La medicina di laboratorio al servizio della persona

Il paziente oncologico situazione odierna e prospettive future

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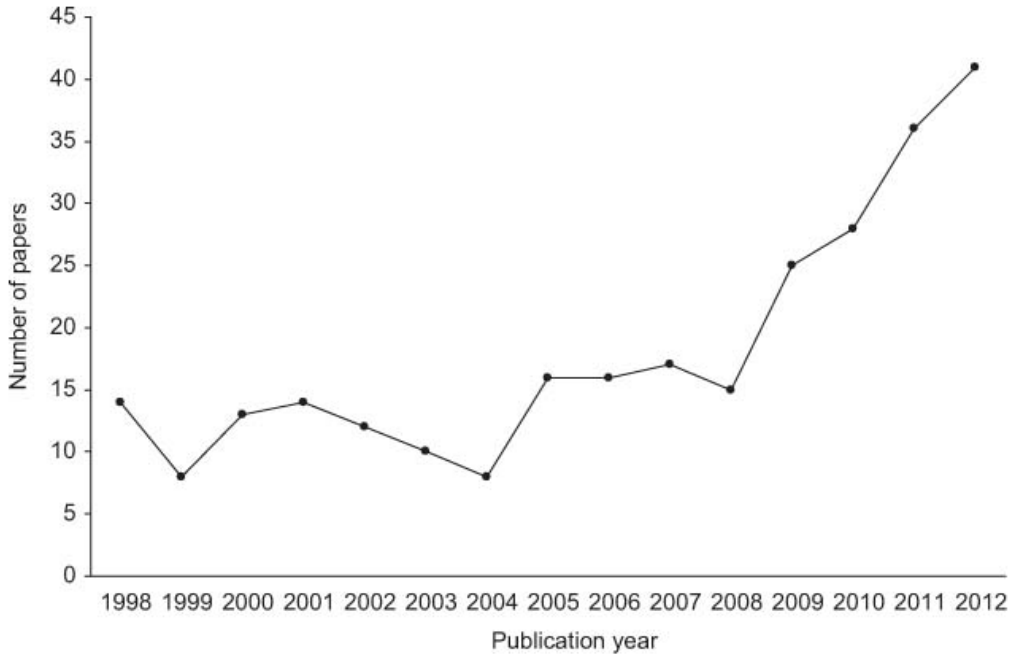
Laboratory medicine and medical oncology: the tale of two Cinderellas



Number of papers on oncological topics in *Clinical Chemistry and Laboratory Medicine*.

- Detection of the host response against tumor
- Biomarkers of treatment toxicity
- Monitoring or predicting the concentrations of anticancer drugs
- **Tumor markers – the old and the new**

A prognostic biomarker informs about a likely cancer outcome (eg, disease recurrence, disease pro- gression, death) independent of treatment received.

A biomarker is predictive if the treatment effect (experimental compared with control) is differ- ent for biomarker-positive patients compared with biomarker-negative patients.

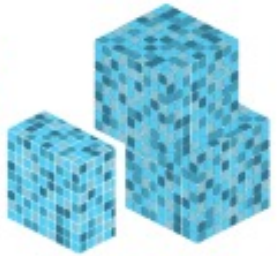
mod. Bohuslav Melichar, Clin Chem Lab Med 2013; 51(1): 99–112

NATIONAL CANCER INSTITUTE
THE CANCER GENOME ATLAS

TCGA BY THE NUMBERS

TCGA produced over

2.5
PETABYTES
of data



To put this into perspective, **1 petabyte** of data is equal to

212,000
DVDs

TCGA data describes **33** DIFFERENT TUMOR TYPES ...including **10** RARE CANCERS

...based on paired tumor and normal tissue sets collected from

11,000
PATIENTS

...using

7 DIFFERENT DATA TYPES

TCGA RESULTS & FINDINGS

MOLECULAR BASIS OF CANCER	Improved our understanding of the genomic underpinnings of cancer	For example, a TCGA study found the basal-like subtype of breast cancer to be similar to the serous subtype of ovarian cancer on a molecular level, suggesting that despite arising from different tissues in the body, these subtypes may share a common path of development and respond to similar therapeutic strategies.
TUMOR SUBTYPES	Revolutionized how cancer is classified	TCGA revolutionized how cancer is classified by identifying tumor subtypes with distinct sets of genomic alterations.*
THERAPEUTIC TARGETS	Identified genomic characteristics of tumors that can be targeted with currently available therapies or used to help with drug development	TCGA's identification of targetable genomic alterations in lung squamous cell carcinoma led to NCI's Lung-MAP Trial, which will treat patients based on the specific genomic changes in their tumor.

