

맞춤 치료와 검사의학





검사 결과

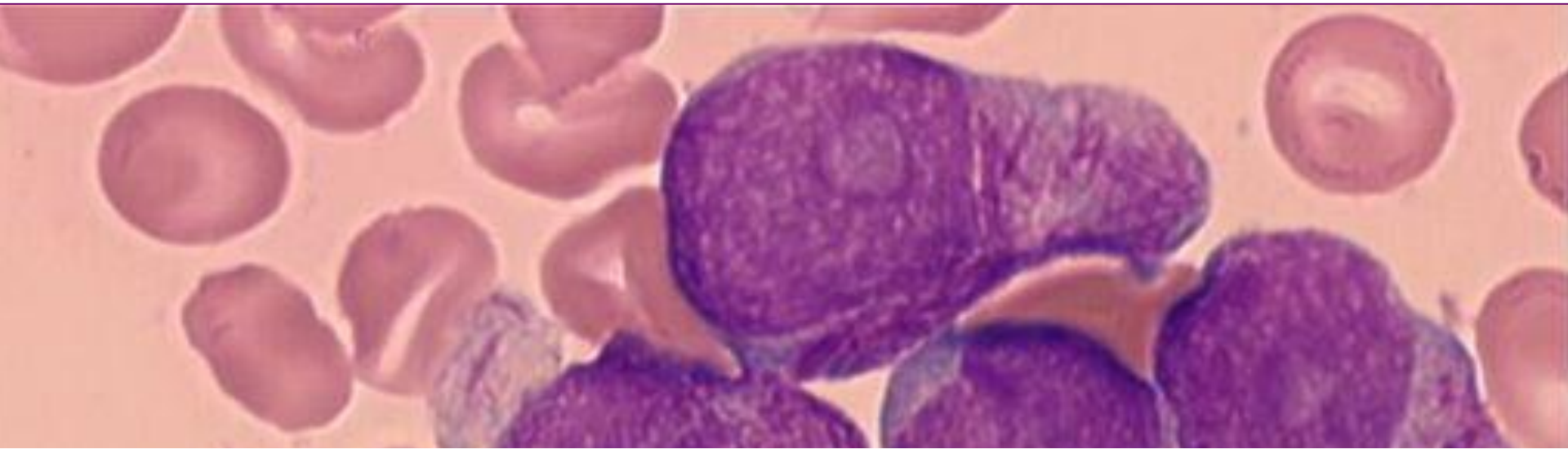
**Hallmark of
Diagnosis**

**Tailored
Treatment**

맞춤치료

Tailored treatment

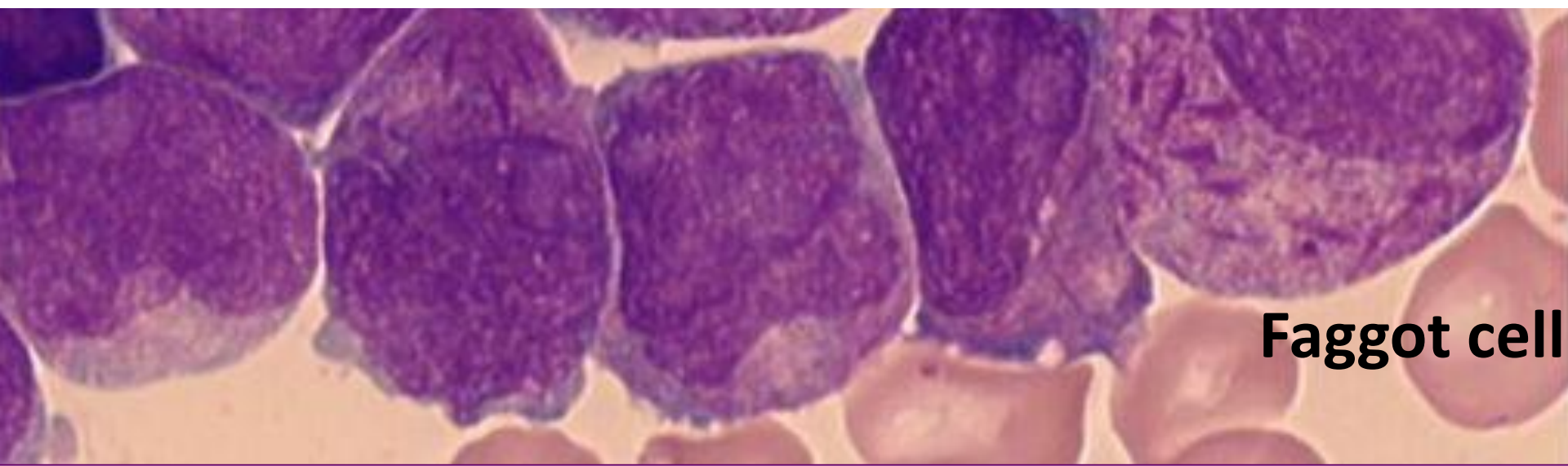
두가지 의미



T(15;17)

PML/RARA

Acute promyelocytoc leukemia M3



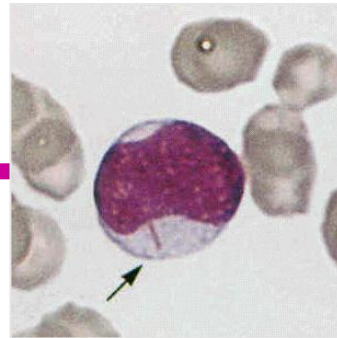
Faggot cell

Acute Promyelocytic Leukemia

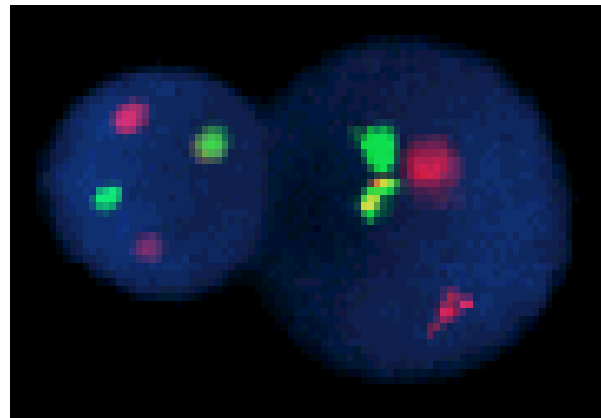
맞춤치료가 가능하다

ATRA

T(15;17)



T(11;17)



응급 t(15;17)
PML/RARA FISH

맞춤 치료

두번째 의미

위험도가 높은 사람
조기환자 발굴 및 예방
차별화된 치료

선천성

암/백혈병

감수성 유전자



똑같은 유전자 변이
다양한 임상 양상



**환경
후성 유전학
스트레스
영양상태
면역반응 능력xa**



유전적 성향

타고난 성향

살다보니.. 생김

타고난...

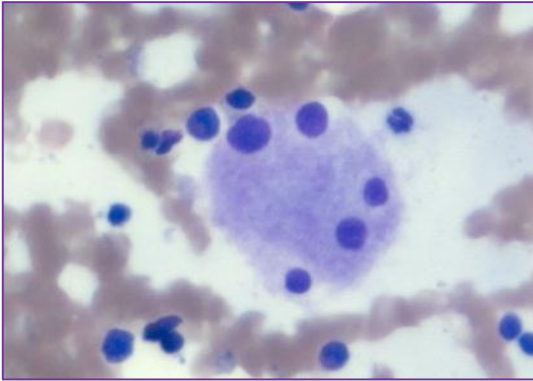
- 유전자 투과도
- 장기에 따라
- 환경에 따라

백혈병감수성 유전자

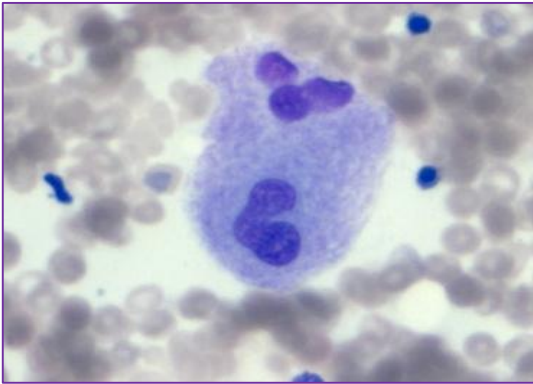
- 매우 높은 백혈병 위험도
- 조기 검색이 중요
- **Genetic counselling:** 가족상담
- 가족 검진
- **WHO 2016 beyond:** 고행암에도.

증례: Genetic predisposition

- 17/F
- 8.7-3500-40K
- 환자골수: MDS
- 여자형제: Dysmegakaryopoiesis
- *GATA2* mutation
- 골수이식공여자: unrelated



