



Personalized Cancer Therapy

(a cohort of one)

Brent Zanke MD PhD FRCPC

FACIT | Fight Against Cancer
Innovation Trust



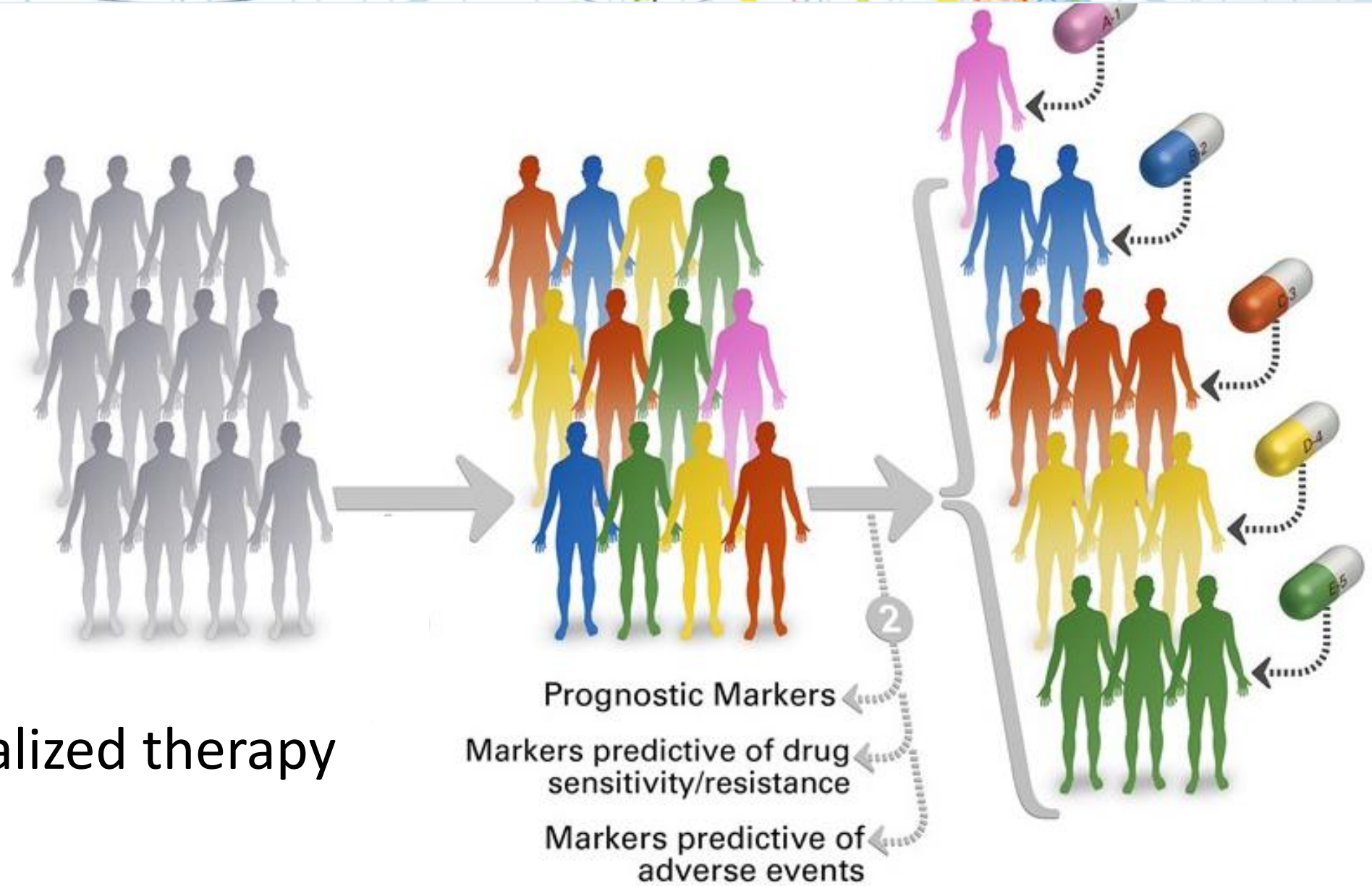
Presenter Disclosure

- **Faculty/Speaker: Brent Zanke**
- **Relationships with financial sponsors:**
 - **Grants/Research Support: None.**
 - **Speakers Bureau/Honoraria: None**
 - **Consulting Fees: None**
 - **Other: Chief Medical Officer, Chairman and Founder of ArcticDx Inc.**



Learning Objectives

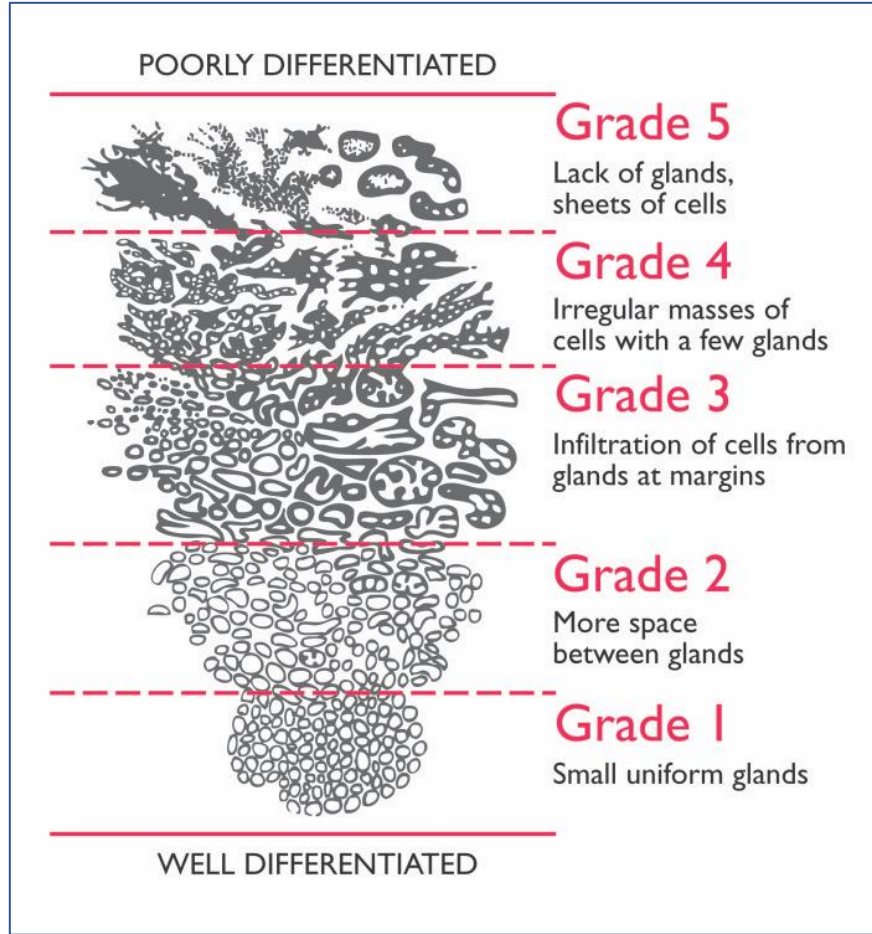
- To understand existing approaches to personalizing cancer therapy
- To learn about new approaches to cancer pharmacogenomics including liquid biopsy and NextGen sequencing.



