Supplementary file 1

Biomarkers for colorectal cancer detection: An insight into colorectal cancer and FDA-approved biomarkers

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Table S1. Summary of sensitivity, specificity, and clinical indications of FDA-approved biomarkers for CRC.

Biomarker/Test	Sensitivity	Specificity	Main Clinical Indications
CEA (Carcinoembryonic Antigen)	~40–70% (higher in advanced stages)	~70–90%	Monitoring treatment response and recurrence; not recommended for primary screening due to low sensitivity.

Biomarker/Test	Sensitivity	Specificity	Main Clinical Indications
CA 19-9	20–40%	80–90%	Prognosis and monitoring; not for primary screening or diagnosis.
KRAS/NRAS/BRAF mutation	Not applicable (qualitative)	Not applicable (qualitative)	Predicting response to anti-EGFR therapy (KRAS/NRAS); prognostic (BRAF); not for screening.
MSI/dMMR	~95% (MSI-H)	~90%	Predicts eligibility for immunotherapy; Lynch syndrome screening.
mSEPT9 (Epi proColon)	68–81%	87–99%	Non-invasive CRC screening (blood test) for average-risk adults.
Cologuard (Stool	92% (CRC); 42% (advanced	87% (CRC)	Non-invasive CRC and advanced adenoma

Biomarker/Test	Sensitivity	Specificity	Main Clinical Indications
DNA/FIT)	adenoma)		screening for average-risk adults ≥45 years.
Shield (cfDNA blood test)	83% (CRC overall); 65% (stage I); 100% (stage II/III); 13% (advanced adenoma)	90%	Non-invasive CRC screening for average-risk adults 45–84; not recommended for adenoma detection.
ColoSense (stool RNA/FIT)	92.6% (CRC)	85.6%	Non-invasive CRC screening; detects CRC and advanced adenomas.

Table S2. Categorization of CRC biomarkers by clinical type and FDA approval status

Biomarker/Test	Type(s)	FDA-Approved	Main Clinical Role/Notes

Biomarker/Test	Type(s)	FDA-Approved	Main Clinical Role/Notes
CEA (Carcinoembryonic Antigen)	Diagnostic, Prognostic	Yes	Used for monitoring, recurrence, and prognosis—not for screening.
CA 19-9	Prognostic	Yes	Prognostic and monitoring; not for screening or diagnosis.
KRAS/NRAS mutation	Predictive	Yes	Predicts response to anti-EGFR therapy; guides targeted therapy.
BRAF mutation	Prognostic, Predictive	Yes	Prognostic for poor outcome; predictive for targeted therapy.
MSI/dMMR	Diagnostic, Prognostic, Predictive	Yes	Diagnostic for Lynch syndrome, prognostic for early-stage CRC, predictive for immunotherapy response.

Biomarker/Test	Type(s)	FDA-Approved	Main Clinical Role/Notes
mSEPT9 (Epi proColon)	Diagnostic	Yes	Non-invasive CRC screening (blood test) for average-risk adults.
Cologuard (Stool DNA/FIT)	Diagnostic	Yes	Non-invasive CRC screening for average-risk adults.
ctDNA (circulating tumor DNA)	Prognostic, Predictive	No (investigational)	Prognostic for recurrence, predictive for adjuvant therapy benefit.
miRNAs (e.g., miR-21, miR-92a)	Diagnostic, Prognostic	No (investigational)	Early detection, prognosis, and therapy response; not yet FDA-approved.
Fusobacterium nucleatum	Diagnostic, Prognostic	No (investigational)	Microbiome marker for detection and prognosis; not FDA-approved.

Table S3. Distinction between FDA-approved and investigational biomarkers for CRC.

Category	FDA-Approved Biomarkers	Investigational/Emerging Biomarkers
Genetic/Epigenetic	KRAS, NRAS, BRAF, MSI/dMMR, mSEPT9, Cologuard, Shield, ColoSense	PIK3CA, SMAD4, SOX17, miRNAs, circRNAs, lncRNAs, microbiome markers
Protein	CEA, CA 19-9	Multi-protein panels, mucins, SFRP2
Liquid Biopsy	ctDNA (monitoring, not screening)	Advanced ctDNA, exosome analysis