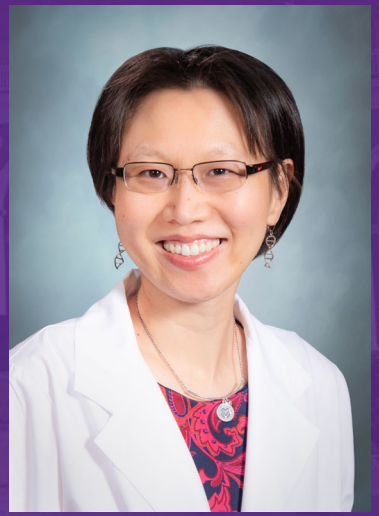
Finding Purpose and Hope:

From Cancer Survivor to Molecular Pathologist



Dr. Yaolin Zhou, MD
Department of Pathology
Associate Professor
East Carolina University – Brody School of Medicine
yaolinz@gmail.com or zhouy20@ecu.edu

Cancer Survivor

Anyone who has ever been diagnosed with cancer no matter where they are in the course of their disease

https://www.cancer.org/cancer/survivorship.html

Survivorship

“Cancer survivorship is often portrayed as a triumphant experience, focusing on recovery and the visible signs of healing….

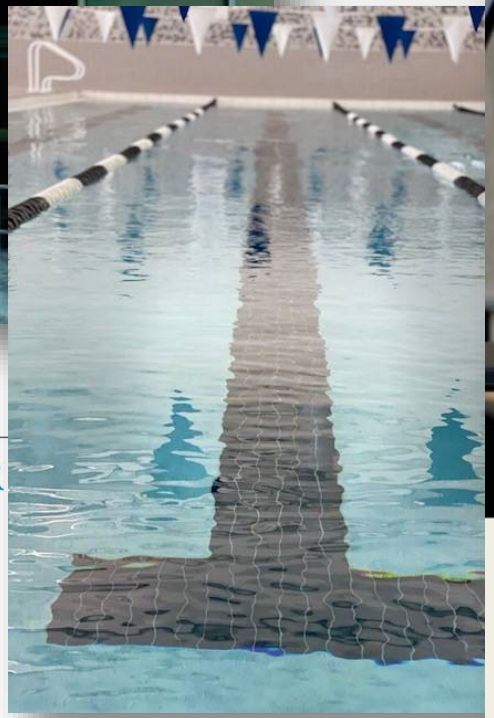
beneath that surface, survivors can experience a variety of physical, emotional, and social challenges that can be just as difficult to manage as the treatment itself.”

https://www.instagram.com/p/DDzkYEoO4sW/

MAYO CLINIC

Duke Health

MASSACHUSETTS
GENERAL HOSPITAL
CANCER CENTER



Listening from both ends of a stethoscope

The story of Mayo Clinic medical student Yaolin Zhou

Pathology

pathos πάθος

"experience" or "suffering"

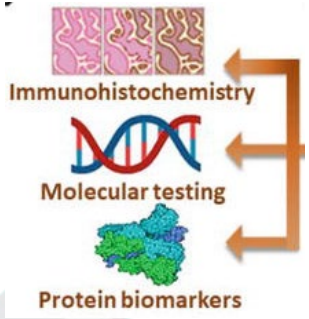
-logia -λογία

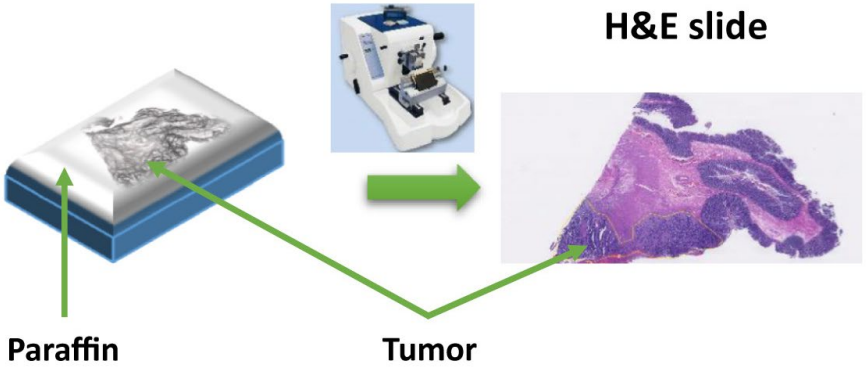
"study of"

Pathologists: Trained physicians who specialize in the diagnosis of many diseases, including cancer, by examining samples from the body (or the entire body!)