Personalized therapy



Bx
→

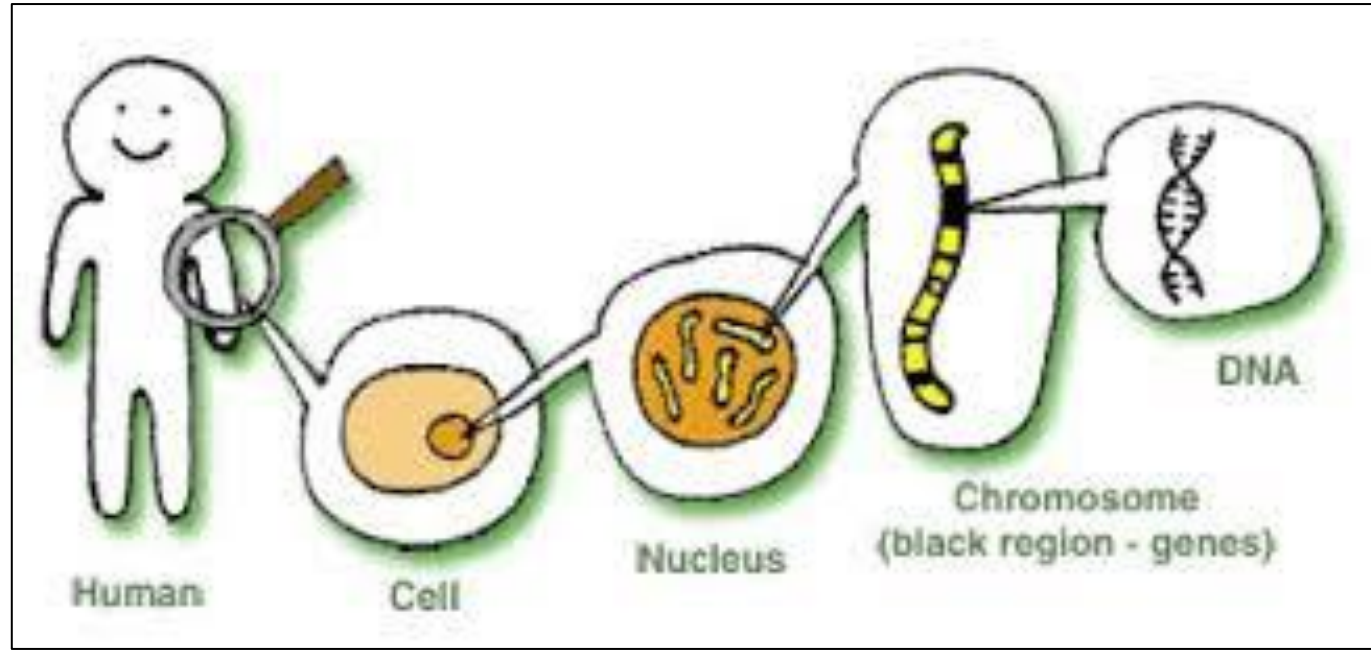


Radical Treatment

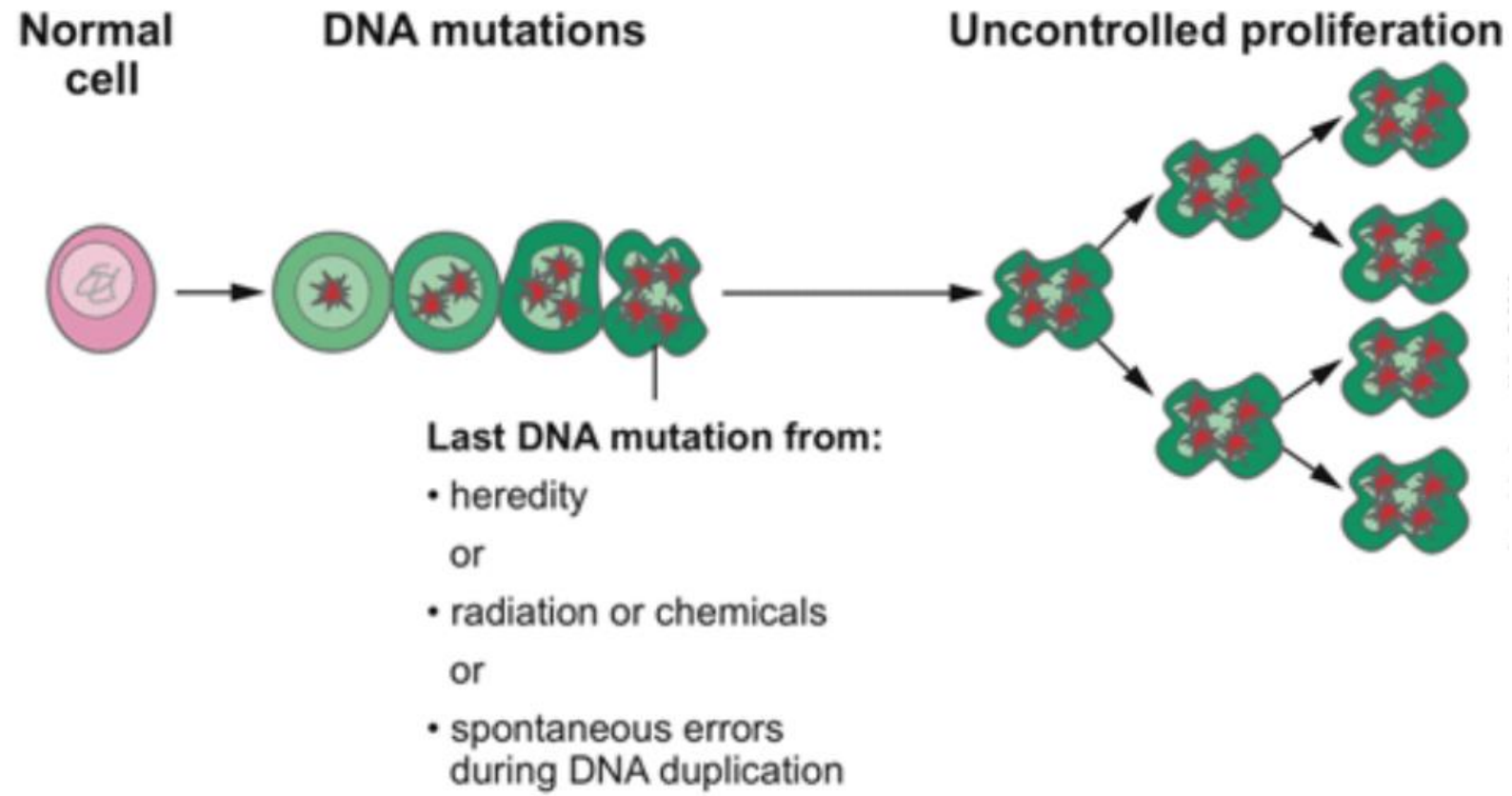


Active Surveillance

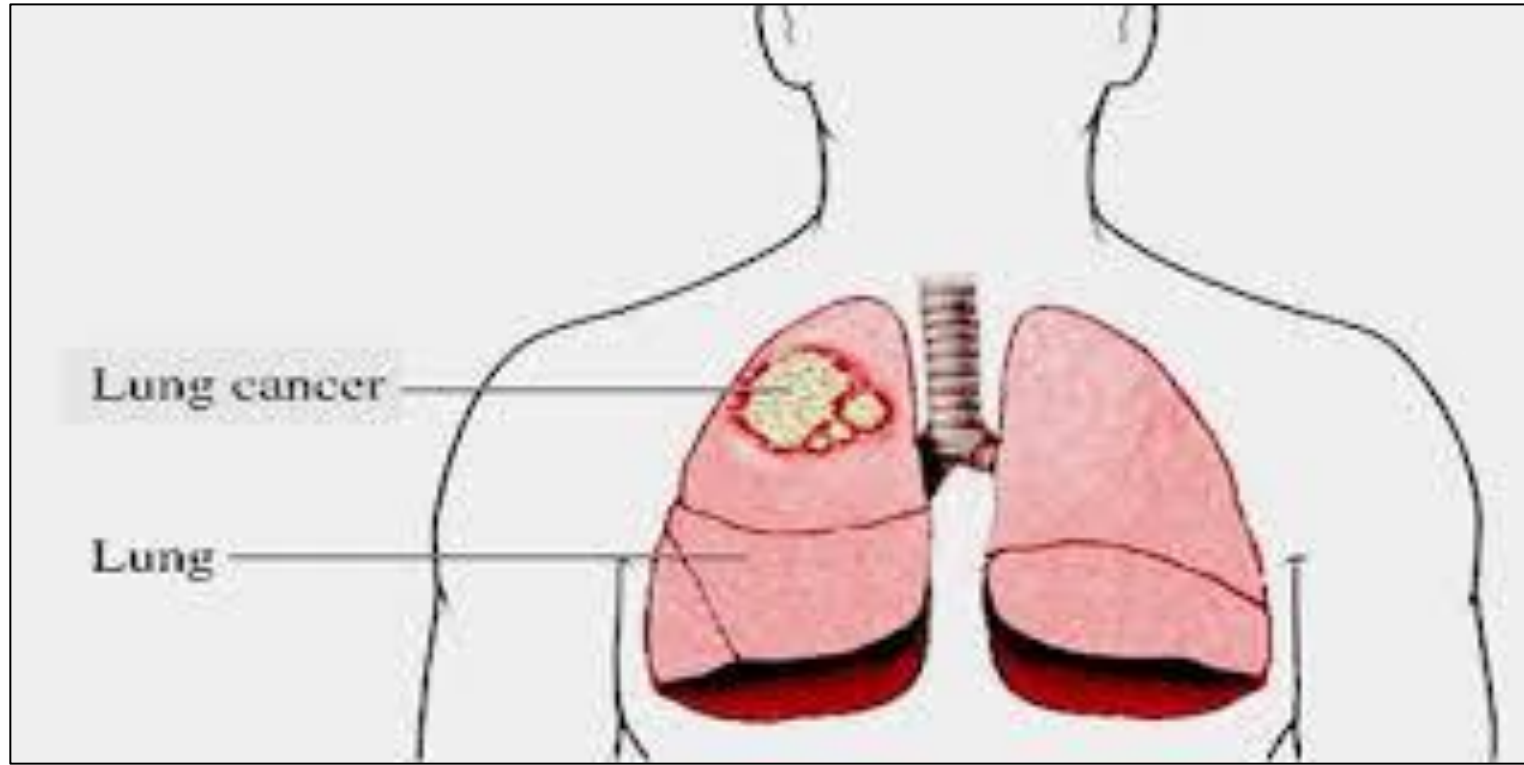
Current Prostate Cancer Personalized Therapy



