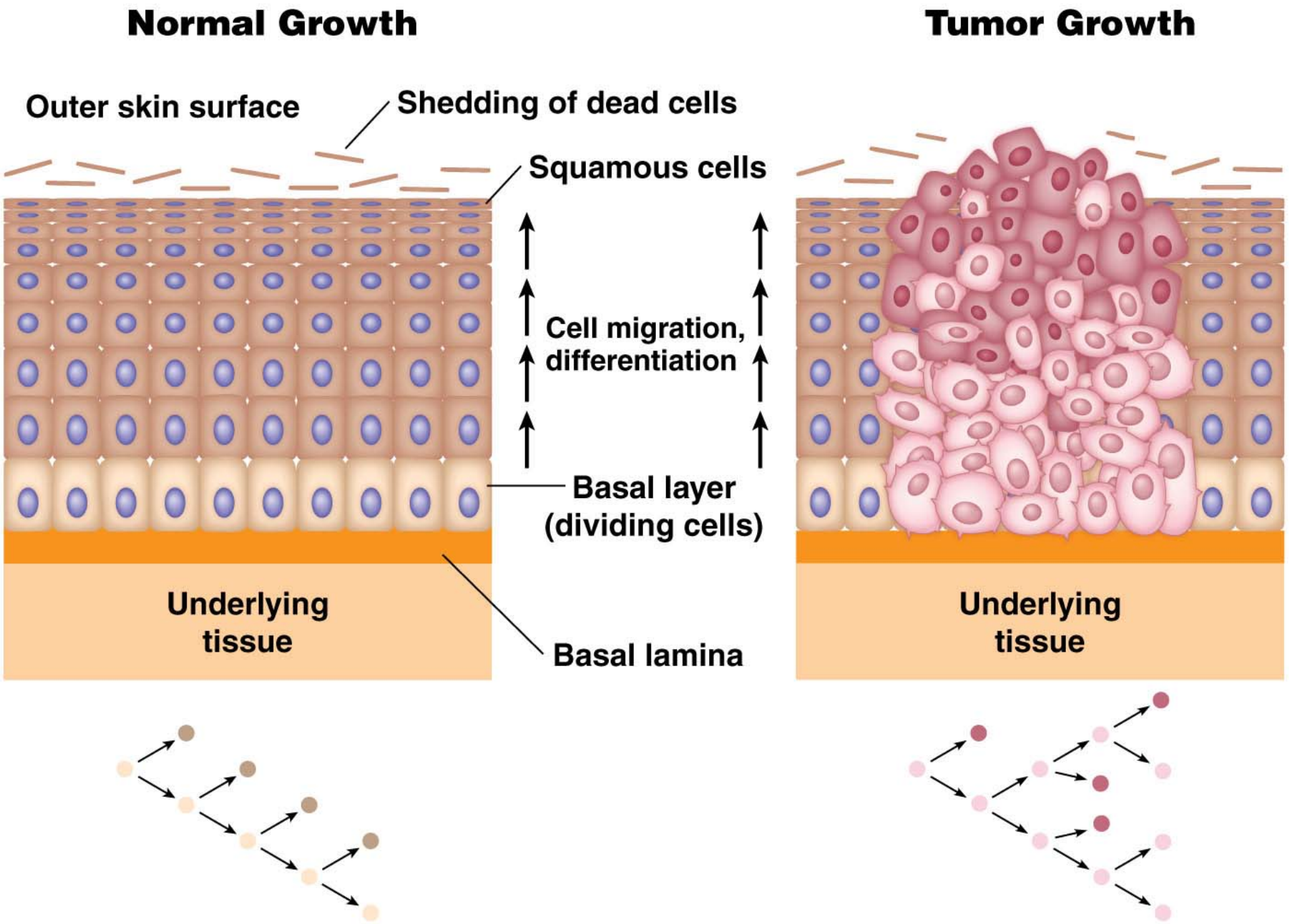
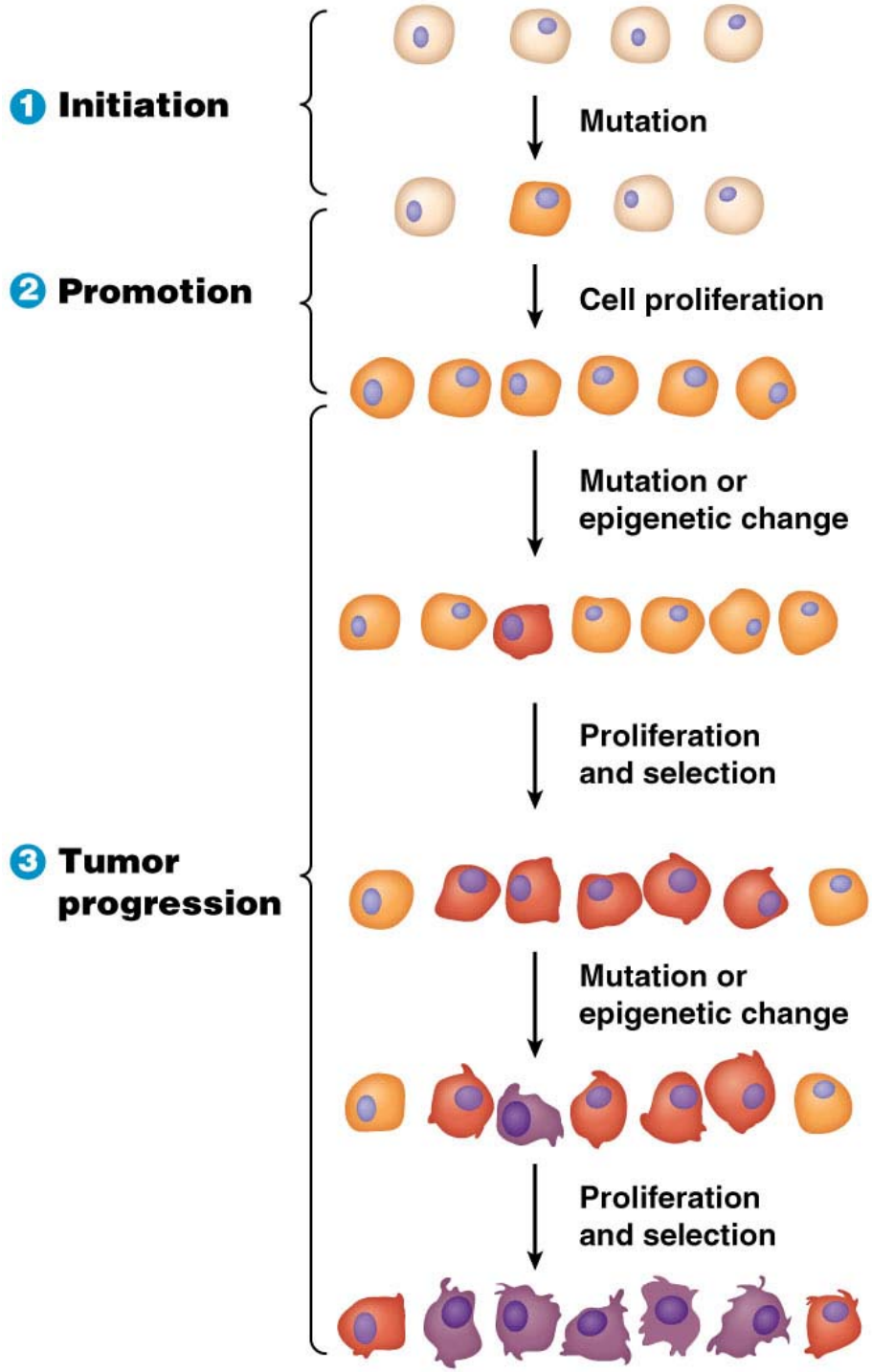
