EVIDENCE-BASED CARE SHEET

Diet, Epigenetics, and Cancer

What We Know

› Epigenetics, which literally means "above" genetics, is the study of modifications made by exogenous or endogenous sources that affect cellular ability to read the genetic information in DNA, impacting genetic expression. Epigenetics focuses on the regulation of how and when certain genes are turned on and off. Theanalysis of overall epigenetic changes across many genes is termed epigenomics. Epigenetics also encompasses the theory that the epigenome can be inherited. The epigenome consists of all the chemical compounds added to an individual's entire DNA[5,8]

› Although the genetic information in DNA can be coded for certain types of cancer, epigenetic modifications to the reading and handling of DNA can alter the heritability and risk of certain cancers. There is some evidence that although some type of cancer can be inherited, the majority of cancers and cancer progression are the result of epigenetic dysregulation due to exposure to environmental factors such as nutrition, physical activity, pathogens, and socioeconomic status (SES). Socioeconomic status can affect an individual's ability to obtain health care. People with low SES may be less likely to get cancer screening tests. As a result, their cancer may have progressed making it more difficult to treat and decreasing survival chances[3,5]

› It is increasingly understood that diet plays a role in cancer prevention, development, and treatment. As a result, a new area of study is emerging,nutri-epigenetics,which focuses on how nutrition regulates a specific gene being turned on or off. Nutri-epigenomics refers to the analysis of the interaction between genes and nutrition and the effects on global gene expression[1,4,5]

- An important distinction between genetic mutation and epigenetic dysregulation is that DNA is definite since the sequence does not change and epigenomes are potentially reversible with intervention. Researchers are currently investigating strategies for targeting epigenomes in order to prevent and treat cancer
- The mechanisms of epigenetic modification typically involve the following:[1,4]
  - Changes in DNA methylation: Methylation is a process in which a methyl group is added to the cytosine base of the DNA molecule, preventing the expression of certain genes
  - Histone modifications: Histones are proteins that provide the structure around which DNA coils, allowing the long DNA strand to fit in the confines of the cell. Histones orchestrate the degree to which the DNA strand is wound. Tightly wound DNA strands (called heterochromatin) are unavailable for cellular transcription, and loose DNA strands (called euchromatin) are accessible to be read and expressed
  - MicroRNAs (miRNA): miRNAs are small, single-stranded RNAs that determine genetic expression by the posttranscriptional silencing of target genes. miRNAs regulate cell proliferation, apoptosis, and differentiation. Abnormal expression of miRNAs is associated with carcinogenesis
    - miRNAs are able to influence epigenetics and, in turn, epigenetic mechanisms (e.g., DNA methylation) are able to impact miRNA expression

› Diet in relation to epigenetics and cancer[1,4,6]

- The dietary nutrients choline, methionine, and folate are significant contributors of methyl groups for DNA methylation reactions[1]

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- Zinc, source of which include seafood, beef, and lamb, inhibits cell proliferation of prostate cancer cells. A deficiency of zinc can potentially increase the risk of developing prostate and esophageal cancer[1]
- A substantial amount of evidence demonstrates the protective role of dietary phytochemicals (i.e., beneficial, plant-derived substances) against certain cancers. Researchers have reported that some of the chemoprotective efficacy of phytochemicals is related to their modulation of epigenetic alterations in cancer cells. The role of phytochemicals in epigenetics is vast and complex; phytochemicals that affect epigenetics include the following:[2,4,6,7]
  - Results of numerous in vitro and animal studies show an inverse association between the intake of tea and its constituent catechins, the most active of which is epigallocatechin-3-gallate (EGCG), and the cell growth of certain cancers. EGCG has demonstrated the ability to modulate the expression of miRNA in hepatocellular carcinoma cells and inhibit DNA methyltransferases (DNMTs) in human esophageal, colon, prostate, and mammary cancer cells[1,4]
  - Genistein, which is found primarily in soybeans, is an isoflavone from the flavonoid class of polyphenol compounds. Results of studies show that the estrogen-like compound genistein appears to inhibit cervical, prostate, colon, and esophageal cancers through its ability to affect histone acetylation and DNA methylation[1]
  - Resveratrol, which is a nonflavonoid polyphenol found in bilberries, blueberries, cranberries, peanuts, and the skin of red grapes, is reported to reduce oxidative stress and inflammation, which potentially reduces the risk of cancer. Results of studies show that resveratrol is able to affect signaling pathways that regulate cellular division, growth, and apoptosis and affect angiogenesis and tumor metastasis. Resveratrol has demonstrated antiproliferative properties in cancer cells of the liver, skin, breast, prostate, lung, and colon[1]
  - Glucosinolates are primarily found in cruciferous vegetables (e.g., cabbage, broccoli, cauliflower, mustard, Brussels sprouts, rapeseed). The degradation products of glucosinolates, isothiocyanates and indoles, appear to have chemopreventive and therapeutic activity. Specifically, they are noted to have potent fungicidal, bactericidal, nematocidal, and allelopathic properties. Isothiocyanates have demonstrated the ability to affect the epigenome by increasing histone acetylation, inhibiting histone deacetylases (HDACs) and DNMTs, and regulating miRNA expression in pancreatic cancer cells[1,4]

What We Can Do

› Learn about the role that diet plays in epigenetics and cancer so you can accurately assess your patients' personal characteristics and health education needs; share this information with your colleagues
› Assess your patients' health and diet history and their risk factors for cancer
› Educate your patients regarding the importance of eating a balanced diet that includes a variety of fruits and vegetables, whole grains, lean proteins, low-fat dairy products, and appropriate dietary fat options
› Emphasize the benefits of consuming a variety of plant-based foods, which are rich in cancer-preventing phytochemicals

Coding Matrix

References are rated using the following codes, listed in order of strength:

- **M** Published meta-analysis
- **SR** Published systematic or integrative literature review
- **RCT** Published research (randomized controlled trial)
- **R** Published research (not randomized controlled trial)
- **C** Case histories, case studies
- **G** Published guidelines
- **RV** Published review of the literature
- **RU** Published research utilization report
- **QI** Published quality improvement report
- **L** Legislation
- **PGR** Published government report
- **PFR** Published funded report
- **PP** Policies, procedures, protocols
- **X** Practice exemplars, stories, opinions
- **GI** General or background information/texts/reports
- **U** Unpublished research, reviews, poster presentations or other such materials
- **CP** Conference proceedings, abstracts, presentation

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