Practicing Physician board-certified Anatomic and Clinical Pathologist, Molecular Genetic Pathologist

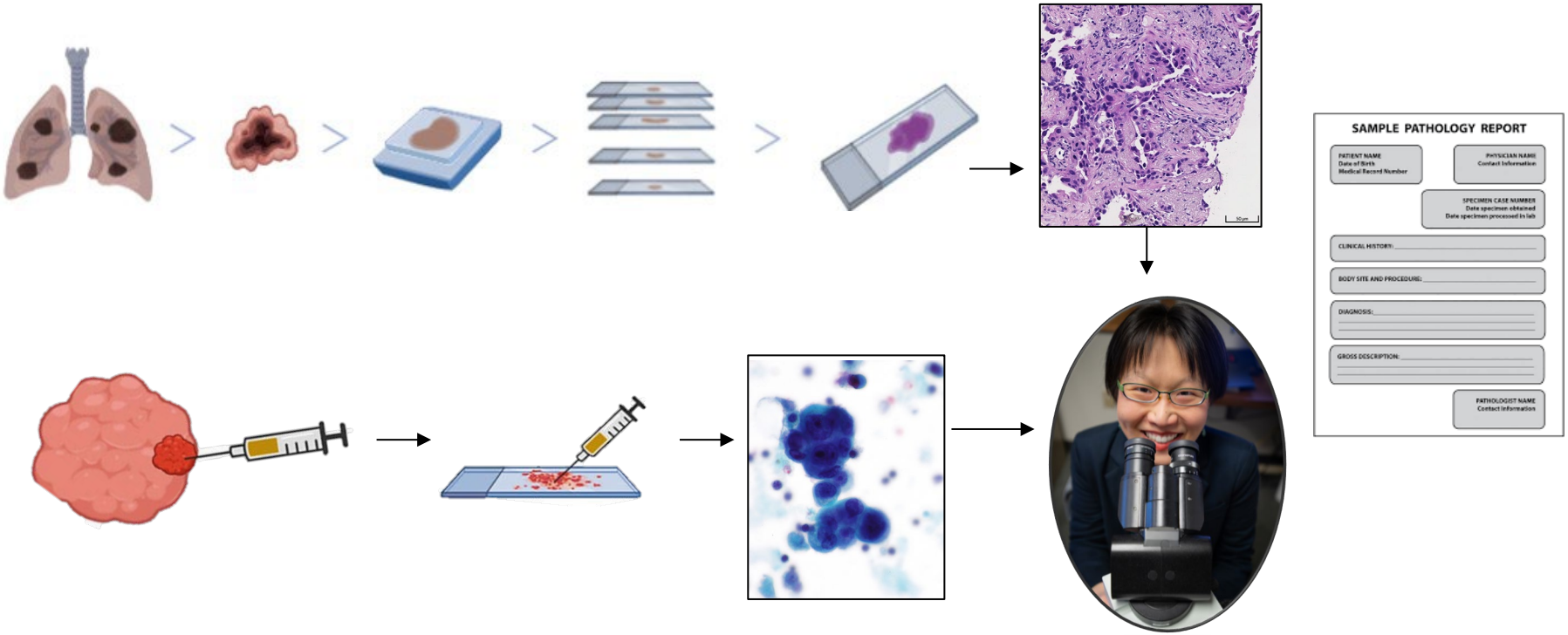
Combine medical knowledge and expertise in genetics and pathology to interpret molecular laboratory tests for the diagnosis, treatment, and prognosis of disease (e.g., mutations in cancers)





ECU

Anatomic Pathology Workflow



https://fabavovutoda.joopsoa.com/gdy?utm_term=pathology+report+format+in+word; https://commons.wikimedia.org/wiki/File:Lung_adenocarcinoma_-_pleural_fluid_-_alt_--_very_high_mag.jpg; https://commons.wikimedia.org/wiki/File:Histopathology_of_lung_adenocarcinoma_with_acinar_pattern.png