THE TEAM

20
COLLABORATING INSTITUTIONS
across the United States and Canada

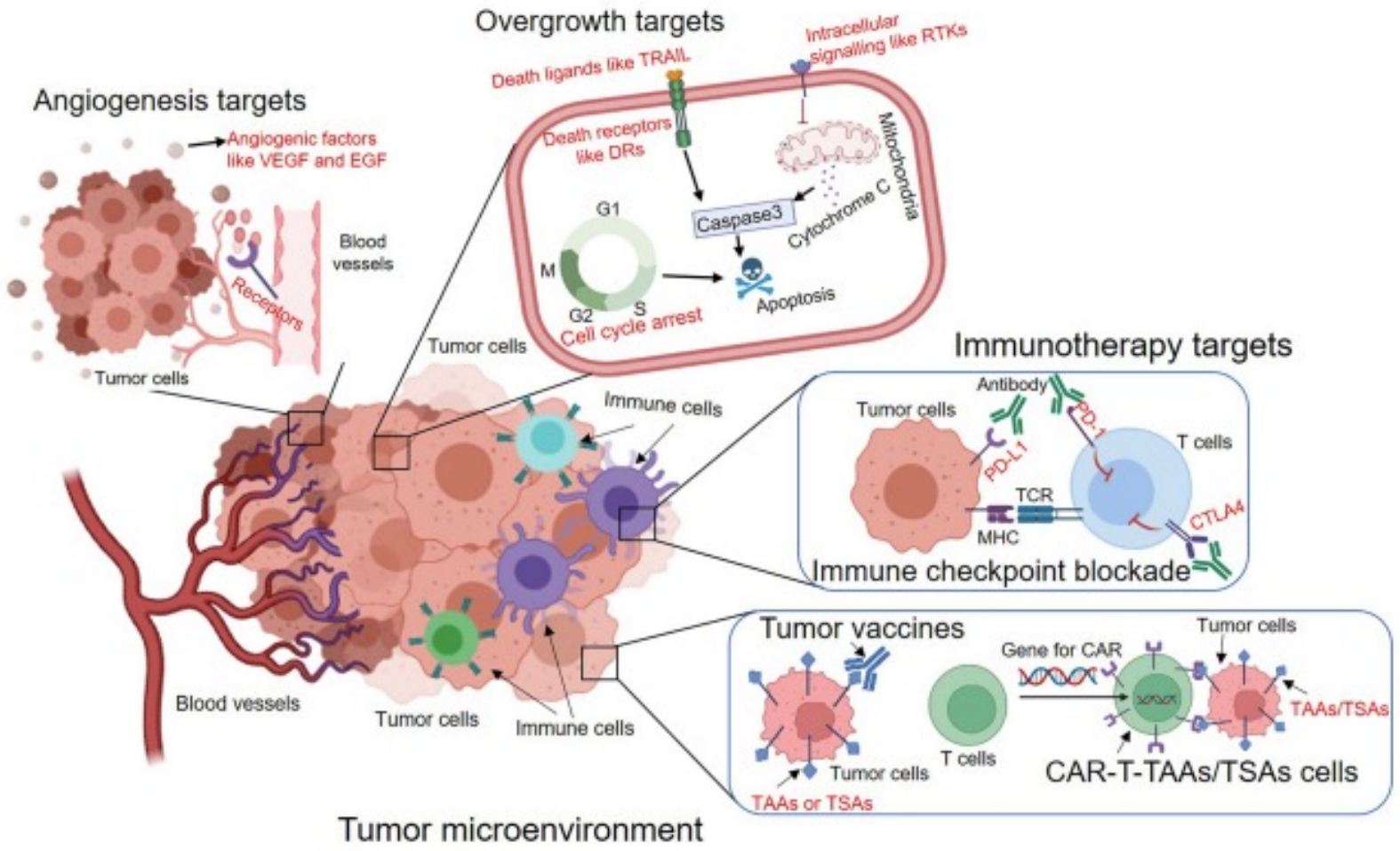
WHAT'S NEXT?

