노스 캐롤라이나
위암연구 심포지엄

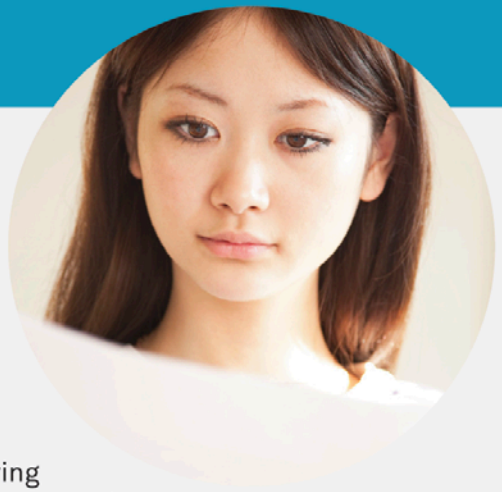
유전학

의학박사 페기 걸리

노스 캐롤라이나 대학
병리학과


Pathology

병리학 보고서를 보는 법
How to Read Your Pathology Report



To diagnose diseases such as cancer, a sample of tissue called a biopsy is taken from a patient and examined by a pathologist to determine if cancer is present.

A pathologist is a medical doctor who specializes in the diagnosis and classification of diseases by looking at tissue or cells under a microscope and by interpreting medical laboratory tests.

The pathologist also is the doctor who examines specimens removed during surgery (resections) for conditions such as cancer, to determine whether a tumor is benign or cancerous, and if cancerous, the exact cell type, grade, and stage of the tumor. In some cases, the pathologist also performs molecular biomarker analysis and reports genetic alterations that may guide targeted therapy for a specific cancer.

The College of American Pathologists has developed the following information to help you understand your pathology report.

Your Surgical Pathology Report

Surgical pathology reports vary somewhat regarding the information they contain. However, each report will document the significant details that affect the management of your diagnosed condition or disease process.

1 Patient Identifiers and Clinical Information

To ensure that the report is about you and your specimen, each pathology report contains your **patient identifiers**—specific information that relates directly to you and includes your name, birth date, and hospital or medical record number. In addition, your pathologist's name and signature and the laboratory's name and address will appear on the report.

The container in which your specimen is sent to the laboratory also is labeled with your patient identifiers and matched to your medical record to ensure that the specimen is from you. After the specimen arrives in the laboratory and is processed and after the final pathology report is prepared, these identifiers are checked repeatedly to ensure the correct information is provided to your medical team.

Case#: 514-124567
Patient: Doe, Jane
DOB: 10/13/1948
Facility: Community Hospital
MR#: 8897786
Age/Sex: 66 yo F
Collected: 07/22/2014
Received: 07/22/2014
Reported: 07/26/2014

Surgical Pathology Report

DIAGNOSIS
1. Infiltrating Ductal Carcinoma, Moderately Differentiated (SBR score 6), Right Breast Core Biopsies.
2. Ductal Carcinoma insitu, high grade.

NOTE: breast marker analysis is pending (HIC and FISH) and an addendum report will be issued. The results were re-viewed by Dr. Mary Beth Shreayder who concurs. Report was faxed to Dr. Surgeon's office on 2/5/11.

Core Biopsies, Low Power | Infiltrating Ductal Carcinoma | Focal Gland Formation

CLINICAL HISTORY: palpable right breast mass; calcifications on mammogram

SITES: right breast core biopsies

GROSS: Received in formalin are 4 cores of white and yellow tissue, each measuring 2.0 X .03 cm in diameter. Totally embedded in one cassette. MB.lad

MICROSCOPIC: Sections reveal infiltrating ductal carcinoma. The tumor is composed of irregular, nests and cords of cells with focal gland formation. Individual cells have irregular nuclei and small nucleoli. Well formed glands make up less than 20% of the tumor. Mitoses are occasionally encountered and these number 4 per 10 hpf. The tumor elicits a desmoplastic stromal reaction. Calcifications are seen within a few neoplastic ducts as well as the stroma. There is a focus of ductal carcinoma in situ involving one core. Nuceli are large and have prominent nucleoli. The duct lumen is filled with necrotic debris. All four core biopsies contain infiltrating carcinoma, the longest tumor segment is 1.7 cm in a 2cm core. Breast Marker analysis is pending and an addendum report will be issued.
adjpm

PREVIOUS BX/PAP HISTORY: FNA cyst left breast, benign (5/5/2005)

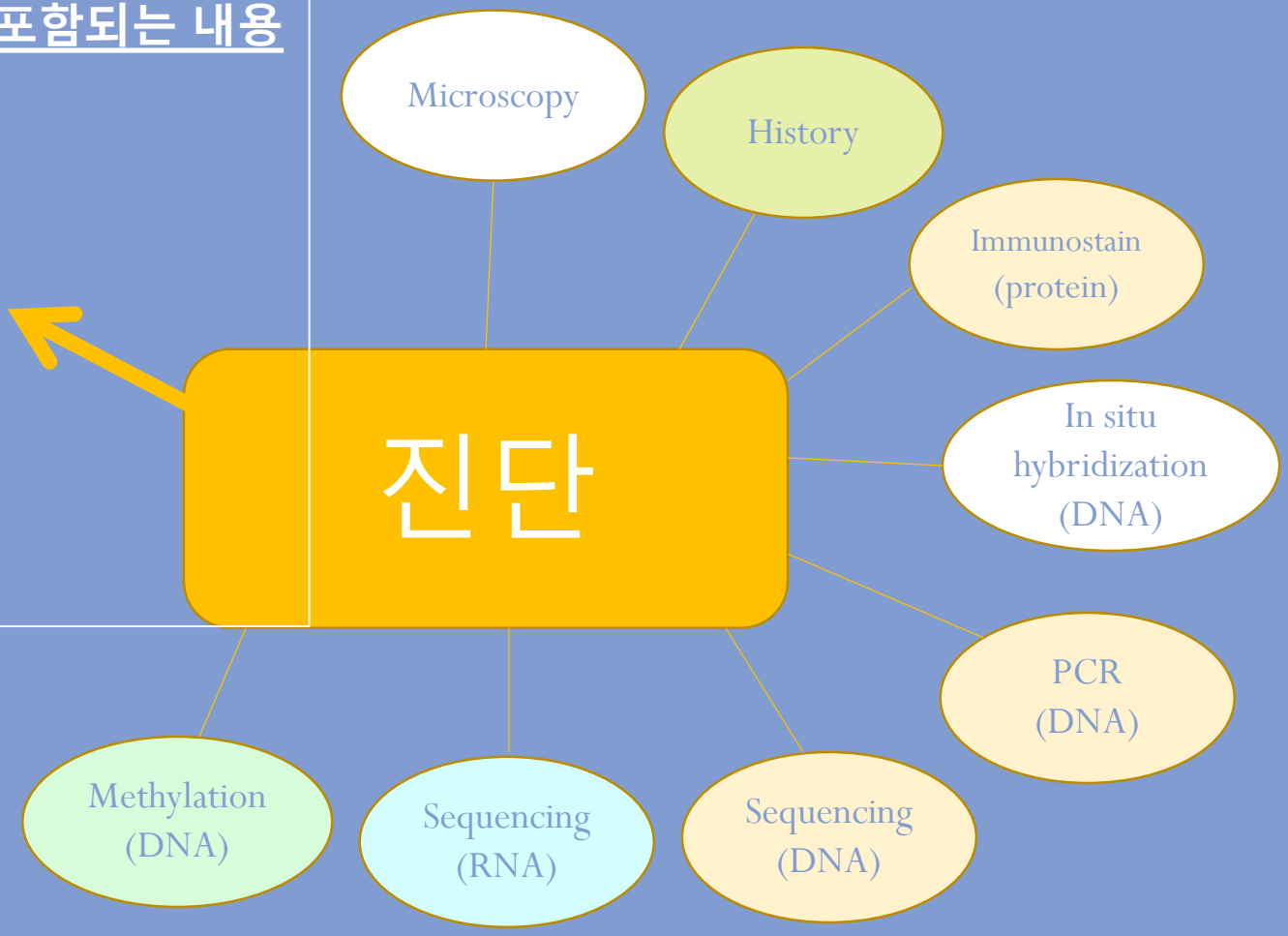
REFERENCES/URLS: www.mybiopsy.org/breast_cancer