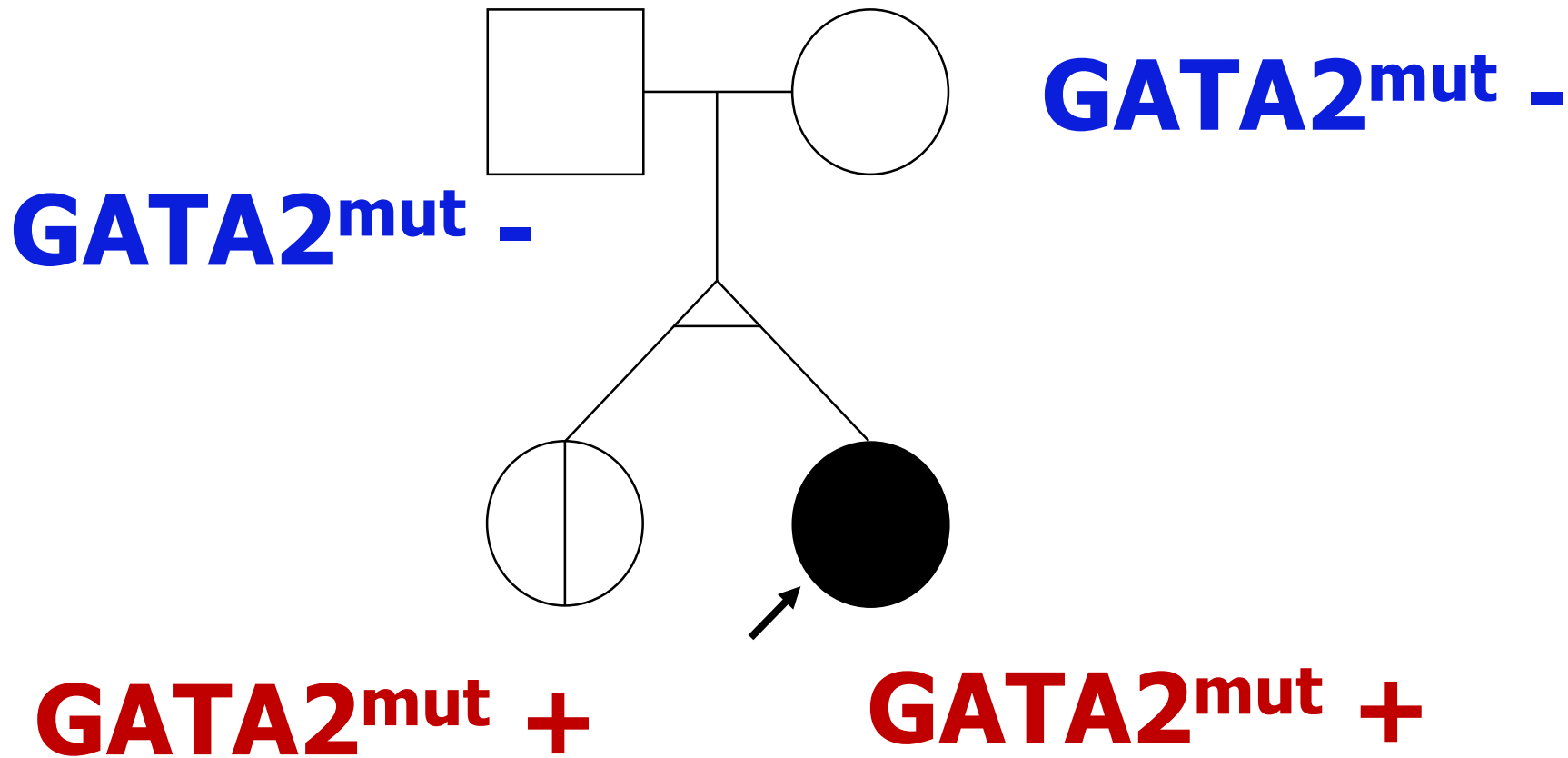
언니
**Dysmegalakaryopoiesis
only**



부모

CBC : 15.3 g/dL – 5550 / μ L – 214K / μ L

CBC : 11.1 g/dL – 4100 / μ L – 254K / μ L



같은 유전자변이를 지녀도

소아에서 발병

성인에서 발현

양상이 다름

Telomere

유전자돌연변이

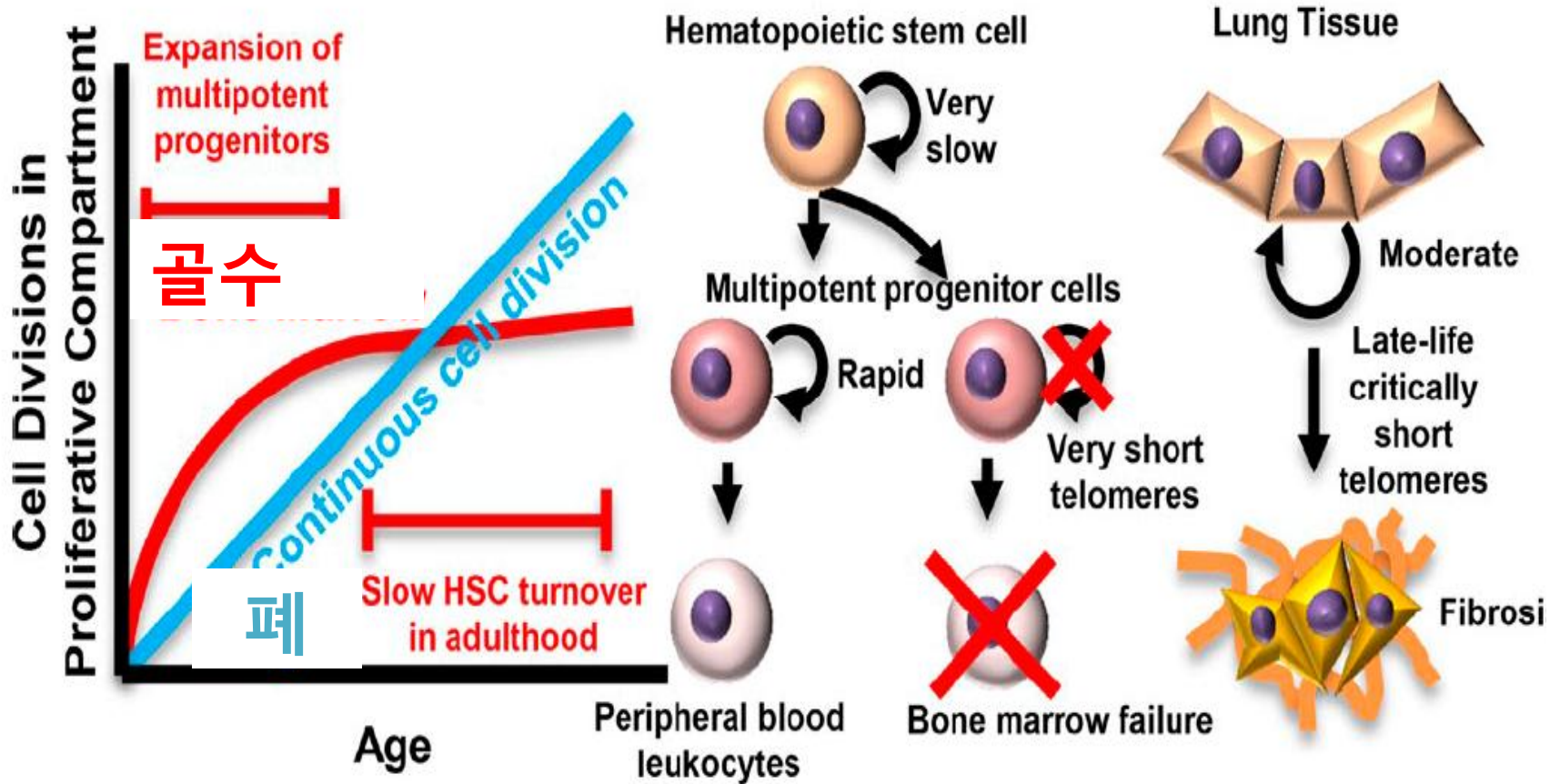
소아

선천성 골수부전

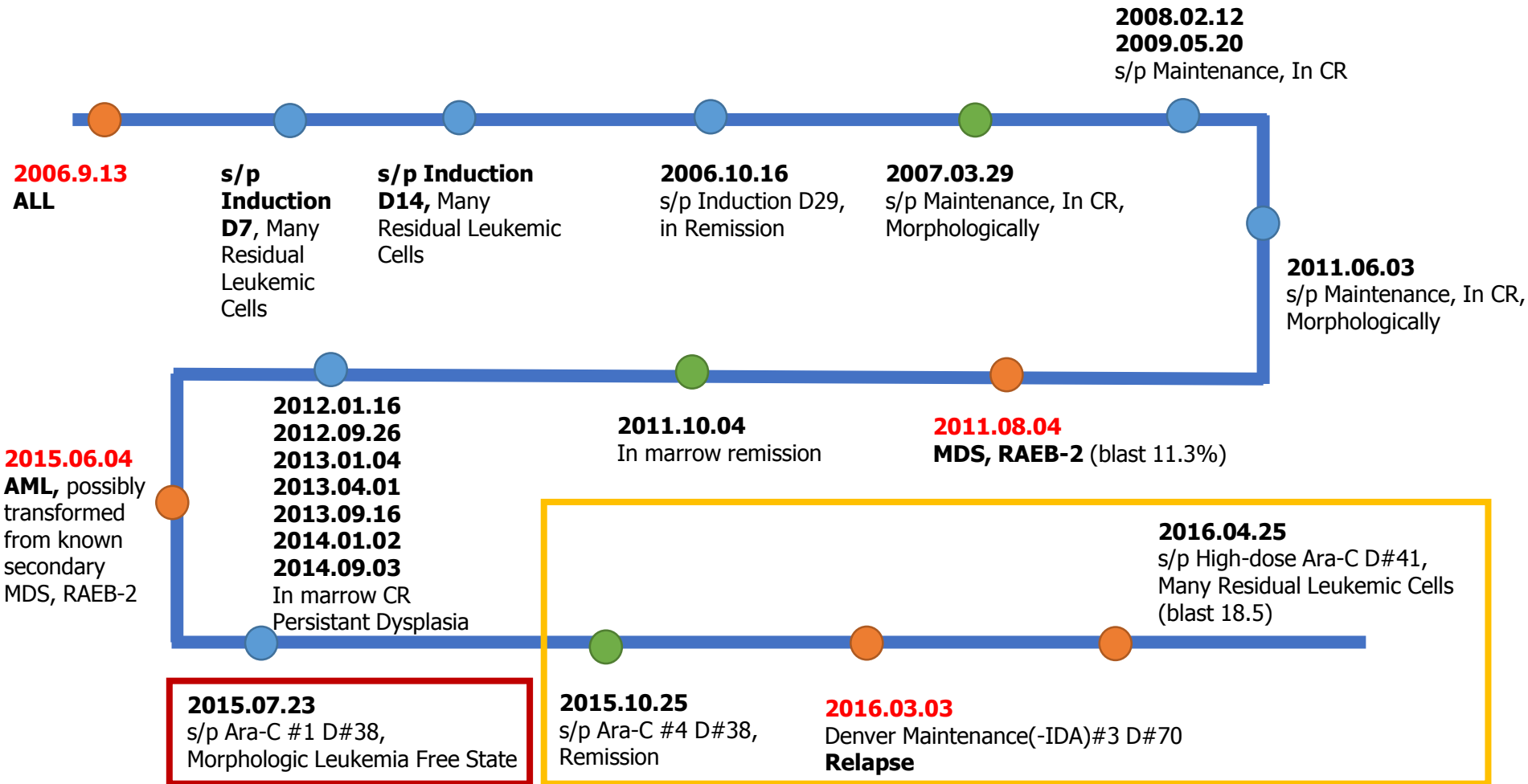
성인

폐섬유화증

Telomere 짧아지는 속도: 장기별로 다르다



BM study X22, 송 **



선천성 감수성 to 골수성백혈병

소아

선천적 변이

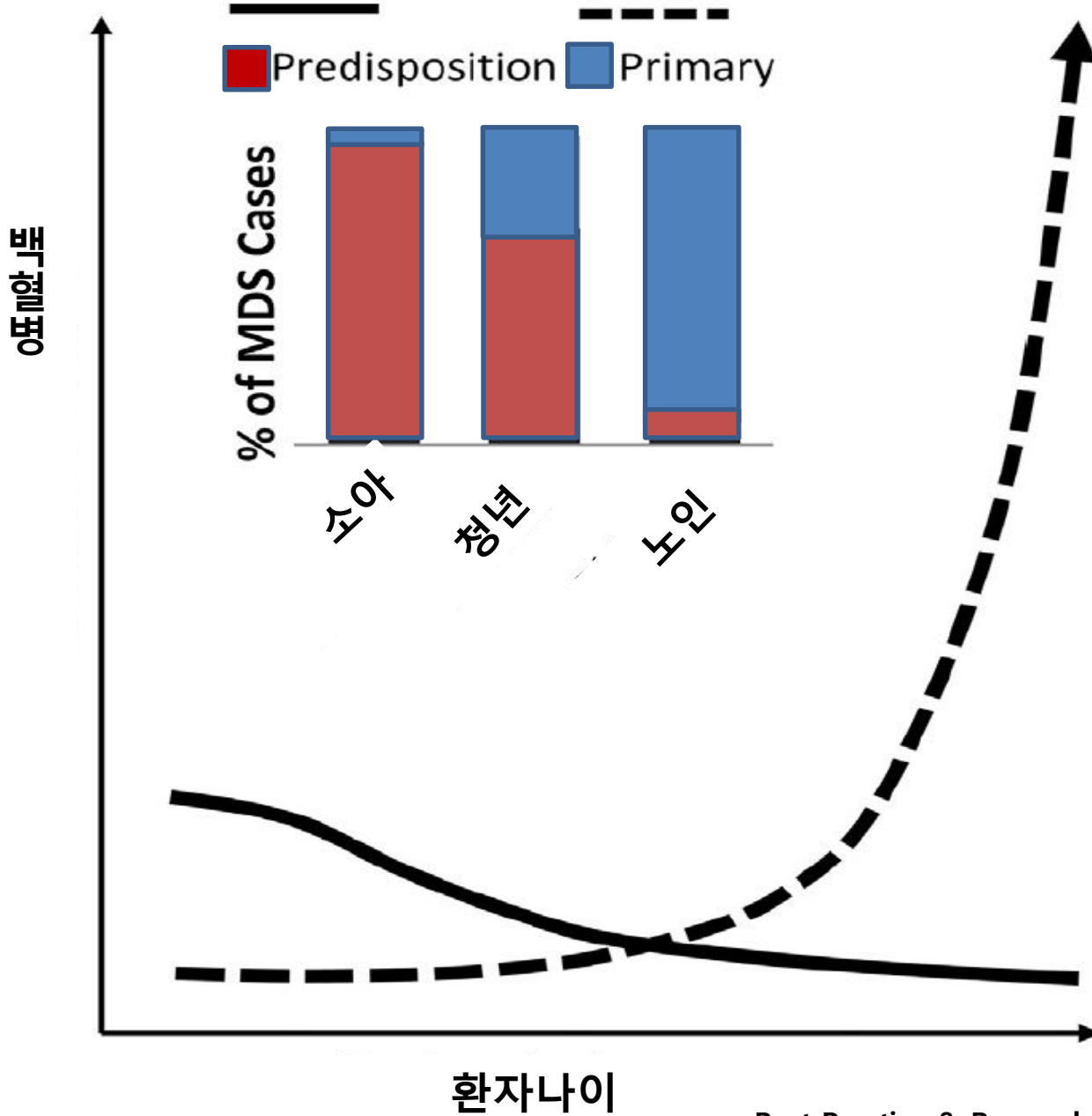
성인

후천적 변이

+

배경- 선천적

요인



New Game

Settings

Instructions

About

Player 1

Player 2



Turns

Rounds

Score

Score

Rounds

Turns

1

0

0

0

0

0

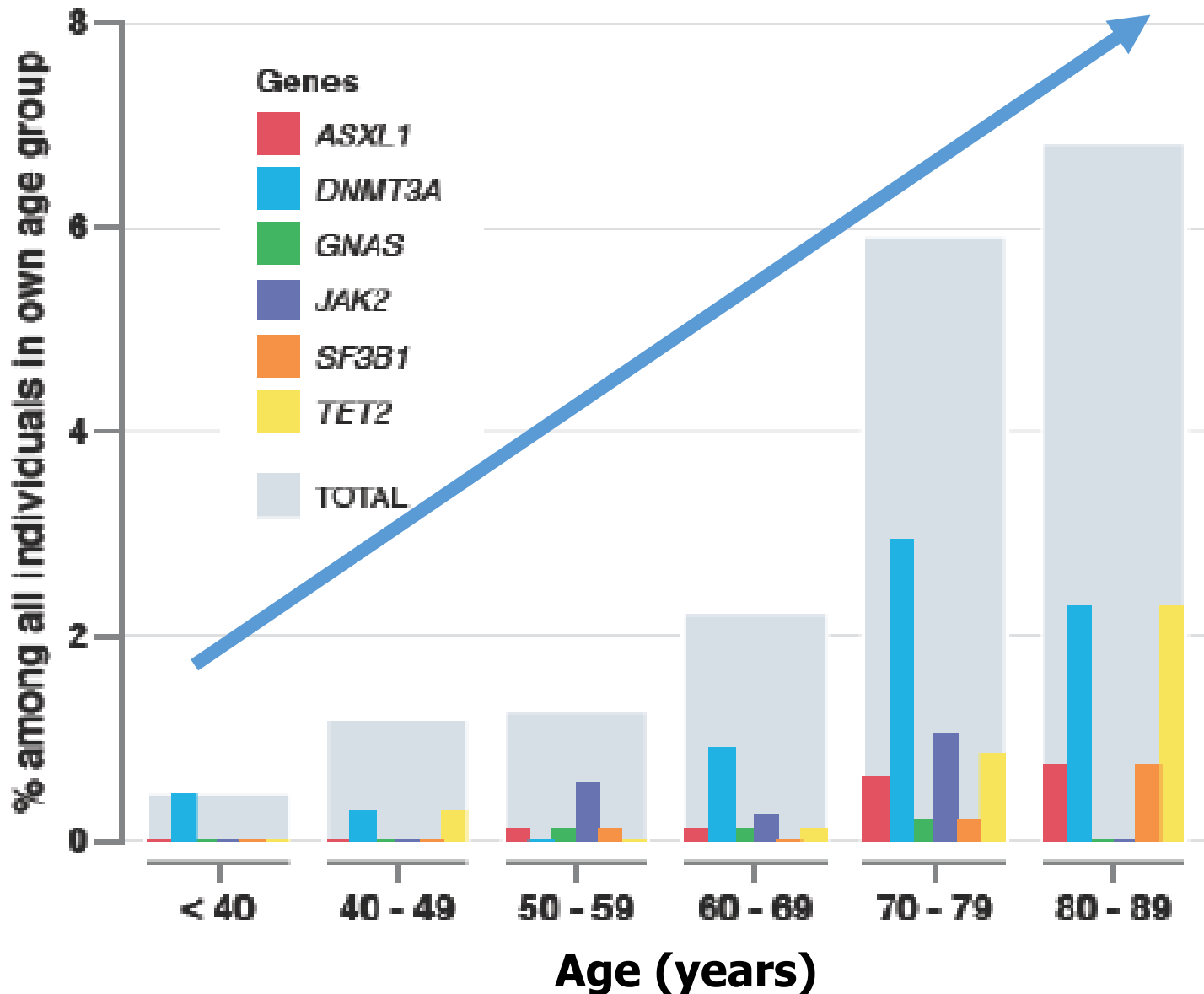


성인

**두종류의
돌연변이**

고령: 의미를 알수 없는 돌연변이

2014 nature medicine



살다보니 생긴
유전자돌연변이

≠ Neoplasm

High probability
for cancer development

정상인에도

