Open Access

Review Article

Emerging Biomarkers and Targeted Therapies Reshaping Clinical Management of Colorectal Cancer

Tamer A. Addissouky [1,2,3]*, Ibrahim El Tantawy El Sayed [2], Majeed M. A. Ali [1]

[1]Al-Hadi University College, Baghdad, Iraq.

[2]Department of Biochemistry, Science Faculty, Menoufia University, Menoufia, Egypt

[3]MLS ministry of health, Alexandria, Egypt. - MLS ASCP, USA.

*Corresponding Author: Tamer A. Addissouky, Al-HADI University College, Baghdad. Iraq. - Department of Biochemistry, Science Faculty, Menoufia University, Egypt. - MLS ministry of health, Alexandria, Egypt. - MLS, ASCP, USA.

Abstract

Background: Colorectal cancer (CRC) is a leading cause of cancer deaths worldwide. Key risk factors include lifestyle, diet, inflammation, and family history. Understanding molecular pathways underlying CRC initiation and progression is critical to guide prevention and treatment.

Purpose: This review summarizes recent advances in CRC screening, therapy, and future directions.

Main body: New stool DNA panels and blood-based assays offer non-invasive options for early CRC detection, though require further validation. Immuno- and targeted therapies matched to tumor molecular profiles have transformed metastatic CRC treatment. Pembrolizumab elicits durable responses in mismatch repair-deficient tumors, and anti-EGFR antibodies cetuximab/panitumumab improve outcomes for left-sided RAS/RAF wild-type CRC. Larotrectinib and entrectinib are highly active in NTRK fusion-positive CRC. Research focusing on new immunotherapies, leveraging the microbiome, and combining multi-omics data to enable precision medicine holds promise. Disparities across groups remain a challenge.

Conclusions: Recent therapeutic advances have significantly improved survival for metastatic CRC patients. Advances in non-invasive diagnostics, next-generation sequencing, and computational approaches will enable more sophisticated molecular profiling and tailored therapy selection. Realizing the potential of emerging immunotherapies and integrating knowledge of the microbiome remain important frontiers.

Keywords: colorectal cancer; immunotherapy targeted therapy; precision medicine biomarkers

Background

Colorectal cancer (CRC) remains one of the most prevalent cancer diagnoses and leading causes of cancer mortality worldwide. Global disease burden has risen in tandem with adoption of certain dietary and lifestyle changes in economically transitioning countries. Understanding key risk factors and pathogenic mechanisms is imperative to guide prevention and treatment strategies [1-3]. Established environmental and lifestyle risk factors for CRC beyond screening non-adherence include smoking, heavy alcohol intake, obesity, consumption of processed or red meat, and low dietary fiber/vegetable intake. Chronic intestinal inflammation is also an important risk factor, as seen in inflammatory bowel disease. Family history of CRC confers increased risk, and several inherited cancer syndromes like Lynch syndrome dramatically predispose to early-onset CRC. Recently, the gut microbiome has emerged as a

potentially important modifiable factor, though mechanisms require further characterization [4-8]. Understanding how these exposures drive CRC initiation and progression at the molecular level remains an area of active investigation. Key pathogenic pathways include chromosomal instability, microsatellite instability, and CpG island methylator phenotype pathways which dictate patterns of genetic mutations arising in tumors. Recent research has also focused on altered metabolic, inflammatory, and immune pathways within the tumor microenvironment which enable growth and metastasis [9].