E-signed by: Alessandro Devillo, MD (310-225-3XXX); secondary review by Mary Beth Shreayder, MD

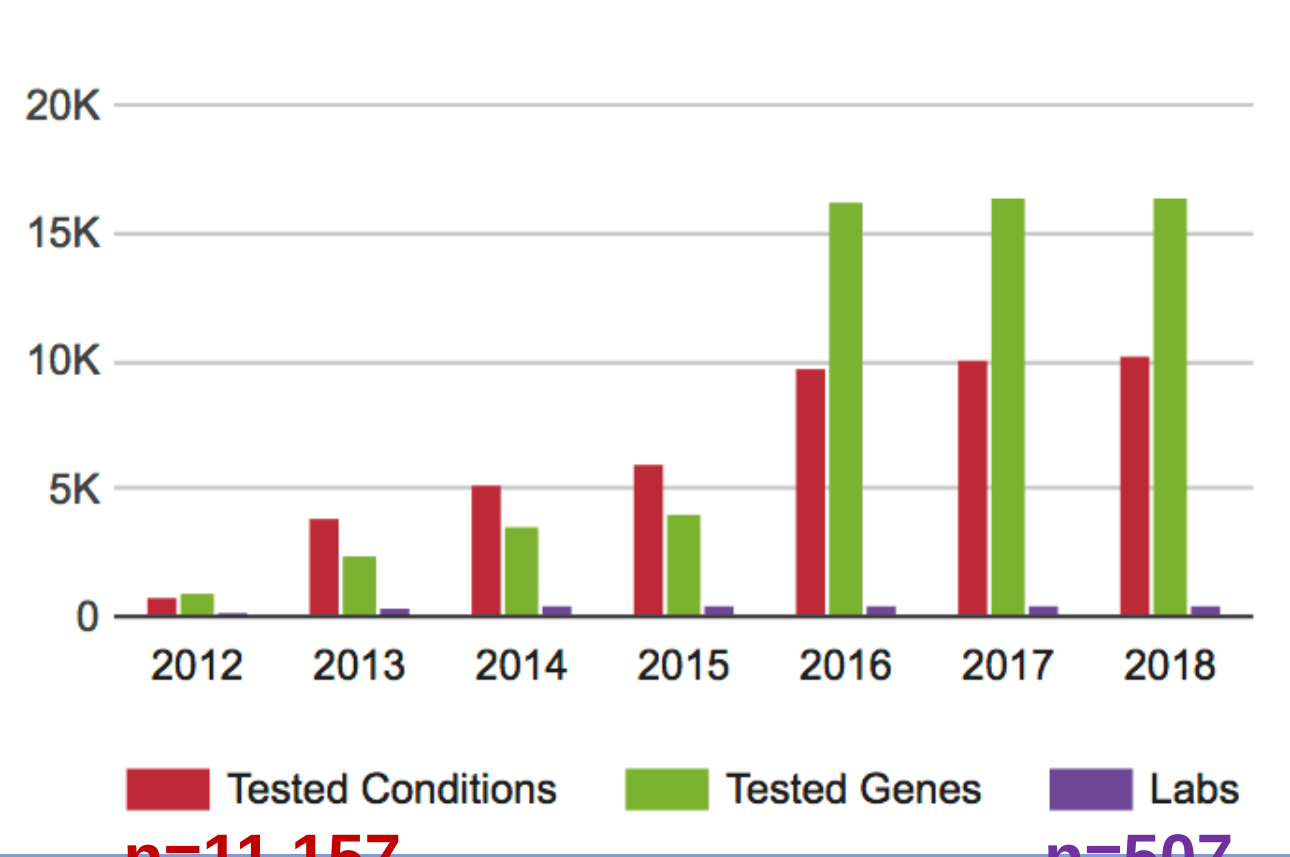
병리학자는 환자의 조직을 분석하여 얻은 데이타를 이용하여 진단을 내린다

환자의 의료기록에 포함되는 내용

수술과정
해부학적 내용
병리학적 내용
암의 크기
병기
마진
침입정도
림프절 상태
보조테스트
해석



2018년 8월 현재 쓰이고 있는 54,862개의 유전자 테스트



n=11,157

n=507

NIH genetic testing registry,
https://www.ncbi.nlm.nih.gov/gtr/

유전자 검사의 활용도

암
전염병
유전병
신원확인
약물유전학

진행된 위암환자에게 일상적으로 쓰이는 유전자검사 두가지

국소적으로 진행되었거나 재발, 또는 전이된 위암, 위식도 접합부암의 암조직에 쓰이는 유전자검사

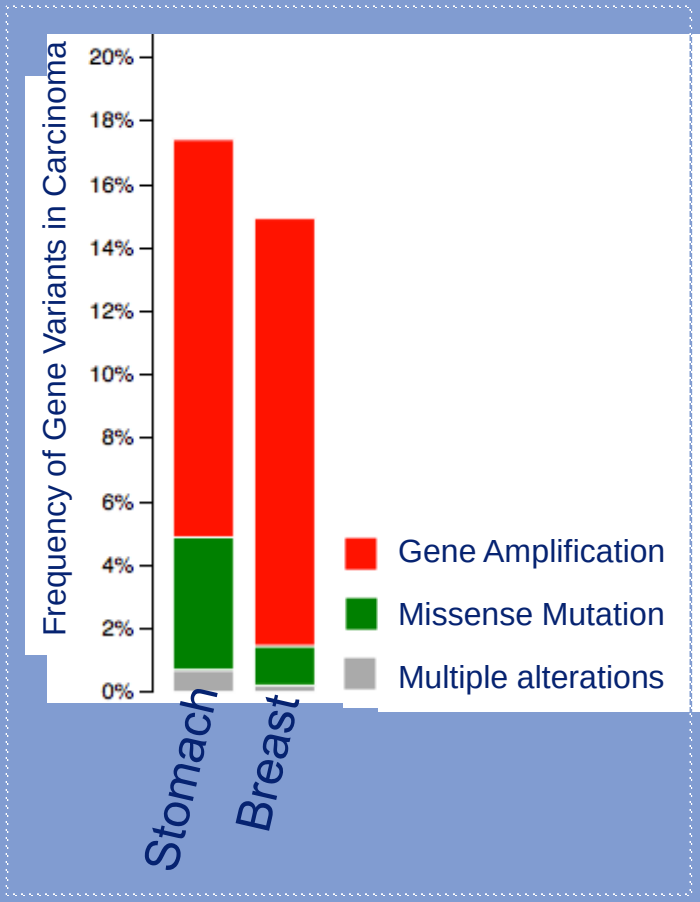
ERRB2 (HER2) 상태:
HER2 표적치료에 더 적합한 환자를 찾기위한 제자리부합법(in situ hybridization)

Microsatellite 불안정 상태:
면역요법에 더욱 적합한 환자를 찾기위해 사용