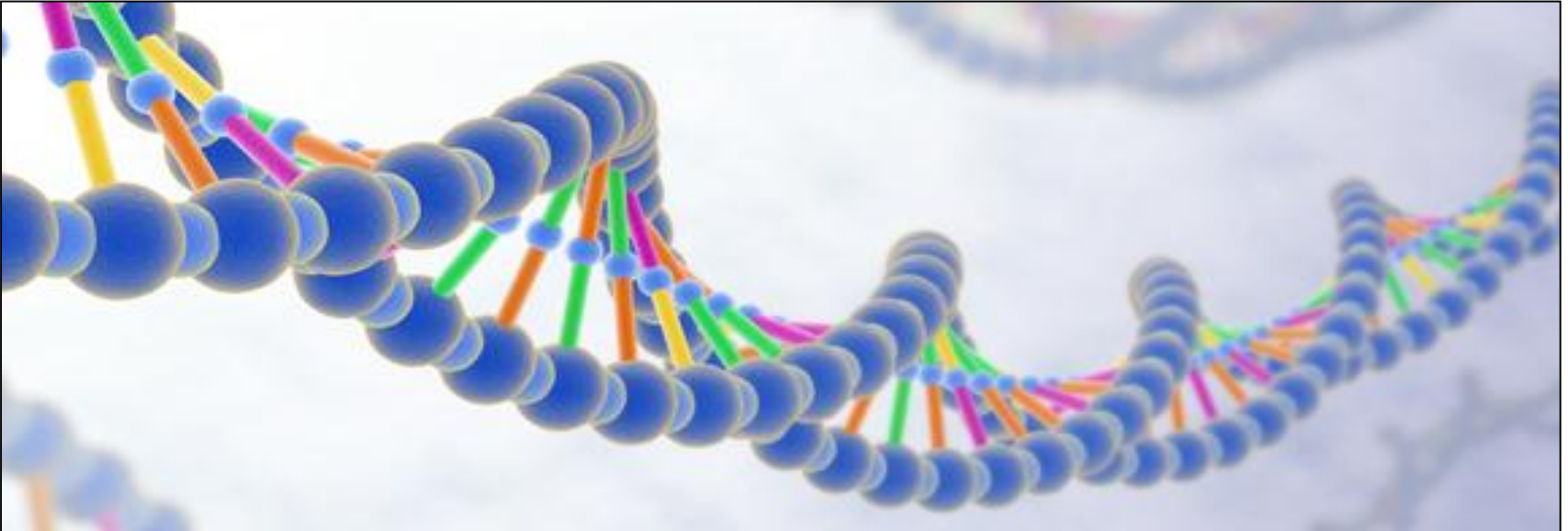
돌연변이는 존재

Susceptibility gene

찾아내고

의미를 부여하는

CAP Hereditary Cancer Syndrome



**Identifying and Communicating Risk for
Hereditary Cancer Syndromes**

유전성 암 증후군

Hereditary Cancer Syndrome

가족성 암

Familial Cancer

2016 WHO classification, revision

Germline

Predisposition

백혈병
고형암

AML WHO 분류: 유전자 중심의 분류

AML **t(8;21)** *AML1/ETO*

AML with abnormal BM eosinophils

inv(16) or **t(16;16)(p13;q22)** *CBFb/MYH11*

APL (AML with **t(15;17)** *PML/RAR α*

AML with **t(9;11)** *MLLT3-MLL*

AML with **t(6;9)**

AML with **Inv(3)**

AML with **t(1;22)**

AML with mutated **NPM1**

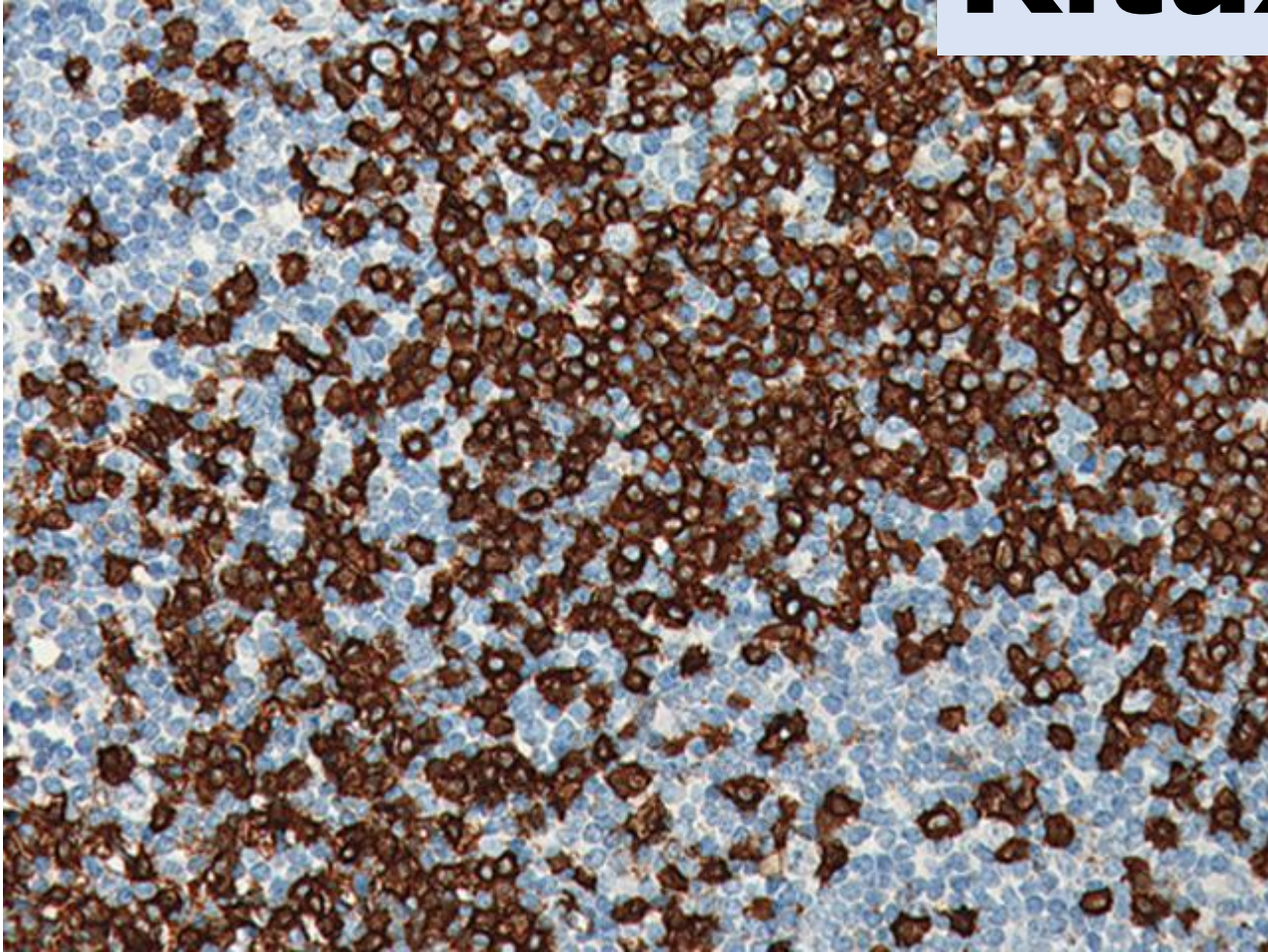
Aml with mutated **CEPBA**

맞춤치료를 위한 검사법

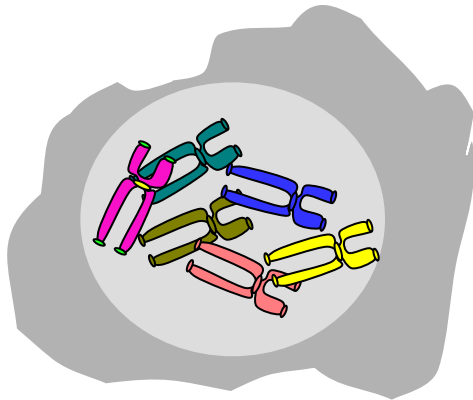
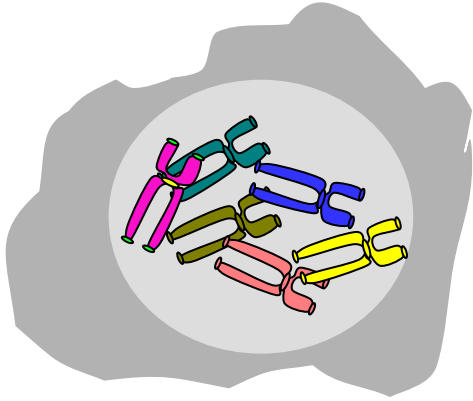
- 분자유전
- 염색체, FISH
- 면역화학염색: CD138, CD20
- 유세포분석

