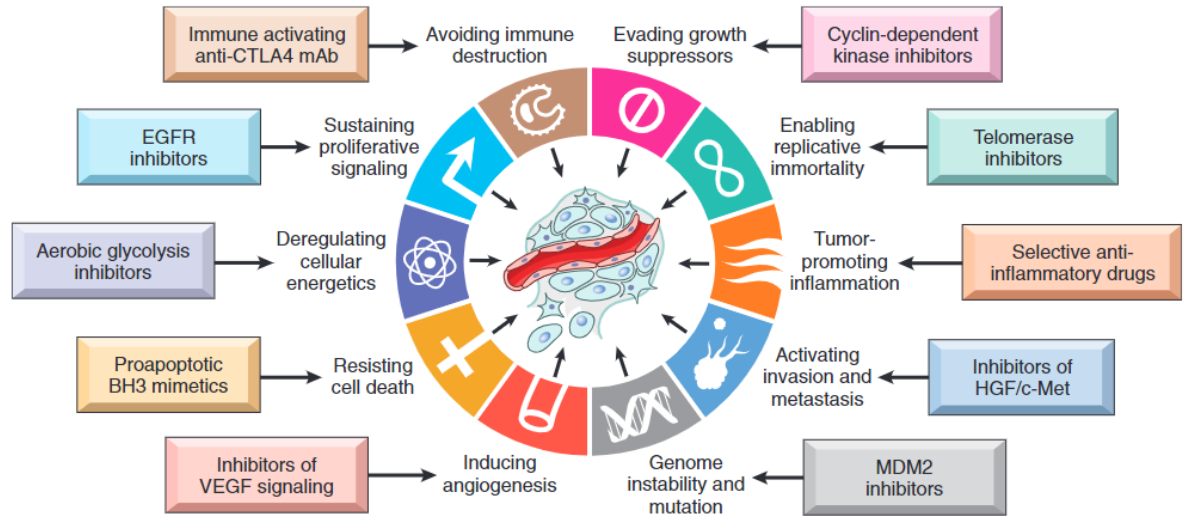


Fig. 6.31 Therapeutic targeting of the hallmarks of cancer. *(From Hanahan D, Weiberg RA: The hallmarks of cancer: the next generation. Cell 144:646, 2011.)*