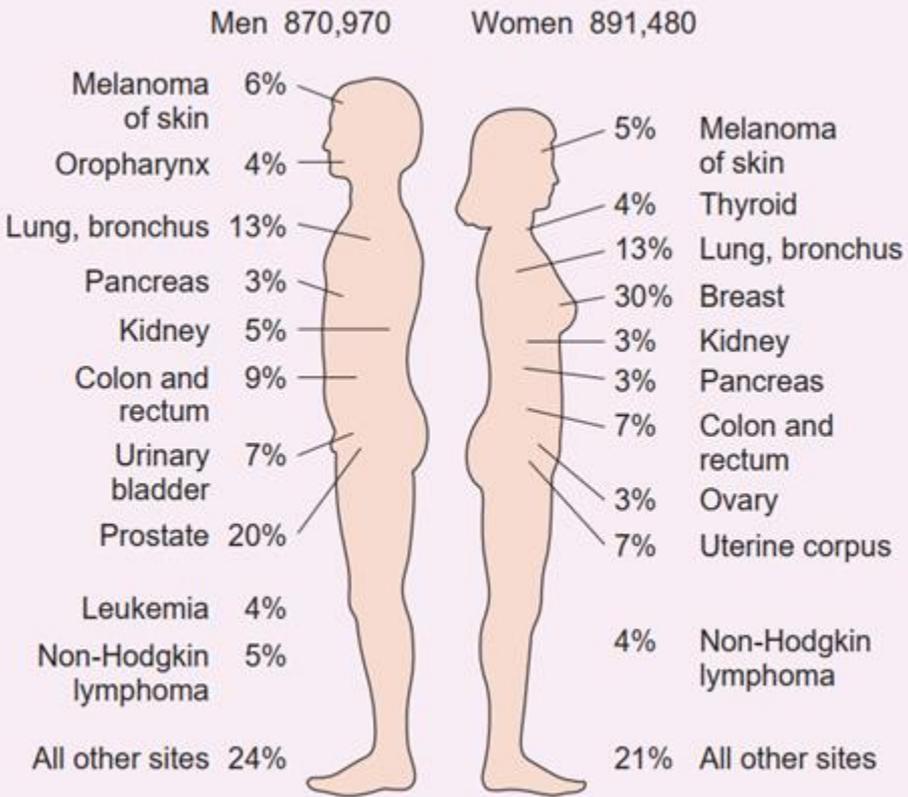


A. 2019 ESTIMATED CANCER INCIDENCE BY SITE AND SEX



B. 2019 ESTIMATED CANCER DEATHS BY SITE AND SEX

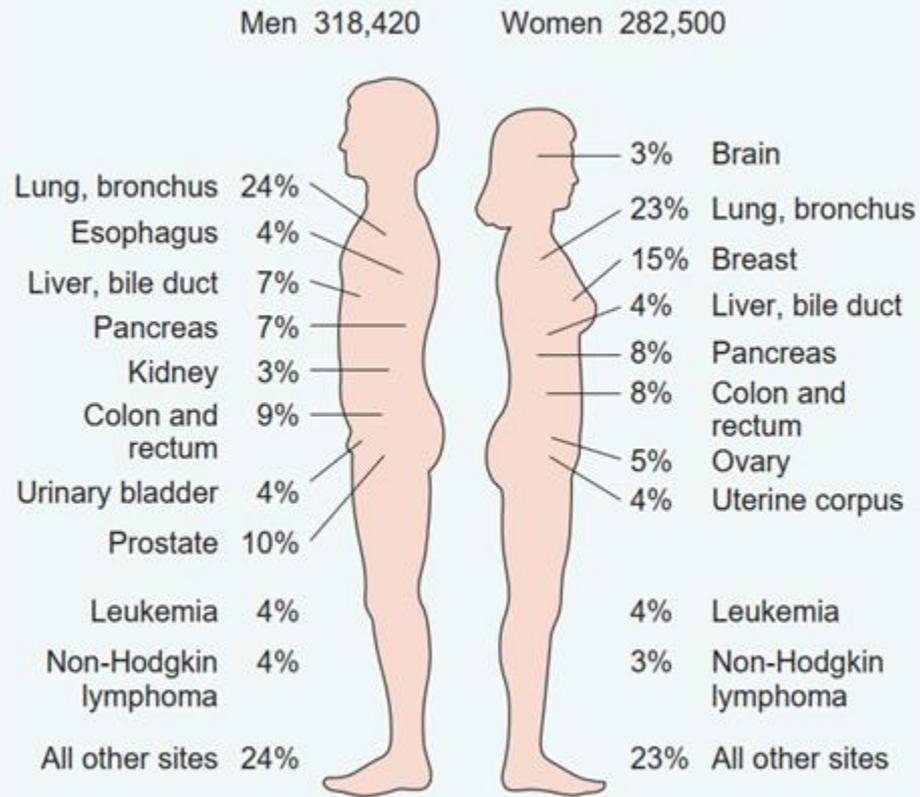


Figure 7.17 Cancer incidence (A) and mortality (B) by site and sex. Excludes basal cell and squamous cell skin cancers and in situ carcinomas except urinary bladder. (Modified from Siegel RL, Miller KD, Jemal A: Cancer statistics, 2017, *CA Cancer J Clin* 67:7–30, 2017.)