Personalized medicine: genetic/proteomic biomarkers distinguish
predisposition/response/toxicity



Cancer arises from DNA mutations in cells



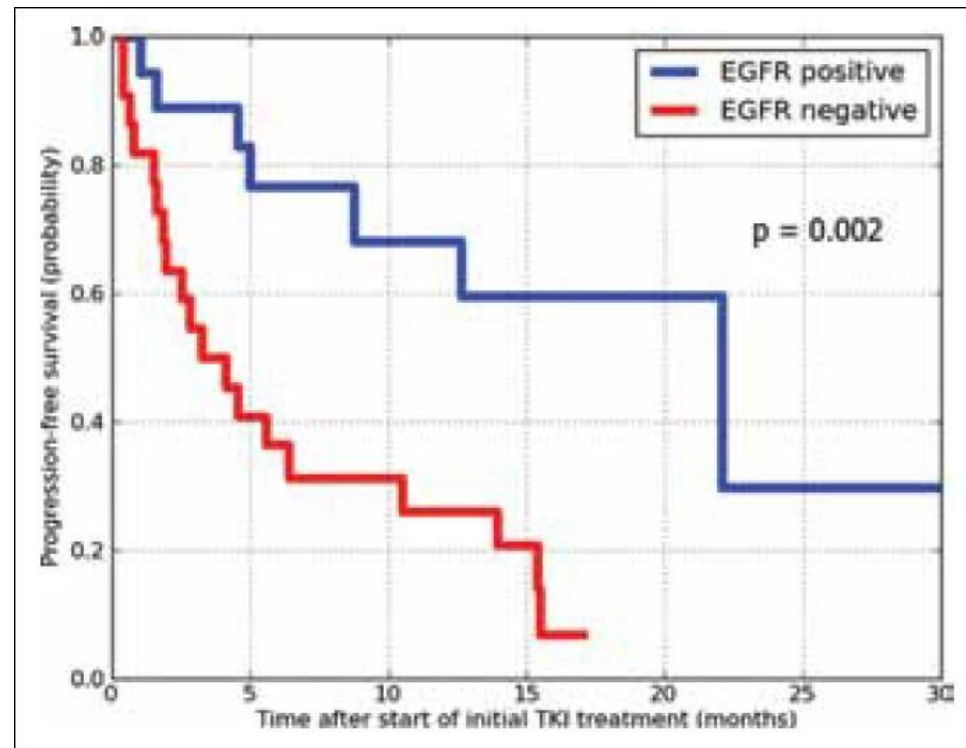
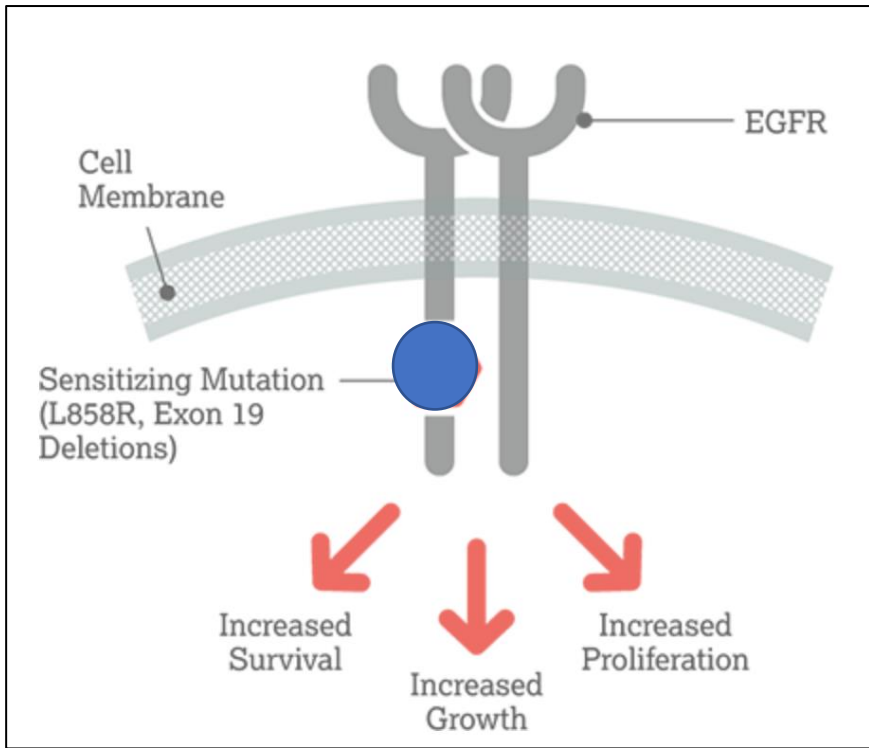
Genetic markers can predict individual sensitivity to lung cancer treatment.



Lung Cancer Genetic Variability affects TKI sensitivity

Epidermal Growth Factor Receptor (EGFR)

Most common sensitizing mutations: exon 19 deletion or L858R point mutation in exon 21



