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REVIEW

Current insights into epigenetics, noncoding RNA interactome and clinical pharmacokinetics of dietary polyphenols in cancer chemoprevention

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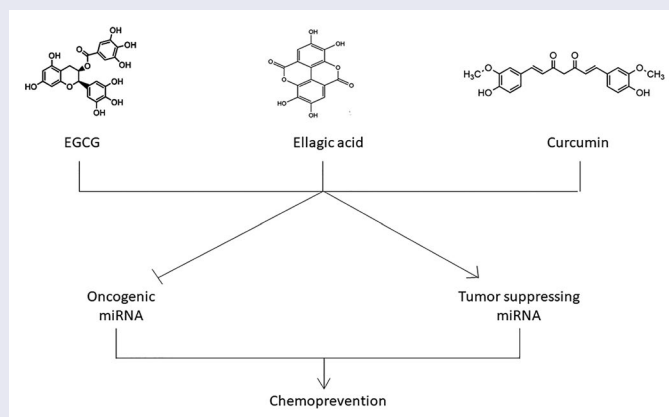
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ABSTRACT

Several studies have reported the health-beneficial effects of dietary phytochemicals, namely polyphenols, to prevent various diseases, including cancer. Polyphenols, like (–)-epigallocatechin-3-gallate (EGCG) from green tea, curcumin from turmeric, and ellagic acid from pomegranate are known to act by modulating antioxidant, anti-inflammatory and apoptotic signal transduction pathways in the tumor milieu. The evolving literature underscores the role of epigenetic regulation of genes associated with cancer by these polyphenols, primarily *via* non-coding RNAs (ncRNAs), such as microRNAs (miRNA) and long noncoding RNA (lncRNA). However, there is little clarity on the exact role(s) played by these ncRNAs and their interactions with other ncRNAs, or with their protein targets, in response to modulation by these dietary polyphenols. Here, we review ncRNA interactions and functional networks of the complex ncRNA interactome with their targets in preclinical studies along with the role of epigenetics as well as key aspects of pharmacokinetics and phytochemistry of dietary polyphenols. We also summarize the current state of clinical trials with these dietary polyphenols. Taken together, this synthetic review provides insights into the molecular aspects underlying the anticancer chemopreventive effects of dietary polyphenols as well as summarizes data on novel biomarkers modulated by these polyphenols for preventive or therapeutic purposes in various types of cancer.

KEYWORDS

Cancer; circRNA; lncRNA; miRNA; ncRNA; pharmacokinetics; polyphenols



Introduction

Despite advances in medical, radiation and surgical oncology, cancer remains particularly difficult to treat owing to several reasons, such as late diagnosis, resistance to chemotherapy and off-tumor toxicity (Global Cancer Observatory 2018a). According to the Global Cancer Observatory database, new incidences of cancer in 2018 amounted to 18,078,957 cases whereas the death toll was 9,555,027 (Global Cancer Observatory 2018a). Furthermore, lung, breast, colorectal,

prostate, stomach and liver cancers accounted for about 50% of the new incidences and deaths in the same timeframe (Global Cancer Observatory 2018a). Nonetheless, and more alarmingly, it is estimated that cancer incidence may rise to 24,112,118 and 29,532,994 cases by 2030 and 2040 (Global Cancer Observatory 2018b). These statistics underscore the need to identify better biomarkers and leads in drug discovery pipelines as also companion diagnostics for diagnosis and prognostication of refractory cancers.

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