Opportunities and Challenges for the Development and Adoption of Multicancer Detection Tests

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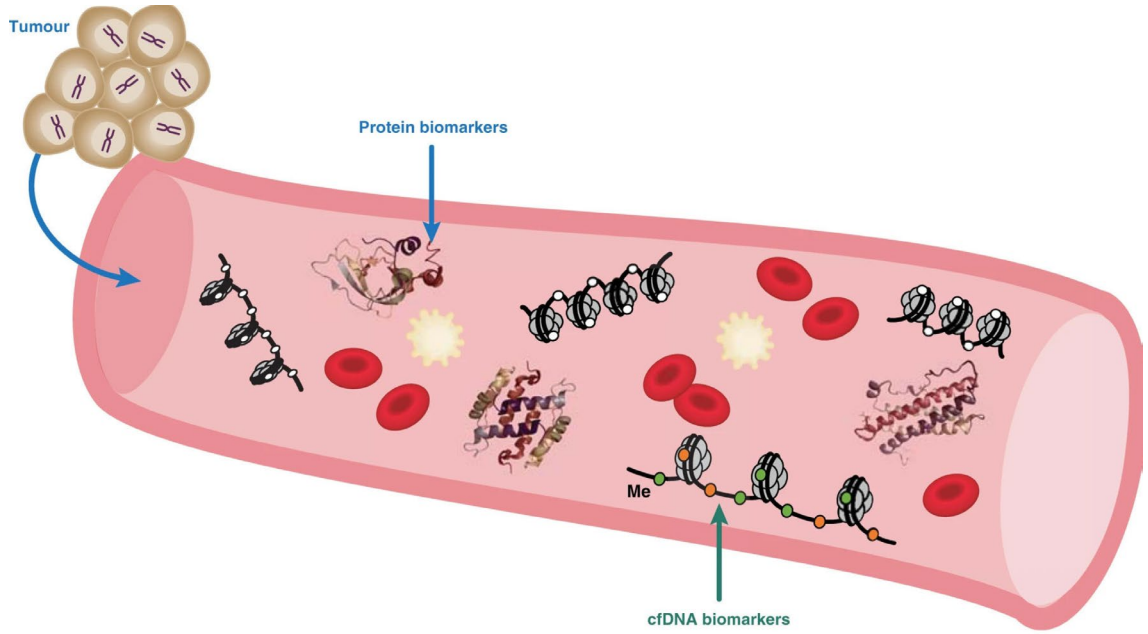
Disclaimers and Disclosures

