



พยาธิวิทยาของเนื้องอก  
(Neoplasia)

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7 กุมภาพันธ์ พ.ศ. 2557

## Terminology

- Neoplasia = Gr. *neos* (new) + *plasia* (growth)
- “Uncontrolled growth of cells whose proliferation **cannot** be controlled by normal regulatory mechanism”
- Neoplastic cells :
  - Autonomous (independent of growth factor and stimuli)
  - Excessive (not response to normal regulators)
  - Disorganized (not follow the rules or normal patterns)

## Terminology

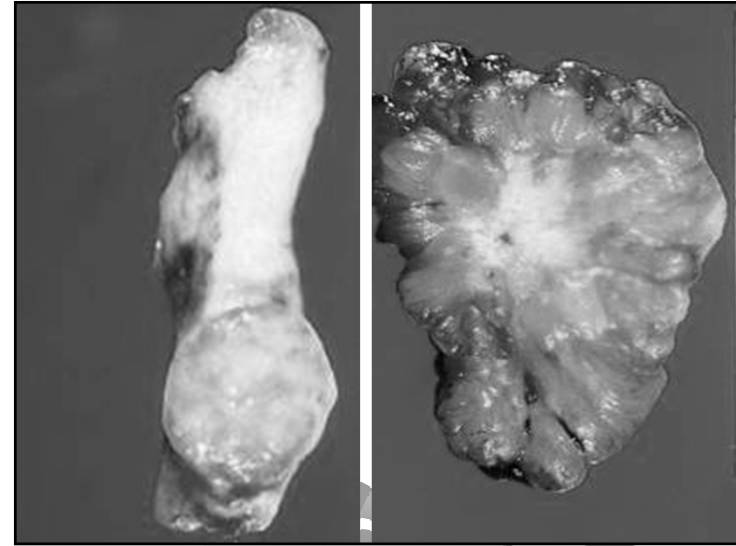
- Tumors = Lat. *tumor* = swelling  
(1 in 5 cardinal signs of inflammation)  
= Gr. *onkos* = swelling
- Oncology, Oncologist
- Tumor (ก้อนเนื้องอก) : benign or malignant
- Cancer = Gr. *karkinos* = crab  
= neoplasm  
= malignant tumor = มะเร็ง

## Classification of Tumors

- Benign and Malignant
  - Macroscopic Features
  - Microscopic Features
    - Differentiation : well, moderate, poorly
    - Anaplasia : loss of differentiation  
(dedifferentiation)
  - Cell Growth
  - Local invasion and Metastasis
- Tumor Type and Tissue of Origin

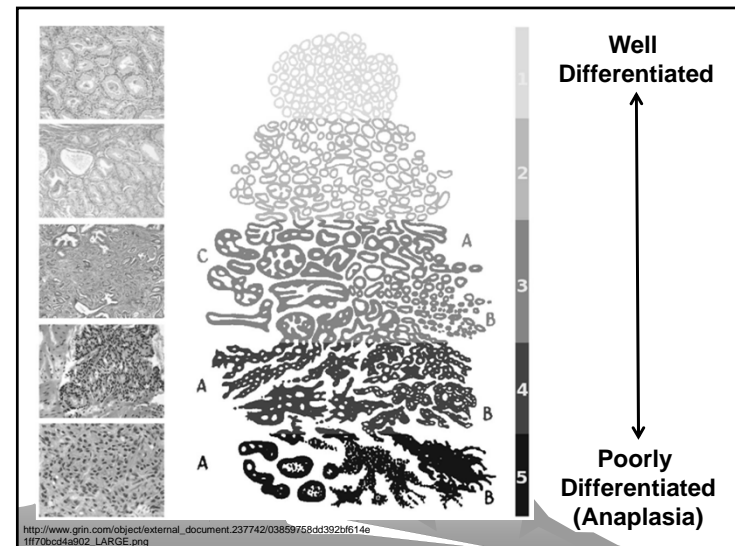
## Macroscopic Features

- Benign tumor :
  - Sharply demarcated
  - Encapsulated
  - Homogenous
  - Easy to remove
- Malignant tumor :
  - Lack a capsule
  - Invade the surrounding tissue
  - Heterogeneous with hemorrhage and necrosis
  - Difficult to totally remove