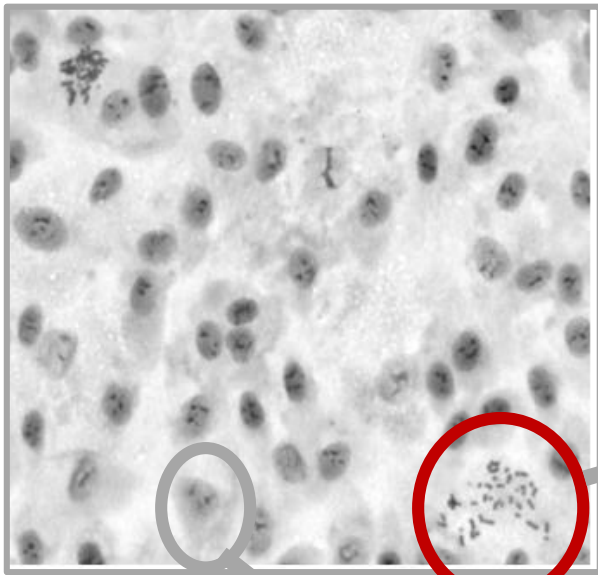
CD20

Anti-CD20 Rituximab



Conventional Cytogenetics

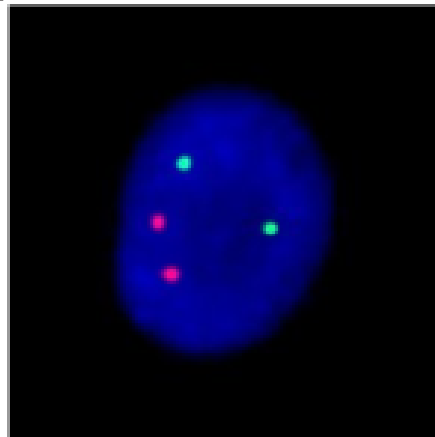




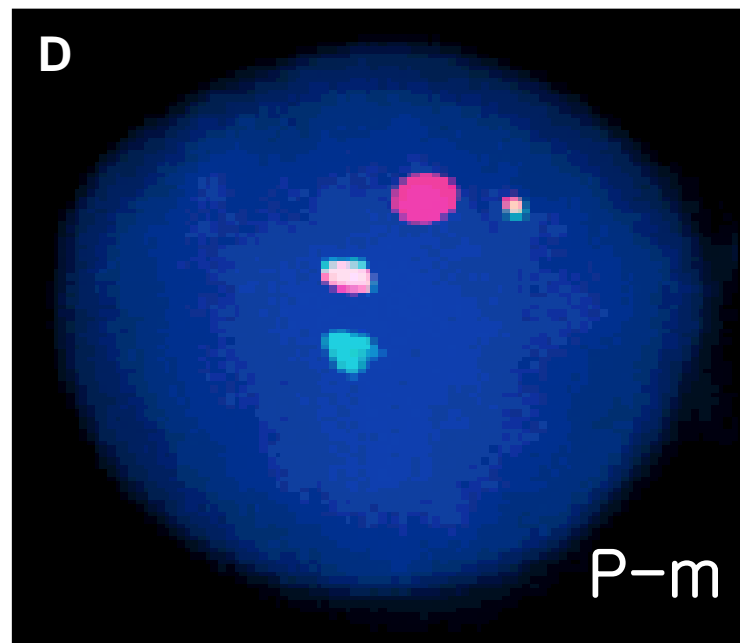
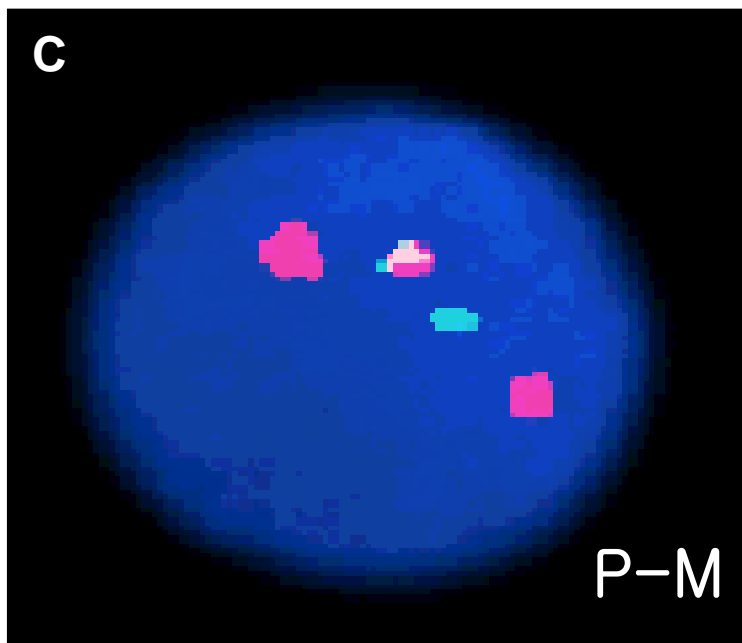
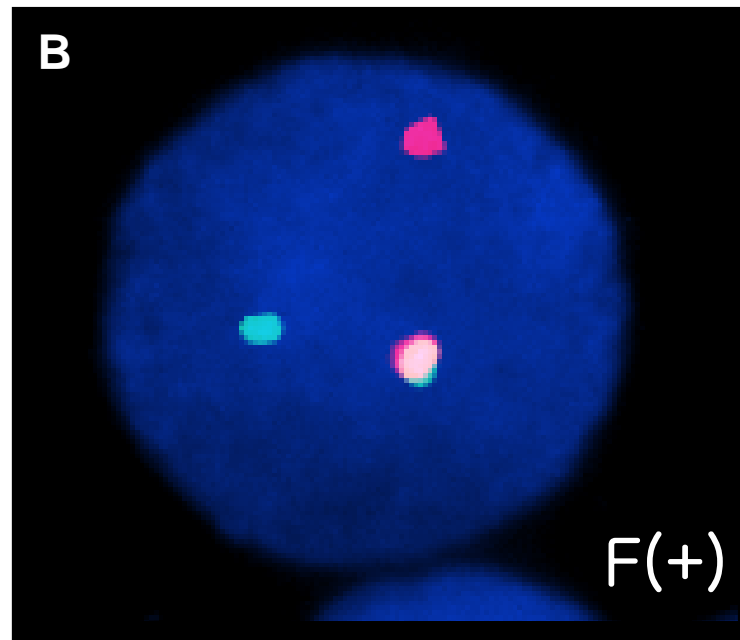
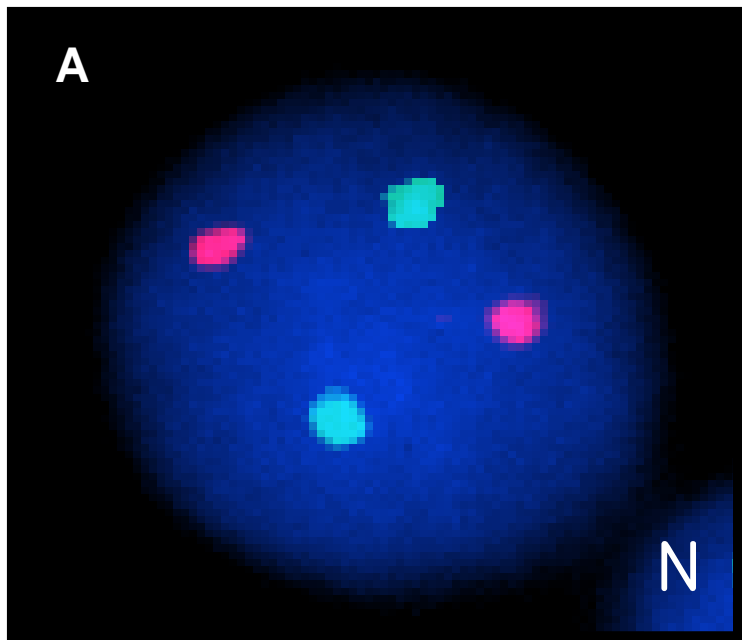
metaphase
-> karyotyping



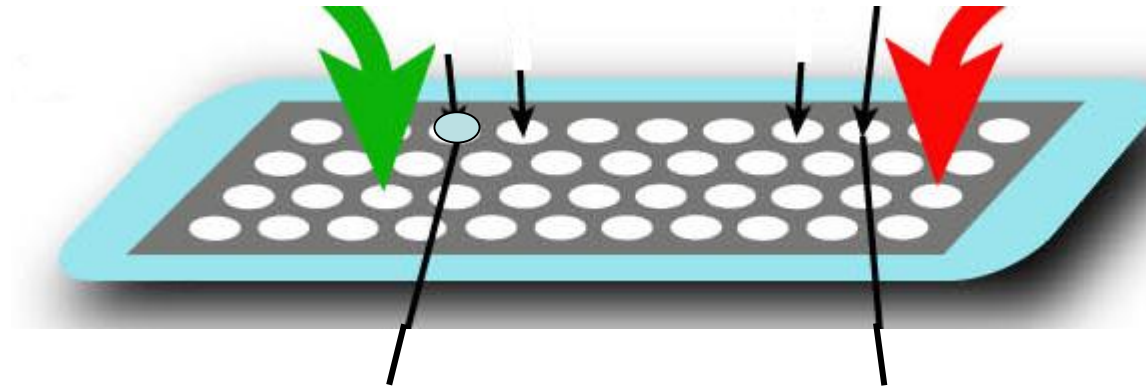
**Nucleus is enclosed with
nuclear membrane**



interphase
Each chromosome count
With FISH

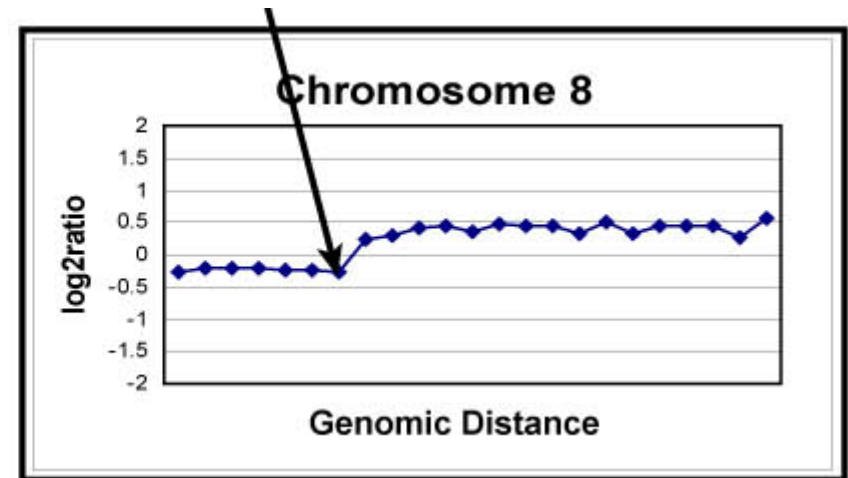
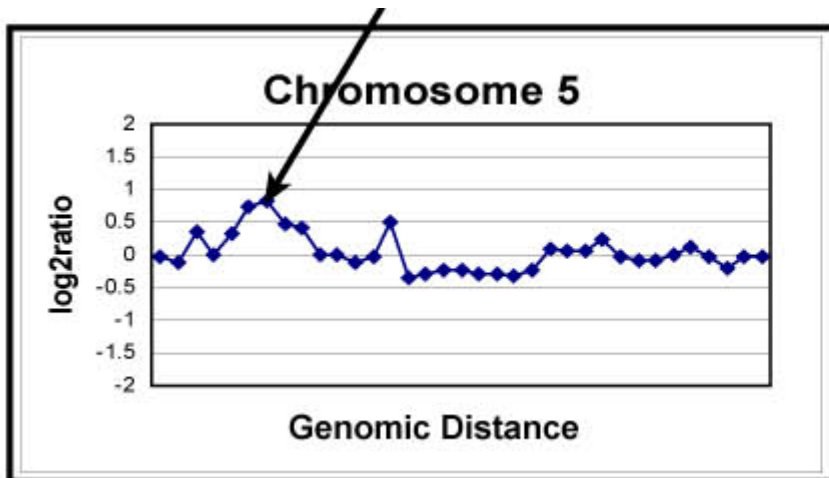