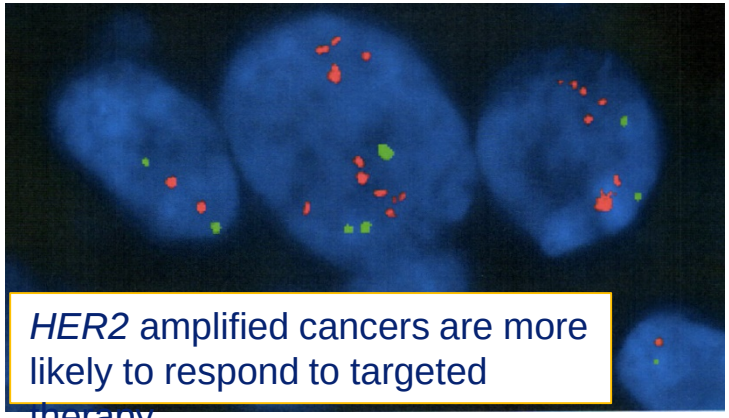
NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018
Gastric Cancer

ERBB2 (HER2) 활성화 : 위암에서 흔히 발생

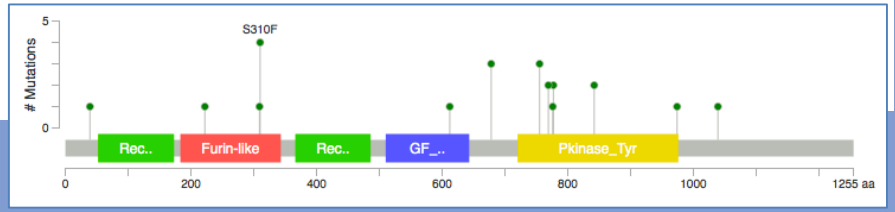


HER2 gene amplification by fluorescence *in situ* hybridization (FISH) using *ERBB2* & cep17 probes



HER2 amplified cancers are more likely to respond to targeted therapy

ERBB2 missense mutation by DNA



cbioportal.org, The Cancer Genome Atlas (TCGA)
PMID: 25079317
PMID:29409051

Microsatellite 가 불안정한 암은 면역요법에 반응도가 높다

"The Story"

MLH1 **유전자 프로모터 메틸화**
→ MLH1 단백질을 발현하지 못함
→ 유전자 불일치 수리에 결함발생
→ 과돌연변이 → 신생항원
→ 면역치료에 대한 더 높은 반응도 (예. PD1 억제제)