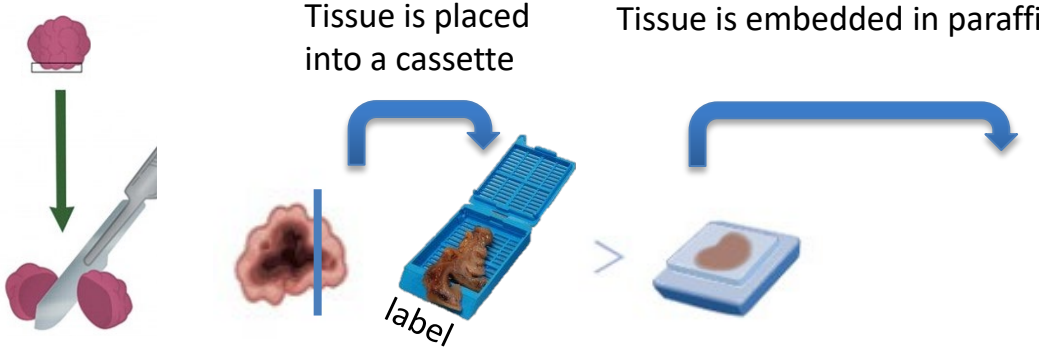
https://www.intechopen.com/chapters/87427 https://uhnbiospecimenservices.com/our-services/digital-pathology-services/

Tissue Processing

Tissue is placed into a cassette

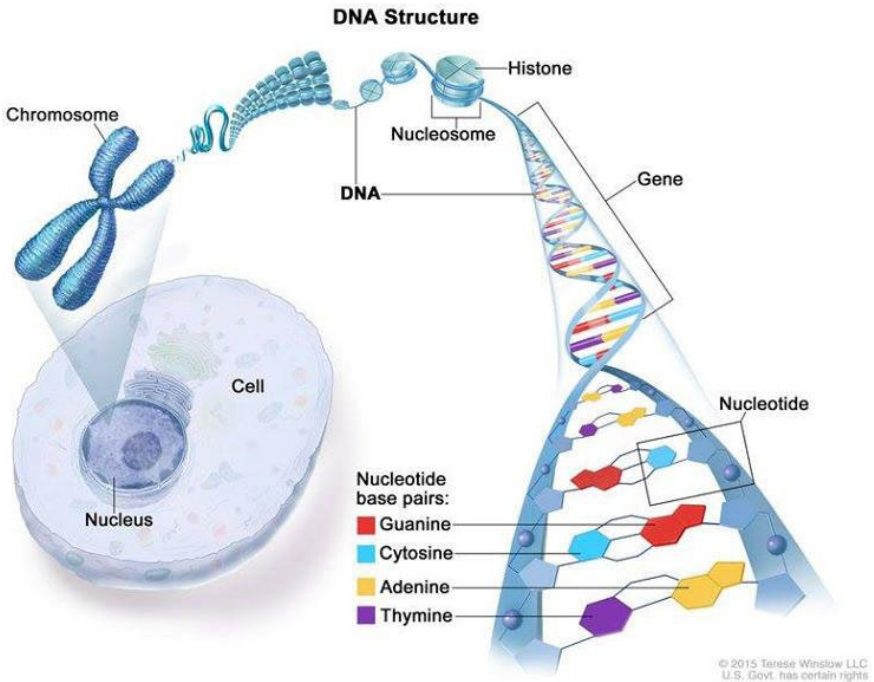
Tissue is embedded in paraffin,

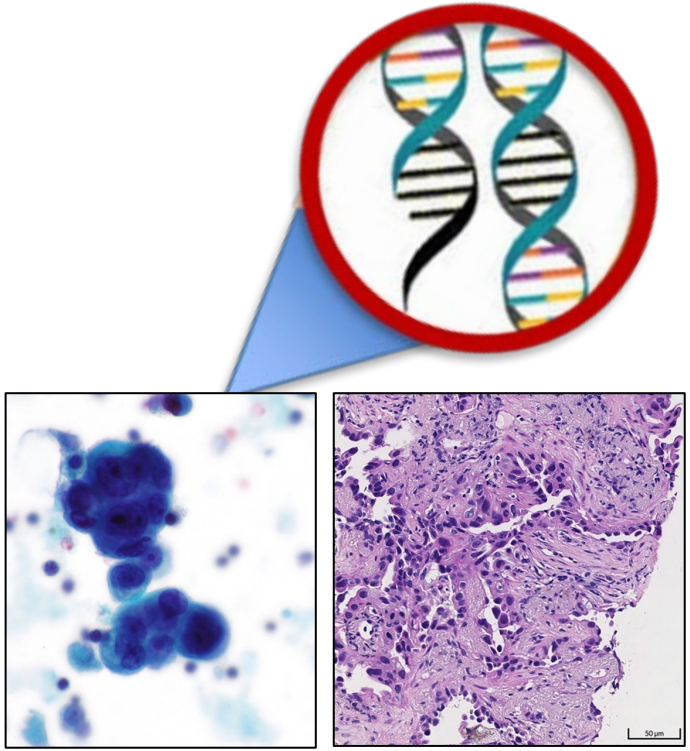
Slides are labeled, stai d viewed under microsco