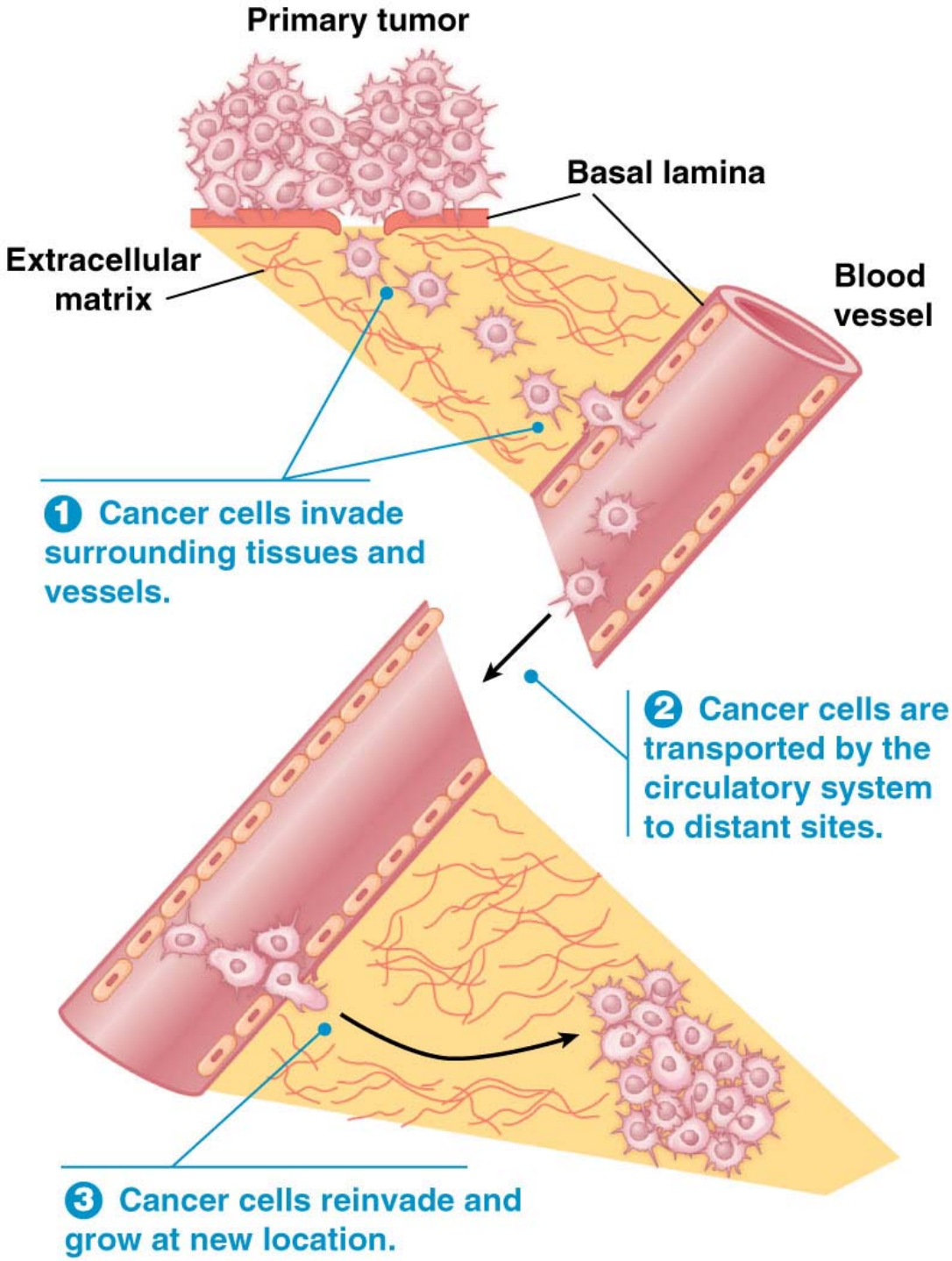
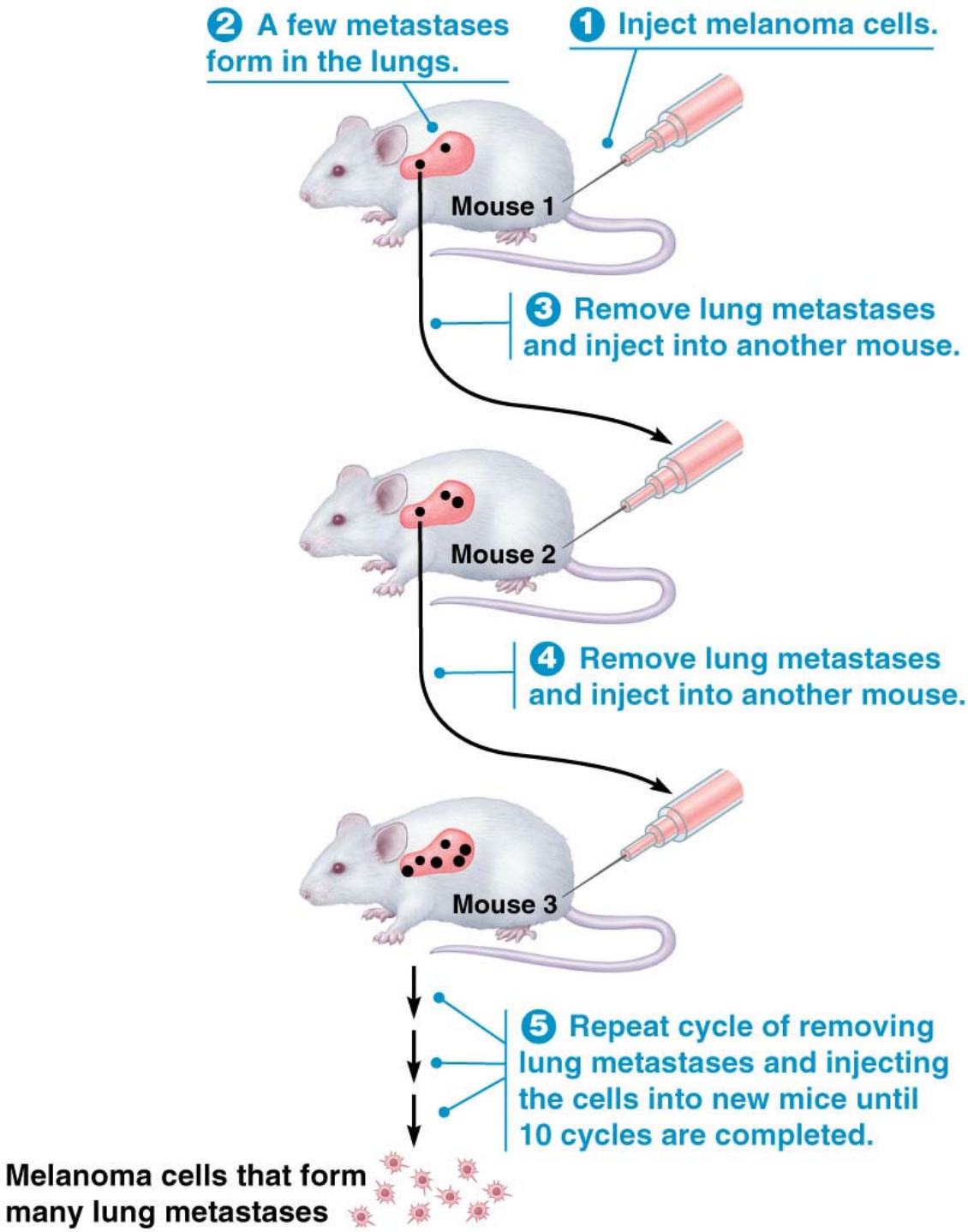