마이크로새틀라이트 불안정성을 알아내기 위한 실험실 테스트

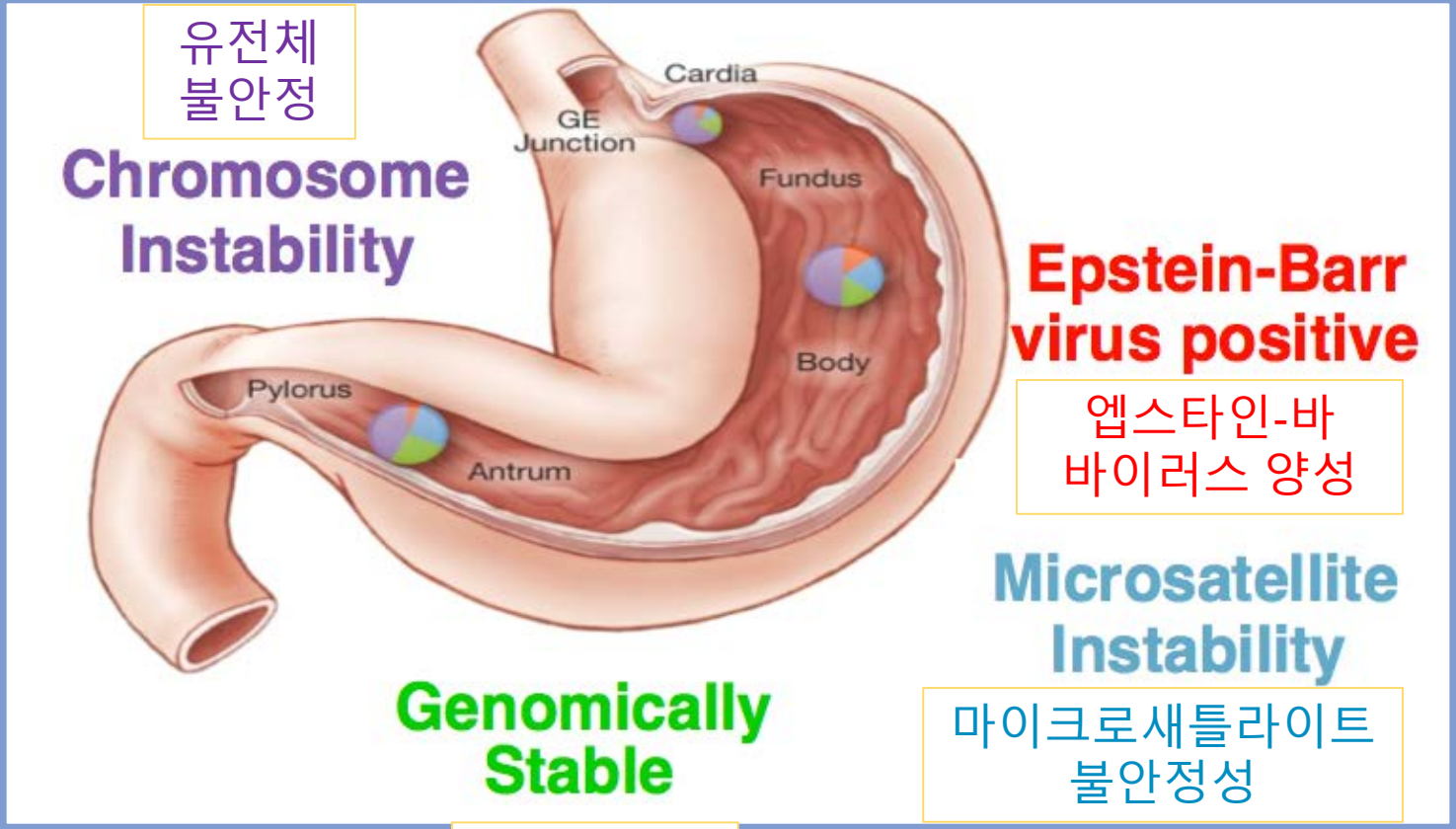
$	*MLH1* 메틸화
$	MLH1 면역염색 (단백질 손실)
$$	마이크로새틀라이트 불안정성(길이, 정상조직과 비교)
$$$	유전자 시퀀싱 패널(마이크로새틀라이트 불안정성, 암세포 돌연변이에 대한 부담)

cbioportal.org, The Cancer Genome Atlas (TCGA)

Le DT, Uram JN, Wang H, et al. PD-1 blockade in tumors with mismatch-repair deficiency. N Engl J Med 2015;372:2509-2520.

