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## Molecular Biomarkers in the Personalized Treatment of Colorectal Cancer

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### Abstract:

Colorectal cancer (CRC) is a disease in which pathogenesis is influenced by genetic and epigenetic events that occur with tumor initiation and progression. Precision oncology is becoming increasingly important in the management and therapy of CRC since large variation exists in individual patient prognosis and response to chemotherapy that is due to molecular heterogeneity. Certain biomarkers have been identified that can be utilized to predict clinical outcome beyond staging, and to inform treatment selection. Molecular testing is routinely performed in clinical practice for the selection of patients for targeted biologic agents or immunotherapy, and is advocated for prognostic stratification. Estimating prognosis can inform treatment decisions with avoidance of under or over treatment and also guide the intensity of patient follow-up. Classifiers of CRC have been developed that integrate genetic and/or epigenetic features which can provide prognostic and predictive information. The mutational status of *KRAS* and *BRAF*<sup>V600E</sup> combined with analysis of the DNA mismatch repair system with/without CIMP has been shown to identify colon cancer subtypes with distinct clinical features and prognoses. Gene expression profiling has also been used to subtype CRCs and can overcome the limitations of single/limited gene testing. A recent effort identified four consensus molecular subtypes of biological relevance that were associated with different patient outcomes. Efforts to validate and refine these subtypes to include additional genomic features are ongoing. In addition to the potential for molecular subtypes to predict therapeutic efficacy, they can inform the development of new agents in a subtype-specific manner to accelerate drug-discovery efforts. The focus of this article is to highlight molecular markers that can inform clinical decision-making in patients with CRC. Molecular profiling-based stratification

**Keywords:** Predictive markers; Prognostic markers; Colorectal cancer; Molecular subtypes; RAS; BRAF; MSI, DNA Mismatch Repair, Immunotherapy; Targeted Therapy; Biologics; anti-EGFR; anti-VEGF

**Conflicts of Interest:** None

### Technological primer:

Molecular testing has become routine in patients with metastatic CRC to select patients for targeted therapy. While analysis of individual genes has been the norm, the use of next-generation sequencing

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