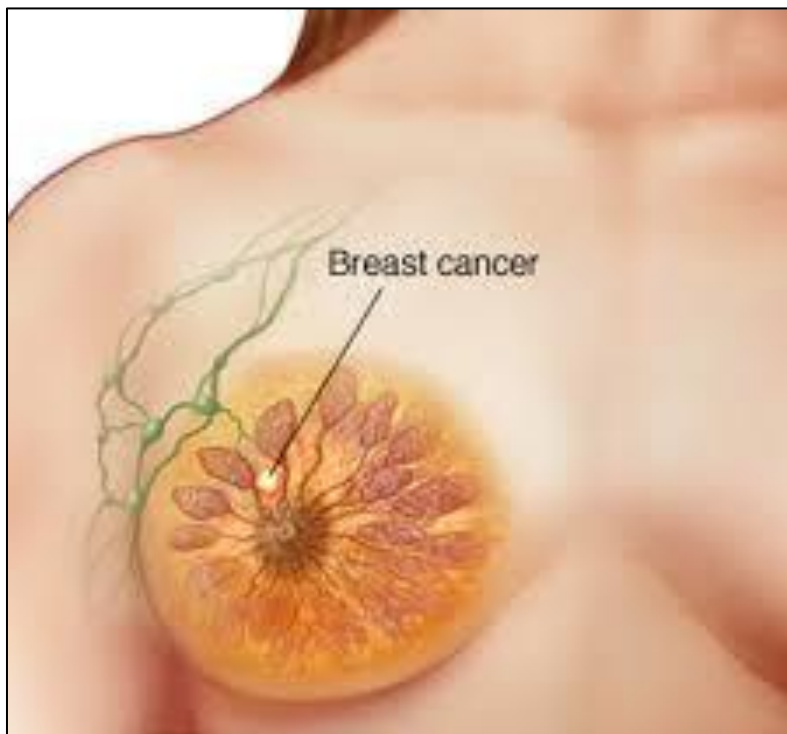


Non-Small Cell Lung Cancer Genetic Testing and Drug Sensitivity

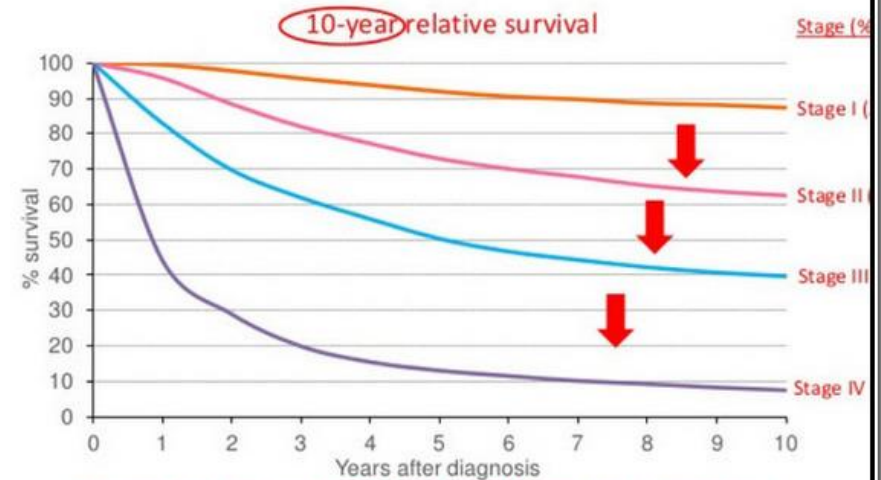
Other important mutations

- ALK (Anaplastic Lymphoma Kinase) – sensitivity to TKI Crizotinib
- ROS1 – RTK – fusion mutations = responsiveness to oral ROS1 TKI
- BRAF S/T Kinase – V600E associated with responsiveness to combination therapy with oral inhibitors of BRAF and MEK
- KRAS. Activating mutations in codon 12 : reduced responsiveness to EGFR TKI
- PD-L1 expression determines sensitivity to check point inhibitors

Breast Cancer: Can good prognosis Stage I, HR+, Her2neg adjuvant candidates be saved adjuvant chemotherapy? A personalized approach.



Female Breast Cancer Survival Rates by Stage of Disease



*Additionally, 20.3% of patients in the US are diagnosed as stage 0 and 5.2% are unknown¹

¹National Cancer Database Analysis: https://oromwell.facs.org/BMark/BM.Cmp/ver10/Docs/fixx_2008. Assessed September 12, 2011
Graph: West Midlands Cancer Intelligence Unit, 2009. <http://info.cancerresearchuk.org/cancerstats/types/breast/survival/stage>. Assessed September 12, 2011.

16 Cancer and 5 Reference Genes From 3 Studies

OncotypeDx

PROLIFERATION

Ki-67
STK15
Survivin
Cyclin B1
MYBL2

OESTROGEN

ER
PR
Bcl2
SCUBE2

$$RS = + 0.47 \times \text{HER2 Group Score} \\ - 0.34 \times \text{ER Group Score} \\ + 1.04 \times \text{Proliferation Group Score} \\ + 0.10 \times \text{Invasion Group Score} \\ + 0.05 \times \text{CD68} \\ - 0.08 \times \text{GSTM1} \\ - 0.07 \times \text{BAG1}$$