Array CGH



**copy number
increase**

deletion



2ND GENERATION
NEXT GENERATION

차세대 염기서열 분석법

**Input
DNA**

Detecting

Fragment

Sequencing

Adapter

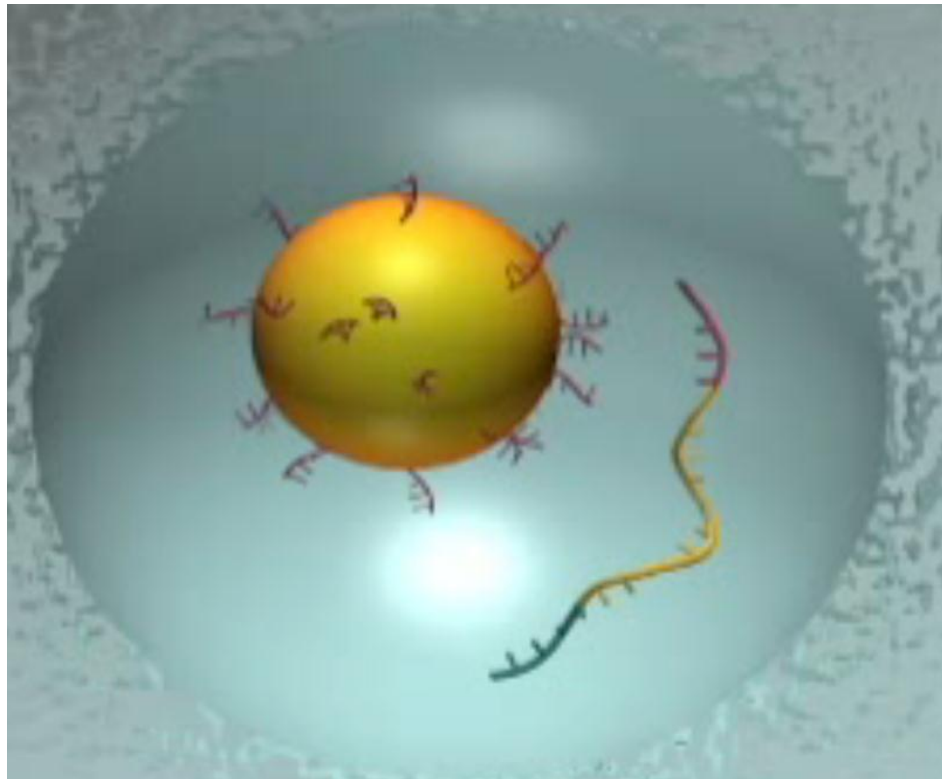
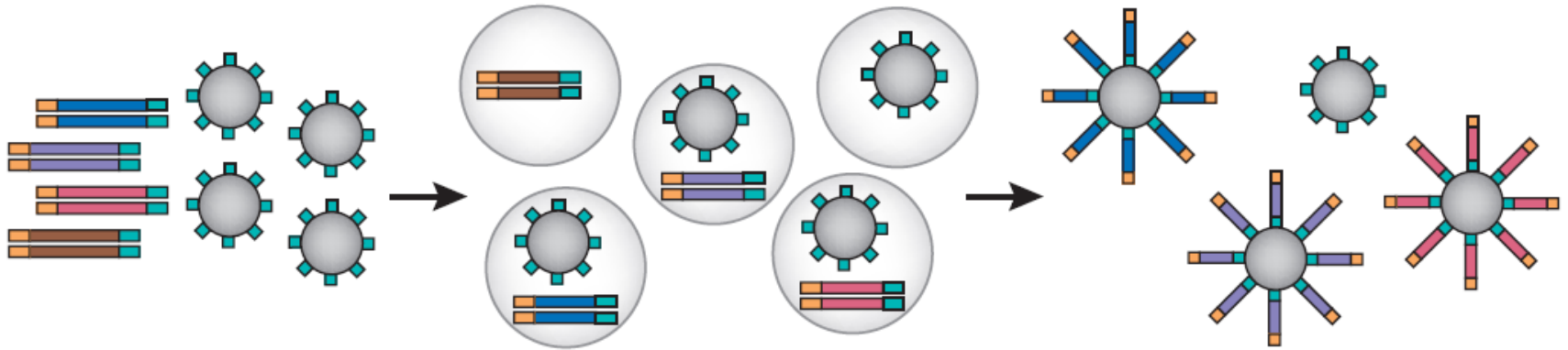
Amplify

Library preparation

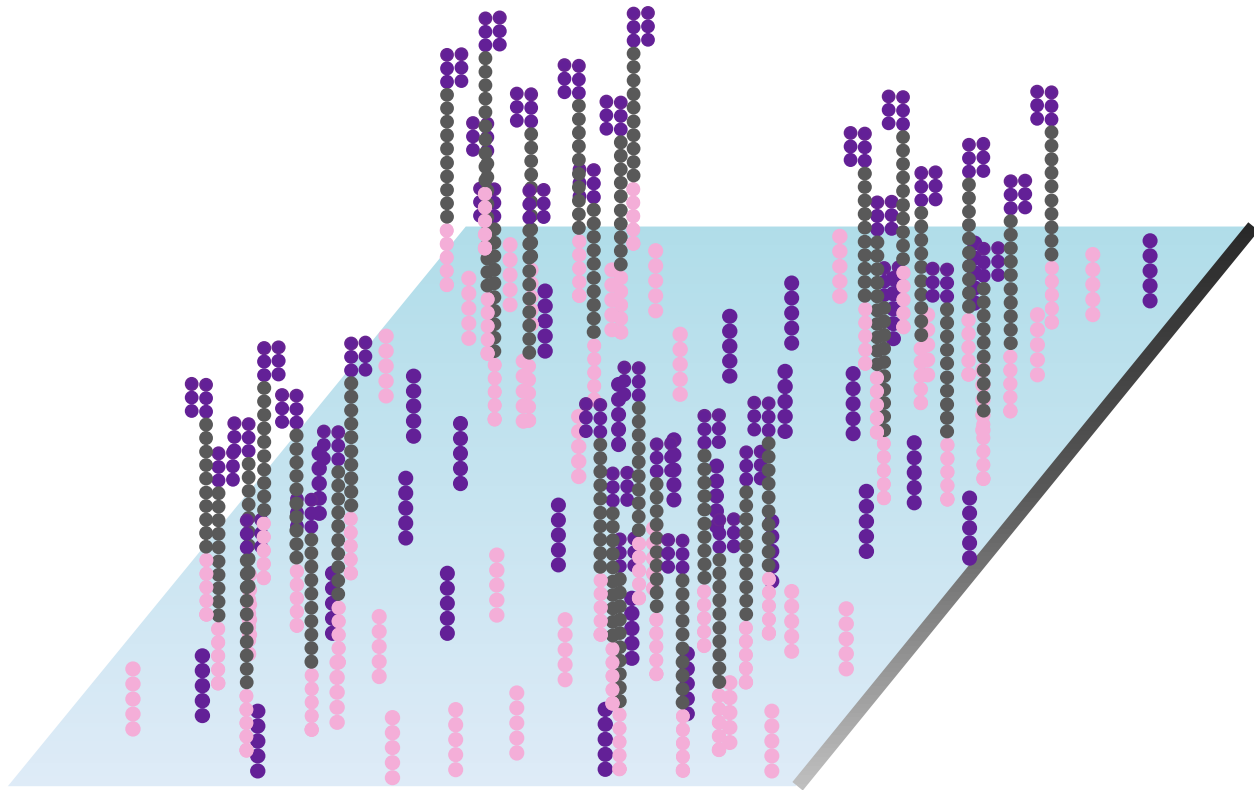
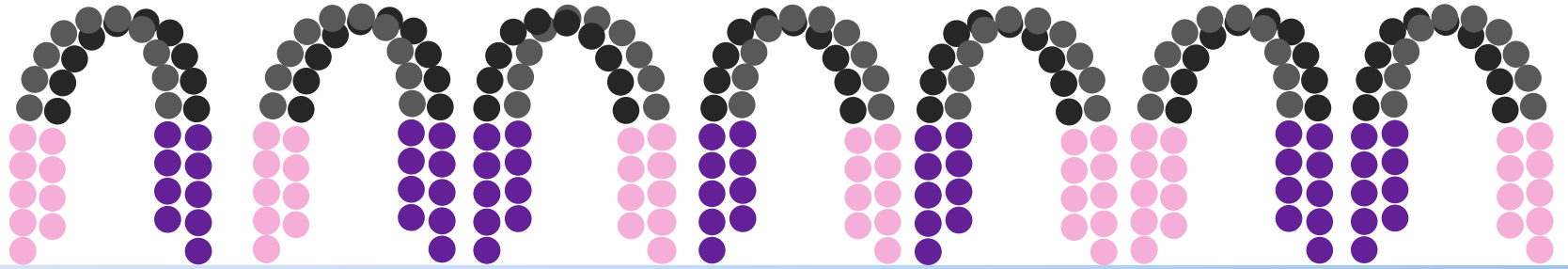


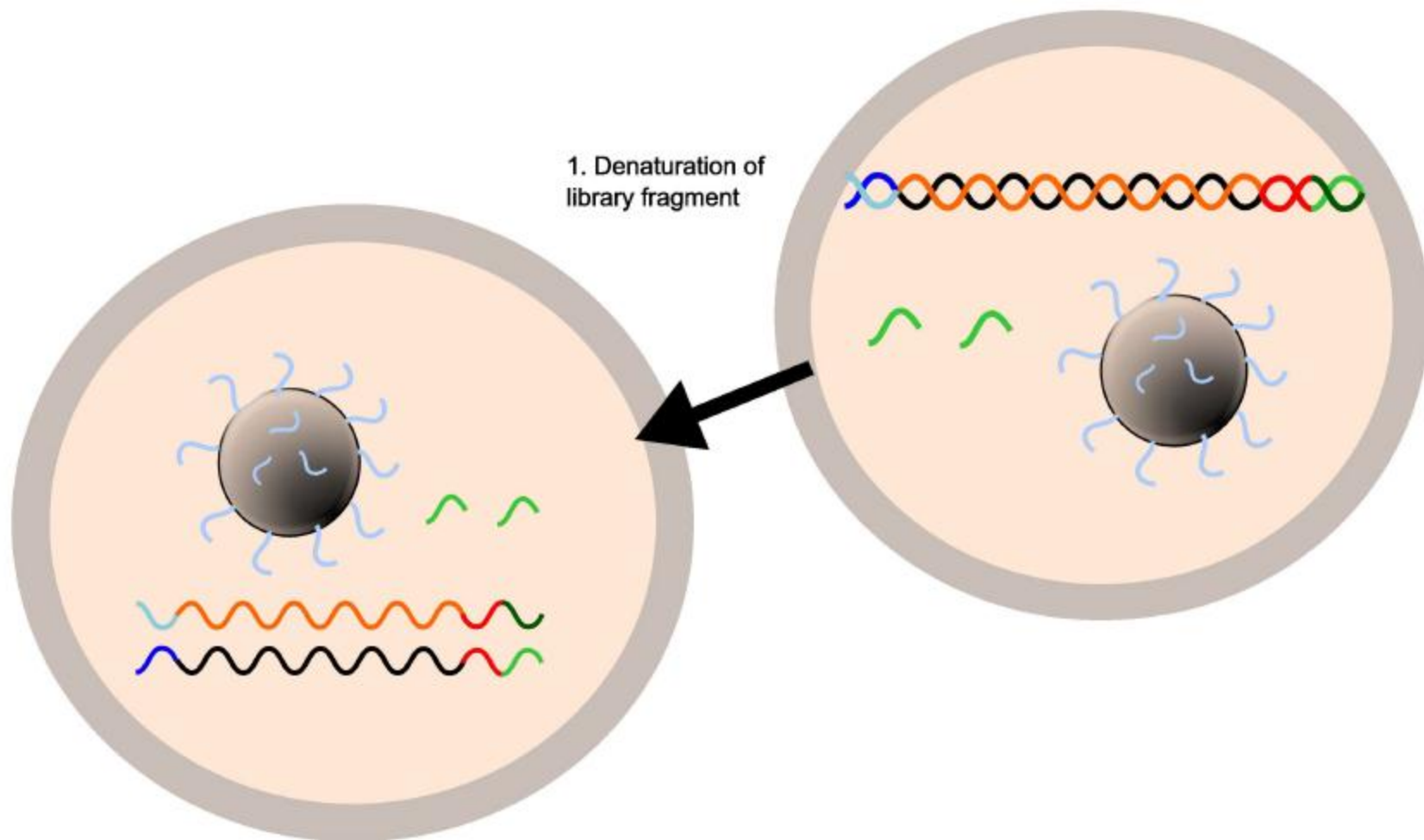
샘플 (DNA)을 무작위적으로 자른 후, 모든 조각의 양쪽 끝에 동일한 adaptor DNA 조각을 붙인다.