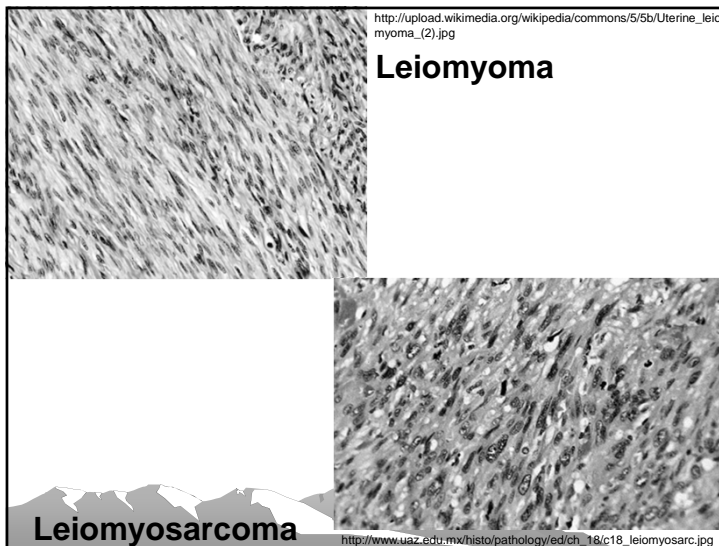
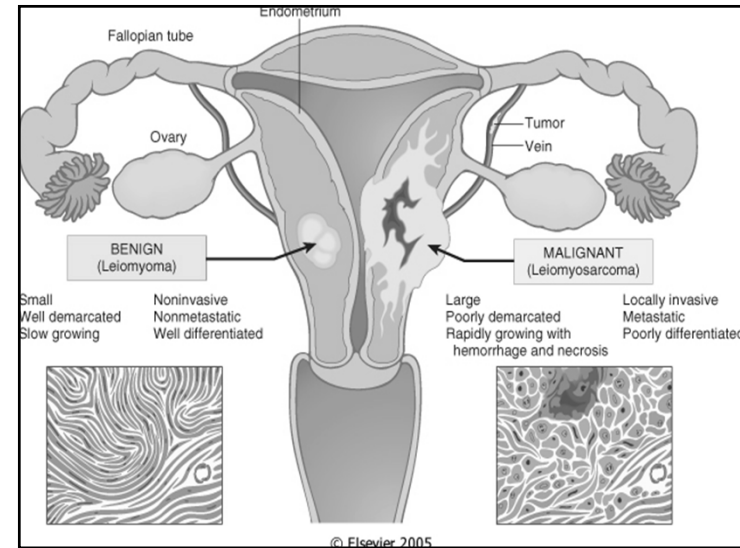
## Microscopic Features

- Benign tumor :
  - Well differentiated (resemble tissue of origin)
  - No anaplasia (anaplasia = dedifferentiation)
- Malignant tumor :
  - Poorly differentiated or undifferentiated
  - Prominent anaplasia (different from normal tissue considerably)



## Cell Growth

- **Benign tumor :**
  - Uniform cell population with regular shape nuclei
  - Slower growth rate
- **Malignant tumor :**
  - Heterogeneous cell population
  - Nuclear pleomorphism (variable in size, shape, and staining properties)
  - High N/C ratio with prominent nuclei
  - Faster growth rate

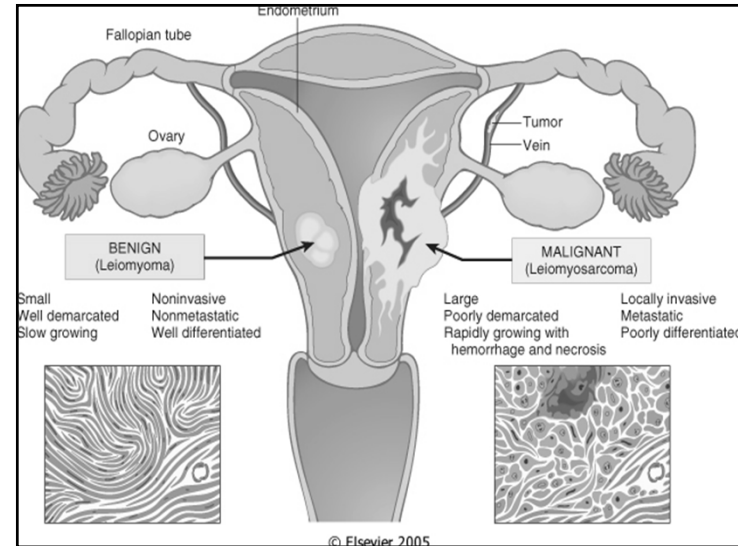


## Local Invasion and Metastasis

- **Benign tumor :**
  - Expansive growth and compress adjacent normal tissue
  - Remain localized
- **Malignant tumor :**
  - Invasion to the surrounding tissue
  - Capable of distant metastasis