The Genomic Data Commons (GDC) houses TCGA and other NCI-generated data sets for scientists to access from anywhere. The GDC also has many expanded capabilities that will allow researchers to answer more clinically relevant questions with increased ease.

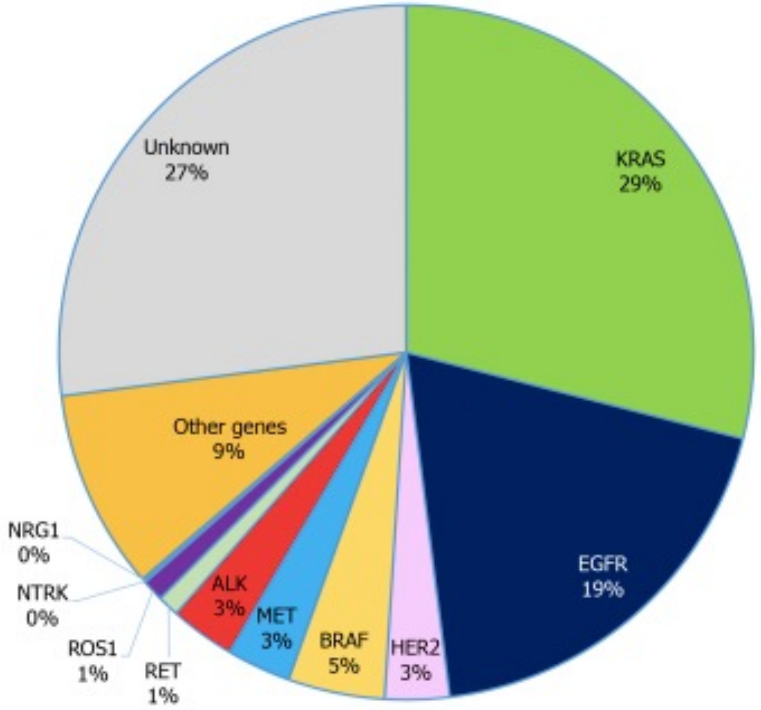
*TCGA's analysis of stomach cancer revealed that it is not a single disease, but a disease composed of four subtypes, including a new subtype characterized by infection with Epstein-Barr virus.