GSTM1

BAG1

INVASION

Stromelysin 3
Cathepsin L2

CD68

REFERENCE

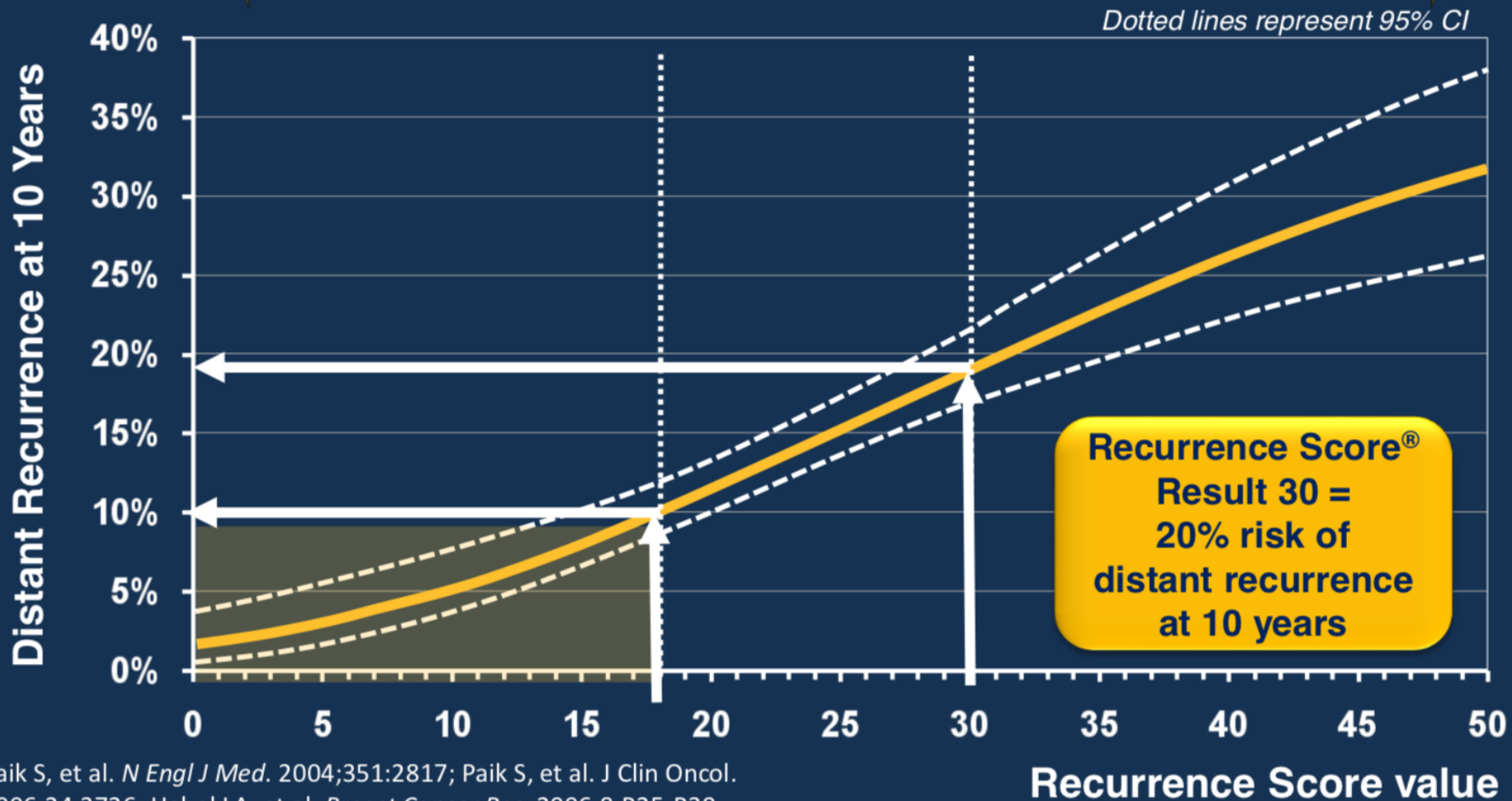
Beta-actin
GAPDH
RPLPO
GUS
TFRC

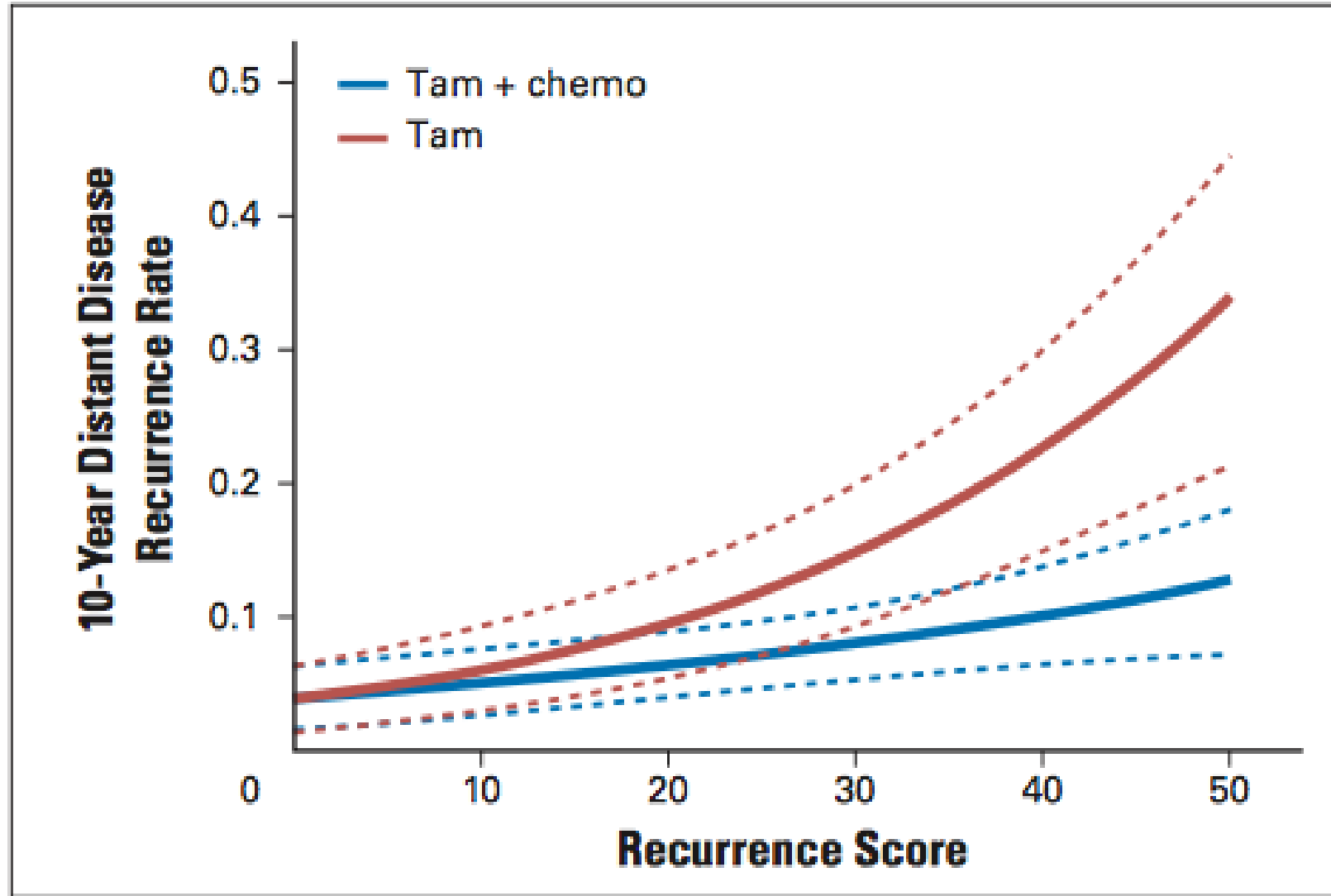
HER2

GRB7
HER2

Category	RS (0 -100)
Low risk	RS <18
Int risk	RS 18 - 30
High risk	RS ≥ 31

What is the 10-year probability of distant recurrence for a patient with a Recurrence Score result of 30?





OncotypeDX score for node negative ER+ tumors (NSABP 20)



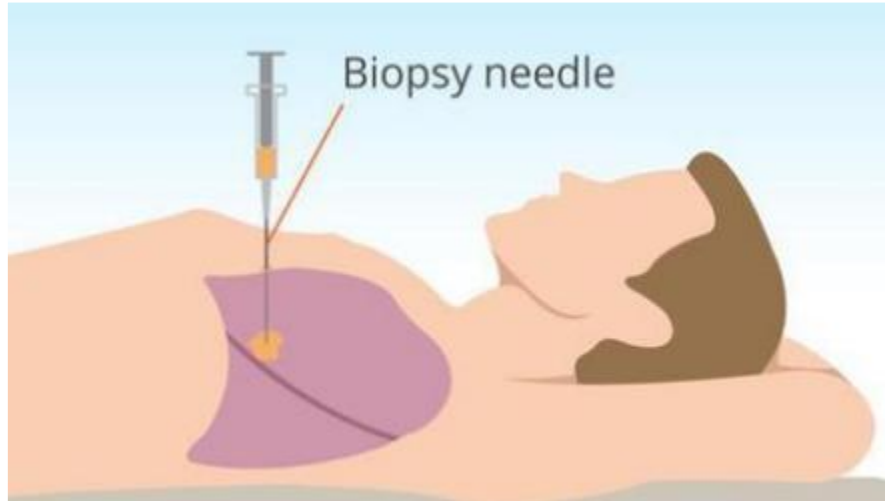
The future of personalized cancer treatment