Emulsion PCR



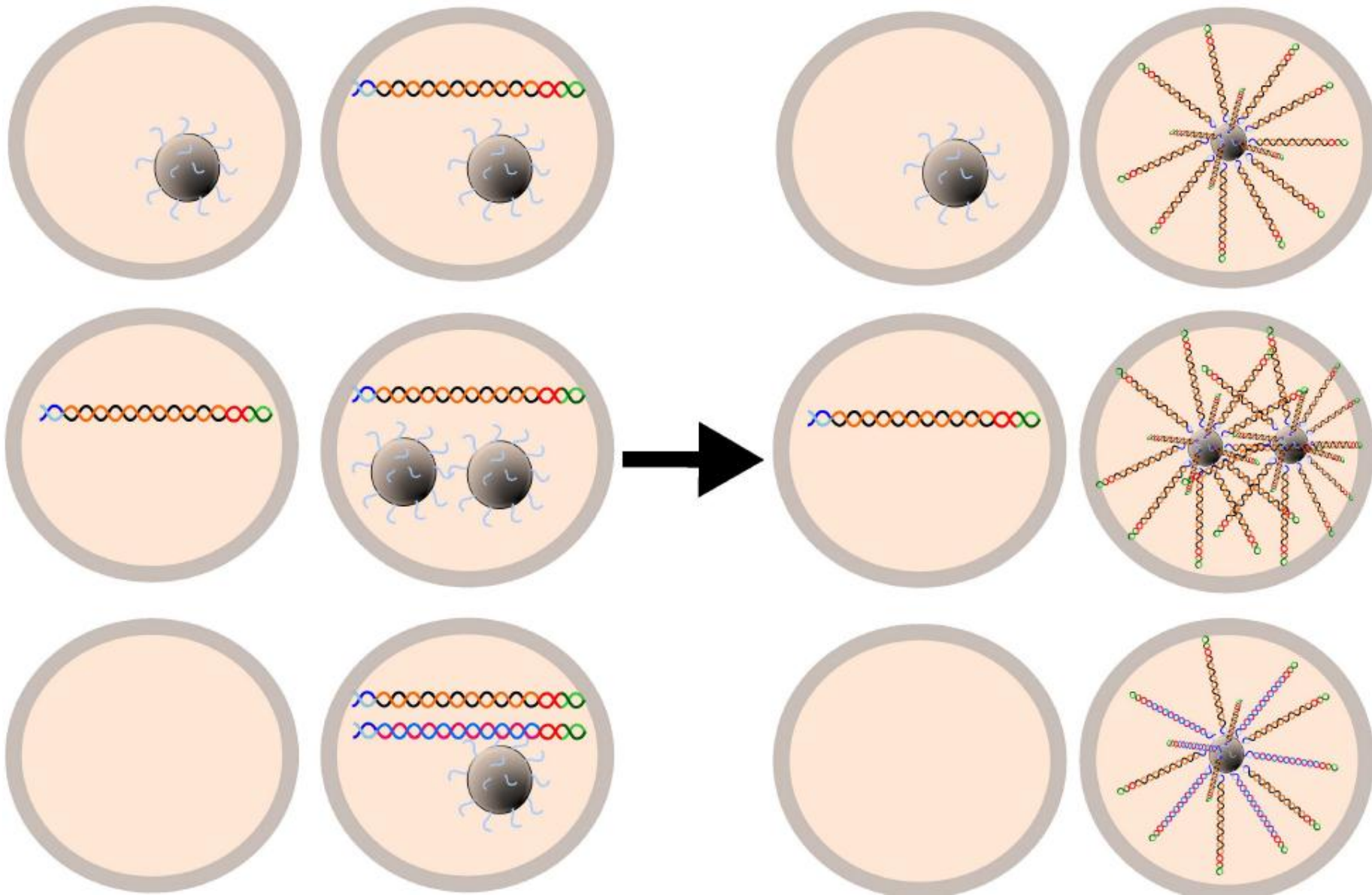
Bridge PCR





Amplified Single Molecule Sequencing Emulsion PCR

different micro reactors : only 15 % are good ones



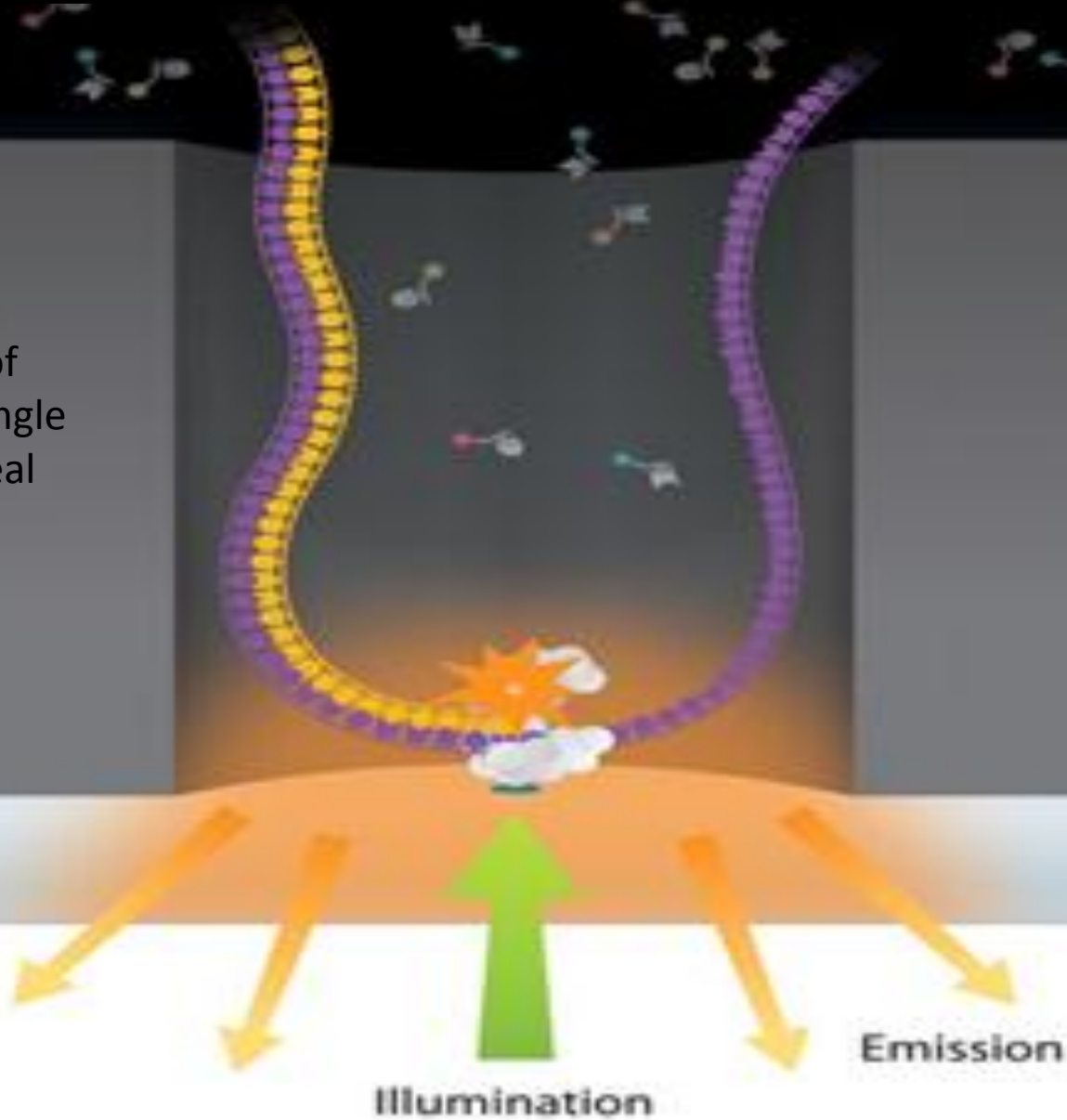
차차세대 염기서열분석법

3RD GENERATION
NEXT NEXT GENERATION

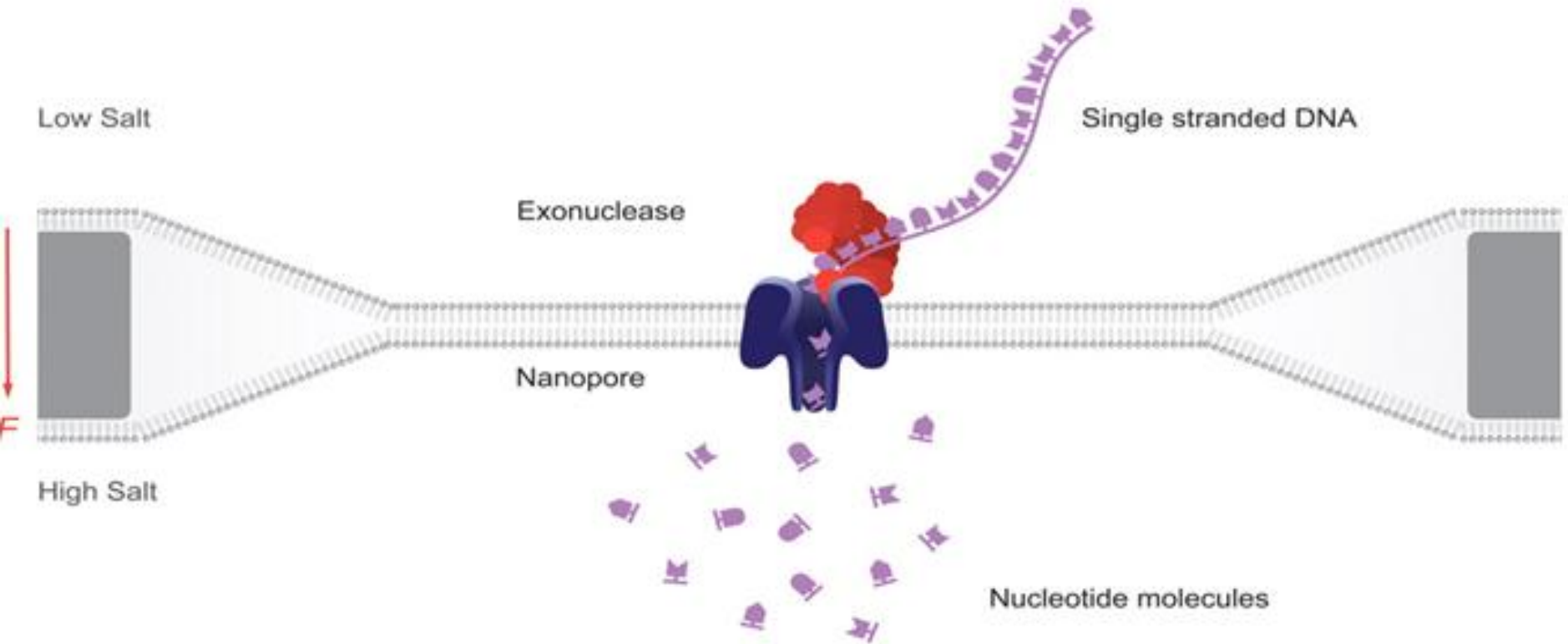
3rd generation

Pacific Biosciences technology

Direct observation of
DNA synthesis on single
DNA molecules in real
time

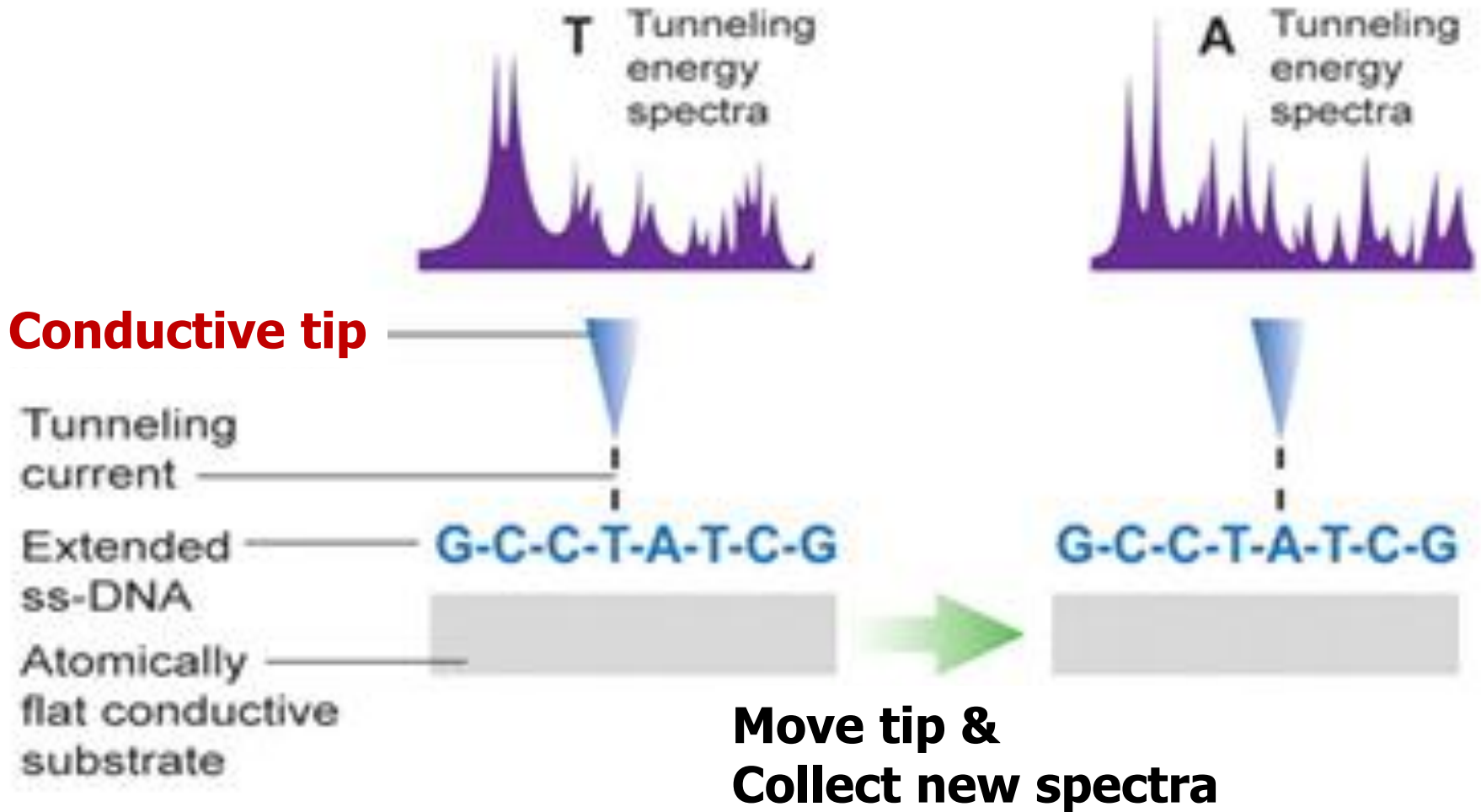


Oxford Nanopore technology

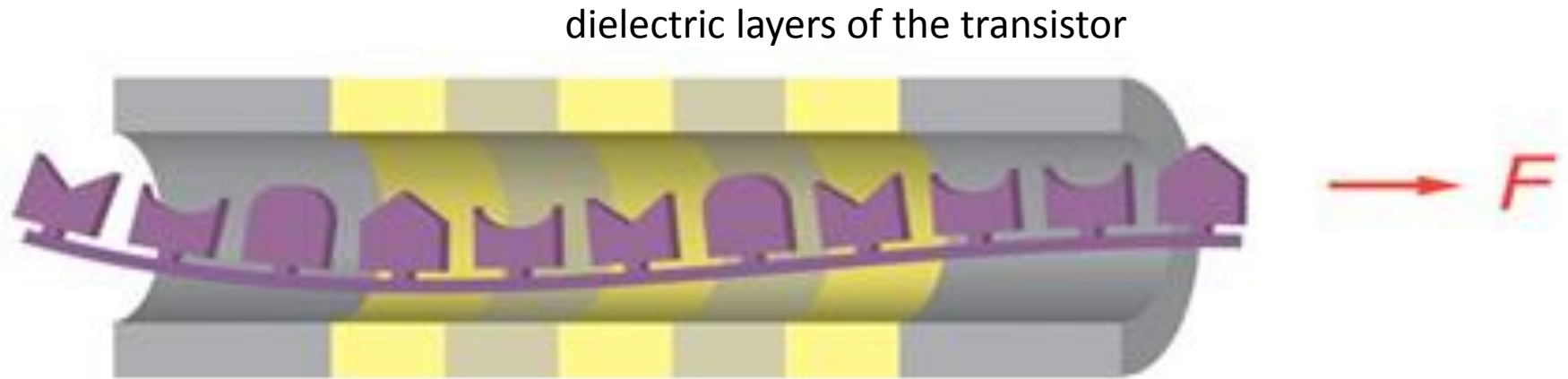


이온농도 차이에 의해 생기는 힘을 이용하여
Nucleotide 가 나노포어에서 하나씩 **translocation** 되는 것을 측정

Sequence DNA by direct inspection using EM



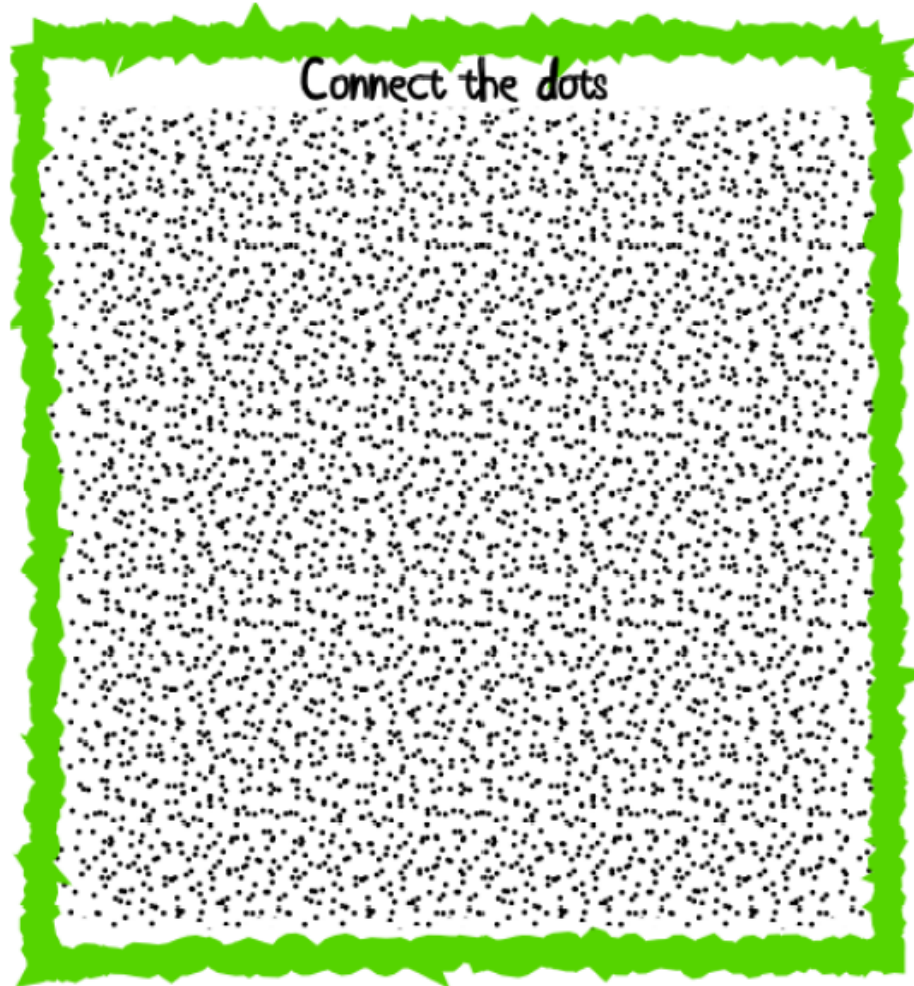
IBM's DNA transistor technology



개개의 ssDNA molecule 이 좁은 slit 을 통과할때