www.cancer.gov/ccg

Overview of major types of molecular targeted therapies



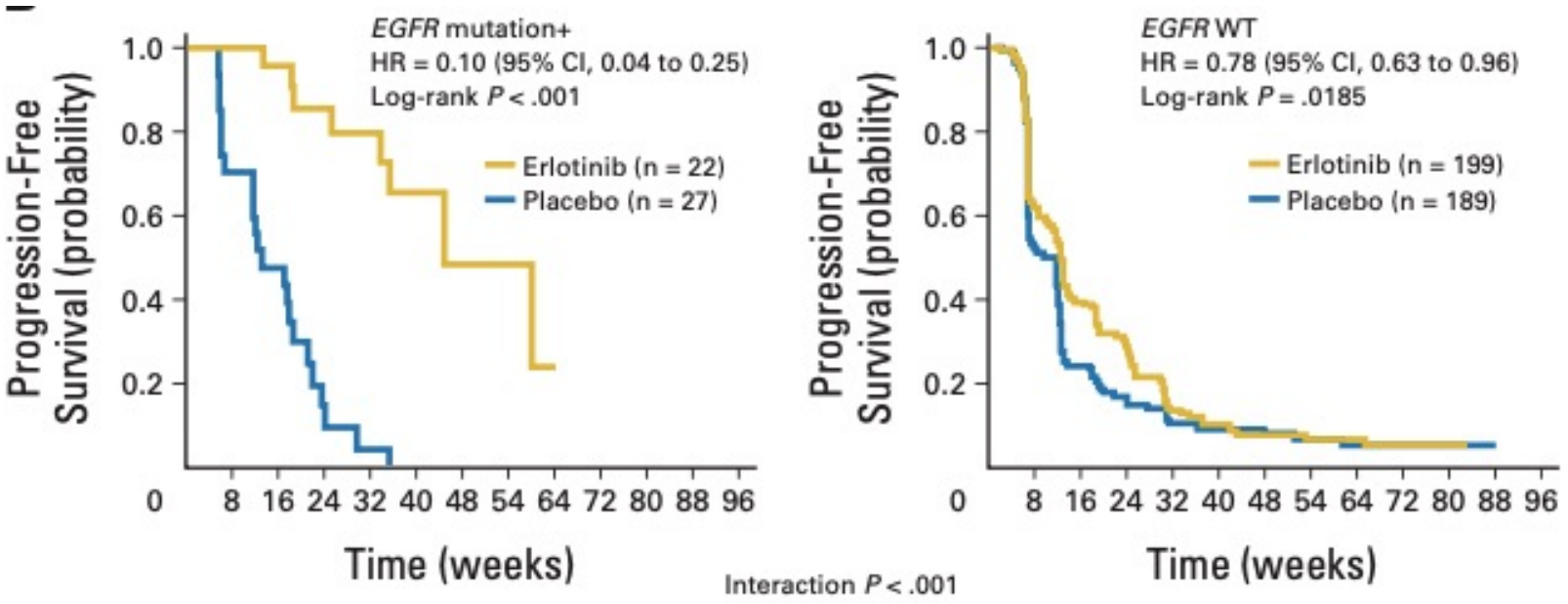
Jue Hou, Front. Oncol, 2022



Incidence of oncogenic drivers in non-small cell lung cancer

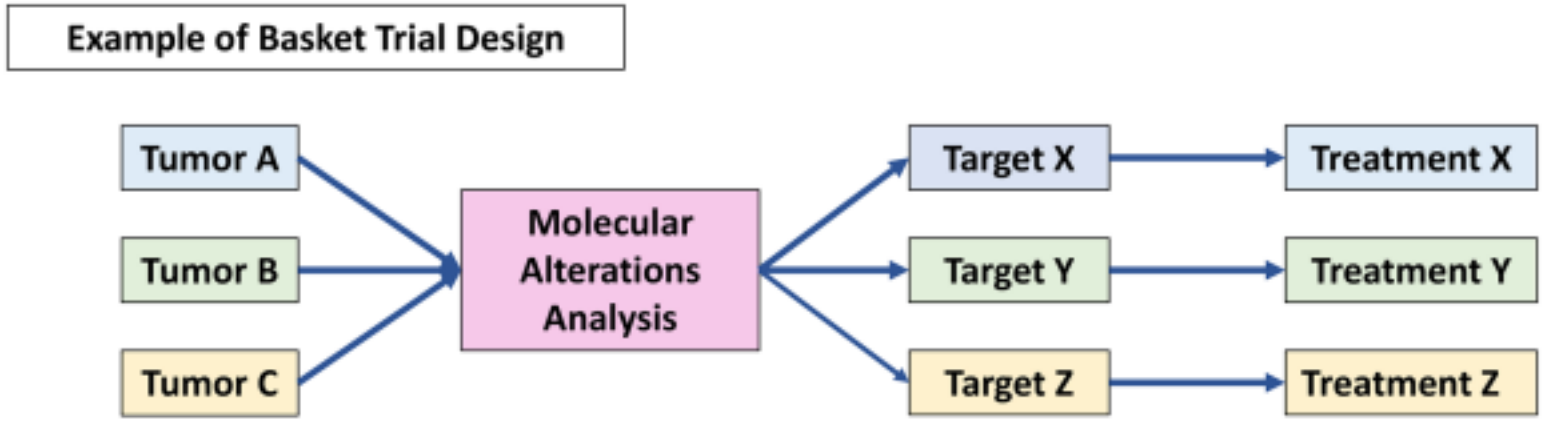
Mathieu Chevallier, World J Clin Oncol 2021