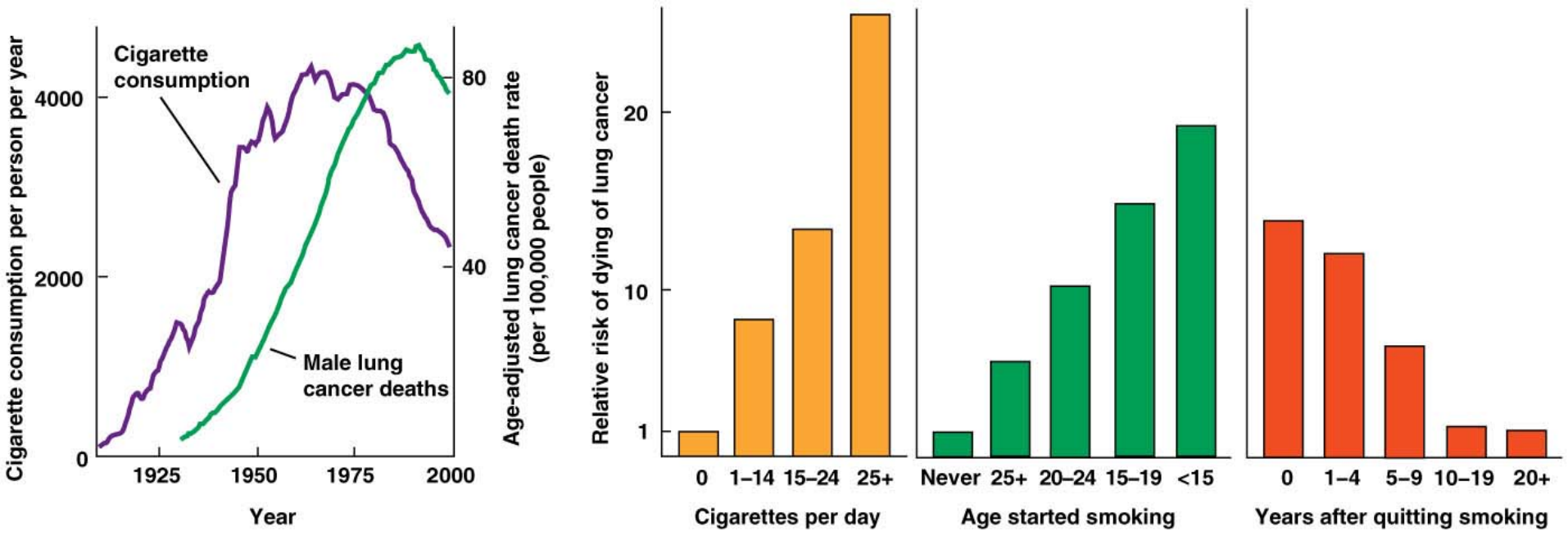
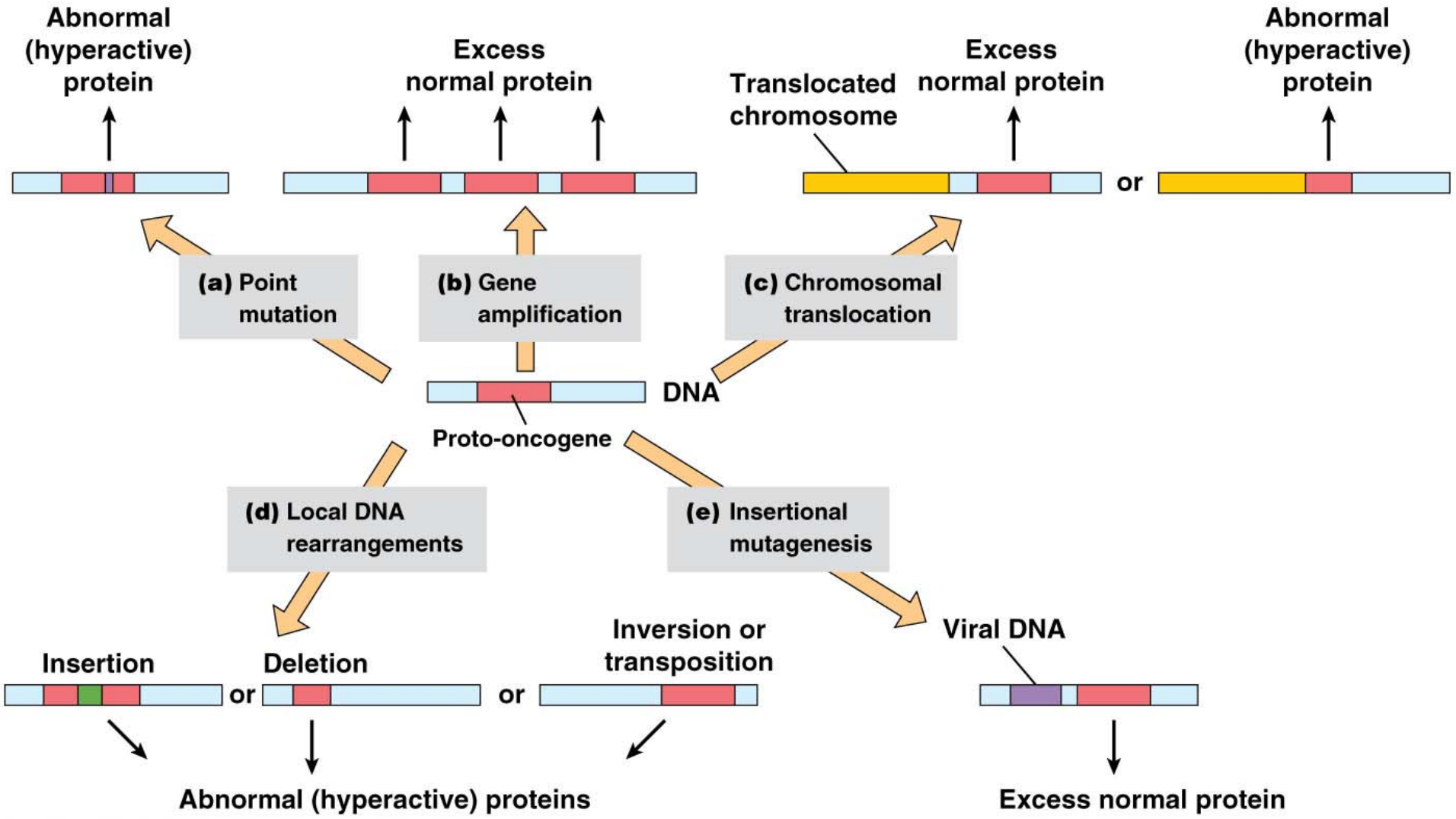