발생하는 electron signal 을 읽어서 DNA 염기를 하나씩 판독

염기서열정보를 얻게 되면 Manual 로 불가



Connect the dots



Connect the dots



맞춤 치료 찾기 방법



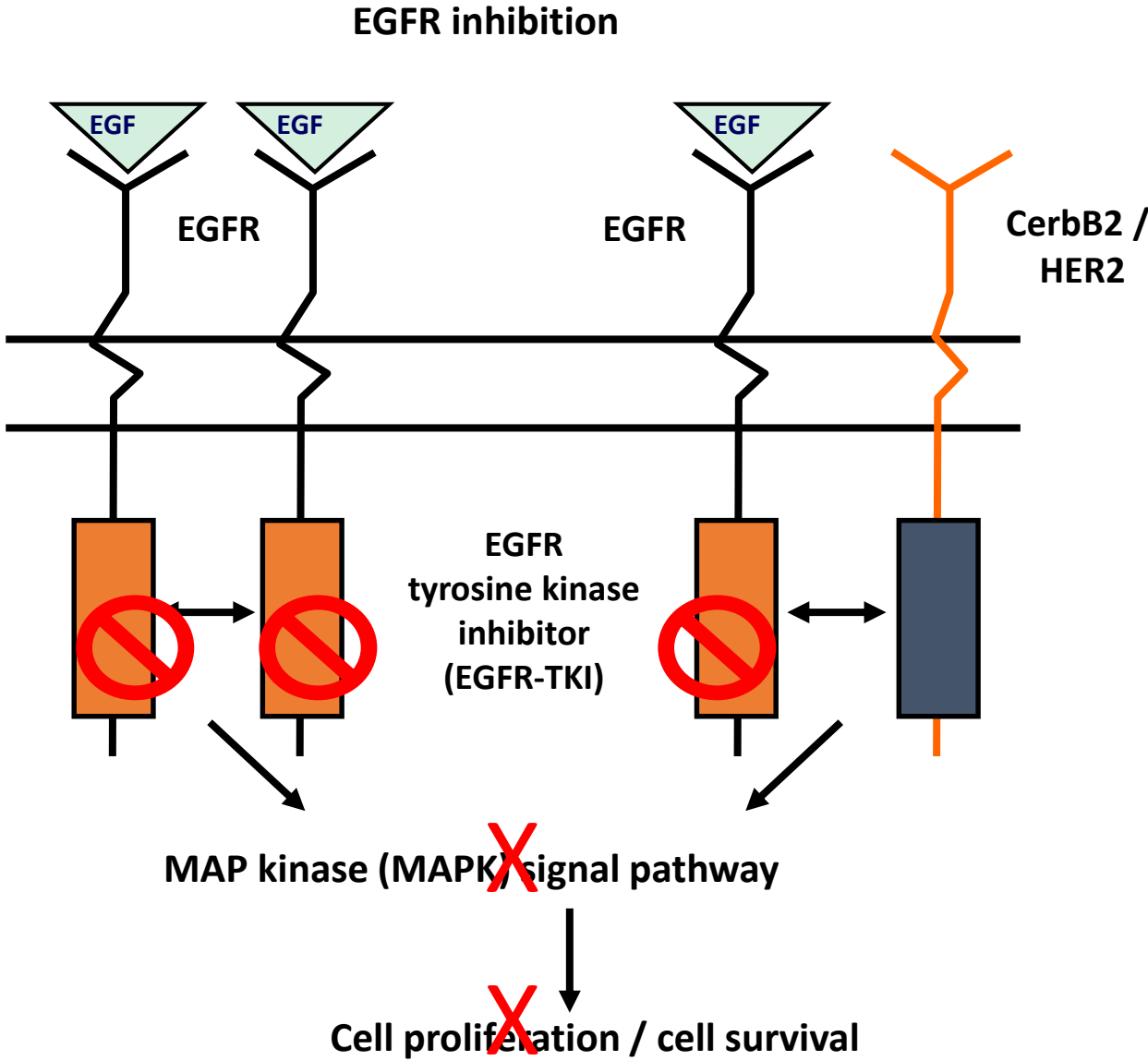
A diagram showing a cross-section of a plant stem. At the top is a wavy orange line representing the epidermis. Below it is a thick grey band representing the cortex. Two orange structures, labeled 'R', represent vascular bundles. Each bundle has a central orange cylinder (xylem) and a crescent-shaped orange structure (phloem) on the outer side. A green oval labeled 'M' is located between the two bundles. At the bottom is a light grey oval representing the pith. A red circle labeled 'L' is positioned at the top left.

L

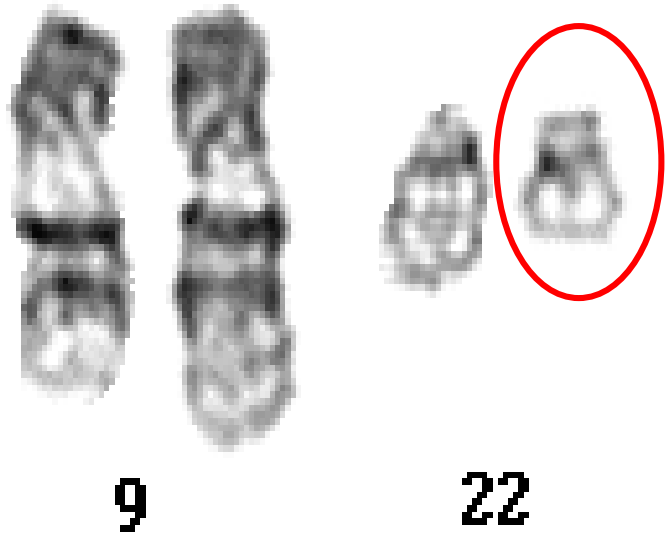
R

M

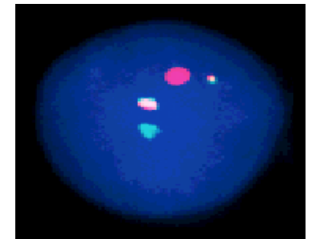
ZD1839 (Iressa)



