

# Molecular Biomarkers

## A review of multiple applications in clinical care of colorectal cancer

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**BACKGROUND:** Advancements in tumor profiling have identified multiple molecular biomarkers that influence tumor growth and behavior. Molecular biomarkers provide clinical prognostic and predictive information, which guides treatment decisions and forms the backbone of precision oncology.

**OBJECTIVES:** This article identifies key predictive and prognostic molecular biomarkers used in the treatment of colorectal cancer and provides greater understanding of their biologic significance and usefulness in guiding treatment decisions.

**METHODS:** A review of the literature and professional guidelines was performed to evaluate approved molecular biomarkers, targeted agents, and tumor testing modalities used for the management and treatment of colorectal cancer, with an emphasis on treatment decision making.

**FINDINGS:** Genomic biomarkers are increasingly used for the prevention, diagnosis, prognostication, and management of colorectal cancer. The introduction of targeted agents and advancements in tumor profiling technologies have increased treatment opportunities and improved clinical outcomes for patients with colorectal cancer.

### KEYWORDS

molecular biomarkers; targeted agents; precision oncology; colorectal cancer

### DIGITAL OBJECT IDENTIFIER

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**COLORECTAL CANCER IS THE THIRD MOST COMMONLY DIAGNOSED** cancer in the United States, excluding skin cancers, and the third leading cause of cancer-related death. In 2020, colorectal cancer is expected to cause an estimated 53,200 deaths (American Cancer Society, 2020). Although the overall death rate from colorectal cancer has been steadily decreasing with improved screening and more effective treatment modalities, the opposite trend has been observed among patients aged 50 years or younger (American Cancer Society, 2020). During the past two decades, the incidence of colorectal cancer in this age group has increased 51%, with an 11% increase in cancer mortality (Siegel et al., 2020). Lynch syndrome, one of the most common forms of inherited cancer predisposition, is caused by germline alterations of DNA mismatch repair (MMR) genes. Lynch syndrome is an autosomal dominant disorder, also known as hereditary nonpolyposis colorectal cancer. Lynch syndrome predisposes patients to developing colon cancer, with a lifetime risk up to 80%, and extracolonic malignancies, including carcinomas of the endometrium, ovary, small bowel, ureter, biliary tract, pancreas, and prostate, as well as a variety of skin cancers (Yurgelun & Hampel, 2018).

Surgery is the one curative modality for stages I–III colorectal cancer. The recommendation for adjuvant chemotherapy in stage II disease is individualized and guided by tumor characteristics (National Comprehensive Cancer Network [NCCN], 2020a). Adjuvant chemotherapy is standard for patients with stage III disease. Chemotherapy, targeted therapy, and immunotherapy have become the standard management strategies for patients with metastatic colorectal cancer (NCCN, 2020a). Targeted agents have increasingly assumed a major role in the treatment of colorectal cancer, with decisions about the most effective treatment being based on tumor profiles and molecular biomarkers (Koncina et al., 2020).

Molecular biomarkers are characteristics of the tumor that can be objectively measured and evaluated and serve as an indicator of normal biologic behavior processes, pathogenic processes, or pharmacologic responses to a specific therapeutic intervention. Prognostic biomarkers estimate the probability of a clinical event, such as disease recurrence or progression, whereas predictive biomarkers determine the likelihood of a favorable or unfavorable response to a specific treatment (Verdaguer et al., 2017). Tumor profiling can identify the molecular biomarkers that influence tumor growth and behavior.