Early Diagnosis and Screening

Detecting colorectal cancer (CRC) at an early stage is critical, as 5-year survival drops precipitously from 90% for localized disease to 14% for metastatic cancer. While screening has improved early diagnosis, novel modalities beyond colonoscopy and stool testing are emerging as depicted in **table 1**. In 2014, Cologuard, a multitarget stool DNA test, was FDA-approved for CRC screening based on superior sensitivity to standard fecal immunochemical testing. However, concerns remain regarding specificity. Plasma-based tests like Epi proColon (methylated SEPT9 DNA) and OncoBEAM (mutant KRAS/NRAS DNA) are now commercially available as screening tools, though evidence is still limited [10-11]. An area of active research is development of blood-based biomarkers for early detection. Circulating tumor cells (CTCs), cell-free tumor DNA, exosomes, miRNAs, proteins, and metabolites are all under study as non-invasive diagnostic markers. Recent advances have identified methylated gene panels, glycosylated protein markers, and metabolite signatures that can discriminate CRC from controls with high accuracy [12-24]. Machine learning and artificial intelligence tools applied to medical imaging and liquid biomarkers show enormous potential to transform early diagnosis. Deep learning algorithms can synthesize diverse data sources into predictive models. However, extensive further validation is required before clinical implementation [25-33]. While colonoscopy remains the gold standard, the advent of stool DNA panels, blood-based assays, and AI-enhanced imaging offer new options for non-invasive screening that could significantly improve early detection and save lives. But rigorous assessment of clinical utility and cost-effectiveness remains needed as these tools continue to evolve [34-35].

Test	Description	Performance vs Colonoscopy
Cologuard	Multitarget stool DNA test (KRAS mutations, aberrant NDRG4/BMP3 methylation, hemoglobin immunoassay)	- Sensitivity: 92% vs 73% for FIT- Sensitivity for precancerous lesions: 42% vs 23% for FIT- Specificity: 87% vs 95% for FIT
Epi proColon	Plasma septin 9 (SEPT9) methylation assay	- Sensitivity: 48% for CRC- Specificity: 91%
OncoBEAM	Plasma RAS mutation assay	- Sensitivity: 55% for CRC - Specificity: 94%
ExoDx	Exosomal protein biomarker stool test	- Sensitivity: 92% for CRC and 69% for advanced adenomas- Specificity: 87%

Table 1. Emerging Non-Invasive Screening Tests for Colorectal Cancer

Advances in Treatment and Innovative Therapeutics

The treatment landscape for colorectal cancer (CRC) has been transformed over the past decade by the arrival of new chemotherapeutic regimens, immunotherapies, targeted agents, and a growing emphasis on precision medicine. Significant gains have been made in systemic therapies for metastatic CRC, extending and improving quality of survival. Several new chemotherapy backbones and combinations have been established through positive randomized phase III trials and endorsed in clinical guidelines. The FOLFOXIRI regimen (folinic acid, 5-fluorouracil, oxaliplatin, and irinotecan) plus bevacizumab has become a standard first-line option for eligible metastatic CRC patients based on significant extensions in median progression-free and overall survival compared to doublet chemotherapy plus bevacizumab. For patients progressing after first-line treatment, addition of the novel vascular endothelial growth factor (VEGF) inhibitors ramucirumab or regorafenib to continuous 5-fluorouracil-based chemotherapy was shown to provide a survival advantage. The multikinase inhibitor regorafenib also showed activity as monotherapy in phase III trials [36-37].