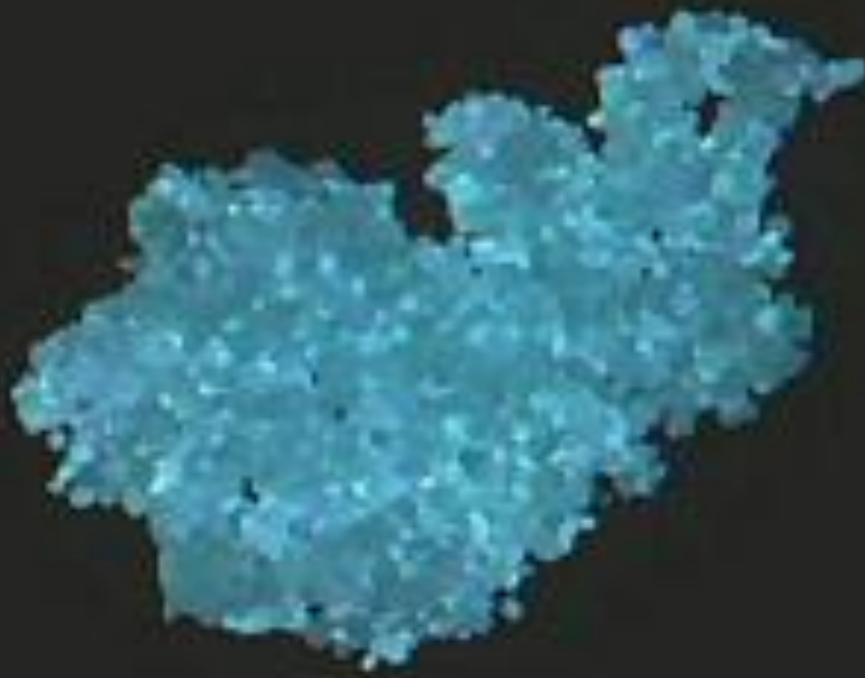
Philadelphia chromosome



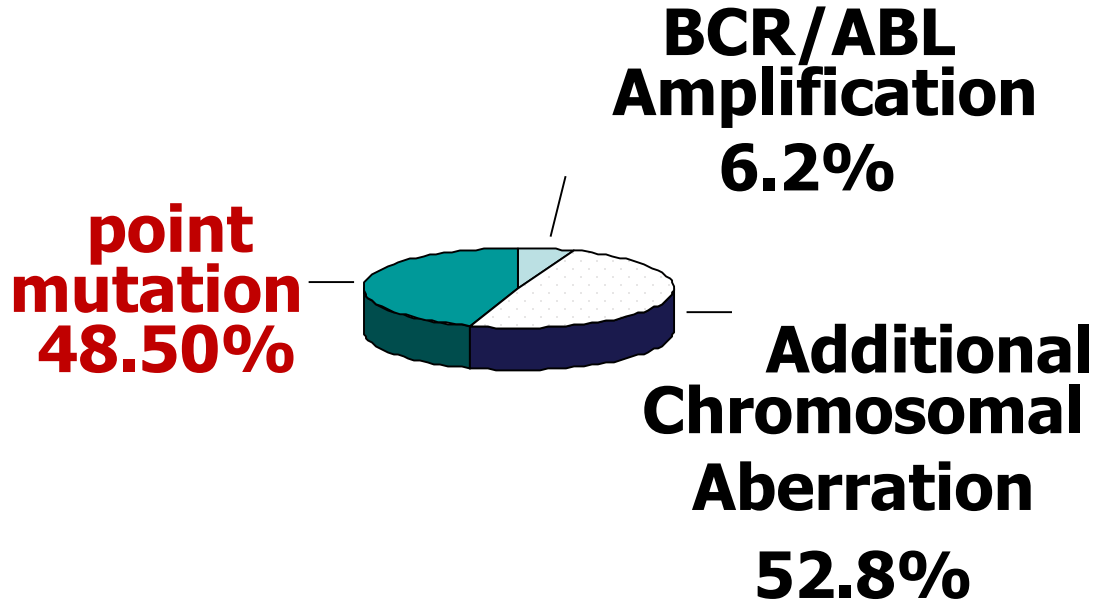
Shortened 22 chromosome
 $t(9;22)$
 $t(9;22)(q22;q13)$



Chronic Myelogenous Leukemia

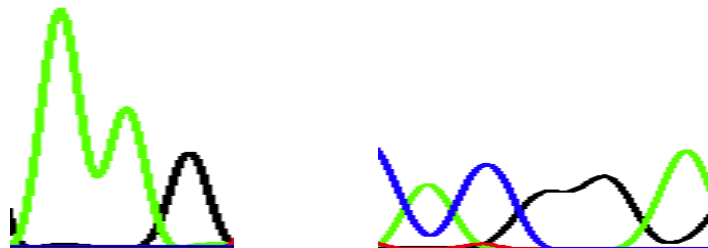
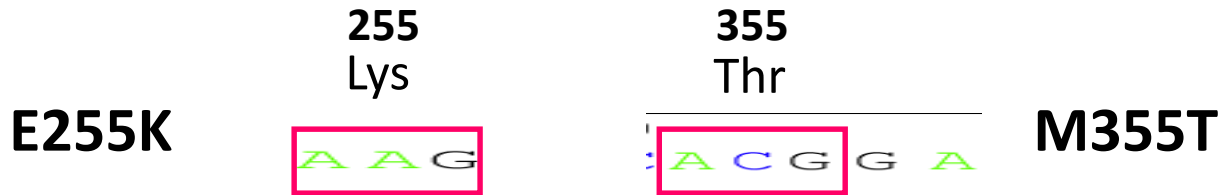
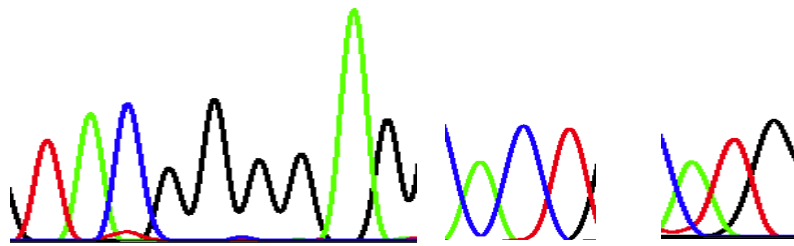
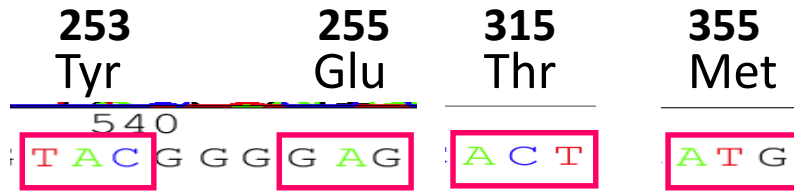


글리벡 내성 기전의 종류



- ① 추가적인 염색체이상
- ② BCR/ABL gene의 point mutation
- ③ BCR/ABL gene amplification

Bcr/Abl ATP binding site



Amplification of Her-2 in breast cancer

A fluorescence microscopy image of breast cancer cells. The nuclei are stained blue with DAPI. Numerous bright red and green spots are visible within the nuclei, indicating the presence of amplified Her-2 receptors. The background is dark, making the fluorescent signals stand out.

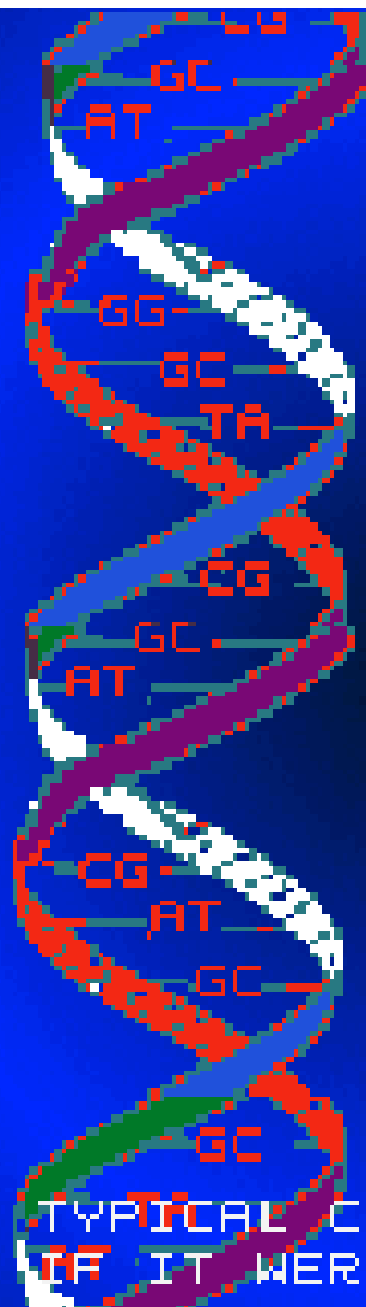
Amplification + Intensive ChemoTx

유전자 돌연변이 없어도..



Histone

Deacetylation



THE LENGTH OF DNA IN A HUMAN CHROMOSOME AVERAGES 3cm WHEN EXTENDED.

YET THE SAME CHROMOSOME MAY BE:-

- ONLY ABOUT 30µm LONG AT INTERPHASE - 1000 TIMES SHORTER!

- ONLY ABOUT 3µm LONG AT METAPHASE - 10,000 TIMES SHORTER!

THE DNA IN A TYPICAL CHROMOSOME WOULD BE ABOUT 20,000µm LONG IF IT WERE THE DIAMETER OF STRING !

유전자 돌연변이 없어도..

Acetylating
agent



Histone
Deacetylation

암의 재발

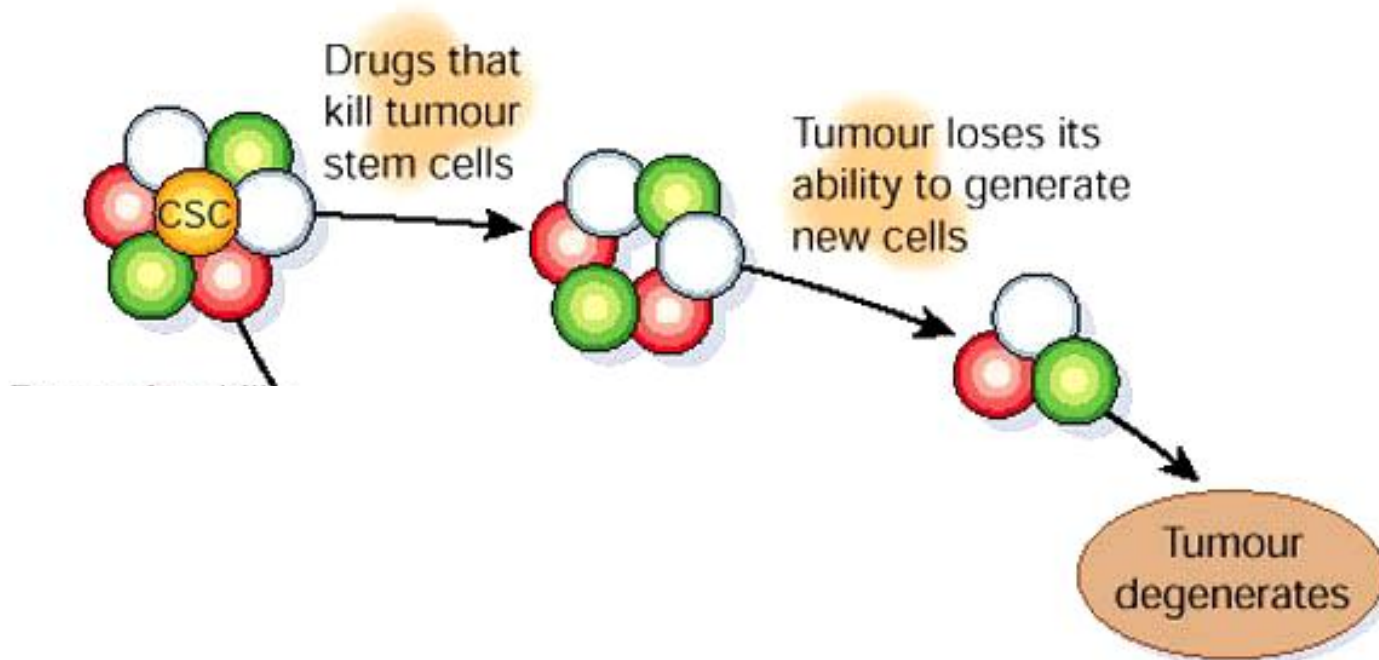
Tumor

heterogeneity

약물감수성

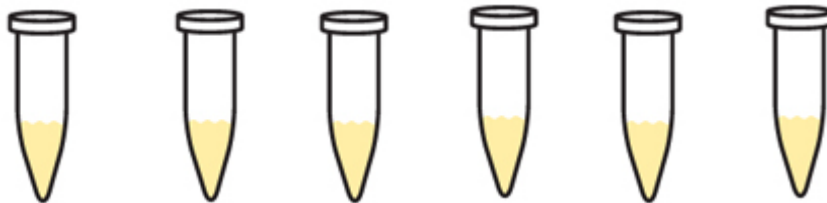
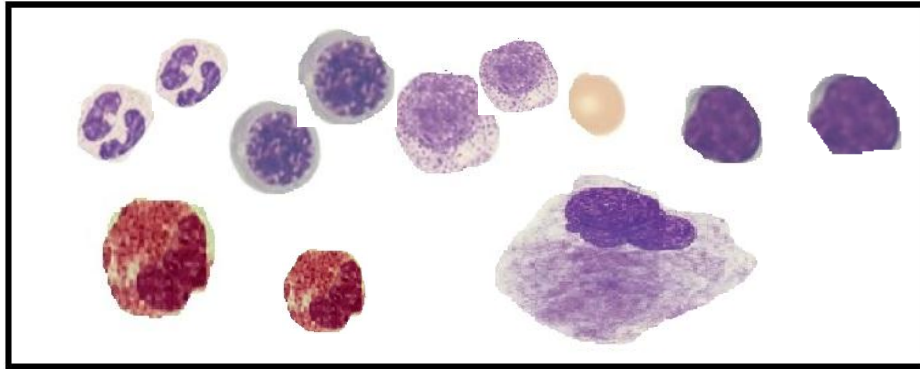
**Single
Cell
Genomics**

암줄기세포와 재발



약물감수성 검사를 위한 단일세포염기분석

DNA level, RNA level



Single Cell PCR

맞춤치료