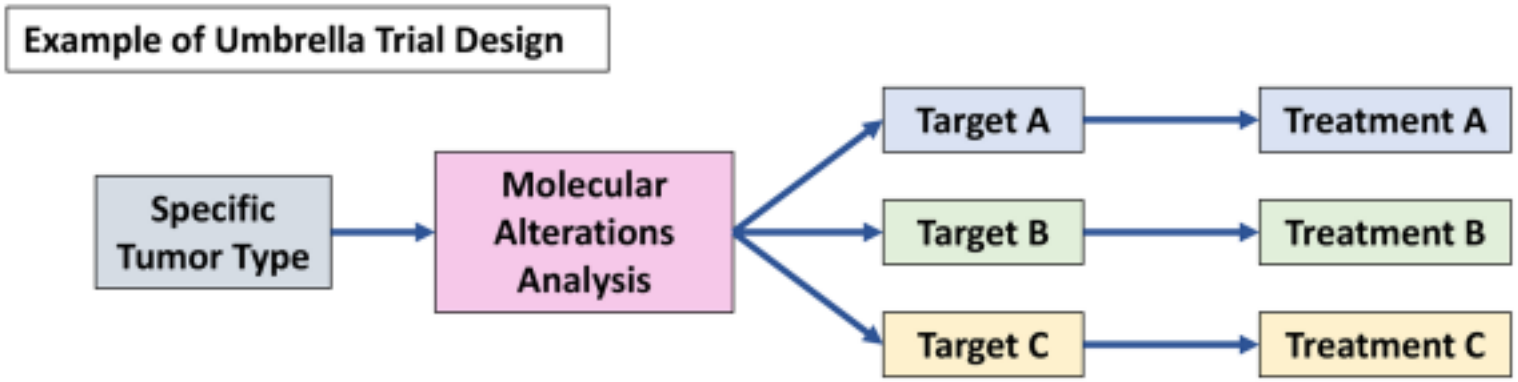
The degree of benefit is greater in the *EGFR* mutation–positive group, suggesting that *EGFR* mutation status is **predictive** of erlotinib response