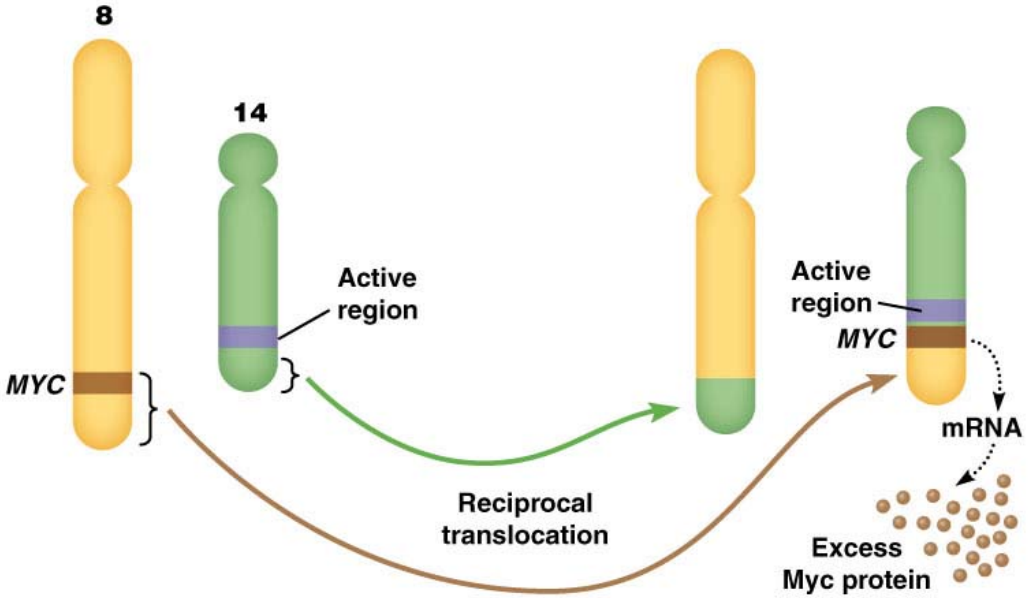




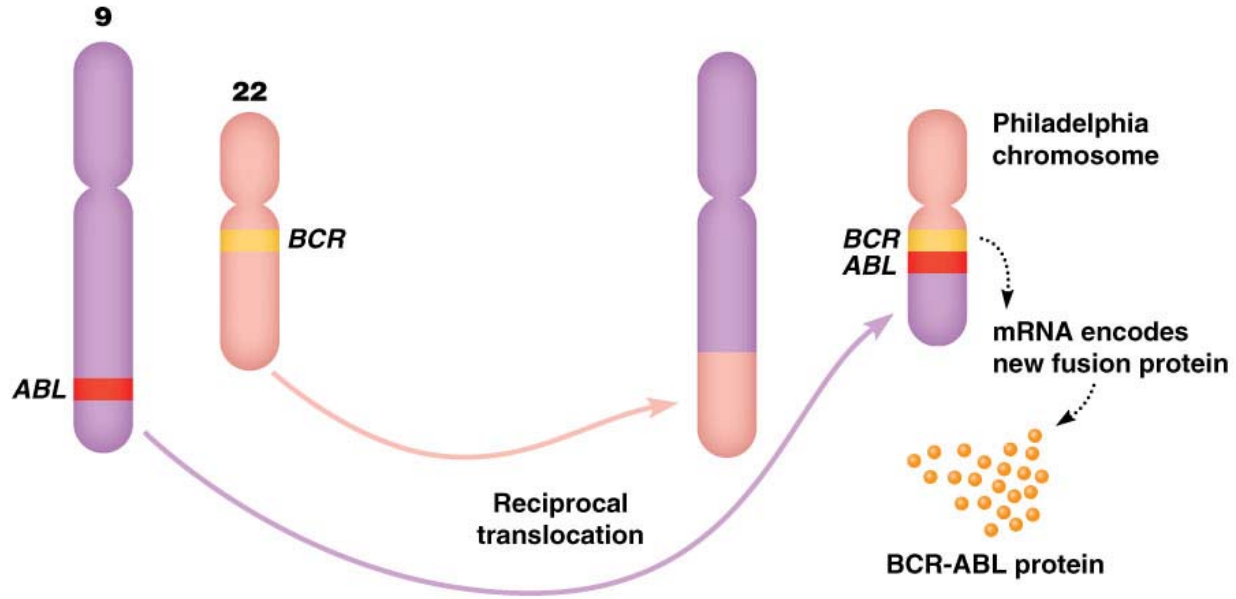








(a) Overexpression of Myc in Burkitt lymphoma



(b) The Philadelphia chromosome and the Bcr-Abl kinase

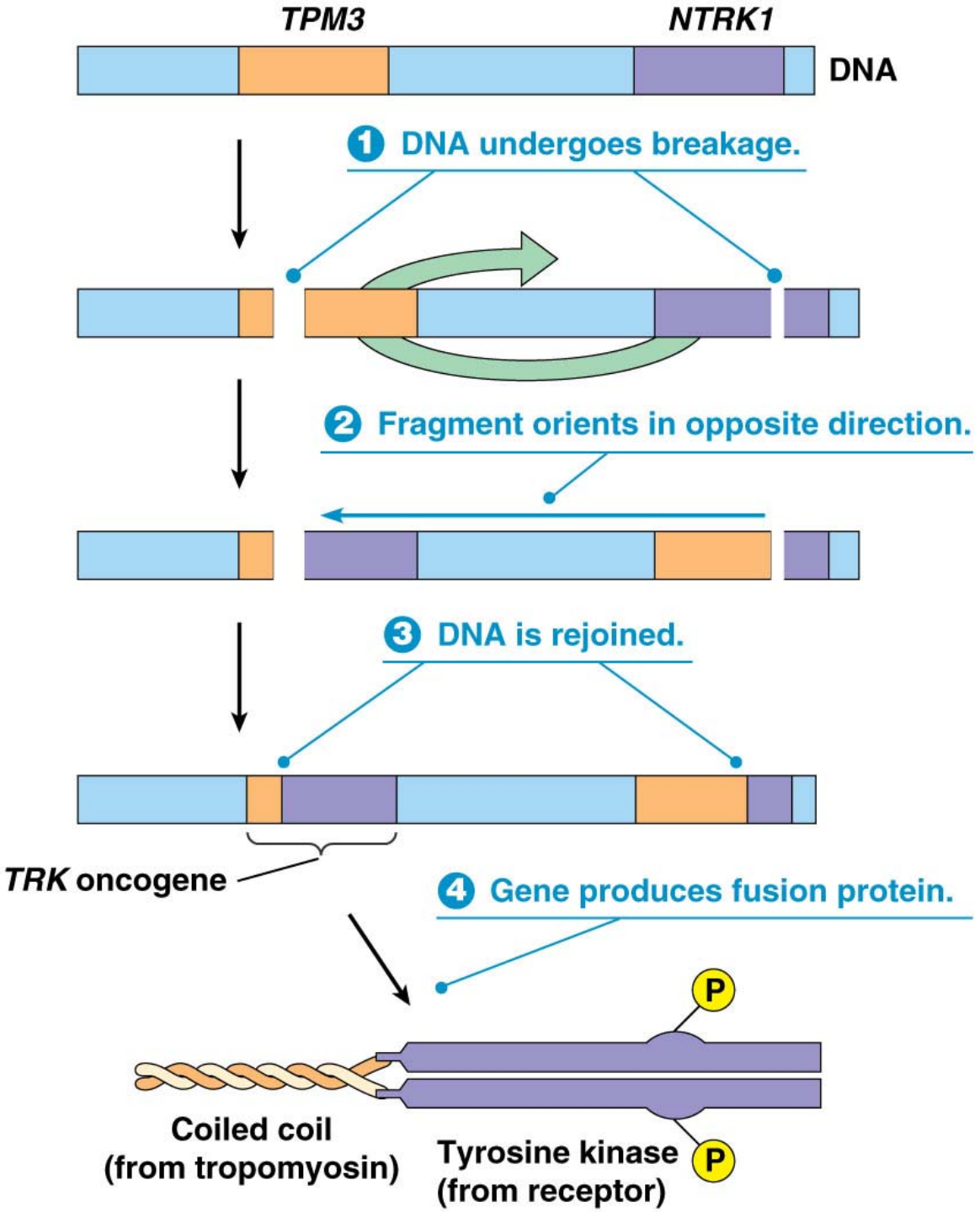


Table 26-1 A Few Examples of Oncogenes Grouped by Protein Function

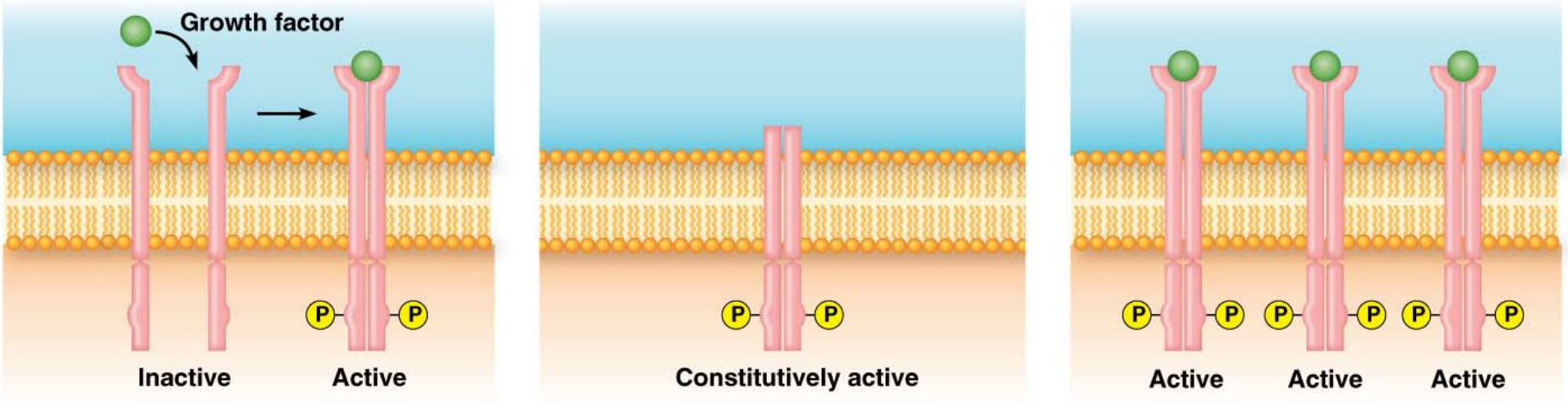
Oncogene Name	Protein Produced	Oncogene Origin	Common Cancer Type*
1. Growth factors			
v-sis	PDGF	Viral	Sarcomas (monkeys)
COL1A1-PDGFB	PDGF	Translocation	Fibrosarcoma
2. Receptors			
v-erb-b	Epidermal growth factor receptor	Viral	Leukemia (chickens)
TRK	Nerve growth factor receptor	DNA rearrangement	Thyroid
ERBB2	Epidermal growth factor receptor 2	Amplification	Breast
v-mpl	Thrombopoietin receptor	Viral	Leukemia (mice)
3. Plasma membrane GTP-binding proteins			
KRAS	Ras	Point mutation	Pancreas, colon, lung, others
HRAS	Ras	Point mutation	Bladder
NRAS	Ras	Point mutation	Leukemias
4. Nonreceptor protein kinases			
BRAF	Raf kinase	Point mutation	Melanoma
v-src	Src kinase	Viral	Sarcomas (chickens)
SRC	Src kinase	DNA rearrangement	Colon
TEL-JAK2	Jak kinase	Translocation	Leukemias
BCR-ABL	Abl kinase	Translocation	Chronic myelogenous leukemia
5. Transcription factors			
MYC	Myc	Translocation	Burkitt lymphoma
MYCL	Myc	Amplification	Small cell lung cancer
c-myc	Myc	Insertional mutagenesis	Leukemia (chickens)
v-jun	Jun	Viral	Sarcomas (chickens)
v-fos	Fos	Viral	Bone (mice)
6. Cell cycle or apoptosis regulators			
CYCD1	Cyclin	Amplification, translocation	Breast, lymphoma
CDK4	Cdk	Amplification	Sarcomas, glioblastoma
BCL2	Bcl-2	Translocation	Non-Hodgkins lymphoma
MDM2	Mdm2	Amplification	Sarcomas, lung, breast, others