### Benign & Malignant Tumors


Characteristics	Benign	Malignant
Histology (differentiation, anaplasia)	- Typical of tissue of origin - Well diff. with no anaplasia	- Poorly diff. - Anaplastic, abnormal cell size and shape
Growth rate	Slow	Rapid
Localization invasion	Local, capsule	Infiltrative
Metastasis	No	Yes
Recurrence	Rare	Common
Prognosis	Good	Poor




- ### Tumor type and Tissue of Origin
- Epithelial tumors
  - Mesenchymal tumors
  - Tumors of blood cells and lymphocytes
  - Tumors of neural cell precursors and neural supporting cells
  - Germ cells tumors

- ### Epithelial tumors
- Benign : suffix – oma
  - Malignant : suffix – carcinoma
  - Squamous cell epithelium
    - Papilloma – Squamous cell carcinoma
  - Glandular/ductal epithelium
    - Adenoma - Adenocarcinoma
  - Transitional epithelium
    - Transitional cell adenoma – Transitional cell CA


## Mesenchymal tumors

- Benign : suffix - oma
  - Malignant : suffix - sarcoma
  - Fibroblast : Fibroma - Fibrosarcoma
  - Fat cell : Lipoma - Liposarcoma
  - Smooth muscle: Leiomyoma - Leiomyosarcoma
  - Striated muscle: Rhabdomyoma - ~-sarcoma
  - Cartilage : Chondroma - Chondrosarcoma
  - Bone : Osteoma - Osteosarcoma
- 


## Tumors of Blood cells and Lymphocytes

- All malignant tumors
  - White blood stem cells – Leukemia
  - Lymphoid cells – Lymphoma
  - Plasma cells – Multiple myeloma
- 

## Tumors of neural cell precursors and neural supporting cells

- Neuroblast : Neuroblastoma (malignant)
  - Glial cells : Glioma (malignant)
  - Meningeal cells : Meningioma (benign)
  - Schwann cells : Schwannoma (benign)
- 

## Germ cell tumors

- Embryonic cells
  - Benign tumor : Teratoma (dermoid cyst)
  - Malignant tumors : Teratocarcinoma  
Seminoma  
(germ cell tumor of the testis)
- 



Teratoma (dermoid cyst): hair, teeth, cartilage, sebaceous

<http://www.med.cmu.ac.th/student/patho/Surapan106.jpg>

## Characteristics of Cancers

- Autonomous and Immortal
  - ↑ Growth-promoting
  - ↓ Growth-inhibiting (apoptosis)
- Angiogenesis, central hemorrhage & necrosis
- Loss of differentiation and increase abnormal features (anaplasia)
- Local invasion
- Distant metastasis


## Causes of Cancer

- Exogenous causes
  - Cancerogenic factors  
(carcinogen, cancer-forming factors)
  - Chemicals
  - Physical agents
  - Viruses
- Endogenous causes
  - Genetic trait, heritability


## Chemical Carcinogens

- Polycyclic aromatic hydrocarbons
  - 3,4-Benzpyrene – tobacco – CA lung
  - Aflatoxin B1 – *Aspergillus flavus* – liver cancer
- Aromatic amines
  - Naphthylamine – azo dyes – bladder cancer
- Nitrosamines
  - Nitrites and nitrates – meat product – CA colon
- Steroid hormones
  - Estrogen – supplement – endometrial cancer


## Physical carcinogens

- Radiation
  - Ultraviolet light (UV)
  - X-rays
  - Radioactive isotopes
  - Atomic bombs
  - Skin cancer (SCC, BCC, melanoma), leukemia, thyroid cancer
- 


## Viral Carcinogens

- Human papilloma virus (HPV)
    - Common warts, genital warts
    - HPV type 16, 18 – Cancer of cervix
  - Epstein-Barr virus (EBV)
    - Burkitt's lymphoma (B-cell neoplasia)
    - Nasopharyngeal carcinoma
  - Hepatitis B virus (HBV)
    - Hepatocellular carcinoma
  - Human T-cell lymphoma/leukemia virus 1 (HTLV-1)
- 

## Genetic Mechanisms of CA

- Altered expression of cellular genes  
“somatic genetic disorders”
    - Nonlethal genetic damage (mutations)
      - Proto-oncogenes
      - Tumor suppressor genes
    - Clonal expansion
    - DNA repair defect
    - Acquire new mutations → malignant properties
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## Proto-oncogenes