Karla V. Ballman, J Clin Oncol 2015

Precision Medicine Clinical Trials Platform

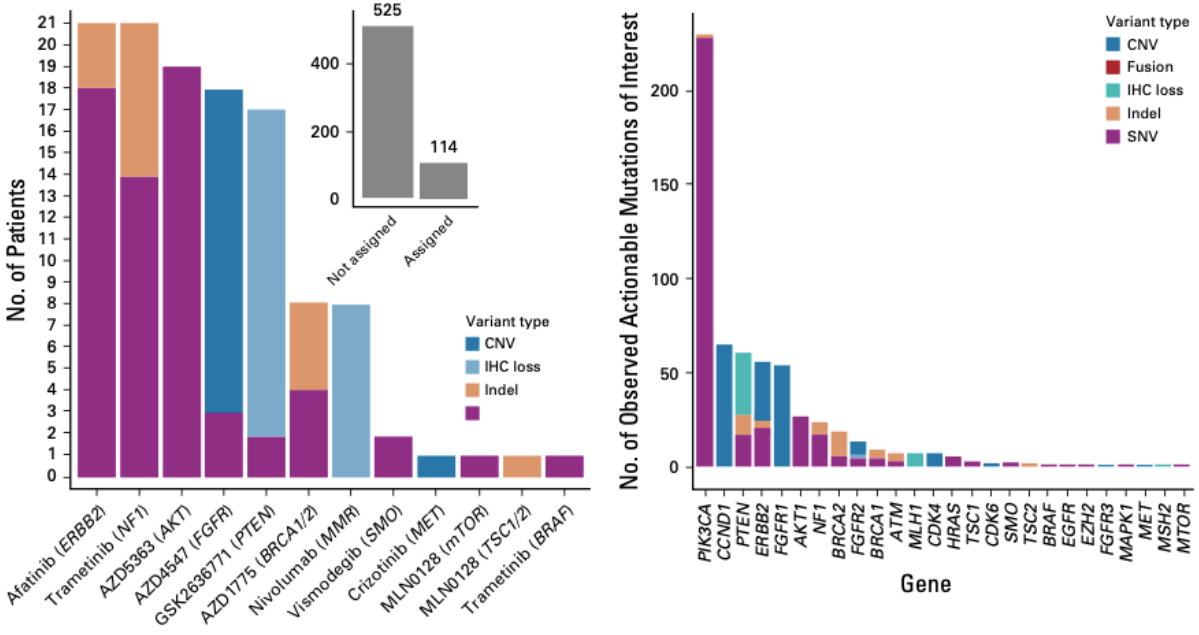




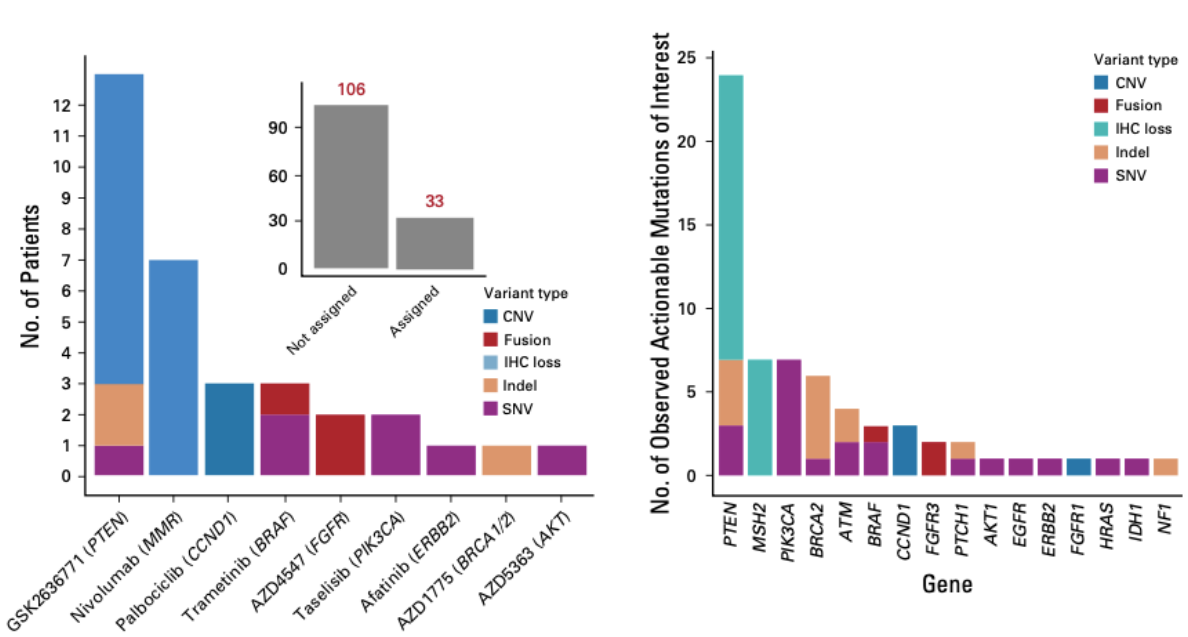
Rabih Said, Cancer J. 2019 ; 25(4): 282–286.

Molecular Landscape and Actionable Alterations in a Genomically Guided Cancer Clinical Trial: National Cancer Institute Molecular Analysis for Therapy Choice (NCI-MATCH)