I work for the Federal Government

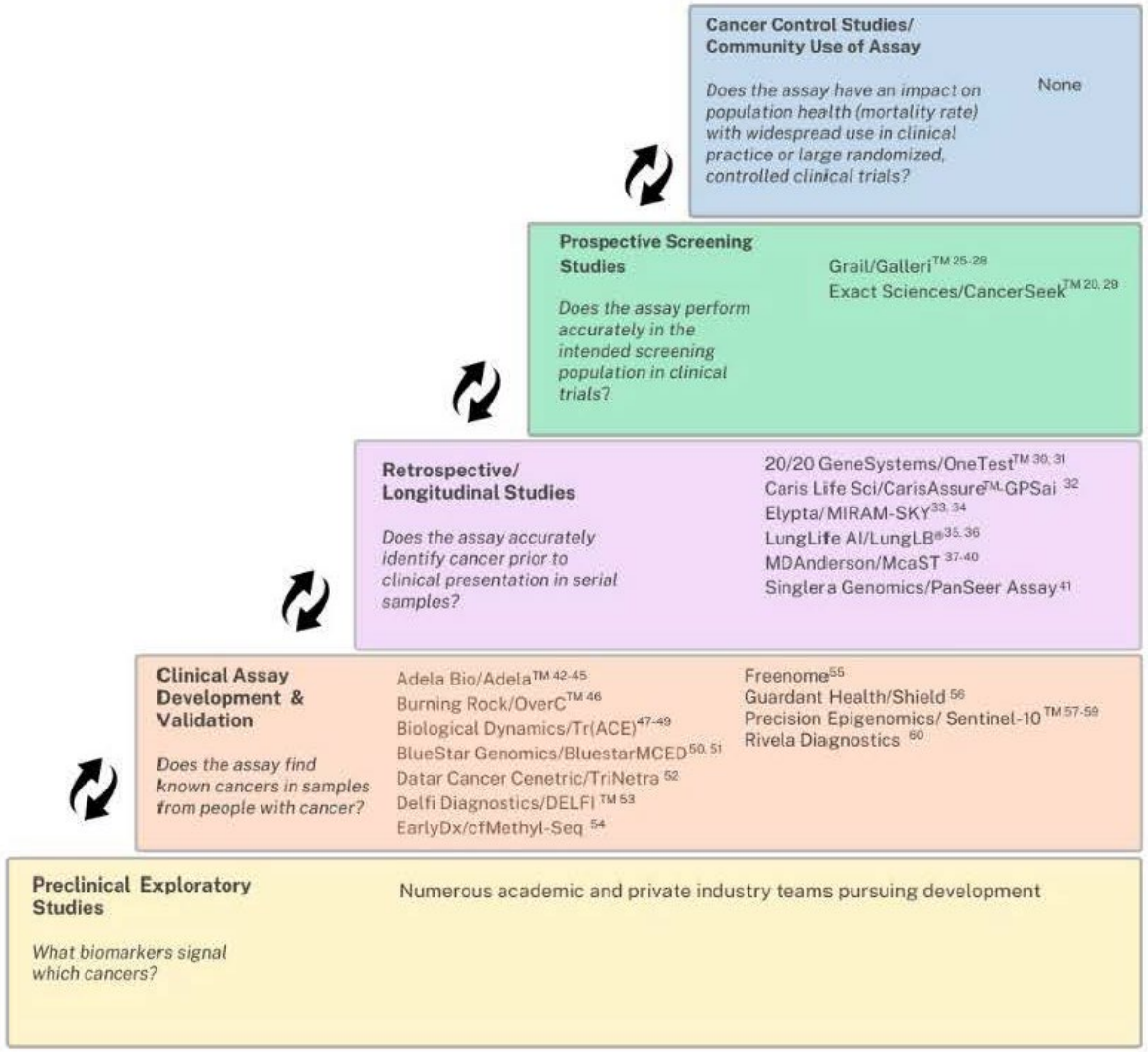
- No Honoraria
- No Consulting Arrangements
- No Stocks in Health Care Sectors

Multi-Cancer Detection Assays: A Potential New Paradigm of Cancer Screening

- Measure biological signals in body fluids that may be shed by cancer cells (known as biomarkers or tumor markers).
- Exploit the shared biology of cancer cells of different tissues to screen for cancers from different organ sites at the same time.
- Utilize high-fidelity/high throughput analytical approaches (e.g. NGS) along with sophisticated statistical algorithms (e.g. ML/AI modeling) to discriminate cancer from non-cancer and to predict the tissue of origin of the cancer signal.



Stage of Biomarker Development of MCD Tests Using Early Detection Research Network 5-phase Framework



Phase 4: Test Sensitivity drops further due to imperfect downstream diagnostic procedure; Specificity of test may drop.

Phase 3: Test Sensitivity drops due to presence of earlier stage disease in presymptomatic, pre-clinical specimens

Phase 2: Test clinical diagnostic performance is most optimistic

Rubinstein, Patriotis et al. CA A Cancer J Clinicians, March 2024; 74:368-382; DOI: (10.3322/caac.21833)