Beyond chemotherapy, arguably the most exciting advances have come in the form of immunotherapy and targeted therapies directed against specific molecular aberrations. After demonstrating remarkable activity in microsatellite instability-high (MSI-H) solid tumors, pembrolizumab and nivolumab have emerged as mainstream options for metastatic CRC patients whose tumors exhibit mismatch repair deficiency (dMMR) or high microsatellite instability (MSI-H). The pivotal phase II CheckMate-142 trial established pembrolizumab as an effective therapy for previously-treated MSI-H/dMMR metastatic CRC, eliciting an immune-related objective response rate of 31%. Building on this, KEYNOTE-177 established pembrolizumab monotherapy as superior to standard chemotherapy in the first-line setting for this population. Ongoing studies are assessing pembrolizumab in combination with chemotherapy backbone, epidermal growth factor receptor (EGFR) inhibitors, or MEK inhibitors as initial therapy for metastatic MSI-H/dMMR CRC. Beyond MSI-H/dMMR disease, research is ongoing into other potential immunotherapy biomarkers and rational combination strategies to extend benefit to broader groups of CRC patients [38-40]. In parallel, monoclonal antibodies and small molecule inhibitors targeting key oncogenic drivers matched to specific biomarkers have moved into standard practice. Cetuximab and panitumumab, monoclonal antibodies directed against EGFR, are now firmly established components of therapy for left-sided RAS/RAF wild-type metastatic CRC. Multiple trials have proven superior outcomes with the addition of these biologics to chemotherapy backbones for this molecularly defined population. Though less common, actionable NTRK and BRAF mutations also now have clinical grade targeted therapies. Larotrectinib and entrectinib, highly selective tropomyosin receptor kinase (TRK) inhibitors, elicit rapid and often durable responses in the small subset of CRC tumors harboring NTRK fusion genes. Encorafenib (BRAF inhibitor) combined with anti-EGFR antibody cetuximab shows excellent efficacy in BRAF-mutant CRC based on the BEACON trial. While these targets affect a smaller proportion of patients, the activity of matched targeted agents is dramatic and provides proof of concept for ongoing biomarker-driven drug development [41-43].

Traditional Medicine

Some traditional herbal medicines and practices derived from ancient healing systems have shown potential anti-cancer benefits against colorectal cancer in preliminary cell line, animal, and early human studies. Most mechanisms relate to anti-inflammatory, antioxidant, and anti-proliferative properties. Curcumin, a polyphenol derived from turmeric, can inhibit growth and metastasis of colorectal cancer cells through regulating multiple signaling pathways. A small clinical trial in colorectal cancer patients found curcumin combined with chemotherapy

reduced tumor cell proliferation compared to chemotherapy alone. Other polyphenols like EGCG from green tea, resveratrol from grapes, and silibinin from milk thistle also demonstrate anti-cancer effects. The traditional Chinese medicine formula PHY906, containing Scutellaria baicalensis (Huang Qin), has been shown in mouse models to normalize intestinal microbiota and reduce chemotherapy-induced toxicity. A phase I/II trial in patients with advanced colorectal cancer suggested PHY906 plus capecitabine improves progression-free survival compared to capecitabine alone. Larger randomized trials of PHY906 are underway [44-47].

Nanomedicine

Nanomedicine utilizes specially engineered nanoparticles (NPs) sized 1-100 nm for cancer imaging, drug delivery, and theranostics. Over the past decade, NP platforms have made significant progress towards clinical implementation for colorectal cancer. Dozens of NP constructs have been studied for colorectal cancer drug delivery, including liposomes, dendrimers, carbon nanotubes, and inorganic nanoparticles. Liposomal irinotecan received FDA approval in 2015 based on improved progression-free survival compared to standard irinotecan in metastatic colorectal cancer. Iron oxide, gold, and silica NPs have demonstrated potential as highly sensitive contrast agents for enhanced colorectal cancer imaging. Tumor-targeted gold NPs also enable photothermal ablation of tumors when exposed to near infrared light. An exciting development is the emergence of theranostics - NPs that integrate therapy and diagnostics into a single platform. For example, new approaches use fluorescent silica NPs to improve tumor visualization during surgery, while loaded with chemotherapeutics for sustained postoperative treatment [48-50].