The Problem

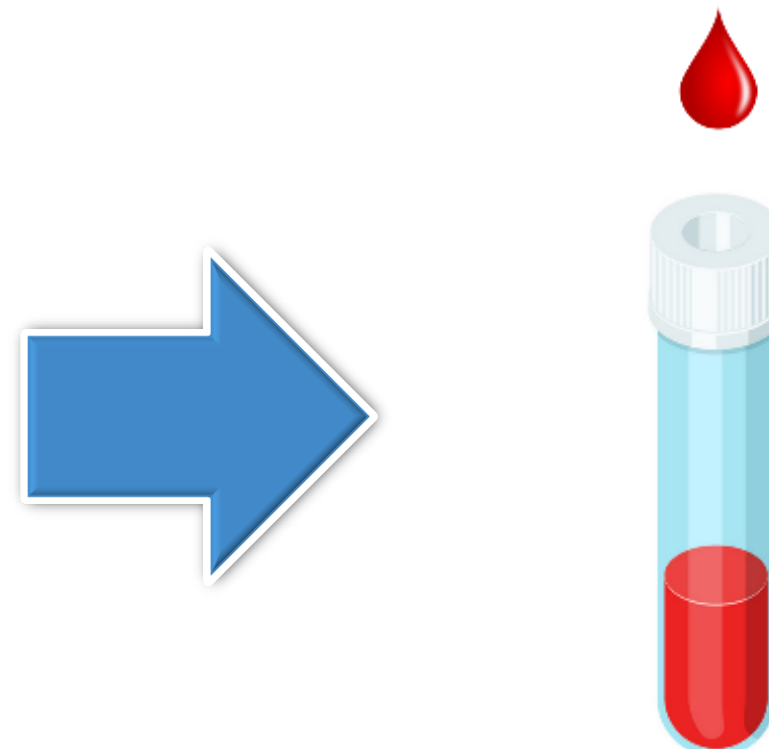
Diagnosis: **Invasive** Tumor Biopsy

- Tumor biopsies are **costly, painful and can result in complications.**

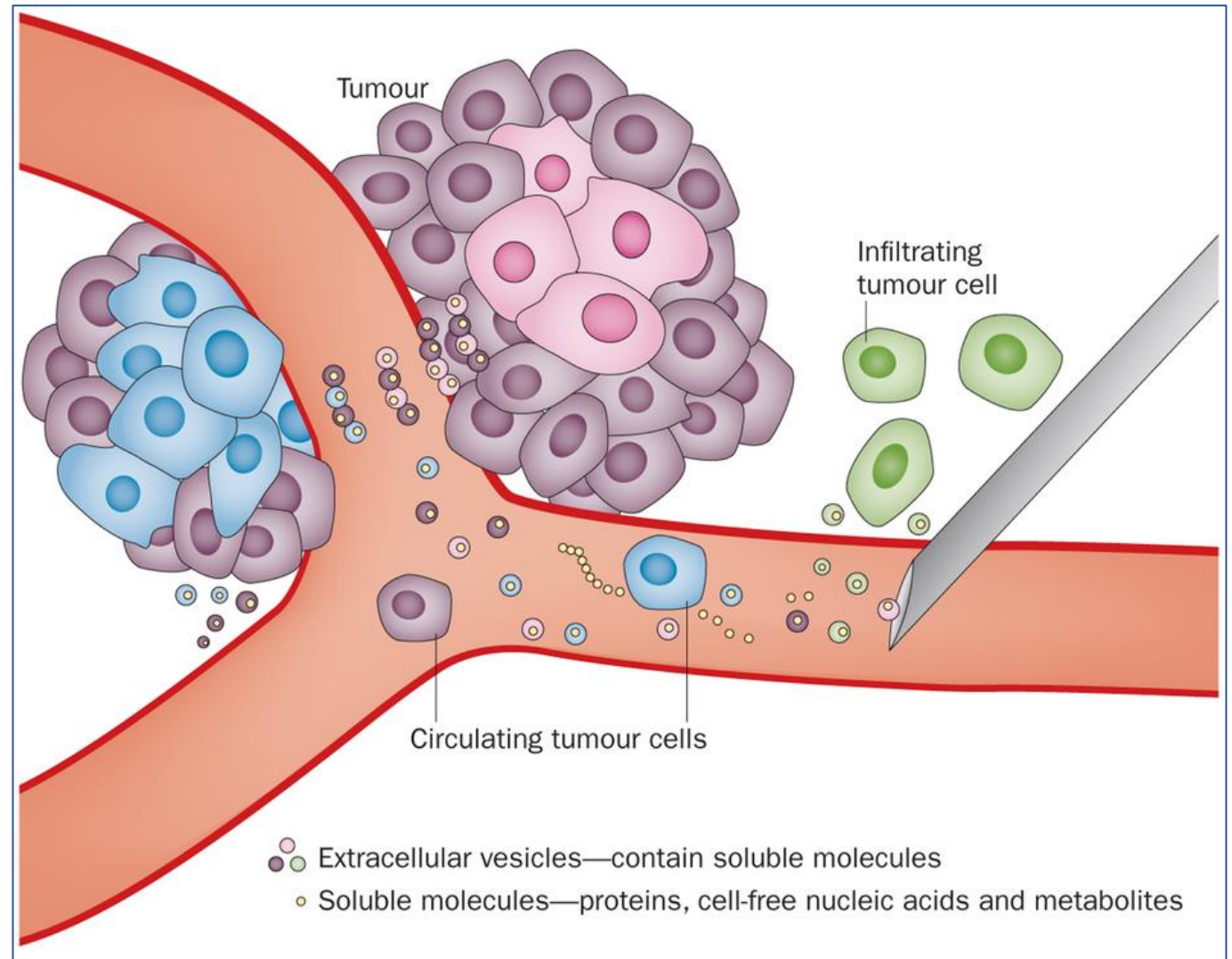


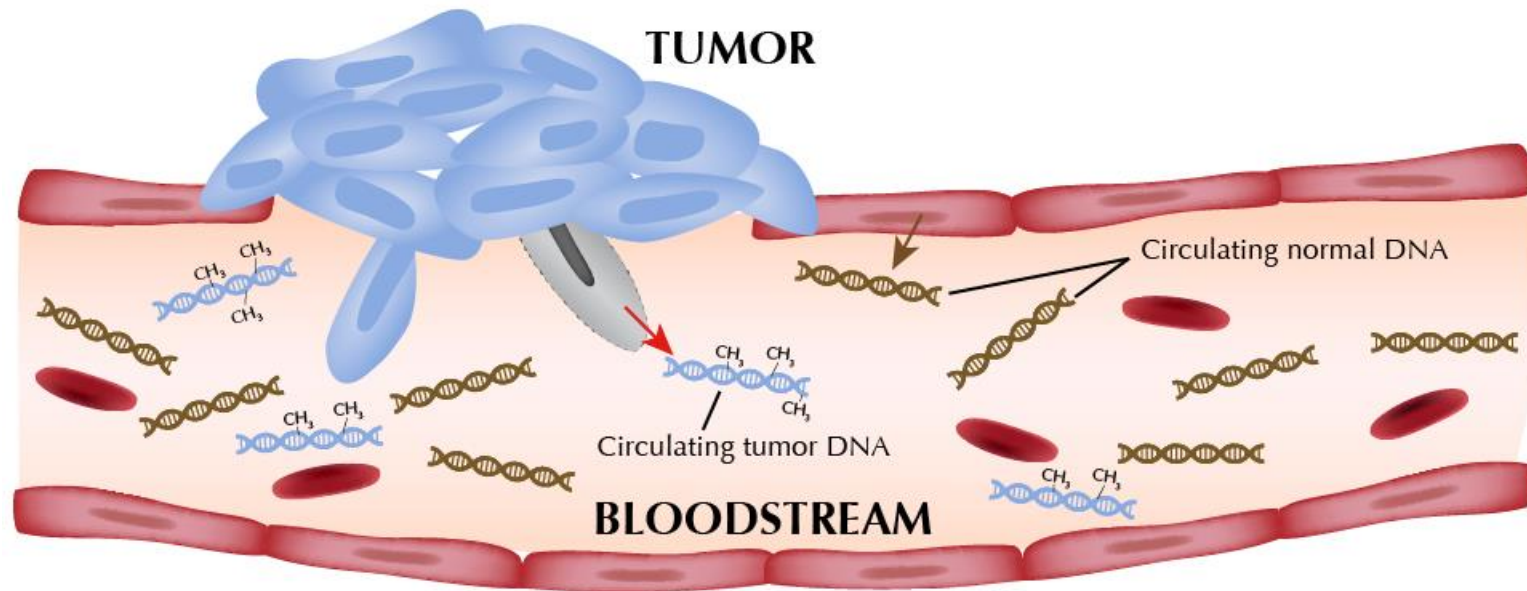
The Proposed Solution

Diagnosis: **Non-Invasive** Liquid Biopsy



Liquid biopsy is less invasive than needle biopsy





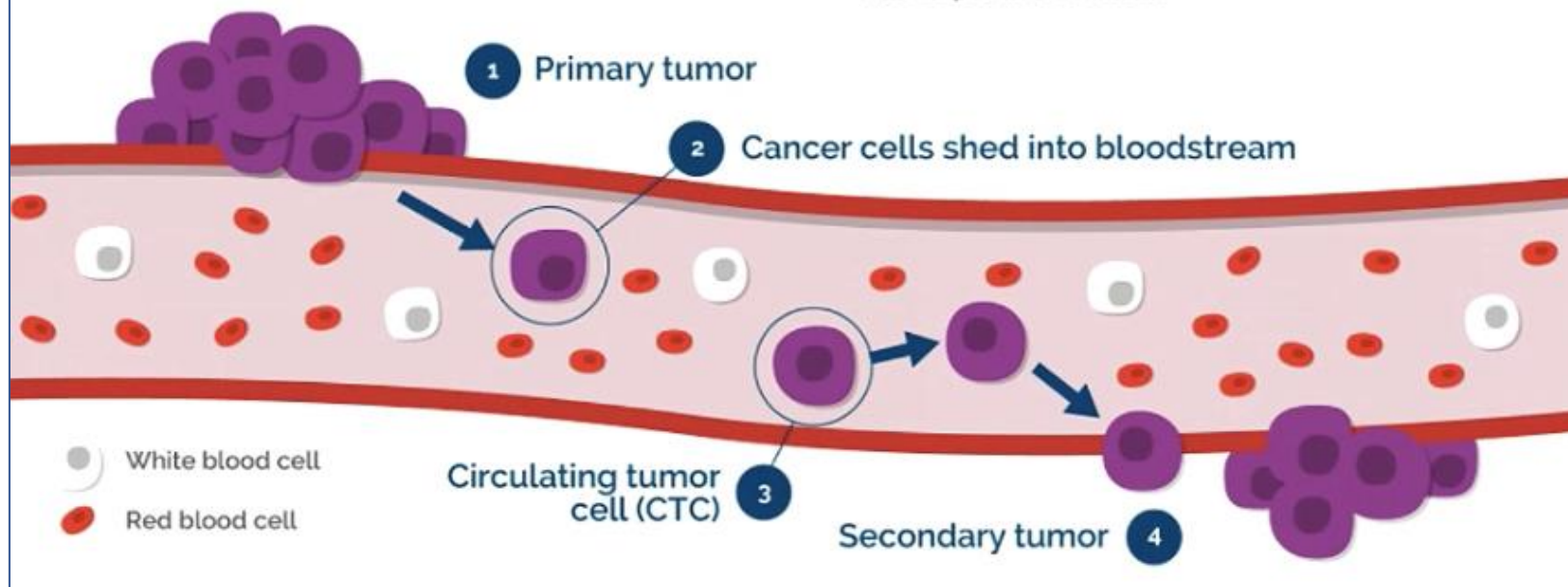
**BLOOD PLASMA
OR SERUM SAMPLE**

CTCs Provide Direct Access to Intact Cancer Biology

Circulating tumor cells (CTCs) detach from a solid tumor and enter in the blood stream.
CTCs play a crucial role in cancer metastasis.