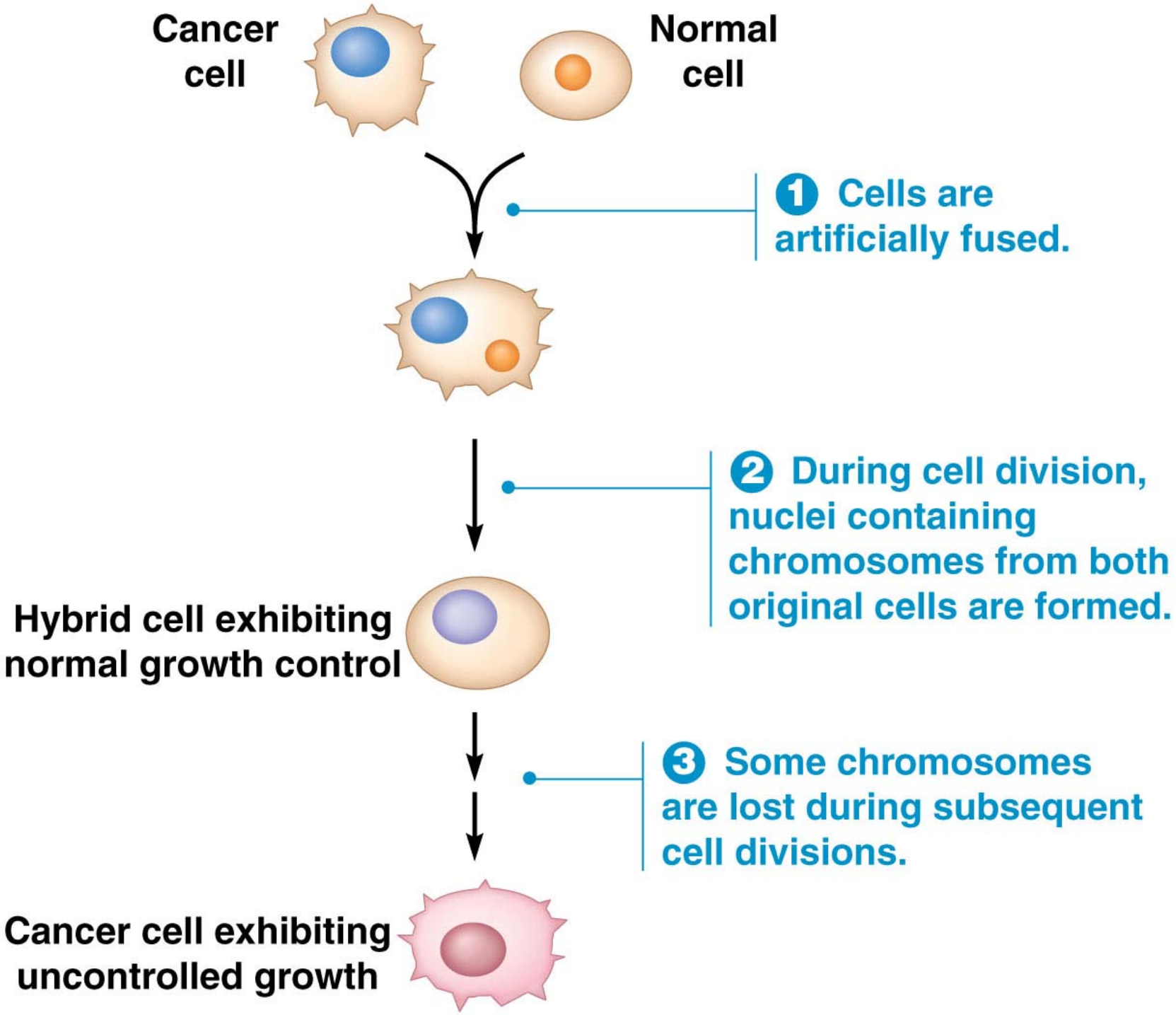
*Cancers are in humans unless otherwise specified. Only the most frequent cancer types are listed.

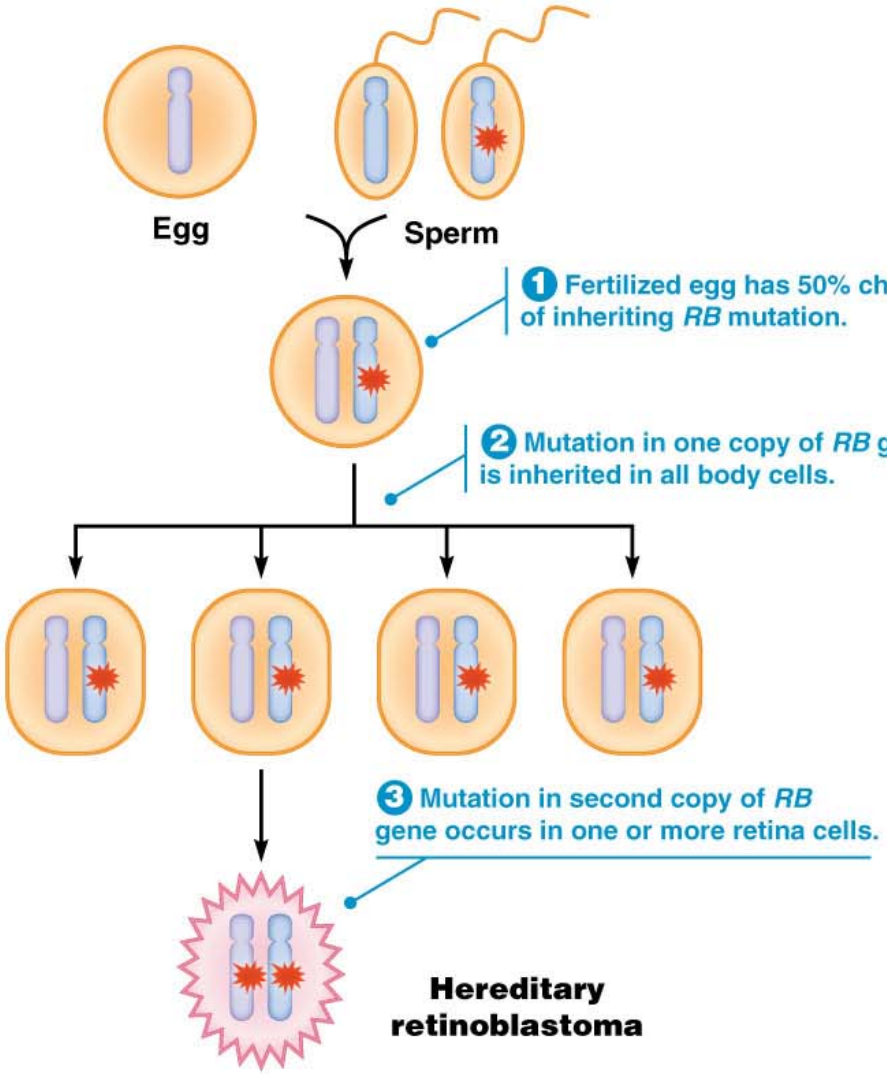
(a) Normal receptor. During normal receptor activation, binding of a growth factor to its receptor promotes the clustering of two receptor molecules, thereby causing the tyrosine kinase activity of each receptor to catalyze phosphorylation of the adjacent receptor (autophosphorylation).