https://www.abacusdx.com/histology/standardization-in-specimen-description-at-the-grossing-station/; https://www.mayo.edu/research/core-resources/pathology-research-core/services/tissue-sectioning; https://www.leicabiosystems.com/knowledge-pathway/steps-to-better-grossing/; https://commons.wikimedia.org/wiki/File:Tissue_processing_-_After_metal_mould_is_removed,_tissue_can_be_seen_in_the_paraffin_block.jpg

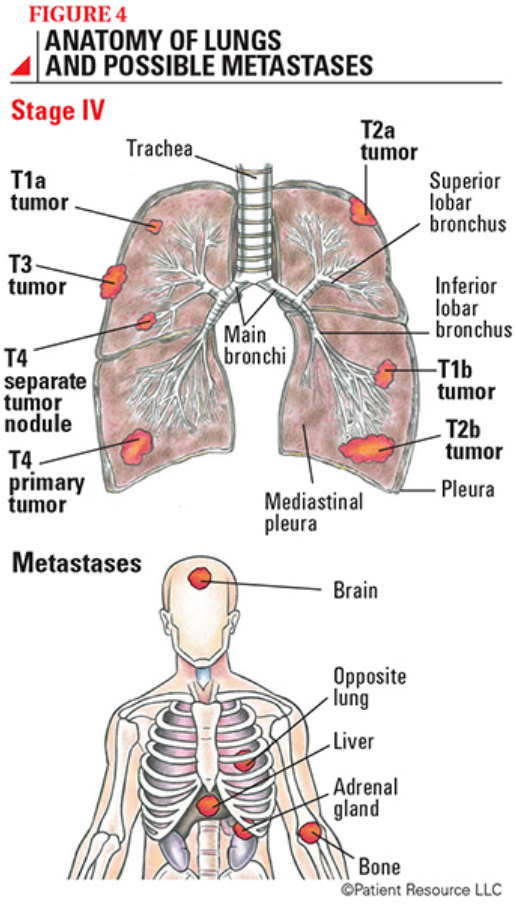
Cancer is caused by DNA changes that are not repaired properly





https://www.cancer.gov/about-cancer/understanding/what-is-cancer
https://commons.wikimedia.org/wiki/File:Lung_adenocarcinoma_-_pleural_fluid_-_alt_--_very_high_mag.jpg
https://commons.wikimedia.org/wiki/File:Histopathology_of_lung_adenocarcinoma_with_acinar_pattern.png