invasive breast cancer

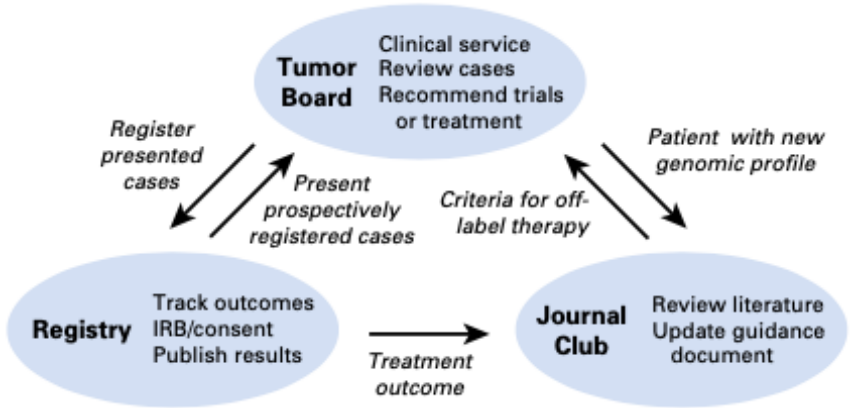


prostate adenocarcinoma

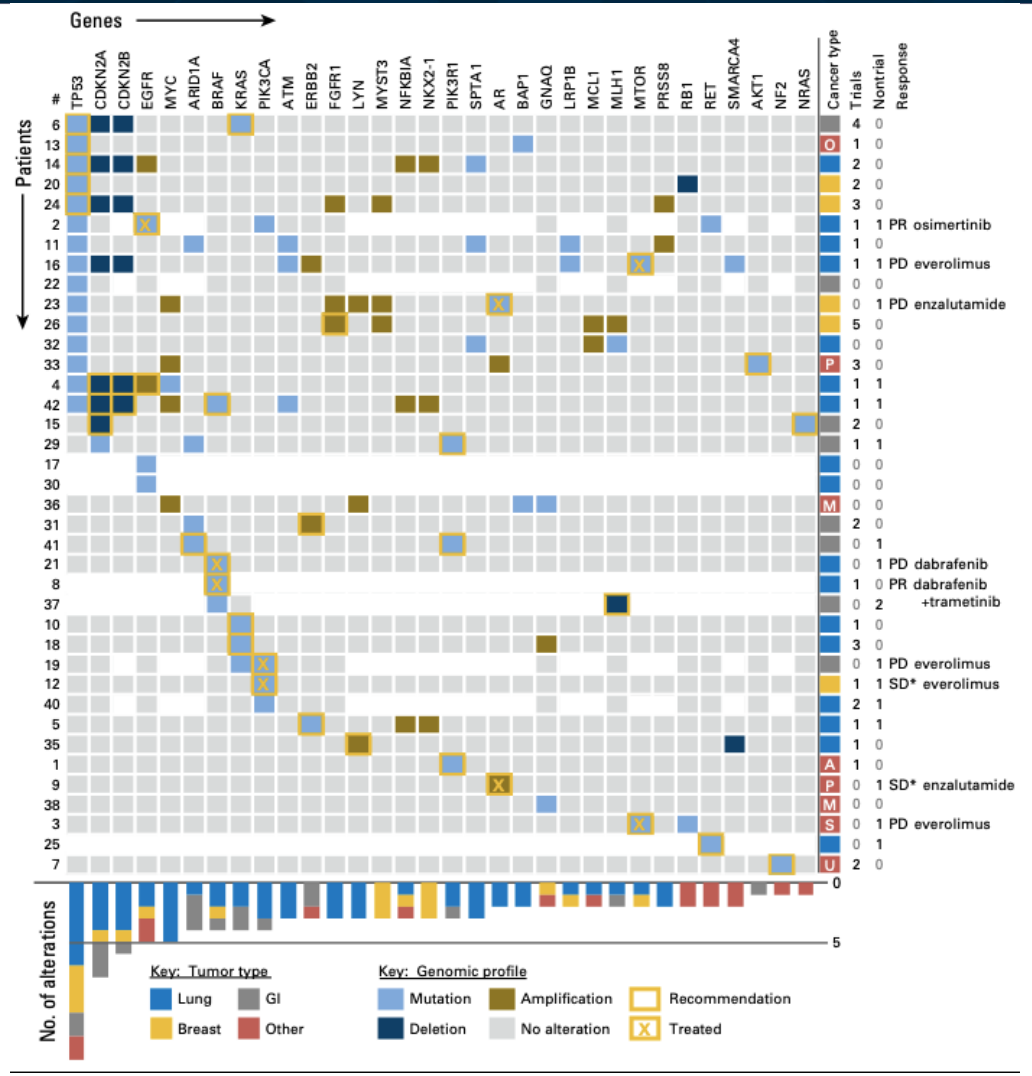


Keith T. Flaherty, J Clin Oncol 38:3883-3894, 2020

Molecolar Tumor Board



Mark E. Burkard, JCO Precision Oncology, 2017



Liquid Biopsies

Fluids biopsied

- Blood
- Urine
- Ascites/pleural fluid
- Cerebrospinal fluid

Examples of Material Isolated/Evaluated

- ctDNA/cfDNA
- CTCs
  - Protein
  - DNA
  - RNA
  - Methylation
  - Functional studies
- Extracellular vesicles

Examples of Clinical Applications

- Assessing immunotherapy response (checkpoint blockade or CAR T-cells)
- Prognostication
- Early cancer detection
- Evaluating residual disease after surgery or drug treatment
- Assessing difficult-to-biopsy cancers
- Understanding tumor heterogeneity
- Detecting potentially actionable alterations
- Early evaluation of response/resistance