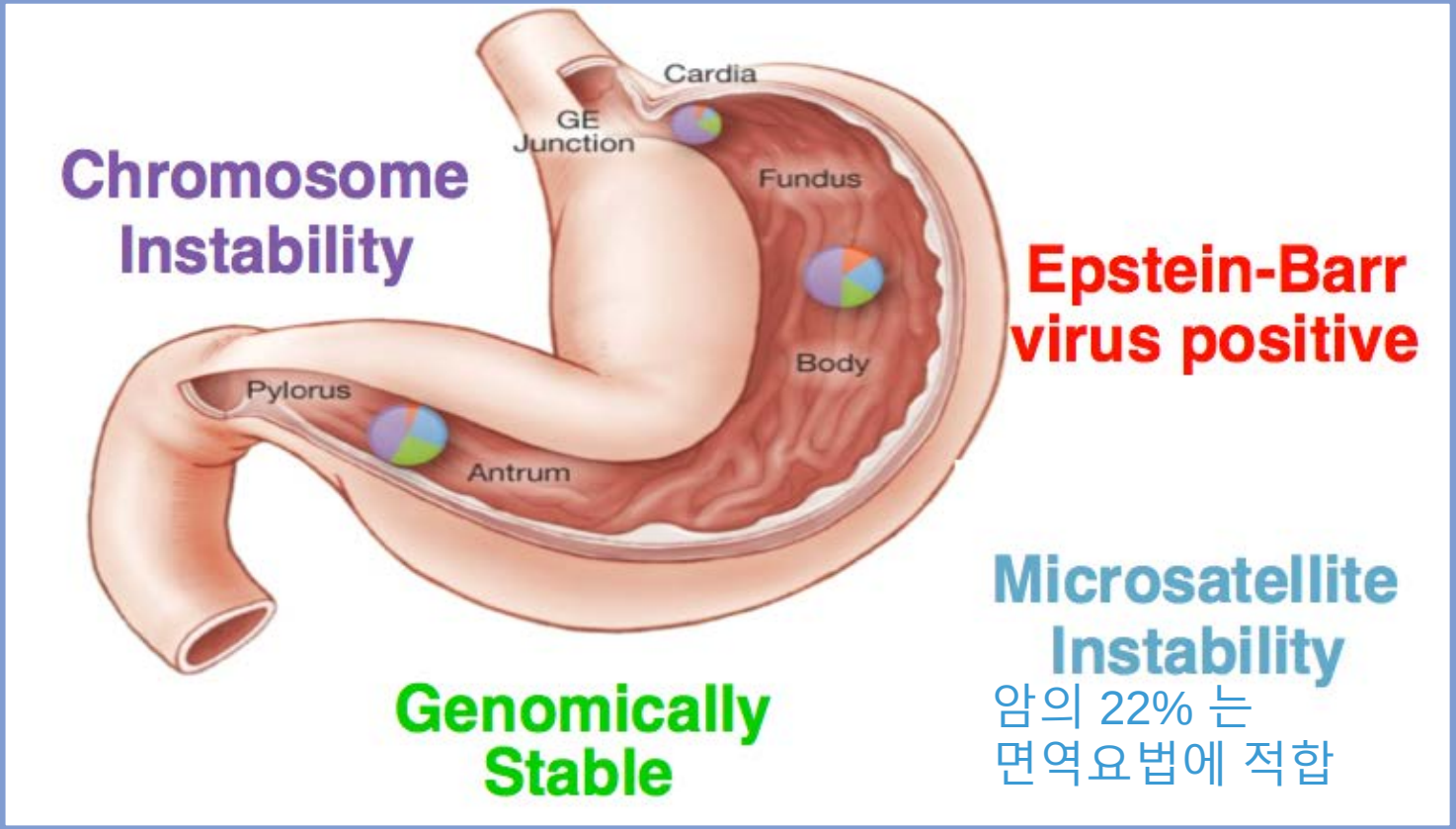
유전자 검사결과에 의해 진행되는 실험적 요법

위암의 네가지 분자생물학적 분류



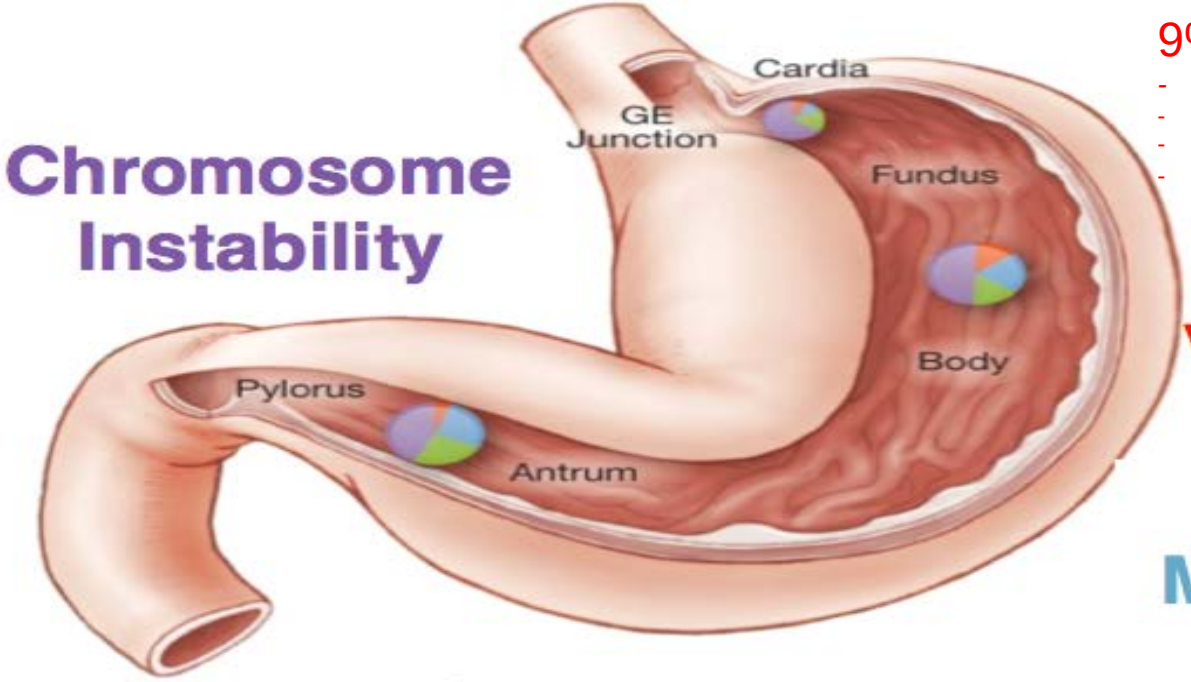
Bass AJ for The Cancer Genome Atlas (TCGA), *Nature*, 513:202, 2014

Four Molecular Subtypes of Gastric Adenocarcinoma



Bass AJ for The Cancer Genome Atlas (TCGA), *Nature*, 513:202, 2014

Four Molecular Subtypes of Gastric Adenocarcinoma



Chromosome Instability

9% of cancers,

- *PIK3CA* mutation
- *JAK2* amplification
- hypermethylation
- immune response gene dysregulation (PD-L1/2)

