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# IMPACT OF LIFESTYLE BEHAVIORS ON CANCER RISK AND PREVENTION

*Evans Mireku*

## ABSTRACT:

Cancer rates are increasing worldwide. To effectively prevent and treat cancer, it is crucial to have a deep understanding of cancer pathology. One key aspect of this is the way tumors alter their metabolic processes to meet their specific energy, bio-synthesis, and redox control requirements. This metabolic reprogramming is considered a defining characteristic of cancer and helps differentiate normal cells from cancer cells in terms of nutrient utilization. Notably, changes in the metabolism of nutrients like glucose, amino acids, and fatty acids have been linked to cancer risk.

Fortunately, lifestyle modifications can play a significant role in controlling these metabolic alterations and reducing the risk of cancer. Adopting a healthy diet, practicing calorie restriction, and engaging in regular physical activity are all lifestyle behaviors that can help improve overall well-being and lower the chances of developing cancer.

In this review, we will explore the concept of metabolic reprogramming in cancer and its implications. Additionally, we will examine the evidence linking lifestyle factors to altered nutrient metabolism,

highlighting the potential of lifestyle interventions in reducing the risk of cancer.

**Keywords:** Pathology, Lifestyle, Cancer, Metabolism, Nutrients, Oncogene. Implications.

## INTRODUCTION:

Cancer is a multifaceted disease influenced by a range of factors, including genetics, environment, and lifestyle choices. While genetics and the environment are beyond our control, the choices we make in our daily lives can greatly impact our risk of developing cancer. This article delves into the importance of lifestyle factors in cancer prevention, focusing on key areas such as diet, exercise, tobacco and alcohol use, and sun exposure. By embracing healthy lifestyle habits, individuals can significantly reduce their chances of developing cancer and enhance their overall health and wellness.



Cancer is a collection of diseases characterized by the uncontrolled growth and invasion of abnormal cells. This transformation occurs through a complex process involving changes in molecular composition and metabolic behavior. The final stage, known as metastasis, can have devastating consequences.

The incidence of cancer cases and deaths is projected to rise significantly in the coming decades. According to Global Cancer Statistics (GLOBOCAN), there were 18.1 million new cancer cases and 9.6 million cancer-related deaths in 2018, making cancer the second leading cause of death worldwide. In the United States alone, over 16.9 million individuals had experienced cancer as of January 2019.

Despite advances in cancer research, treatment challenges persist as cancer cells develop resistance to

therapies and often reappear as more aggressive secondary tumors.

The risk factors for cancer are closely tied to population growth and social development. Changes in lifestyle associated with societal evolution have contributed to the rise of metabolic diseases such as diabetes, obesity, and cancer. Dietary factors also play a role, with red and processed meats increasing the risk of colorectal cancer, while calcium, fiber, milk, and whole grains lower the risk.

These effects can be attributed to the impact on immune response, inflammation, and nutrient imbalances that contribute to colorectal cancer development. Additionally, cancer cells exhibit distinct metabolic adaptations, driven by both genetic mutations and the tumor microenvironment, to support their energy needs, biosynthesis, and redox balance.



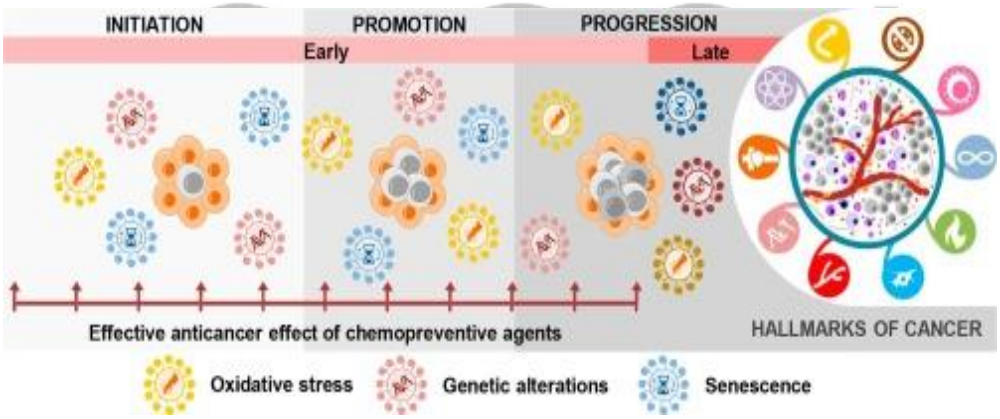
This review aims to explore the significance of molecular and metabolic changes in understanding cancer pathology and emphasizes the importance of lifestyle factors in reprogramming nutrient metabolism. It strongly advocates for lifestyle modifications as a means of cancer prevention and treatment.

