From fork to fight: Exploring dietary patterns in colorectal cancer prevention

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ABSTRACT

Epigenetic alterations, particularly aberrant DNA methylation, are a hallmark of cancer and offer promising applications in early detection, disease monitoring, and risk stratification. Advances in genome-scale methylation profiling and machine learning have enhanced the potential of these biomarkers across diverse cancer types. This presentation highlights the evolution of epigenetic biomarkers, and focuses on recent studies in breast cancer and small intestinal neuroendocrine tumours (siNETs). In a large prospective case–control study nested within the EPIC-Heidelberg cohort (n=702), reduced representation bisulphite sequencing (RRBS) was used to profile DNA methylation in buffy coat samples. Cancer-specific methylation changes were detected in regions associated with SURF6 and REXO1/CTB31O20.3, with signal intensity correlating with time to diagnosis. A machine learning classifier based on these features achieved 76.5% accuracy in predicting future breast cancer cases. These findings support the use of blood-based methylation signatures for early risk stratification. In a separate multi-omics study of siNETs, transcriptomic, genetic, and DNA methylation profiling identified four molecular subtypes with distinct biological features and clinical relevance. These included subtypes linked to specific enteroendocrine differentiation patterns, an immune-enriched subtype, and a mesenchymal-like subtype associated with poor prognosis and treatment resistance, likely driven by cancer-associated fibroblast infiltration. DNA methylation was instrumental in distinguishing multifocal from unifocal tumours, underscoring its utility in tumour classification and outcome prediction. Collectively, these findings demonstrate the utility of epigenetic biomarkers in cancer detection and prognosis. They highlight the potential of methylation profiling in both common and rare cancers to inform personalised care, early intervention, and targeted treatment strategies.

Keywords: DNA methylation, epigenetic biomarkers, risk stratification, predictive biomarkers, neuroendocrine tumours