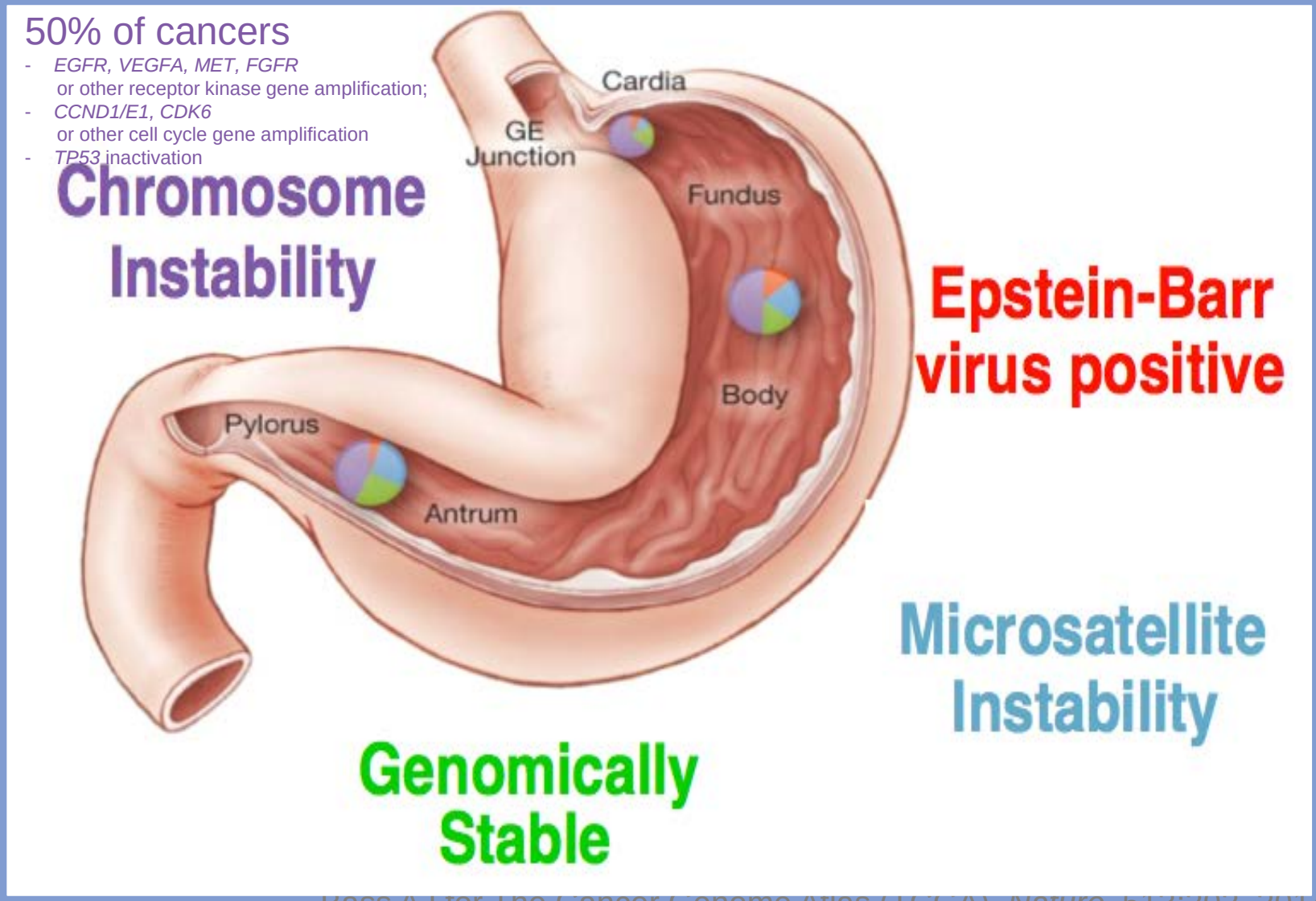
Epstein-Barr virus positive

Microsatellite Instability

Genomically Stable

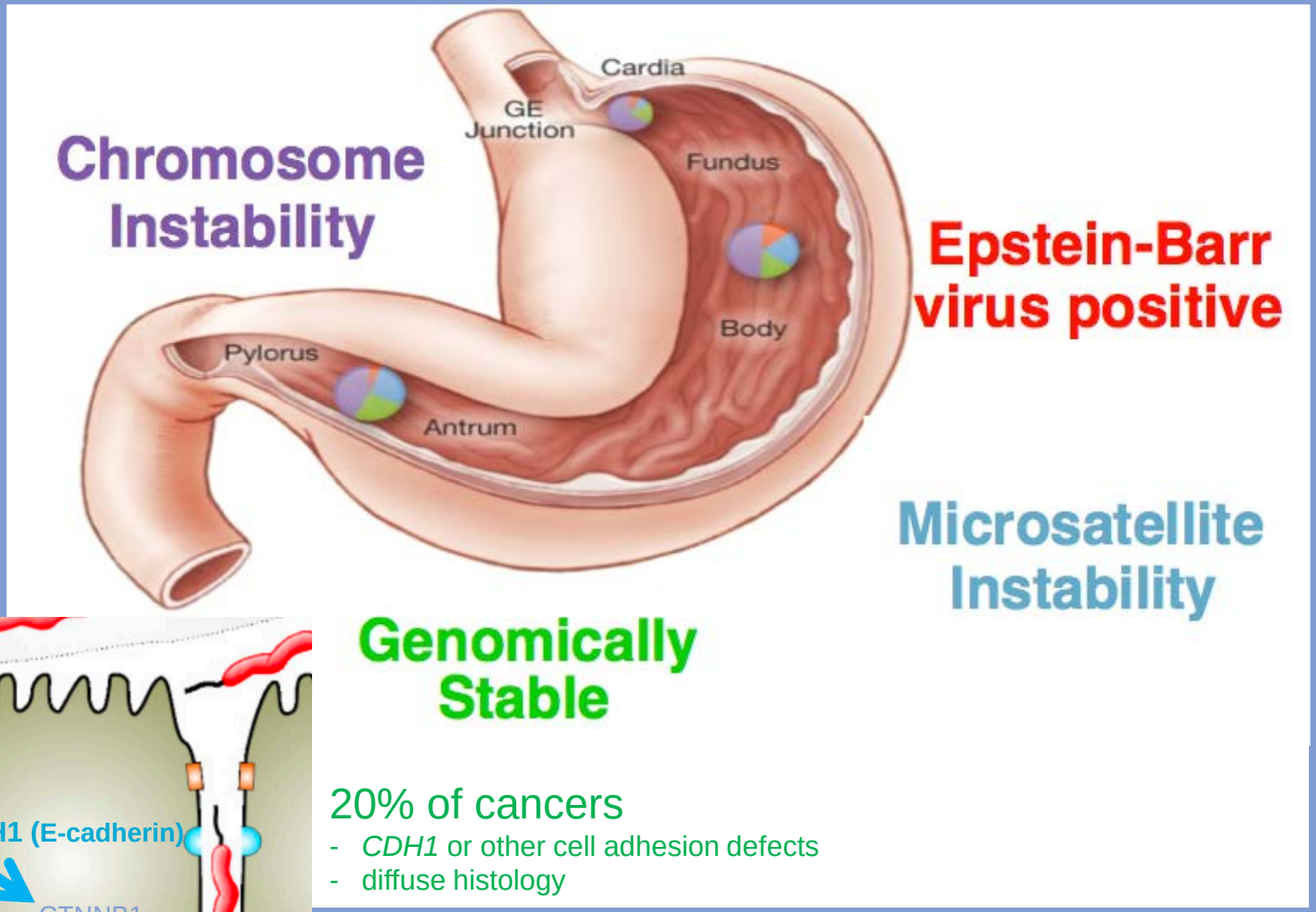
Bass AJ for The Cancer Genome Atlas (TCGA), *Nature*, 513:202, 2014

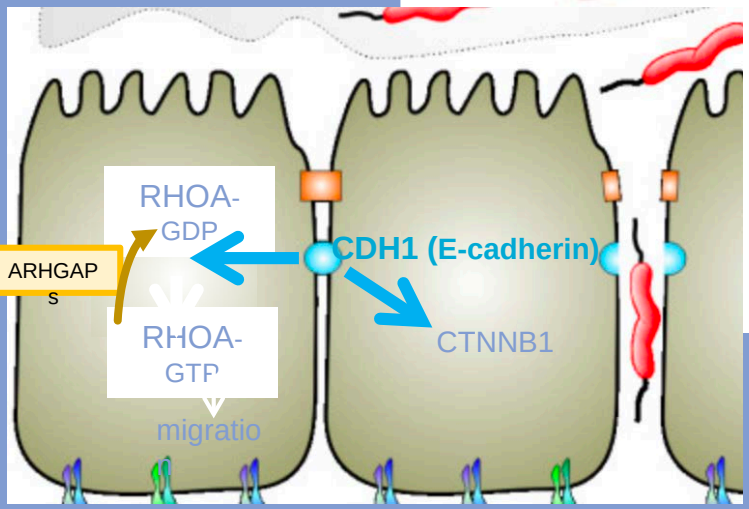
Four Molecular Subtypes of Gastric Adenocarcinoma