Challenges to CTC isolation

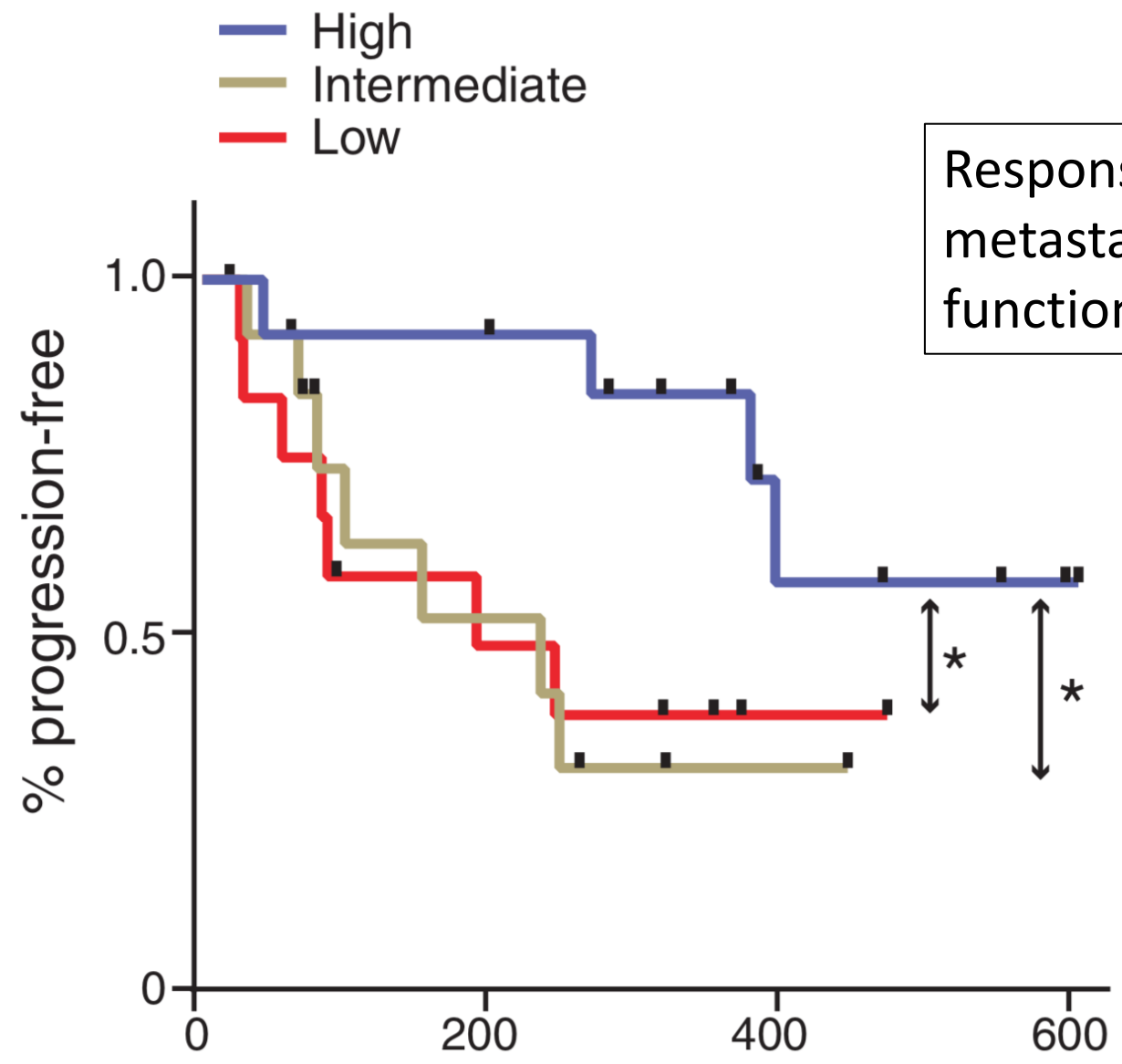
- **Extremely rare:** 1-100 CTCs per mL of blood
- **Other cells:** millions of WBCs and billions of RBCs per mL of blood

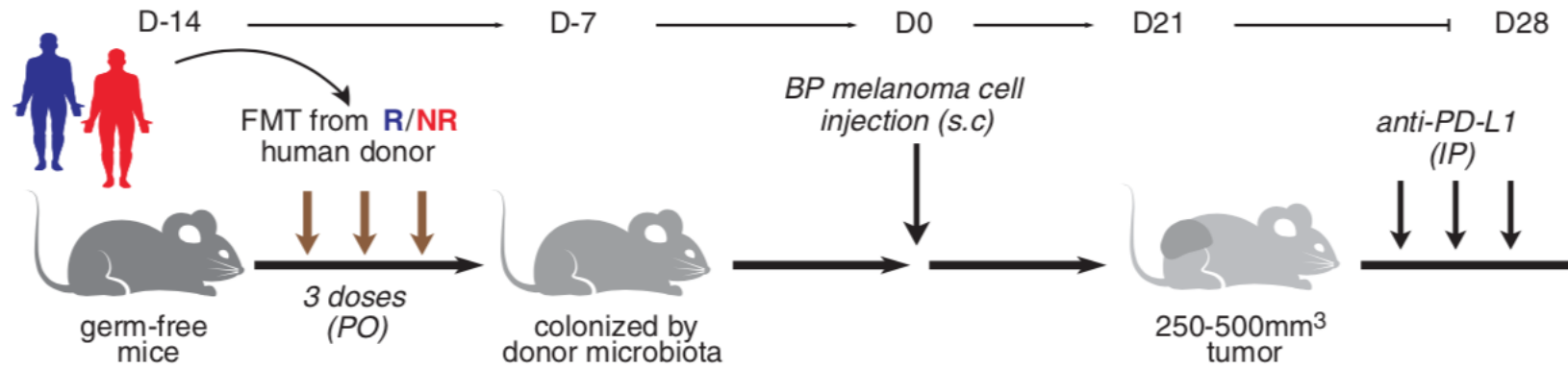




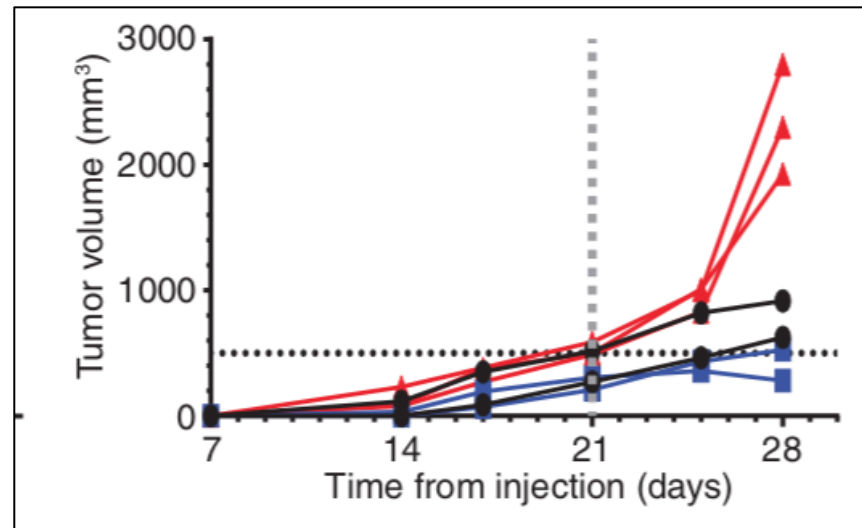
Bacterial diversity can affect efficacy of cancer treatment

Your DNA may not be the only thing personal about you!