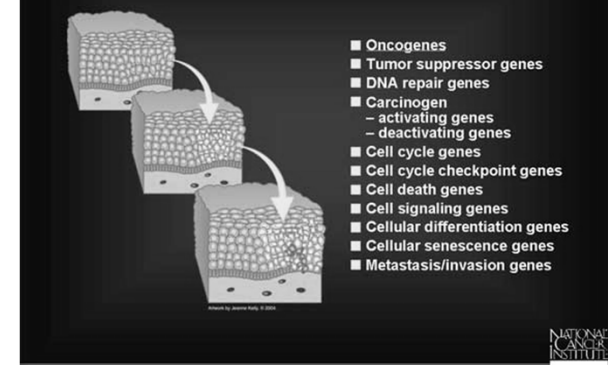
- Proto-oncogenes → mutation → oncogenes  
→ oncoproteins → promote autonomous cell growth → cancer
  - Ex. Growth factors (PDGF), Growth factor receptors (EGFR), cytoplasmic signal molecules (K-RAS), nuclear transcription factors (c-myc)
- 

## Tumor Suppressor Genes

- Growth inhibitory signals
  - Rb gene: retinoblastoma, osteosarcoma
  - P53: most human cancers (breast and colon CA)
  - BRCA-1/BRCA-2: breast & ovarian cancers
    - 3% all breast cancer
    - 80% familial breast cancer
- Evasion of apoptosis (anti-apoptosis)
  - Bcl-2

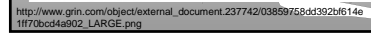
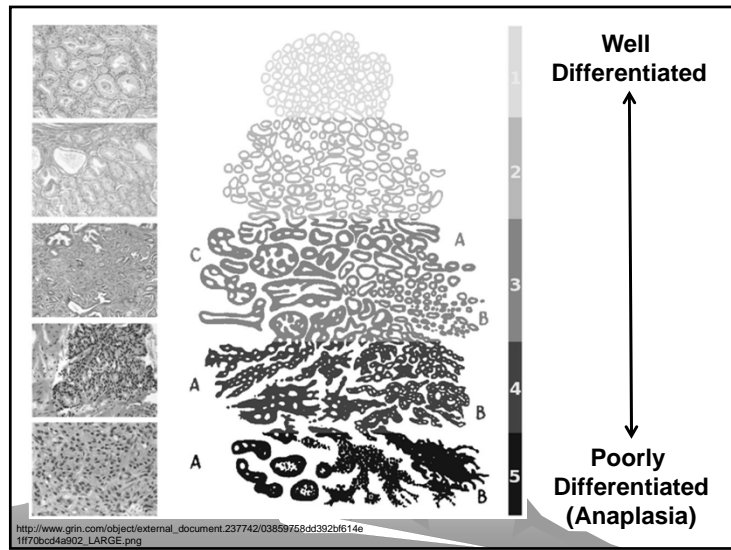


## Cancer-Associated Mutations

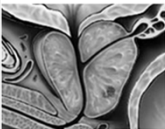
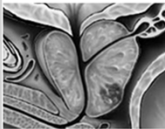
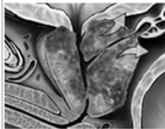
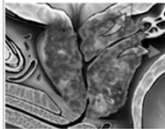
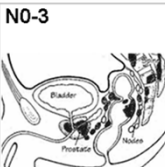
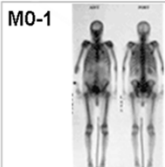


## Grading and Staging

- Grading: histologic characterization of tumor cells and is basically a determination of the degree of anaplasia (grade 1, 2, 3, 4)
- Staging: location and pattern of spread of a tumor within the host
  - International Centre Center → TNM (tumor, Node, Metastasis)
  - American Joint Committee → Stage 0 - IV