Future Directions

While recent years have seen impressive advances in colorectal cancer across multiple fronts, significant opportunities and challenges remain to further progress. Exciting new innovations in treatment, diagnostics, and prevention on the horizon warrant expanded research. Novel immunotherapies offer new paradigms in activating anti-tumor immunity. Beyond immune checkpoint inhibitors like pembrolizumab, ongoing research is exploring cancer vaccines, CAR T cells, oncolytic viruses, and combination immunotherapies. These approaches aim to generate more durable responses than current options [51-53]. Leveraging the microbiome therapeutically also holds promise. Fecal microbial transplantation to restore intestinal homeostasis and probiotics/prebiotics to prevent colitis show potential to reduce colorectal cancer risk. Additional research is needed to identify mechanisms and optimal approaches [54-56]. Expanding our understanding of colorectal cancer genetics and immunology will enable more sophisticated molecular profiling, guiding personalized precision medicine. Multi-omics integration and systems biology modeling will provide a more comprehensive view of CRC carcinogenesis [57]. Detecting pre-malignant polyps and early-stage tumors remains challenging. Development and validation of blood or stool biomarkers, through proteomics, metabolomics, and epigenetics, is a key priority. AI-enhanced imaging and endoscopy could also improve screening [58-59]. Disparities persist in CRC incidence and outcomes across socioeconomic, geographic, and racial/ethnic groups. Resolving these inequities requires coordinated efforts targeting risk factor reduction, screening access, diagnosis delays, and treatment availability [60]. Multidisciplinary collaboration harnessing new technologies will accelerate progress

against colorectal cancer. Advances in genomics, immunotherapy, nanomedicine, applied AI, and precision diagnostics bring hope for improved outcomes and will shape the future of CRC research.

Conclusions:

Recent years have witnessed remarkable progress in the treatment of metastatic colorectal cancer, with median overall survival improving from around 12 months with older chemotherapy regimens to over 30 months with modern combination strategies incorporating targeted agents and immunotherapies matched to specific biomarkers. Looking forward, leveraging rapid advances across fields including genomics, immunotherapy, nanotechnology, and artificial intelligence offers immense opportunities to further advance screening, diagnosis, prevention, and therapeutic decision-making for colorectal cancer. Key priorities include developing and validating non-invasive biomarker approaches to enable earlier detection, expanding insights into colorectal cancer genetics and immunology to extend precision medicine approaches to larger groups of patients, further characterizing the role of the microbiome in colorectal carcinogenesis and response to therapy, designing innovative clinical trial methodologies to efficiently assess emerging immunotherapies and targeted agents matched to lower frequency biomarkers, and applying cutting-edge computational tools to synthesize diverse multi-omics data sources into predictive models guiding personalized therapy selection while accounting for inter- and intra-tumor heterogeneity.

Recommendations:

Several recommendations can be made to accelerate progress against colorectal cancer:

- Expand research and clinical validation of emerging non-invasive screening technologies like stool/blood biomarker panels and AI-enhanced medical imaging to improve early detection.
- Develop and implement standardized molecular profiling of colorectal tumors at diagnosis using next-generation sequencing and immunohistochemistry to match patients to targeted therapies and immunotherapies.
- Design and support innovative clinical trials focusing on novel immunotherapies, integrating multi-omics data, and utilizing master protocols that assign therapy by genomic profile rather than cancer type.
- Investigate the therapeutic potential of the gut microbiome through basic mechanistic studies and clinical trials of interventions like fecal transplant, pre/probiotics, and synbiotics.
- Promote data sharing, collaboration between academia and industry, and leverage big data and AI to enable precision oncology and understand mechanisms of treatment resistance.
- Prioritize reducing disparities in prevention, screening, diagnosis, and treatment across all populations through coordinated policy and community outreach efforts.
- Fund research into novel nanotechnology platforms for colorectal cancer drug delivery, theranostics, and enhanced imaging.
- Train more clinician-scientists qualified to advance molecular pathology, computational biology, immunotherapy, and clinical trials focused on targeted therapies.

Abbreviations:

CRC - Colorectal Cancer

EGFR - Epidermal Growth Factor Receptor

CMS - Consensus Molecular Subtypes

NPs - Nanoparticles

AI - Artificial Intelligence

FIT - Fecal Immunochemical Test

dMMR - Mismatch Repair Deficient

MSI-H - Microsatellite Instability-High

PD-1 - Programmed Death-1

PFS - Progression-Free Survival

OS - Overall Survival

Declarations:

References

1. Brenne, S.S., Madsen, P.H., Pedersen, I.S. *et al.* (2023). Colorectal cancer detected by liquid biopsy 2 years prior to clinical diagnosis in the HUNT study. *Br J Cancer* **129**, 861–868.