Fecal transplant: A new frontier in personalized medicine



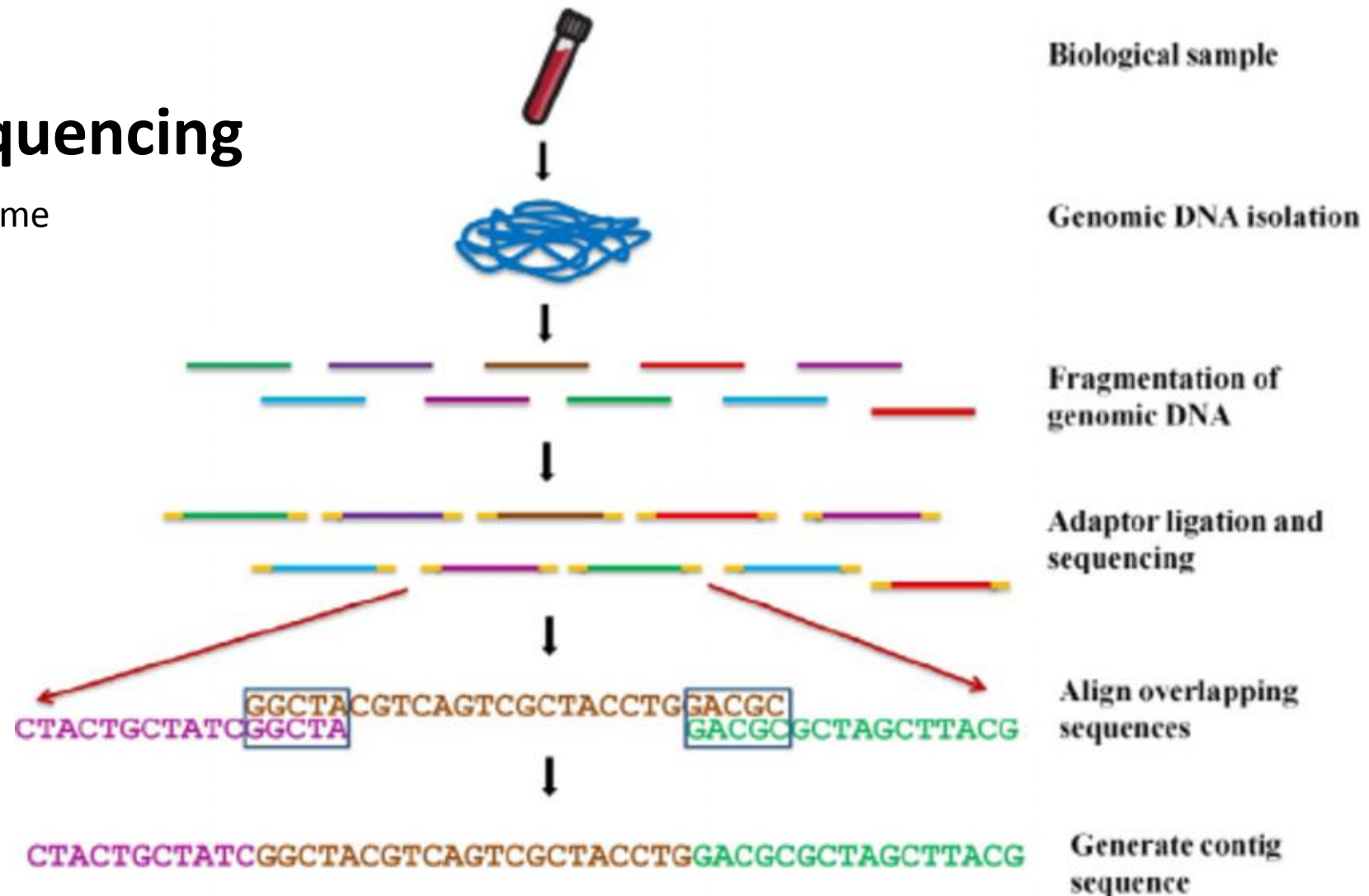
Drug sensitivity influenced by gut bacterial composition

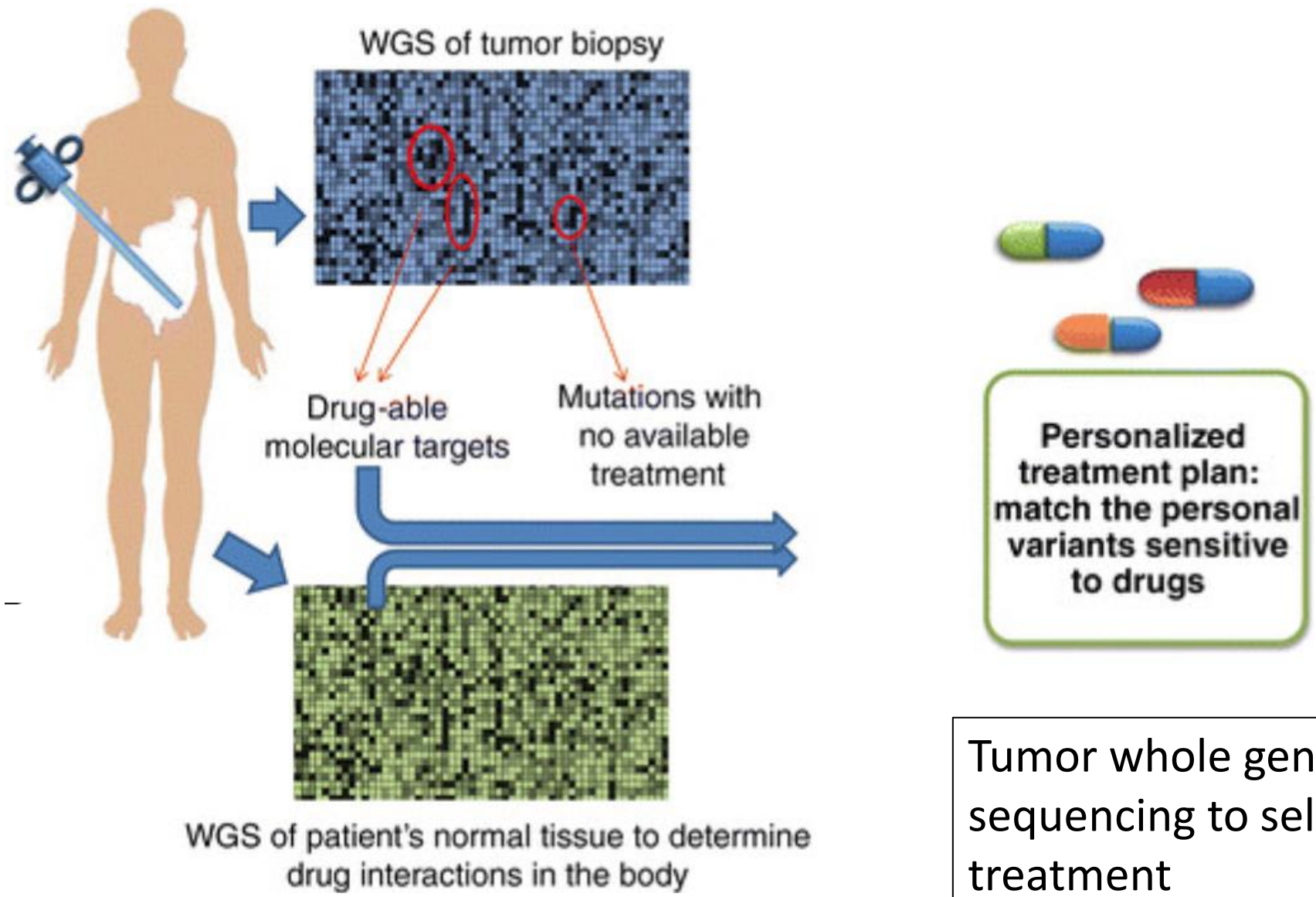
An increasingly important management partner



NextGen Sequencing

\$1000 genome





Tumor whole genome sequencing to select treatment



Summary

- Sequencing technologies are becoming inexpensive
- Big data and artificial intelligence are resolving complexity into order
- Less invasive techniques are evolving to allow frequent sampling and personalized treatment selection.
- This will result in better outcomes and (?) less expensive care.