Liquid Biopsy (Blood) vs. Tissue Biopsy

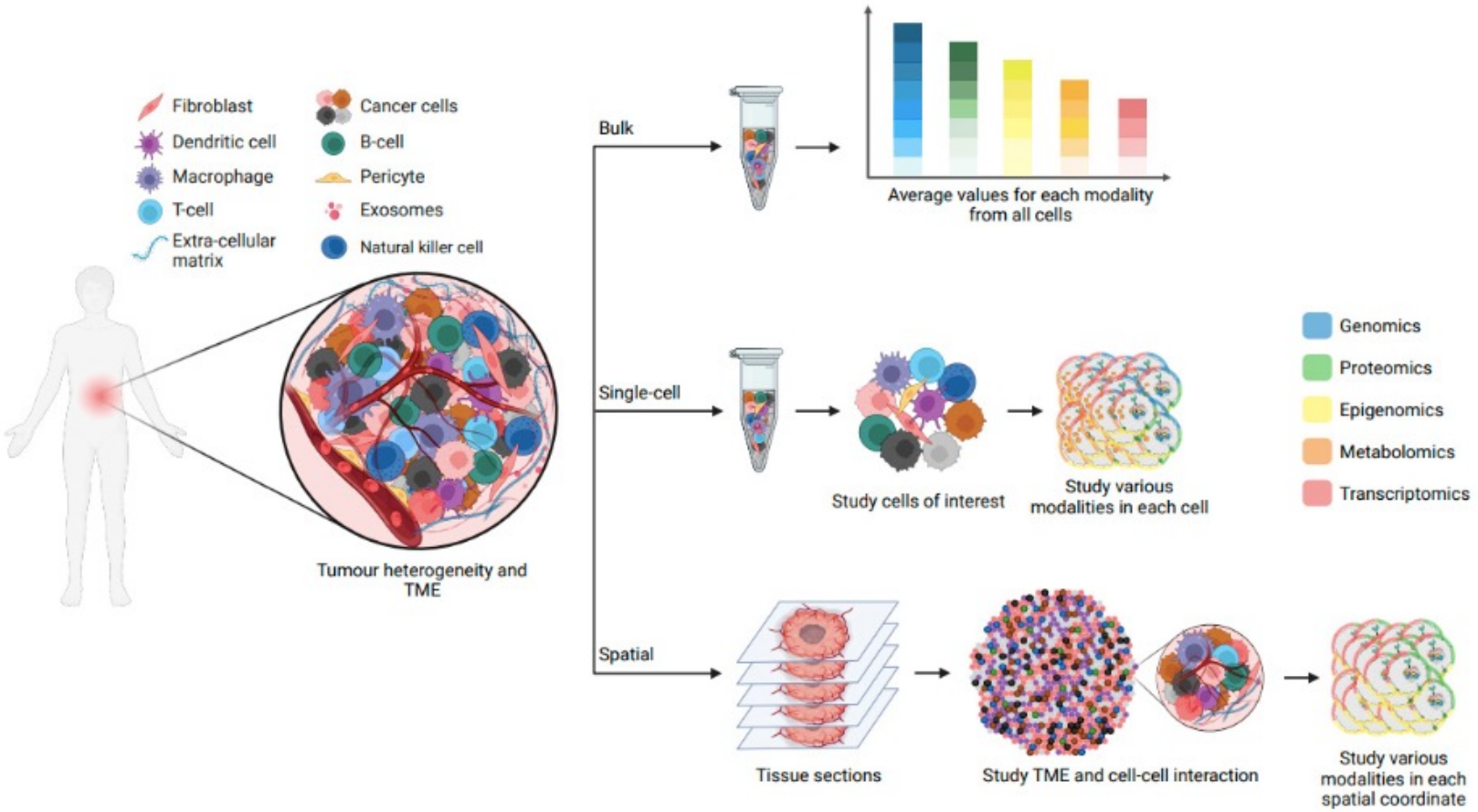
Advantages

- Non-invasive
- Less expensive than tumor biopsy
- Detect material shed from multiple tumor sites
- Can be obtained serially for screening, determining therapeutic response, and assessing for minimal residual disease

Disadvantages

- Low amounts of tumor DNA shed
- Reproducibility concerns from different assays/vendors
- DNA alterations may be confounded by CHIP
- Tumor-derived material may not be shed homogeneously from all sites
- Can be technically challenging (CTC isolation)

Mina Nikanjam, Journal of Hematology & Oncology (2022) 15:131



Arghavan Ashouri , *Genes* 2023, *14*, 1856

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GRAZIE

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