2. Addissouky, T.A., El Sayed, I.E.T., Ali, M.M.A. et al. (2024). Oxidative stress and inflammation: elucidating mechanisms of smoking-attributable pathology for therapeutic targeting. Bull Natl Res Cent 48, 16.

3. Saraiva MR, Rosa I, Claro I. (2023). Early-onset colorectal cancer: A review of current knowledge. World J Gastroenterol. 29(8):1289-1303.

4. Malinowska, D., Milewski, R. & Żendzian-Piotrowska, M. (). Risk factors of colorectal cancer: the comparison of selected nutritional behaviors of medical and non-medical students. *J Health Popul Nutr* **42**, 50 (2023).

5. T A Addissouky, A E El Agroudy, A A Khalil, (2023). Developing a Novel Non-invasive Serum-based Diagnostic Test for Early Detection of Colorectal Cancer, *American Journal of Clinical Pathology*, Volume 160, Issue Supplement_1, Page S17.

6. Addissouky TA, El Tantawy El Sayed I, Ali MMA, Wang Y, El Baz A, et al. (2023). Can Vaccines Stop Cancer Before It Starts? Assessing the Promise of Prophylactic Immunization Against High-Risk Preneoplastic Lesions *J Cell Immunol.* 5(4):127-126.

7. T A Addissouky, A A Khalil, (2020). Detecting Lung Cancer Stages Earlier By Appropriate Markers Rather Than Biopsy And Other Techniques, American Journal of Clinical Pathology, Volume 154, Issue Supplement_1, Pages S146–S147.

8. Hua H, Jiang Q, Sun P, Xu X. (2023). Risk factors for early-onset colorectal cancer: systematic review and meta-analysis. *Front Oncol.* 13:1132306.

9. Kitsel Y, Cooke T, Sotirchos V, Sofocleous CT. (2023). Colorectal Cancer Liver Metastases: Genomics and Biomarkers with Focus on Local Therapies. *Cancers (Basel).* 15(6):1679.

10. Stürzlinger H, Conrads-Frank A, Eisenmann A, Invansits S, Jahn B, et. al., (2023). European Network for Health Technology Assessment (EUnetHTA). Stool DNA testing for early detection of colorectal cancer: systematic review using the HTA Core Model® for Rapid Relative Effectiveness Assessment. *Ger Med Sci.* 21: Doc06.

11. Lazar NJ, Khreisat A, AlKloub R, Al-Hillan A, Duffy M. (2023). Inappropriate Multi-Target Stool DNA Use for Colorectal Cancer Screening: Risks, Compliance, and Outcomes. *Cureus.* 15(6): e40506.

12. Capuozzo M, Ferrara F, Santorsola M, Zovi A, Ottaiano A. (2023). Circulating Tumor Cells as Predictive and Prognostic Biomarkers in Solid Tumors. *Cells.* 12(22):25900.

13. T A Addissouky, A A Khalil, A E El Agroudy, (2023). Assessment of potential biomarkers for early detection and management of Glomerulonephritis patients with diabetic diseases, *American Journal of Clinical Pathology*, Volume 160, Issue Supplement_1, November, Pages S18.

14. Addissouky TA, Ali M, El Tantawy El Sayed I, Wang Y. (). Revolutionary Innovations in Diabetes Research: From *Biomarkers to Genomic Medicine.* IJDO 2023; 15 (4) :228-242.

15. Addissouky TA, El Tantawy El Sayed I, Ali MMA, Wang Y, El Baz A, et al. (2024). Shaping the Future of Cardiac Wellness: Exploring Revolutionary Approaches in Disease Management and Prevention. *J Clin Cardiol.*;5(1):6-29.