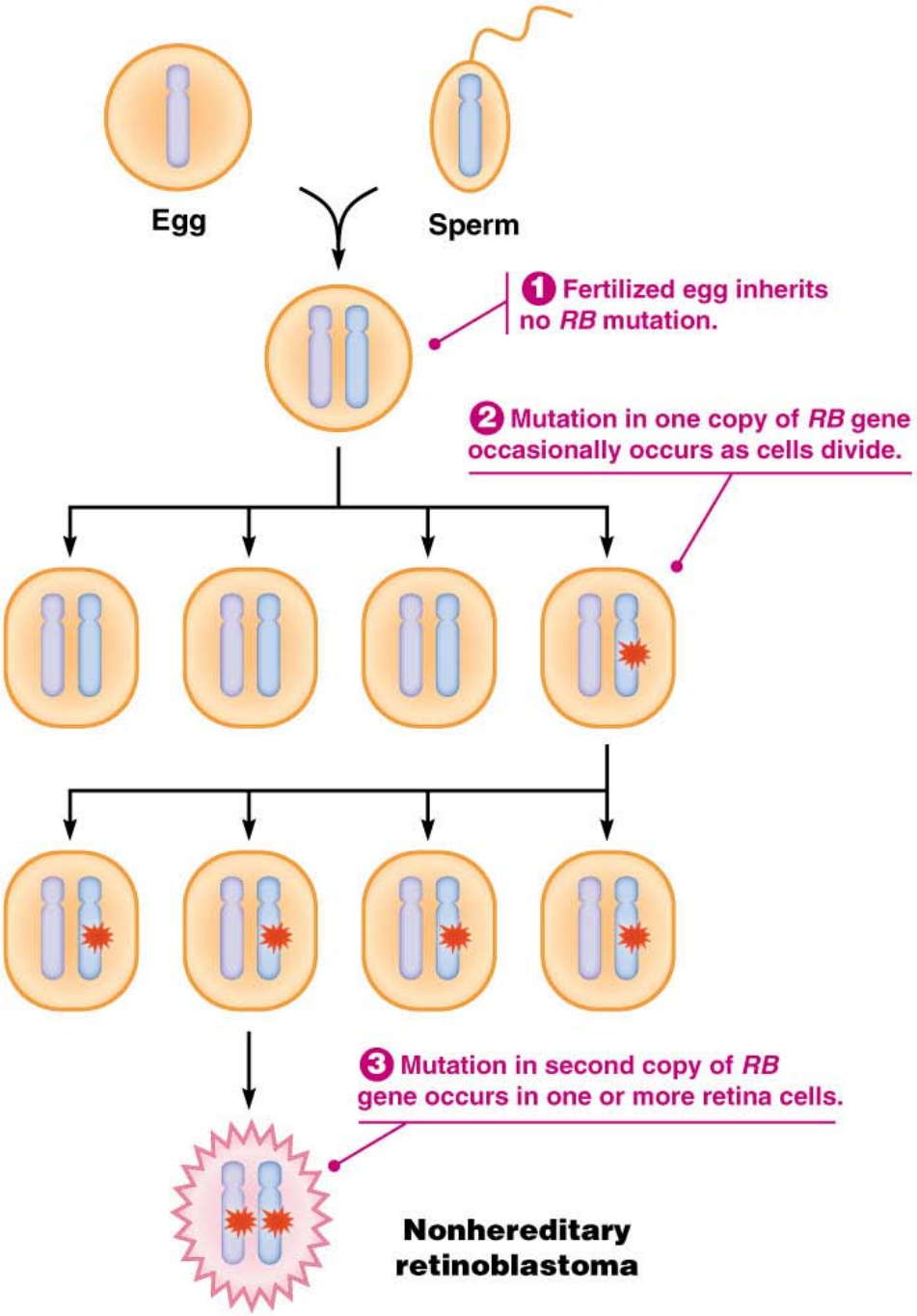
(b) Mutant receptor. Some oncogenes encode mutant receptors whose tyrosine kinase is permanently activated. Below is a mutant receptor missing its growth factor binding site, which makes the receptor constitutively active—that is, it exhibits tyrosine kinase activity even in the absence of growth factor.

(c) Amplified receptor. Amplified oncogenes produce normal receptors but in excessive quantities, which also leads to excessive receptor activity.