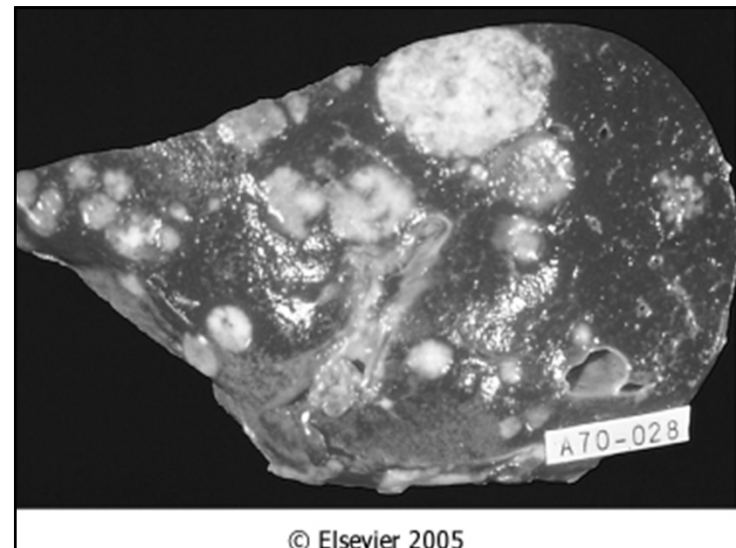
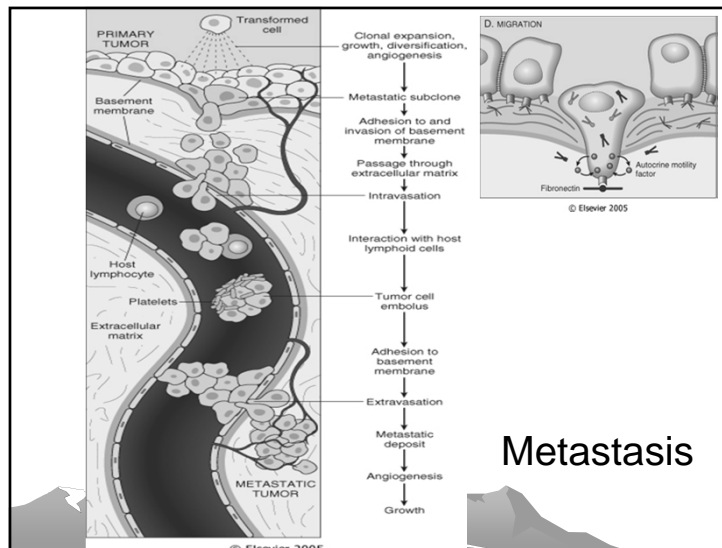


T1	T2	T3	T4
			
<p><b>T1</b> Clinically inapparent, tumor not palpable or visible by imaging</p> <p><b>T1a</b> Incidental finding during transurethral resection of prostate; &lt; 5% of tissue resected</p> <p><b>T1b</b> Incidental finding during transurethral resection of prostate; &gt; 5% of tissue resected</p> <p><b>T1c</b> Tumor identified by needle biopsy (e.g. because of elevated PSA)</p>	<p><b>T2</b> Tumor confined within prostate (palpable or visible on TRUS)</p> <p><b>T2a</b> Involves half of a lobe or less</p> <p><b>T2b</b> Involves more than half of a lobe one lobe but not both lobes</p> <p><b>T2c</b> Tumor involves both lobes</p>	<p><b>T3</b> Tumor extends through prostatic capsule, bladder neck or seminal capsule</p> <p><b>T3a</b> Unilateral extracapsular extension</p> <p><b>T3b</b> Bilateral extracapsular extension</p> <p><b>T3c</b> Tumor invades seminal vesicle(s)</p>	<p><b>T4</b> The tumor has spread or attached to tissues next to the prostate (other than the seminal vesicles)</p> <p><b>T4a</b> The tumor has spread to the neck of the bladder, the external sphincter (muscles that help control urination), or the rectum.</p> <p><b>T4b</b> The tumor has spread to the floor and/or the wall of the pelvis.</p>
		<p><b>N0</b> Cancer has not spread to any lymph nodes.</p> <p><b>N1</b> Cancer has spread to a single regional lymph node (inside the pelvis) and is not larger than 2 centimeters</p> <p><b>N2</b> Cancer has spread to one or more regional lymph nodes and is larger than 2 centimeters (3/4 inch), but not larger than 5 centimeters</p> <p><b>N3</b> Cancer has spread to a lymph node and is larger than 5 centimeters</p> <p><b>M0</b> The cancer has not metastasized (spread) beyond the regional lymph nodes</p> <p><b>M1</b> The cancer has metastasized to distant lymph nodes (outside of the pelvis), bones, or other distant organs such as lungs, liver, or brain</p>	

http://edoc.hu-berlin.de/dissertationen/kaiser-smone-2004-06-10/HTML/kaiser2.html\_76b64ef.png