16. Liu, Y.; Deng, S.; Song, Z.; Zhang, Q.; Guo, Y et. al., (2021). MLIF Modulates Microglia Polarization in Ischemic Stroke by Targeting EEF1A1. *Frontiers in Pharmacology*, *12*.

17. Addissouky TA, Ali MMA, El Tantawy El Sayed I, Wang Y. (2023). Recent Advances in Diagnosing and Treating Helicobacter pylori through Botanical Extracts and Advanced Technologies. *Arch Pharmacol Ther.* 5(1):53-66.

18. Addissouky, T.A., et al. (2020). efficiency of mixture of olive oil and figs as an antiviral agent: a review and perspective, *International Journal of Medical Science and Health Research*, Volume 4, Issue 4, Aug, page 107-111.

19. T A Addissouky, A A Khalil, A E El Agroudy, (2023). Assessing the Efficacy of a Modified Triple Drug Regimen Supplemented with Mastic Gum in the Eradication of Helicobacter pylori Infection, American Journal of Clinical

Pathology, Volume 160, Issue Supplement_1, November, Page S19.

20. Addissouky, T.A., Wang, Y., El Sayed, I.E., et al. (2023). Recent trends in Helicobacter pylori management: harnessing the power of AI and other advanced approaches. Beni-Suef Univ J Basic Appl Sci 12, 80.

21. Lawrence, R., Watters, M., Davies, C.R. *et al.* (2023). Circulating tumour cells for early detection of clinically relevant cancer. *Nat Rev Clin Oncol* **20**, 487–500.

22. Bittla P, Kaur S, Sojitra V, Zahra A, Hutchinson J, et. al.,. (2023). Exploring Circulating Tumor DNA (CtDNA) and Its Role in Early Detection of Cancer: A Systematic Review. Cureus. Sep 22;15(9): e45784.

23. Buk Cardoso, L., Cunha Parro, V., Verzinhasse Peres, S. *et al.* (2023). Machine learning for predicting survival of colorectal cancer patients. *Sci Rep* **13**, 8874.

24. Zhang B, Shi H, Wang H. (2023). Machine Learning and AI in Cancer Prognosis, Prediction, and Treatment Selection: A Critical Approach. *J Multidiscip Healthc.* 16:1779-1791.

25. Addissouky, T.A., Sayed, I.E.T.E., Ali, M.M.A. et al. (2024). Latest advances in hepatocellular carcinoma management and prevention through advanced technologies. *Egypt Liver Journal* 14, 2.

26. Addissouky TA, Ali MMA, El Tantawy El Sayed I, Wang Y, El Baz A, et al. (2023). Preclinical Promise and Clinical Challenges for Innovative Therapies Targeting Liver Fibrogenesis. Arch Gastroenterol Res. 4(1):14-23.

27. Addissouky, T.A., Wang, Y., Megahed, F.A.K. et al. (2021). Novel biomarkers assist in detection of liver fibrosis in HCV patients. *Egypt Liver Journal* 11, 86.

28. Addissouky, T.A., Ayman E. El-Agroudy, Abdel Moneim A.K. El-Torgoman and 1Ibrahim E. El-Sayed, (2019). Efficacy of Biomarkers in Detecting Fibrosis Levels of Liver Diseases. IDOSI Publications, World Journal of Medical Sciences, Volume 16, Issue (1): PP. 11-18.

29. Addissouky, T.A., Ayman E. El Agroudy, Abdel Moneim A.K. El-Torgoman, et. al., (2019). Efficiency of alternative markers to assess liver fibrosis levels in viral hepatitis B patients, Allied Academies Publications, Biomedical Research, Volume 30, Issue (2): PP. 351-356.

30. Addissouky, T.A., (2019). Detecting Liver Fibrosis by Recent Reliable Biomarkers in Viral Hepatitis Patients, *American Journal of Clinical Pathology*, Volume 152, Issue Supplement_1, Page S85,

31. El Agroudy, A. E., Elghareb, M. S., Addissouky, T. A., Elshahat, E. H., & Hafez, E. H. (2016). Serum hyaluronic acid as a non-invasive biomarker to predict liver fibrosis in viral hepatitis patients. Journal of Biochemical and Analytical Research, 43(2), 108377.