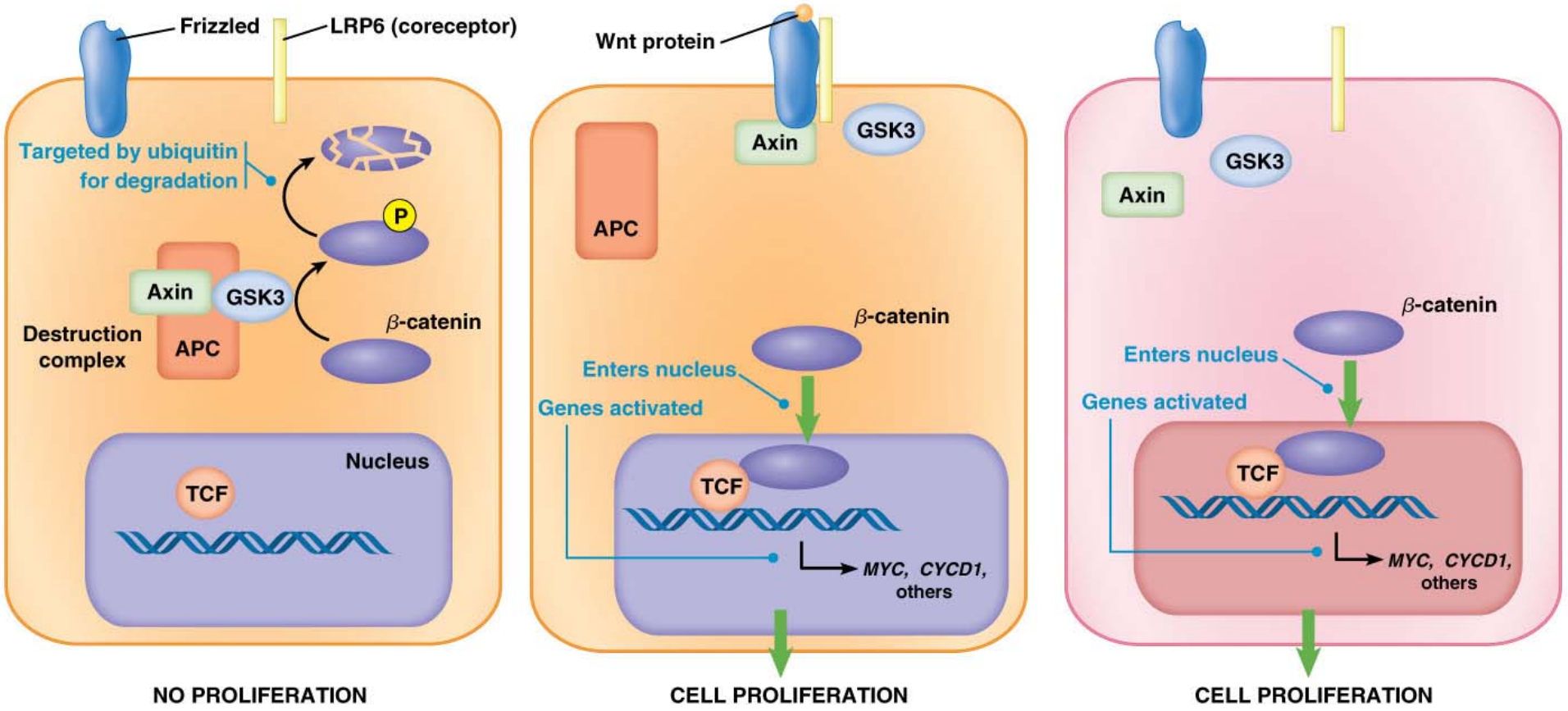


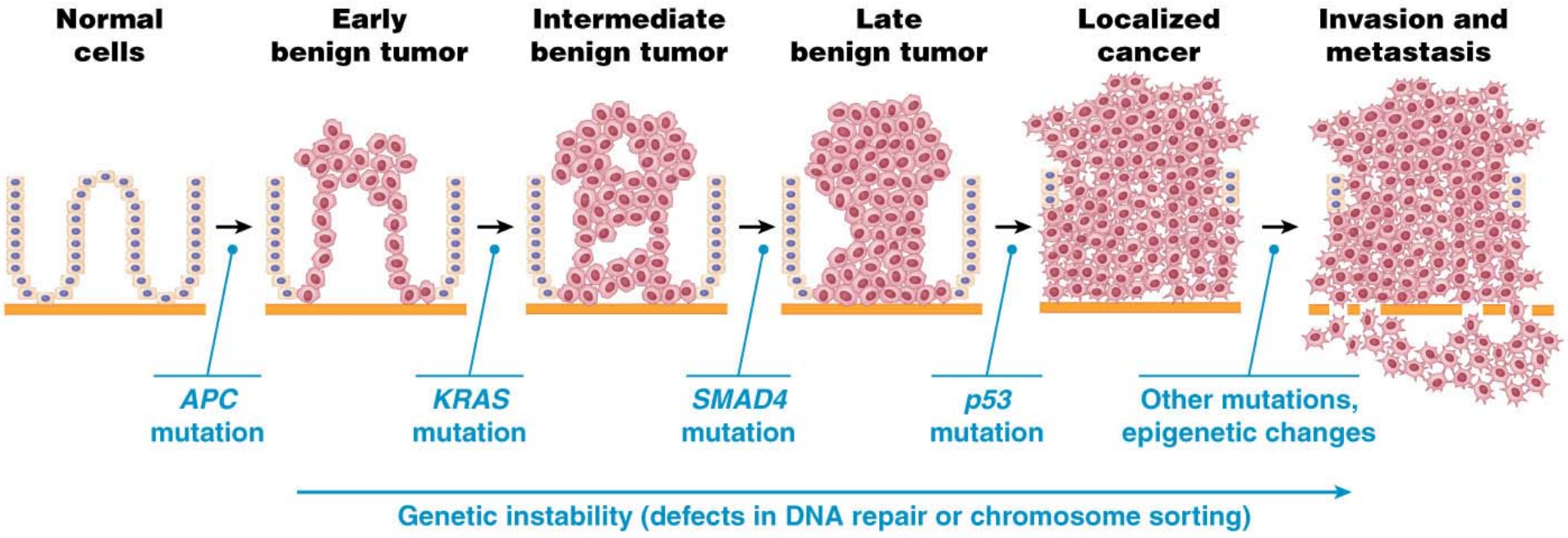


(a) Normal cell (without Wnt proteins). β-catenin is targeted for degradation by the APC-axin-GSK3 destruction complex, which catalyzes phosphorylation of β-catenin. Phosphorylated β-catenin is linked to ubiquitin and degraded by proteasomes. The resulting absence of β-catenin maintains pathway in the OFF position.

(b) Normal cell (with Wnt proteins). The Wnt pathway is turned ON when Wnt proteins activate cell surface Wnt receptors, which bind axin. This prevents assembly of the destruction complex. β-catenin enters the nucleus and binds to TCF, forming a complex that activates genes that control cell proliferation, including *MYC* and *CYCD1* (a cyclin gene).

(c) Cancer cell (with or without Wnt proteins). Some cancer cells have loss-of-function mutations in the *APC* gene. In the absence of functional APC protein, the destruction complex cannot form, β-catenin accumulates, enters the nucleus, and locks the Wnt pathway in the ON position.





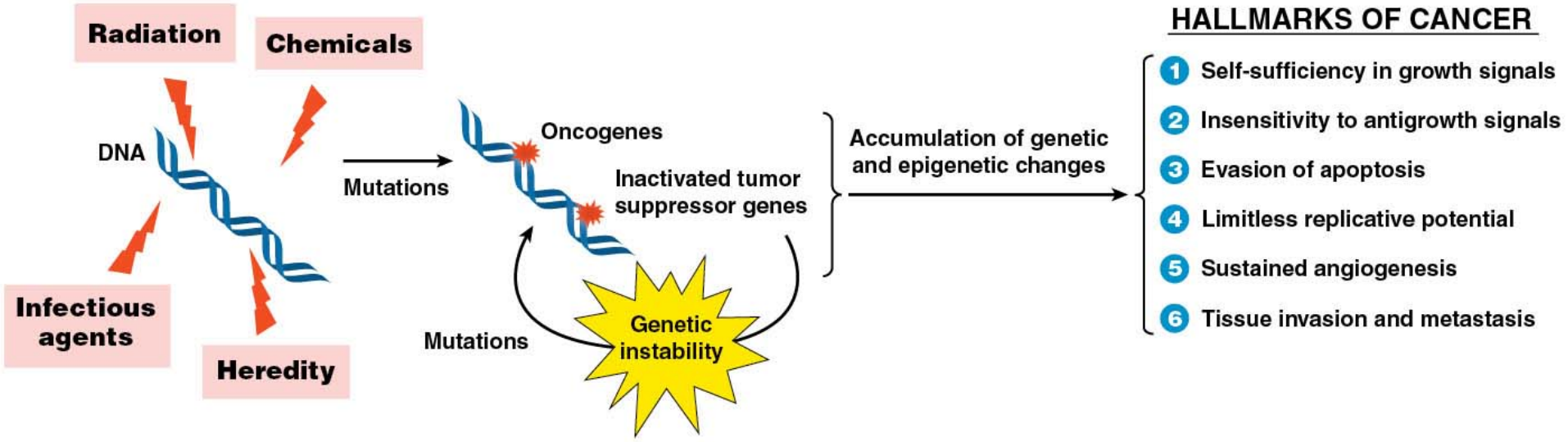


Table 26-3 Some Differences in the Microscopic Traits of Benign and Malignant Tumors

Trait	Benign	Malignant
Nuclear size	Small	Large
N/C ratio (ratio of nuclear to cytoplasmic volume)	Low	High
Nuclear shape	Regular	Pleomorphic (irregular shape)
Mitotic index	Low	High
Tissue organization	Normal	Disorganized
Differentiation	Well differentiated	Poorly differentiated
Tumor boundary	Well defined	Poorly defined
	↓	↓