Bass AJ for The Cancer Genome Atlas (TCGA), *Nature*, 513:202, 2014

Four Molecular Subtypes of Gastric Adenocarcinoma



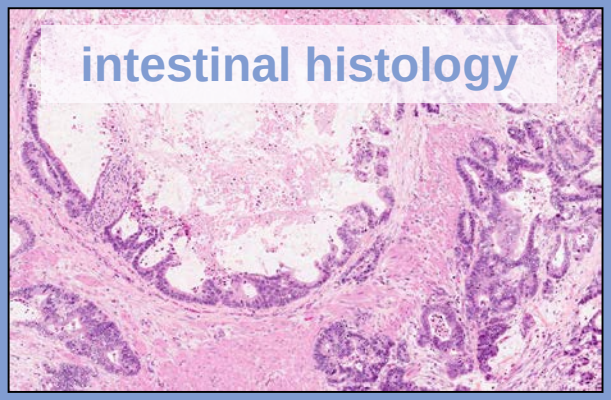


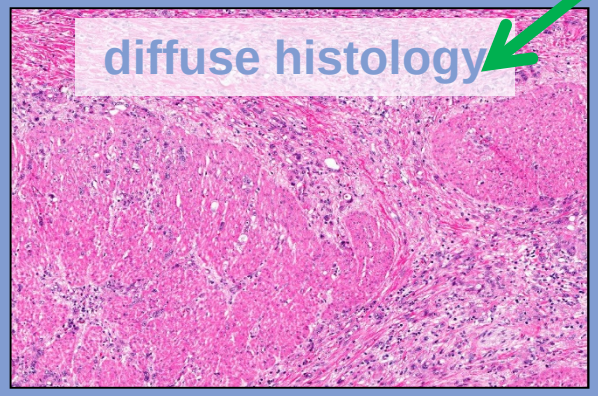
20% of cancers

- *CDH1* or other cell adhesion defects
- diffuse histology

Bass AJ for The Cancer Genome Atlas (TCGA), *Nature*, 513:202, 2014

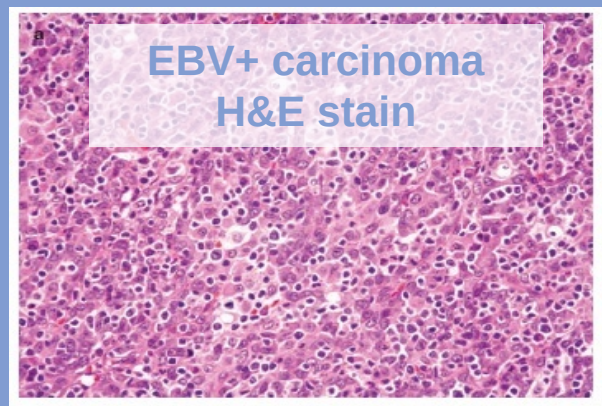
위암의 조직학적 분류

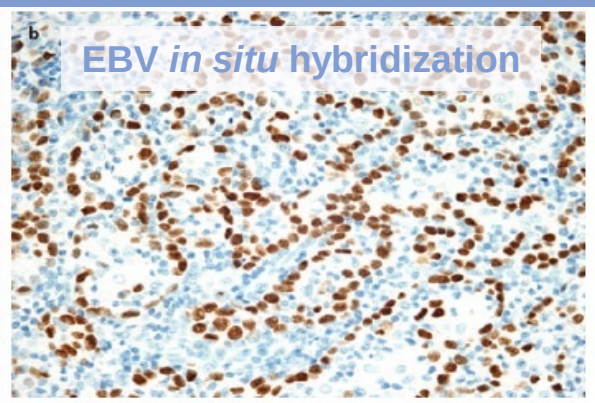




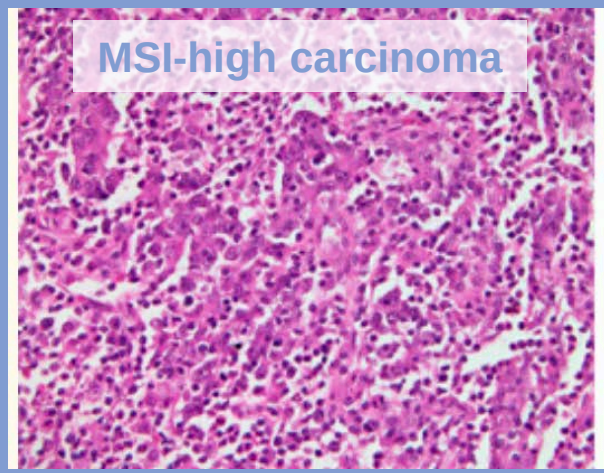
'Genomically Stable', Infiltrating single cells, cell adhesion defects