Biomarker	Specific Alterations	Indications	Result Interpretation Significance	Assays Techniques*
Must Test (Broad Molecular Profiling Recommended) **				
EGFR	Exons 18-21 (exon 19 deletions, p.L858R point mutation in exon 21)	Therapy with EGFR-targeted tyrosine kinase inhibitors (TKIs)	Responsiveness to EGFR-targeted TKIs (e.g., afatinib, erlotinib, osimertinib)	NGS, PCR-based assays NSCLC stage IB–IIIA and stage IIIB
	Exon 20 in-frame duplication or insertion	Therapy with EGFR-targeted TKIs	Primary resistance to traditional EGFR-targeted TKI therapy; responsiveness to EGFR-targeted TKIs specific for exon 20 insertion	
	T790M	Arises in response to and as a mechanism of resistance to first- and second-generation EGFR TKIs	Third generation TKIs are typically efficacious. If identified in the absence of prior EGFR TKI therapy, genetic counseling and possible germline genetic testing are warranted. Identification of germline *EGFR* p.T790M confers a high risk for lung cancer regardless of smoking status.	
ALK	Rearrangements: The most common fusion partner is *EML4*	Therapy with targeted inhibitors	Predicts response to oral ALK TKIs (e.g., alectinib, brigatinib, lorlatinib,ceritinib, crizotinib)	FISH, IHC, NGS, RT-PCR††
ROS1	Rearrangements; common fusion partners: *CD74, SLC34A2, CCDC6, GOPC* (FIG)	Therapy with targeted inhibitors	Predicts responsiveness to oral ROS1 TKIs (e.g., ceritinib, crizotinib)	FISH†, RT-PCR††, NGS†††; IHC as a screening with FISH or molecular confirmation of positive IHC results
BRAF	Point mutations Most common p.V600E	Therapy with targeted inhibitors	Predicts response to BRAF/MEK inhibitors (e.g., dabrafenib-trametinib, vemurafenib)	NGS, Sanger sequencing, PCR-based assays, IHC after extensive validation
KRAS*	Point mutations Codon 12, 13, 61, 146	Therapy with targeted inhibitors	Predicts response to sotorasib (*KRAS* G12C); diminished likelihood of another targetable oncogenic alteration; prognostic of poor survival when compared to patients with tumors without *KRAS* mutation	NGS, PCR-based assays
MET	Exon 14 skipping alterations	Therapy with targeted inhibitors	Predicts response to oral MET TKIs (e.g., capmatinib, crizotinib)	NGS†††
RET	Rearrangements Common fusion partners: *KIF5B, NCOA4, CCDC6*	Therapy with targeted inhibitors	Predicts response to oral RET TKIs (e.g., selpercatinib, pralsetinib,cabozantinib, vandetanib)	FISH†, RT-PCR††, NGS†††
***ERBB2* (HER2)**	Mutations (insertion/duplications in exon 20, substitutions at codon S310, amplifications)	Therapy with targeted inhibitors	Predicts response to fam-trastuzumab deruxtecan-nxki (alternative ado-trastuzumab emtansine)	NGS, PCR-based methods
NTRK1/2/3	Rearrangements * To date, no specific clinicopathologic	Therapy with targeted inhibitors	Predicts response to oral TRK inhibitors (e.g., larotrectinib, entrectinib)	FISH, IHC, RT-PCR††, NGS†††



https://www.sitcancer.org/connectedold/p/patient/resources/cancer-types/lung
https://www.amp.org/AMP/assets/File/education/MIMP/LungCancer.pdf?pass=94

https://www.kurlanassociates.com/understanding-the-sales-force/2018/how-the-cheesecake-factory-menu-can-make-you-a-better-closer/

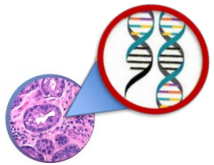
ECU Medical Center Molecular Pathology Workflow

Combine medical knowledge and expertise in genetics and pathology to interpret molecular laboratory tests for the diagnosis, treatment, and prognosis of disease

Pathologist signs report → Request for Molecular Testing → Molecular Pathologist → Material sent to lab

Review Send-Out

- *Medical necessity*
- *Specimen adequacy*
- *Recommend testing*

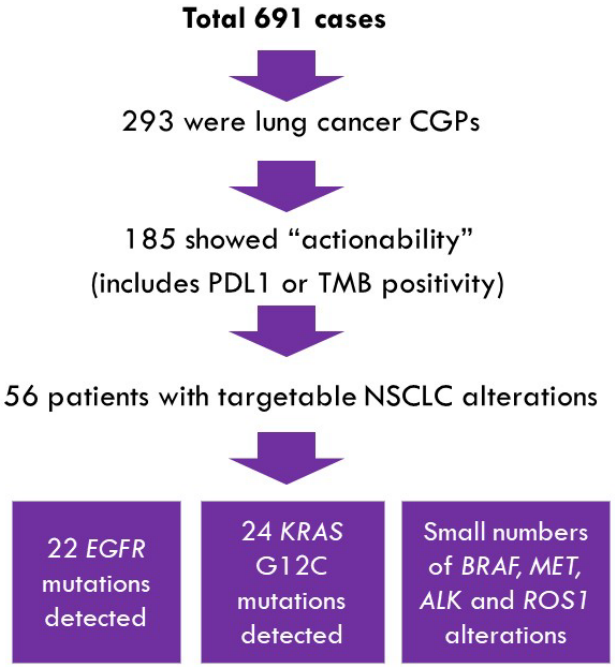


Molecular Consultation (May 2023)