Examples of MCD Assays

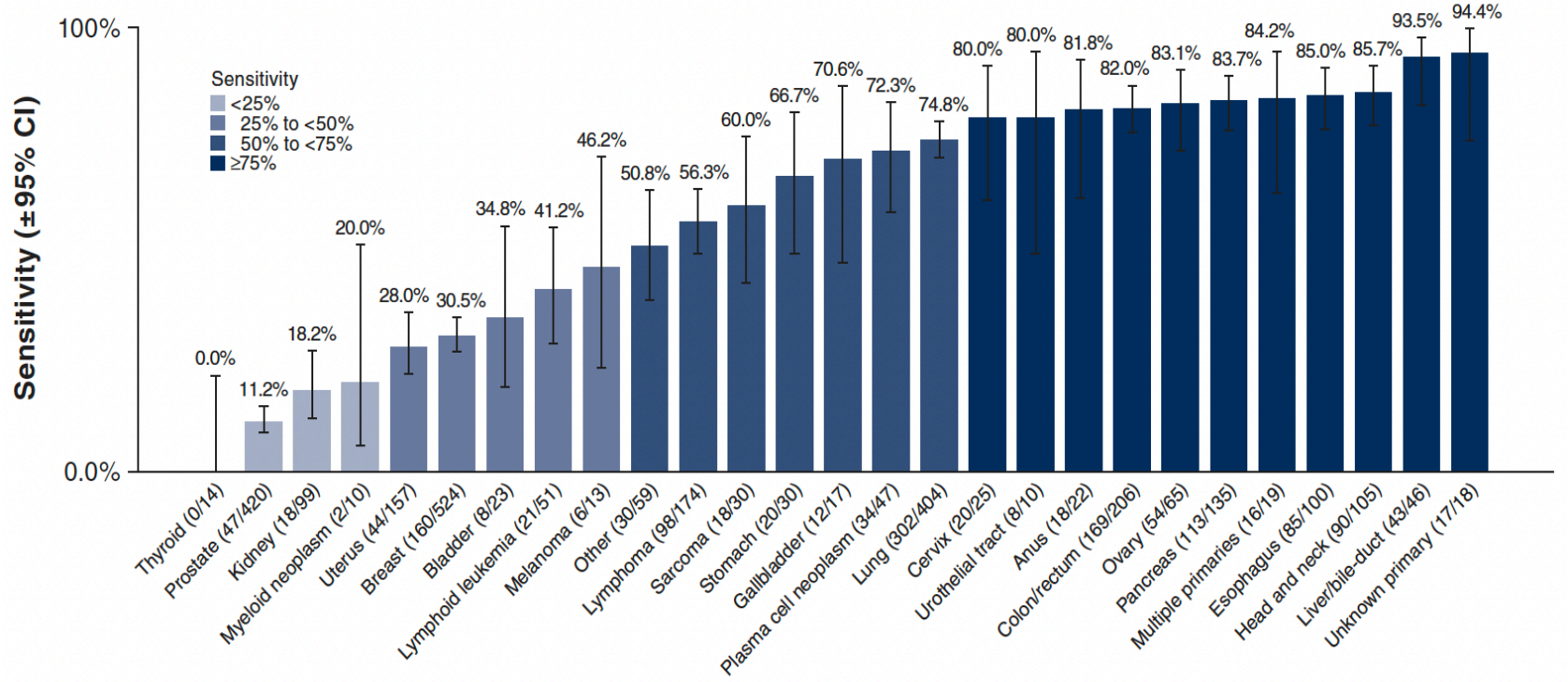
Company	Assay	Technology	Targeted Cancers															
			Lung	CRC	Breast	Pancreas	Liver	Esophagus	Stomach	Ovary	Prostate	Bladder	Kidney	Uterine	Head & Neck	Lymphoma	Leukemia	Plasma Cell Neo
Adela Bio	adela™	cfMeDIP-seq; cfDNA fragmentomics	■	■	■	■						■	■				■	
Biological Dynamics	**Tr(ACE)**	EV proteins; AI	■			■				■	■	■	■	■				
Bluestar Genomics/ ClearNote Health	**Avantect-MCD**	cfDNA 5hmC-seq; fragmentomics	■	■	■	■				■				■				
Burning Rock	**OverC™**	Deep-targeted BS ELSA-seq	■	■		■	■	■		■								
Caris Life Sci	MI GPSai™	cfDNA/cfRNA NGS; AI	■	■	■				■				■	■				
Delfi Dignostics	DELFI	cfDNA fragmentomics	■	■		■			■	■								
Early Diagnostics	**cfMethyl-Seq**	cfDNA mC-NGS	■	■	■		■		■	■								
Elypta	**MIRAM**	UHPLC-MS GAGs/SKY			■				■			■			■	■		
Exact Sciences	CancerSEEK	cfDNA NGS; protein markers	■	■	■	■	■	■	■	■								
Freenome	**FMBT**	Multi-Omics/AI	■	■	■	■	■	■	■	■	■	■	■	■				
Guardant	**GH MCD**	cfDNA-mC NGS; cfDNA fragmentomics	■	■	■	■	■	■		■	■	■	■	■				
Grail	Galleri™	CpG-cfDNA NGS	■	■		■	■	■	■	■		■			■	■		■
LungLifeAI	**LungLB®**	CTC FISH; Imaging AI	■		■		■						■					
Natera	Signatera™	cfDNA NGS; protein markers	■	■	■	■	■			■		■		■				
Oncodea	OncodeAI	Structural fingerprints: proteins, DNA, RNA,	■	■	■						■							
Precision Epigenomics	**Sentinel-10™**	CpG-cfDNA qPCR	■	■	■	■	■											
20/20 Gene Systems	**OneTest**	Circul. Cancer Ag's; AI	■	■	■	■	■		■	■	■							
MD Anderson CC	**McaST**	Raman Spectra profile of exosomes	■	■	■	■	■		■									
Ryerson U/St Michael's Hosp	**Quantum Sensor/OncoProfiler**	Immune Cell SERS/ML	■	■	■			■		■	■	■	■	■	■			