32. El Agroudy, A. E., Elghareb, M. S., Addissouky, T. A., Elshahat, E. H., & Hafez, E. H. (2016). Biochemical study of some non-invasive markers in liver fibrosis patients. *Journal of Biochemical and Analytical Research*, 43(2), 108375.

33. Yin Z, Yao C, Zhang L, Qi S. (2023). Application of artificial intelligence in diagnosis and treatment of colorectal cancer: A novel Prospect. *Front Med (Lausanne).* 10:1128084.

34. Zheng S, Schrijvers JJA, Greuter MJW, Kats-Ugurlu G, Lu W, et. al., (2023). Effectiveness of Colorectal Cancer (CRC) Screening on All-Cause and CRC-Specific Mortality Reduction: A Systematic Review and Meta-Analysis. *Cancers (Basel).* 15(7):1948.

35. Jayasinghe M, Prathiraja O, Caldera D, Jena R, Coffie-Pierre JA, et. al.,. (2023). Colon Cancer Screening Methods: 2023 Update. *Cureus.* 15(4): e37509.

36. Shin AE, Giancotti FG, Rustgi AK. (2023). Metastatic colorectal cancer: mechanisms and emerging therapeutics. *Trends Pharmacol Sci.* 44(4):222-236.

37. Kumar A, Gautam V, Sandhu A, Rawat K, Sharma A, Saha L. (2023). Current and emerging therapeutic approaches for colorectal cancer: A comprehensive review. World J Gastrointest Surg. 15(4):495-519.

38. Kamrani, A., Nasiri, H., Hassanzadeh, A. *et al.* (2024). New immunotherapy approaches for colorectal cancer: focusing on CAR-T cell, BiTE, and oncolytic viruses. *Cell Commun Signal* **22**.

39. Manzi J, Hoff CO, Ferreira R, Pimentel A, Datta J, Livingstone AS, Vianna R, Abreu P. (2023). Targeted Therapies in Colorectal Cancer: Recent Advances in Biomarkers, Landmark Trials, and Future Perspectives. *Cancers (Basel).* 15(11):3023.

40. Li F, Lin Y, Li R, Shen X, Xiang M, et. al., (2023). Molecular targeted therapy for metastatic colorectal cancer: current and evolving approaches. *Front Pharmacol.* 14:1165666.

41. Wu, X., Xu, L., Li, X. *et al.* (2023). A HER2-targeting antibody-MMAE conjugate RC48 sensitizes immunotherapy in HER2-positive colon cancer by triggering the cGAS-STING pathway. *Cell Death Dis* **14**, 550.

42. Wang, Fang, Kai Fu, Yujue Wang, Can Pan, et al. (2023). "Small-molecule Agents for Cancer Immunotherapy." *Acta Pharmaceutica Sinica B*,

43. Chen X, Chen LJ, Peng XF, Deng L, Wang Y, Li JJ, Guo DL, Niu XH. (2024). Anti-PD-1/PD-L1 therapy for colorectal cancer: Clinical implications and future considerations. Transl Oncol. 40:101851.

44. Chen, JF., Wu, SW., Shi, ZM. *et al.* (2023). Traditional Chinese medicine for colorectal cancer treatment: potential targets and mechanisms of action. *Chin Med* **18**, 14.

45. Bu, Fan, Yifeng Tu, Ziang Wan, and Shiliang Tu. (2023). "Herbal Medicine and Its Impact on the Gut Microbiota in Colorectal Cancer." *Frontiers in Cellular and Infection Microbiology 13*.

46. Chen JF, Wu SW, Shi ZM, Hu B. (2023). Traditional Chinese medicine for colorectal cancer treatment: potential targets and mechanisms of action. *Chin Med.* 18(1):14.