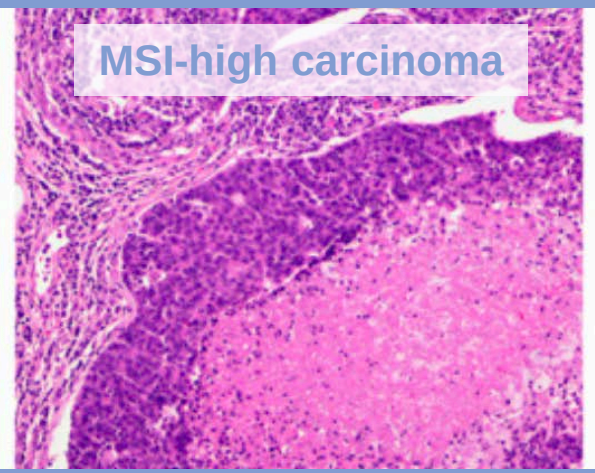
현미경





엡스타인-바 바이러스 분류





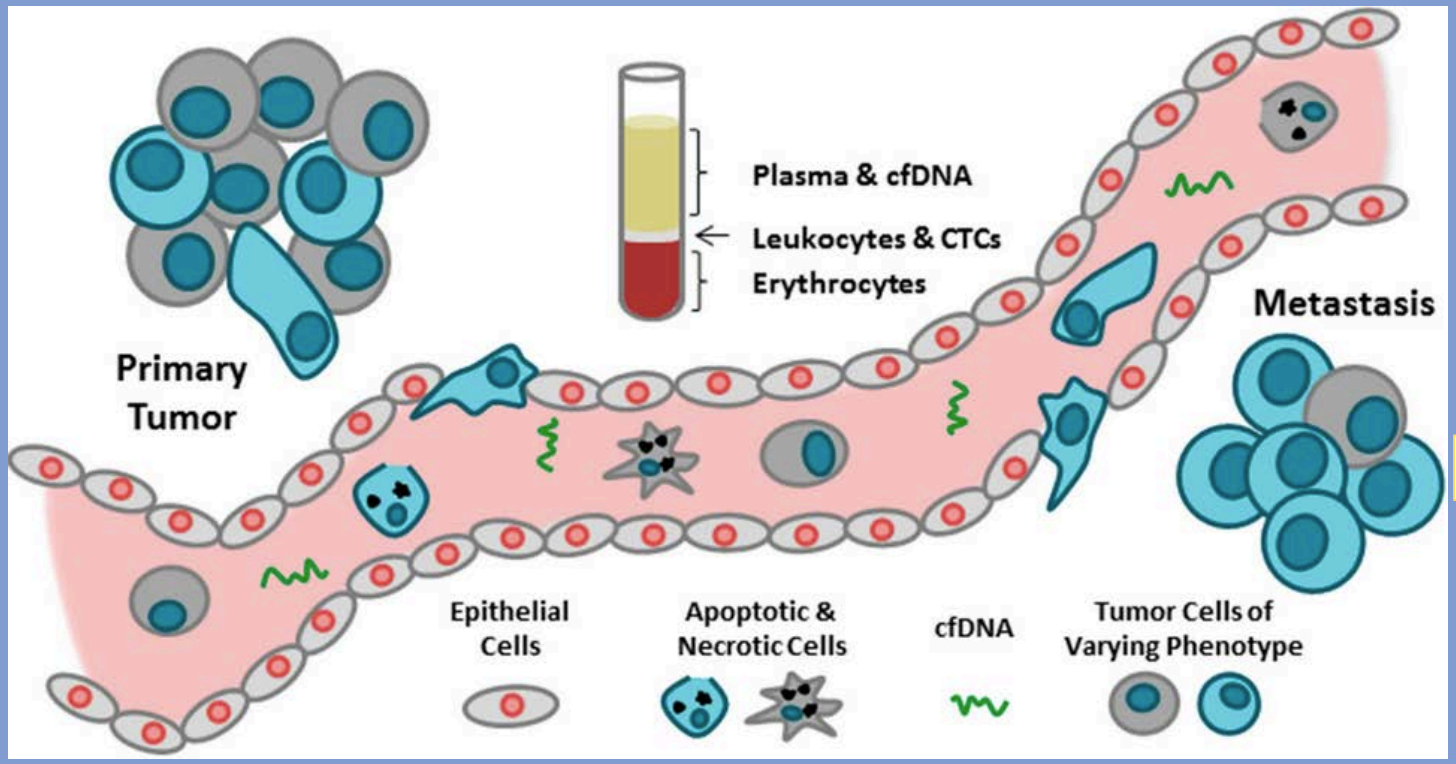
마이크로새틀라이트 불안정성 분류

PMID: 26371427

암치료의 효능 모니터링

혈액중의 셀 프리 유전자는 시스테믹한 암 유전자형을 나타낸다

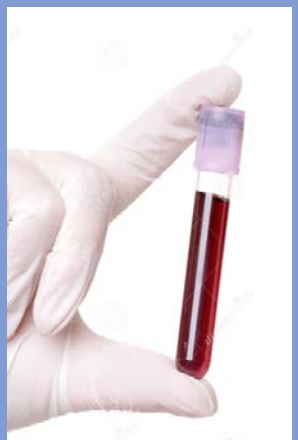
1차 암



전이된 암

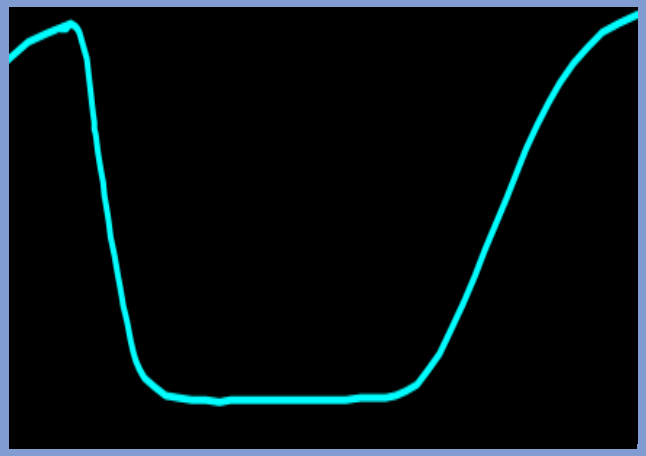
Lowes LE et al, *Int J Mol Sci* 2016, 17: 1505

혈액돌연변이 패널은 암의 유전자형을 알고 있는 환자를 모니터하는데 쓰임



Input: 10mL blood

- 암치료의 효능을 모니터; 재발여부를 예상
- 약 저항성 돌연변이를 탐지
- 체세포변이체에서 생식세포를 구분해 냄



암예방

위암의 가족력
(암환자 5-10% 가 해당)

Hereditary diffuse gastric cancer (*CDH1*)
Lynch (*MLH1, MSH2, MSH6, PMS2, EPCAM, MUTYH)*
Juvenile polyposis (*SMAD4, BMPR1A*)
Peutz-Jeghers (*STK11*)
Familial adenomatous polyposis (APC)

Li-Faumeni (*TP53*)
Cowden (*PTEN*)
Ataxia telangiectasia (ATM)
Bloom (BLM)
Breast and Ovarian Cancer (BRCA1/2)
Xeroderma pigmentosum (7 genes)

Inquire about cancer predisposition syndromes when cancer occurs below age 50, or when other blood relatives also have cancer

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018
Gastric Cancer

암환자에 대한 유전자 검사의 향후 활용가능성

고위험군 환자를 알아냄
암의 조기 발견
치료법에 대한 반응을 예측
치료 진행중 암상태를 모니터

요 약

위암치료(HER2 억제제, 면역요법)는 유전적상태의 영향을 점점 다 많이 받는다

유전자검사를 이용하여 바이러스, 박테리아, 인간유전자를 특성화하는 것이 가능해졌다

유전적 분석은, 연속된 혈액샘플을 통해 암치료의 효능을 모니터할 수 있는 암표적을 밝혀낼 수 있다

Thank You to colleagues at University of North Carolina & Lineberger Comprehensive Cancer Center

노스 캐롤라이나
위암교육 심포지엄

궁금한 점?