- MCD assays are optimized to detect a defined, small set of cancer types, or “index cancer types”, based on their training on available specimens from cancer cases and matched controls.
- MCD assays measure biological features that are common among most cancers, hence they can detect cancer types outside the “bucket’ of index cancer types.

Variability of Performance within MCD Test

Sensitivity

- Wide range of sensitivities across cancer types

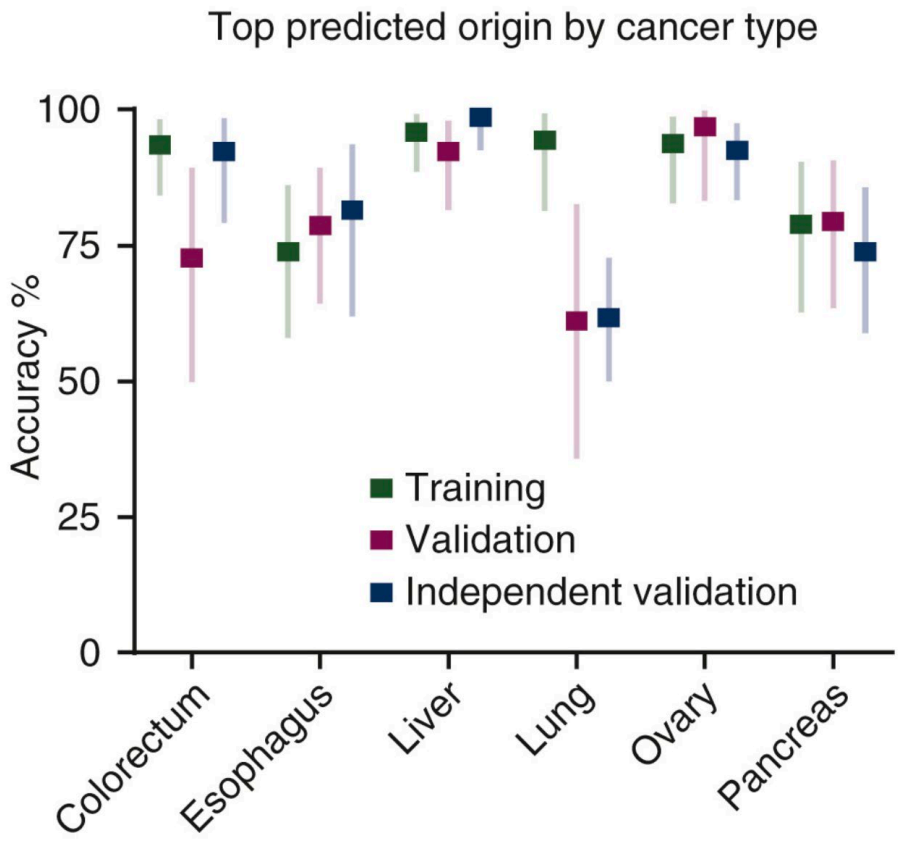


Klein EA, Richards D, Cohn A, *et al*. Ann Oncol. 2021 Sep;32(9):1167-1177. doi: 10.1016/j.annonc.2021.05.806. Epub 2021 Jun 24. PMID: 34176681.

Variability of Performance within MCD Test

Tissue-of-Origin (TOO) Prediction

- Variable range of TOO accuracies across cancer types.
- No TOO provided for cancers outside the "bucket" of index cancers although sensitivity of detection may be similar.
  - ➢**Potential impact on diagnostic odyssey triggered by a positive MCD test.**



Gao Q, Lin YP, Li BS, *et. al.* Ann Oncol. 2023 May;34(5):486-495. doi: 10.1016/j.annonc.2023.02.010. Epub 2023 Feb 26. PMID: 36849097.

Thank You

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