

### **Advances and Ongoing Challenges in Colorectal Cancer**

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#### **Abstract**

Colorectal cancer (CRC) remains a major global health concern, with a rising incidence among younger adults and persistently high mortality in advanced stages, despite significant scientific and technological progress. Its etiology is multifactorial, involving lifestyle factors, genetic susceptibility, chronic inflammation, and gut microbiome dysbiosis. Recent advances in screening, molecular profiling, surgery, and systemic therapies have substantially reshaped CRC management. This narrative review was conducted through a comprehensive literature search of PubMed/MEDLINE, Scopus, and Web of Science databases, covering publications from January 2015 to June 2025. Peer-reviewed articles addressing CRC epidemiology, molecular pathways, screening and diagnostic strategies, surgical management, systemic therapies, and emerging treatment modalities were selected. Evidence was qualitatively synthesized and organized into clinically relevant thematic domains. Recent progress in CRC screening, including advanced endoscopic imaging, fecal DNA testing, and blood-based biomarkers, has improved early detection, although implementation remains uneven. Molecular characterization – such as MSI-H/dMMR status, RAS/RAF mutations, HER2 amplification, and consensus molecular subtypes – guides prognostic assessment and personalized therapy. Surgical resection remains the cornerstone of curative-intent treatment, with minimally invasive and robotic approaches reducing morbidity while maintaining oncologic safety. Techniques such as complete mesocolic excision and total mesorectal excision, along with multimodal strategies for advanced disease, have expanded therapeutic options. Despite these advances, challenges persist, including therapeutic resistance, tumor heterogeneity, limited immunotherapy efficacy in microsatellite-stable disease, and rising early-onset CRC. Future progress relies on precision medicine, ctDNA-guided monitoring, microbiome-targeted strategies, and optimized surgical selection.

**Keywords:** colorectal cancer, molecular pathways, screening and diagnosis, colorectal surgery, targeted therapie