47. Guo S, Chen M, Li S, Geng Z, Jin Y, Liu D. (). Natural Products Treat Colorectal Cancer by Regulating miRNA. Pharmaceuticals (Basel). 2023 Aug 9;16(8):1122.

48. Dezfuli, A.A.Z., Abu-Elghait, M. & Salem, (2023). S.S. Recent Insights into Nanotechnology in Colorectal Cancer. *Appl Biochem Biotechnol.*

49. Kasi PB, Mallela VR, Ambrozkiewicz F, Trailin A, Liška V, et. al., (2023). Theranostics Nanomedicine Applications for Colorectal Cancer and Metastasis: Recent Advances. Int J Mol Sci. 24(9):7922.

50. Jain A, Bhattacharya S. (2023). Recent advances in nanomedicine preparative methods and their therapeutic

potential for colorectal cancer: a critical review. *Front Oncol.* 13:1211603.

51. Rastin, Farangis, Hossein Javid, Mahsa A. Oryani, Nastaran Rezagholinejad, et. al., (2024). "Immunotherapy for Colorectal Cancer: Rational Strategies and Novel Therapeutic Progress." *International Immunopharmacology 126*, (2024): 111055.

52. He X, Lan H, Jin K, Liu F. (2023). Can immunotherapy reinforce chemotherapy efficacy? a new perspective on colorectal cancer treatment. Front Immunol. 14:1237764. doi: 10.3389/fimmu.2023.1237764. PMID: 37790928; PMCID: PMC10543914.

53. Wu Y, Zhuang J, Qu Z, Yang X, Han S. (2023). Advances in immunotyping of colorectal cancer. *Front Immunol.* 14:1259461.

54. Algrafi AS, Jamal AA, Ismaeel DM. (2023). Microbiota as a New Target in Cancer Pathogenesis and Treatment. *Cureus.* 15(10): e47072.

55. Liu, Yali, Harry C. H. Lau, Wing Y. Cheng, and Jun Yu. (2024). "Gut Microbiome in Colorectal Cancer: Clinical Diagnosis and Treatment." *Genomics, Proteomics & Bioinformatics 21*, no. 1 (2023): 84-96.

56. Knisely A, Seo YD, Wargo JA, (2023). Chelvanambi M. Monitoring and Modulating Diet and Gut Microbes to Enhance Response and Reduce Toxicity to Cancer Treatment. *Cancers (Basel).* 15(3):777.

57. Yang G, Yu XR, Weisenberger DJ, Lu T, Liang G. (2023). A Multi-Omics Overview of Colorectal Cancer to Address Mechanisms of Disease, Metastasis, Patient Disparities and Outcomes. *Cancers (Basel).* 15(11):2934.

58. Ruiz-Bañobre J, Goel A. (2021). Genomic and epigenomic biomarkers in colorectal cancer: From diagnosis to therapy. Adv Cancer Res. 151:231-304.

59. Deris Zayeri, Z., Parsi, A., Shahrabi, S. *et al.* (2023). Epigenetic and metabolic reprogramming in inflammatory bowel diseases: diagnostic and prognostic biomarkers in colorectal cancer. *Cancer Cell Int* **23**, 264.

60. Lozano P, Randal FT, Peters A, Aschebrook-Kilfoy B, Kibriya MG, et. al., (2023). The impact of neighborhood disadvantage on colorectal cancer screening among African Americans in Chicago. *Prev Med Rep.* 34:102235.

To Submit Your Article Click Here: **Submit Manuscript**

Ready to submit your research? Choose Auctores and benefit from:

➢ fast, convenient online submission
➢ rigorous peer review by experienced research in your field
➢ rapid publication on acceptance
➢ authors retain copyrights
➢ unique DOI for all articles
➢ immediate, unrestricted online access

At Auctores, research is always in progress.

Learn more https://auctoresonline.org/journals/cancer-research-and-cellular-therapeutics