Before ordering molecular testing, what specimen is highest yield, testing strategy	Interpreting molecular results, for clinical care (diagnostic or therapeutic implications)

Molecular Tumor Board (Jan 2025)

Lung Cancer Patient Impact



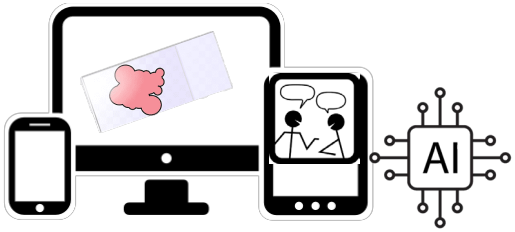
***EGFR* mutation demographics:**

14 B (9 F, 5M) / 6 W (4 F, 2 M) / 1 Asian F

- ✓ Lung cancer is more likely to result an actionable mutation ($p<0.001$)
- ✓ Lung cancer patients are more likely to receive apt Rx than other tumor types ($p=0.007$)
- ✓ Within lung, adenocarcinoma cases are more likely to receive guideline concordant Rx than other lung sub types (Fishers exact test; $p=0.01$)

Patients whose results are referenced in the EHR have approximately **3.76 times** higher odds of receiving targeted therapy compared to patients whose results are not referenced ($p= 0.015$, significant).

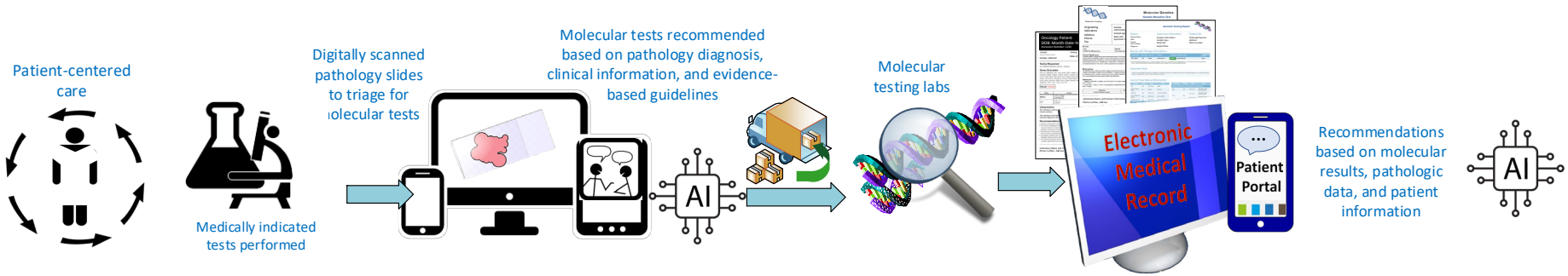
Demographic differences in comprehensive genomic profiling and targeted therapy use among cancer patients in a rural hospital system [Accepted Abstract], Association for Molecular Pathology 2025 Annual Meeting, Boston, MA.