## Invasion and Metastasis

- Invasion of extracellular matrix
- Invasion into vascular
- Vascular dissemination
  - Lymphatic → lymph nodes
  - Blood vessels → distant organs
- Tumor implantation
  - Favoring new location → homing

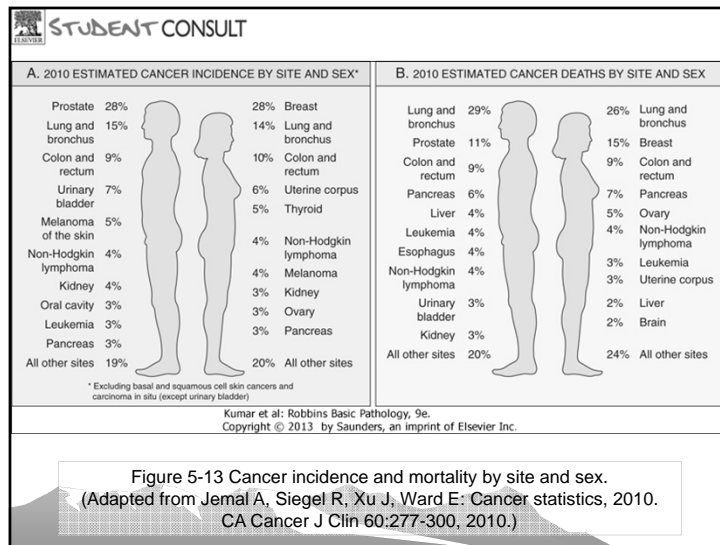
## Effects of cancer on body

- Location & impingement on adjacent structures
- Functional activity such as hormone
- Bleeding & secondary infections
- Initiation of acute symptoms (rupture, infarction)



## Effect of cancer on body

- Cachexia: overall weight loss and generalized weakness due to
  - Anorexia (loss of appetite)
  - High metabolism by cancer cells
  - Therapeutic effect → nausea, vomiting
- Pain: patient-controlled analgesia
- Fear, depression
- Paraneoplastic syndromes: venous thrombosis, cushing syndrome, hypercalcemia



## In Thailand 2010

- ข้อมูลจากสถาบันมะเร็งแห่งชาติ ปี 2010  
([http://www.nci.go.th/File\\_download/Nci%20Cancer%20Registry/hospital-based%202010.pdf](http://www.nci.go.th/File_download/Nci%20Cancer%20Registry/hospital-based%202010.pdf))
- มะเร็งที่พบบ่อยที่สุดในผู้ชาย ได้แก่  
Trachea, bronchus and lung (23.6%),  
Colon and rectum (21.5%), Liver and bile duct (17.3%)
- มะเร็งที่พบบ่อยที่สุดในผู้หญิง ได้แก่  
Breast (47.8%), Cervix uteri (16.2%), Colon & rectum (10.4%)



## In Thailand 2011

- ข้อมูลจากสถาบันมะเร็งแห่งชาติ ปี 2011 (หน้า 15)


([http://www.nci.go.th/th/File\\_download/Nci%20Cancer%20Registry/Hospitalbase2011.pdf](http://www.nci.go.th/th/File_download/Nci%20Cancer%20Registry/Hospitalbase2011.pdf))

- มะเร็งที่พบบ่อยที่สุดในผู้ชาย ได้แก่

Colon and rectum (16.2%), Trachea, bronchus and lung (15.5%), Liver and bile duct (15.3%)

- มะเร็งที่พบบ่อยที่สุดในผู้หญิง ได้แก่

Breast (37.5%), Cervix uteri (14.4%), Colon & rectum (9.6%)




## ความรู้เพิ่มเติมเกี่ยวกับโรคมะเร็ง

- สถาบันมะเร็งแห่งชาติ <http://www.nci.go.th/index.html>

- ความรู้ทั่วไปเกี่ยวกับโรคมะเร็ง

<http://www.nci.go.th/th/Knowledge/index.html>



## References

- Damjanov I., "**Pathology for the Health Professions, 4<sup>th</sup> edition.**", Elsevier Saunders, 2012, p. 67-90.
  - Kumar V., Abbas A.K., Aster J.C., "**Robbins Basic Pathology, 9<sup>th</sup> edition.**" Elsevier Saunders, 2013, p.161-214.
  - Kumar V., Abbas A. K., Fausto N., "**Robbins and Cotran Pathologic Basis of Disease, 7<sup>th</sup> edition.**", Elsevier Saunders, 2005, p. 3-46.
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