A. Worldwide variation of cancer incidence in males

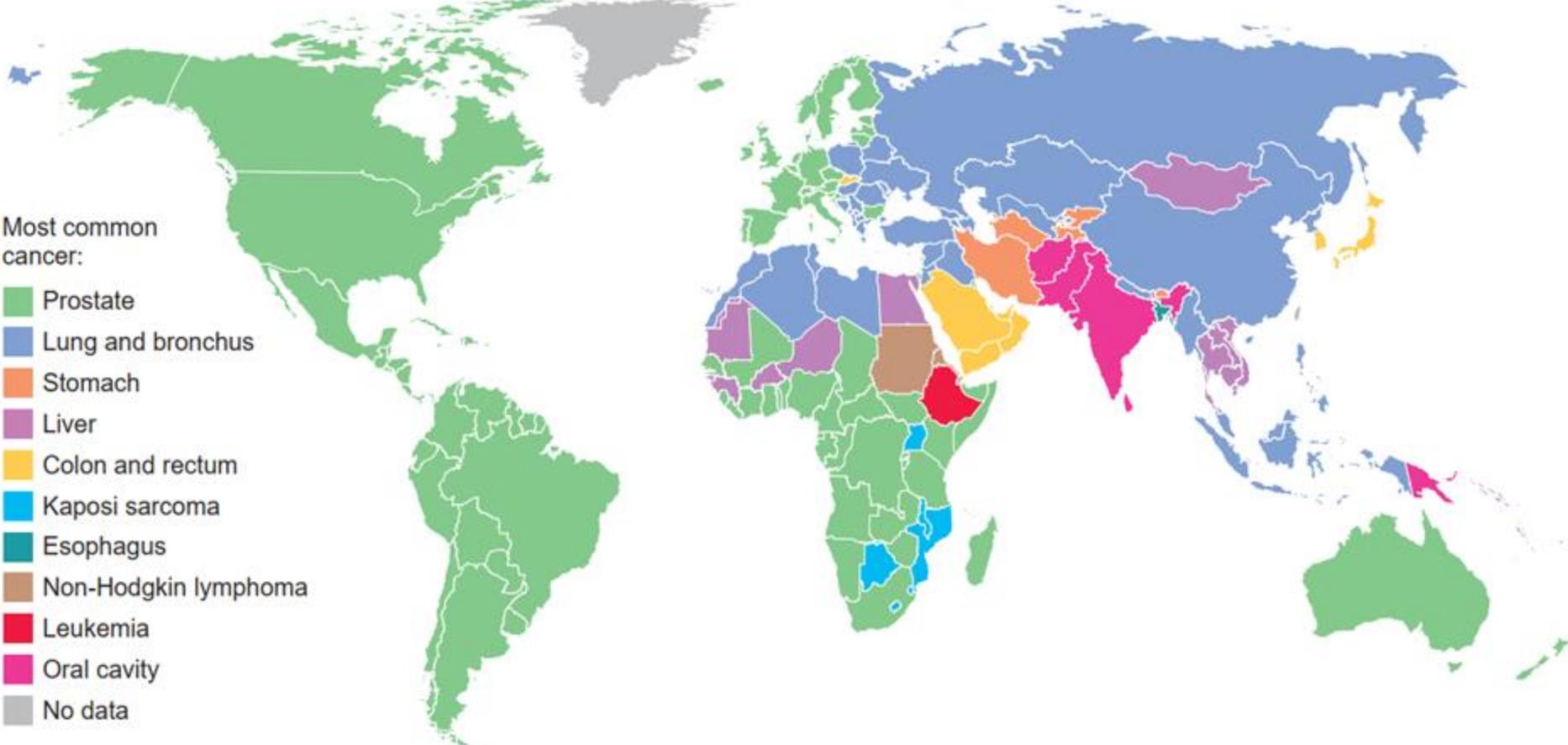


Table 7.3 Occupational Cancers

Agents or Groups of Agents	Human Cancers for Which Reasonable Evidence Is Available	Typical Use or Occurrence
Arsenic and arsenic compounds	Lung carcinoma, skin carcinoma	By-product of metal smelting; component of alloys, electrical and semiconductor devices, medications and herbicides, fungicides, and animal dips
Asbestos	Lung, esophageal, gastric, and colon carcinoma; mesothelioma	Formerly used for many applications because of fire, heat, and friction resistance; still found in existing construction as well as fire-resistant textiles, friction materials (i.e., brake linings), underlayment and roofing papers, and floor tiles
Benzene	Acute myeloid leukemia	Principal component of light oil; despite known risk, many applications exist in printing and lithography, paint, rubber, dry cleaning, adhesives and coatings, and detergents; formerly widely used as solvent and fumigant
Beryllium and beryllium compounds	Lung carcinoma	Missile fuel and space vehicles; hardener for lightweight metal alloys, particularly in aerospace applications and nuclear reactors
Cadmium and cadmium compounds	Prostate carcinoma	Uses include yellow pigments and phosphors; found in solders; used in batteries and as alloy and in metal platings and coatings
Chromium compounds	Lung carcinoma	Component of metal alloys, paints, pigments, and preservatives
Nickel compounds	Lung and oropharyngeal carcinoma	Nickel plating; component of ferrous alloys, ceramics, and batteries; by-product of stainless-steel arc welding
Radon and its decay products	Lung carcinoma	From decay of minerals containing uranium; potentially serious hazard in quarries and underground mines
Vinyl chloride	Hepatic angiosarcoma	Refrigerant; monomer for vinyl polymers; adhesive for plastics; formerly inert aerosol propellant in pressurized containers

Carcinogenesis

DNA Mutation>> Monoclonal cells>> overgrowth

Mutation: Point mutation, translocation, amplification

Target of tumor genes:

***Proto oncogene: mutation>>oncogene>>oncoprotein .**

***Apoptotic gene: BCL-2 (anti apoptotic)>> overexpression.**

***Tumor suppressor genes: RB, P53**

Unlimited replicative capacity : Telomere, Telomerase,

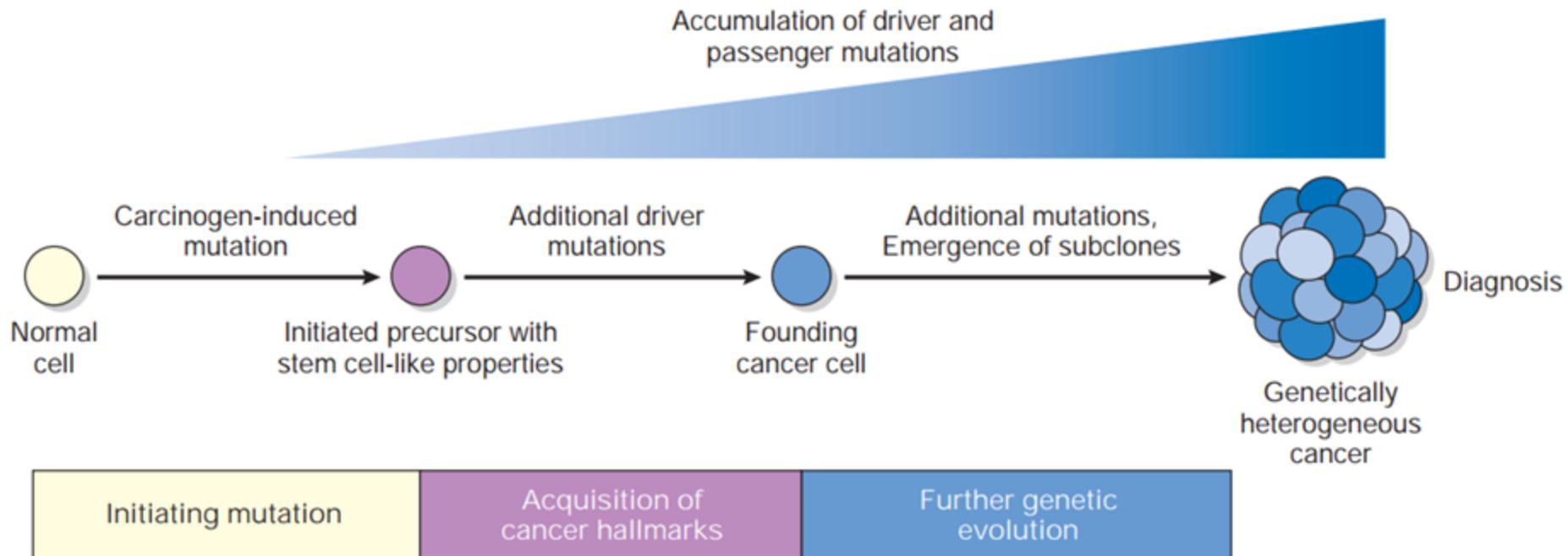


Table 7.5 Selected Oncogenes, Their Mode of Activation, and Associated Human Tumors

Category	Proto-Oncogene	Mode of Activation in Tumor	Associated Human Tumor
Growth Factors			
PDGF- β	<i>PDGFB</i>	Overexpression	Astrocytoma
Fibroblast growth factors	<i>HST1</i> <i>FGF3</i>	Overexpression Amplification	Osteosarcoma Stomach cancer Bladder cancer Breast cancer Melanoma
TGF- α	<i>TGFA</i>	Overexpression	Astrocytomas
HGF	<i>HGF</i>	Overexpression	Hepatocellular carcinomas Thyroid cancer
Growth Factor Receptors			
EGF-receptor family	<i>ERBB1 (EGFR)</i> <i>ERBB2 (HER)</i>	Mutation Amplification	Adenocarcinoma of lung Breast carcinoma
FMS-like tyrosine kinase 3	<i>FLT3</i>	Point mutation or small duplications	Leukemia
Receptor for neurotrophic factors	<i>RET</i>	Point mutation	Multiple endocrine neoplasia 2A and B, familial medullary thyroid carcinomas
PDGF receptor	<i>PDGFRB</i>	Amplification, translocation	Gliomas, leukemias
Receptor for KIT ligand	<i>KIT</i>	Point mutation	Gastrointestinal stromal tumors, seminomas, leukemias