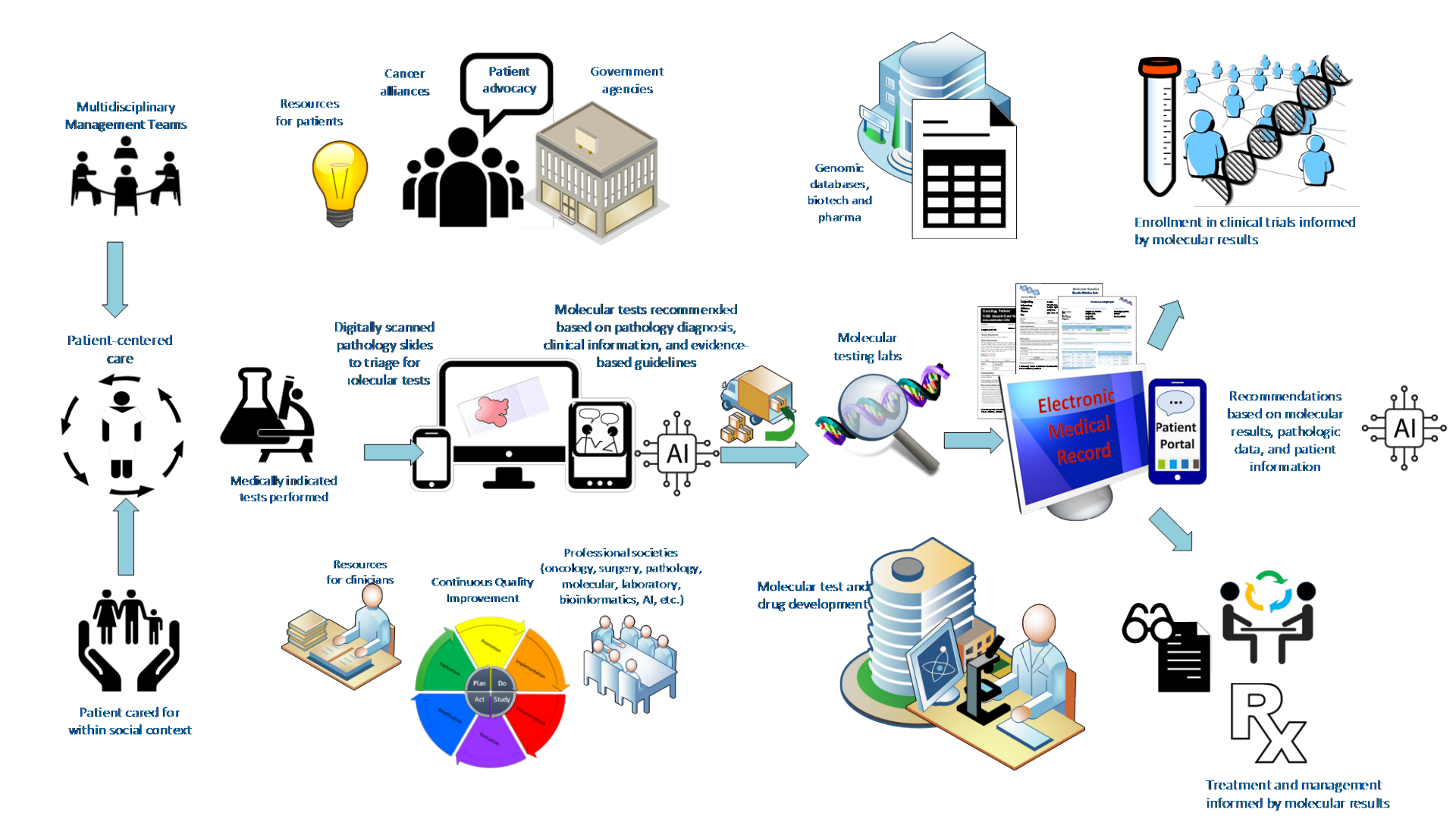


Molecular Path Chat

GPT-5

Precision Oncology Resource


Patient-centered care
Medically indicated tests performed
Digitally scanned pathology slides to triage for olecular tests
Molecular tests recommended based on pathology diagnosis, clinical information, and evidence-based guidelines
AI
Molecular testing labs
Electronic Medical Record
Patient Portal
Recommendations based on molecular results, pathologic data, and patient information
AI


Multidisciplinary Management Teams
Patient-centered care
Patient cared for within social context
Resources for patients
Cancer alliances
Patient advocacy
Government agencies
Genomic databases, biotech and pharma
Enrollment in clinical trials informed by molecular results
Digitally scanned pathology slides to triage for molecular tests
Medically indicated tests performed
Molecular tests recommended based on pathology diagnosis, clinical information, and evidence-based guidelines
AI
Molecular testing labs
Electronic Medical Record
Patient Portal
Recommendations based on molecular results, pathologic data, and patient information
AI
Resources for clinicians
Continuous Quality Improvement
Plan
Do
Study
Act
Professional societies (oncology, surgery, pathology, molecular, laboratory, bioinformatics, AI, etc.)
Molecular test and drug development
Rx
Treatment and management informed by molecular results

Pathology

pathos πάθος

"experience" or "suffering"

-logia -λογία

"study of"

"*only collaborative efforts* can fully realize the potential of molecular pathology and oncology therapeutics for all cancer patients."

https://www.jmdjournal.org/article/S1525-1578(23)00210-6/fulltext

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https://www.flickr.com/photos/polsifter/4047982682