ALK receptor	<i>ALK</i>	Translocation Point mutation	Adenocarcinoma of lung, certain lymphomas Neuroblastoma
Proteins Involved in Signal Transduction			
GTP-binding (G) proteins	<i>KRAS</i> <i>HRAS</i> <i>NRAS</i> <i>GNAQ</i> <i>GNAS</i>	Point mutation Point mutation Point mutation Point mutation Point mutation	Colon, lung, and pancreatic tumors Bladder and kidney tumors Melanomas, hematologic malignancies Uveal melanoma Pituitary adenoma, other endocrine tumors
Nonreceptor tyrosine kinase	<i>ABL</i>	Translocation	Chronic myelogenous leukemia Acute lymphoblastic leukemia
RAS signal transduction	<i>BRAF</i>	Point mutation	Melanomas, leukemias, colon carcinoma, others
Notch signal transduction	<i>NOTCH1</i>	Point mutation, translocation	Leukemias, lymphomas, breast carcinoma
JAK/STAT signal transduction	<i>JAK2</i>	Point mutation, translocation	Myeloproliferative disorders Acute lymphoblastic leukemia
Nuclear Regulatory Proteins			
Transcriptional activators	<i>MYC</i> <i>NMYC</i>	Translocation Amplification	Burkitt lymphoma Neuroblastoma
Cell Cycle Regulators			
Cyclins	<i>CCND1 (cyclin D1)</i>	Translocation Amplification	Mantle cell lymphoma, multiple myeloma Breast and esophageal cancers
Cyclin-dependent kinase	<i>CDK4</i>	Amplification or point mutation	Glioblastoma, melanoma, sarcoma

Inhibitors of Cell Cycle Progression

<i>RB</i>	Retinoblastoma (RB) protein	Inhibitor of G ₁ /S transition during cell cycle progression	Familial retinoblastoma syndrome (retinoblastoma, osteosarcoma, other sarcomas)	Retinoblastoma; osteosarcoma; carcinomas of breast, colon, lung
<i>CDKN2A</i>	p16/INK4a and p14/ARF	p16: Negative regulator of cyclin-dependent kinases; p14, indirect activator of p53	Familial melanoma	Pancreatic, breast, and esophageal carcinoma; melanoma; certain leukemias

Inhibitors of Pro-growth Programs of Metabolism and Angiogenesis

<i>VHL</i>	von Hippel–Lindau (VHL) protein	Inhibitor of hypoxia-induced transcription factors (e.g., HIF1 α)	von Hippel–Lindau syndrome (cerebellar hemangioblastoma, retinal angioma, renal cell carcinoma)	Renal cell carcinoma
<i>STK11</i>	Liver kinase B1 (LKB1) or STK11	Activator of AMPK family of kinases; suppresses cell growth when cell nutrient and energy levels are low	Peutz-Jeghers syndrome (GI polyps, GI cancers, pancreatic carcinoma, and other carcinomas)	Diverse carcinomas (5%–20% of cases, depending on type)
<i>SDHB, SDHD</i>	Succinate dehydrogenase complex subunits B and D	TCA cycle, oxidative phosphorylation	Familial paraganglioma, familial pheochromocytoma	Paraganglioma

Inhibitors of Invasion and Metastasis

<i>CDH1</i>	E-cadherin	Cell adhesion, inhibition of cell motility	Familial gastric cancer	Gastric carcinoma, lobular breast carcinoma
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Enablers of Genomic Stability

<i>TP53</i>	p53 protein	Cell cycle arrest and apoptosis in response to DNA damage	Li-Fraumeni syndrome (diverse cancers)	Most human cancers
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Carcinogens:

Chemical :Aromatic hydrocarbons, Aromatic amines and amides.

Physical: UV rays: SKin

Radiation: Lymphoma, leukemia.

Viruses: HPV: Cervix.

HBV: Liver

EBV: Burkitt lymphoma, nasopharyngeal.

Hormones: Estrogenes, Androenes

Clinical aspects of tumor

*Benign :

- Obstruction. - Vital organs. - Functioning
- Benign > malignant.

*Malignant : Destruction. - Organ failures. - Paraneoplastic syndrome

Malnutrition: anorexia, anemia, GI obstruction, cachexia (TNF)

IHC: 1:Diagnostic: Vimentin, CK, LCA, S100

2: Prognostic: Her2, ER, PR

Table 7.12 Selected Tumor Markers

Tumor Markers	Tumor Types
Hormones	
Human chorionic gonadotropin	Trophoblastic tumors, nonseminomatous testicular tumors
Calcitonin	Medullary carcinoma of thyroid
Catecholamine and metabolites	Pheochromocytoma and related tumors
Ectopic hormones	See Table 7.11
Oncofetal Antigens	
α -Fetoprotein	Liver cell cancer, nonseminomatous germ cell tumors of testis
Carcinoembryonic antigen	Carcinomas of the colon, pancreas, lung, stomach, and heart
Lineage-Specific Proteins	
Immunoglobulins	Multiple myeloma and other gammopathies
Prostate-specific antigen and prostate-specific membrane antigen	Prostate cancer
Mucins and Other Glycoproteins	
CA-125	Ovarian cancer
CA-19-9	Colon cancer, pancreatic cancer
CA-15-3	Breast cancer