## MOLECULAR BIOLOGY OF CANCER:

Decades of extensive research into cancer have unequivocally demonstrated that cancer is a complex ailment characterized by intricate alterations in the genetic makeup. The progression of cancer is intricately linked to mutations that give rise to oncogenes, enhancing their function, and tumor suppressor genes, diminishing their function. Scientific evidence strongly supports the notion that tumorigenesis stems from a

series of events that drive the conversion of normal human cells into highly aggressive and invasive tumors, a process intricately tied to genomic instability. Moreover, it is evident that the evolution of cancer is mirrored by modifications in six key hallmarks: the presence of ample growth signals, resistance to growth-inhibiting signals, uncontrolled replicative potential, sustained angiogenesis, tissue invasion, and metastasis.

Fig.1 Alteration of molecular biology during cancer development.




Normal and cancer cells alike rely on growth signals to transition from a dormant state to an active proliferation phase. These signals are transmitted through transmembrane receptors, essential for initiating cell division. While normal cells necessitate these signals to proliferate, oncogenes can mimic growth factors, driving uncontrolled cell division in cancer cells. For instance, the Ras signaling cascade, constitutively active in25% of human tumors, floods cells with mitogenic signals independently of their usual regulatory mechanisms.

In addition to heightened growth signals, cancer cells exhibit resistance to anti-proliferative cues. These signals, received via cell surface receptors, typically inhibit cell division or induce differentiation. However, cancer cells often evade these signals, disrupting pathways like the retinoblastoma protein signaling to promote continuous cell cycle progression.

Unrestrained cell growth in cancer is not only governed by proliferation rates but also by resistance to apoptosis, the programmed cell death process. While normal cells undergo apoptosis in response to various triggers, cancer cells often evade this fate by mutating key regulators like the p53 tumor suppressor gene.



Furthermore, telomere maintenance distinguishes cancer cells from normal cells, with cancer cells upregulating telomerase to extend telomeres, enabling limitless replication. Angiogenesis, the formation of new blood vessels, is crucial for tumor growth, as it provides oxygen and nutrients. Tumors manipulate angiogenic processes by altering the balance between inducers like Vascular Endothelial Growth Factor (VEGF) and inhibitors, promoting the growth of blood vessels.

Tissue invasion and metastasis mark the advanced stages of cancer progression, where primary tumors infiltrate surrounding tissues and spread to distant sites, forming secondary colonies. This metastatic

spread, often fatal, involves changes in integrin expression that support cancer cell invasion and degradation of surrounding tissue components, facilitating metastasis.

## DIET AND NUTRITION:

Consuming a nutrient-dense diet comprising fruits, vegetables, whole grains, and lean proteins can play a significant role in lowering the likelihood of developing various forms of cancer. These foods are packed with vital nutrients, antioxidants, and dietary fiber that bolster the immune system, aid in DNA repair, and combat inflammation. On the flip side, diets abundant in processed foods, red meats, saturated fats, and sugars have been linked to higher cancer risks. Embracing a well-rounded, plant-centric diet not only aids in cancer prevention but also promotes overall well-being.



Contrary to traditional beliefs, a novel hallmark of cancer involves disrupting cellular energetics. Nutrients play a crucial role in cell survival by supplying the necessary elements for energy production and biosynthesis. The balance of nutrients is carefully regulated to uphold cellular homeostasis and proliferation. Thus, any aberration in nutrient metabolism, such as glucose, amino acid, and lipid metabolism, can precipitate various metabolic disorders, including cancer.

Essential for cell survival, nutrients provide the building blocks for energy production and biosynthesis. Following digestion, nutrients break down into simpler components that enter the bloodstream for further metabolic processes in various cell types.

Maintaining a delicate balance of nutrients is vital for sustaining cellular equilibrium and proliferation. Consequently, disturbances in cellular metabolism can give rise to a spectrum of metabolic disorders, including cancer.

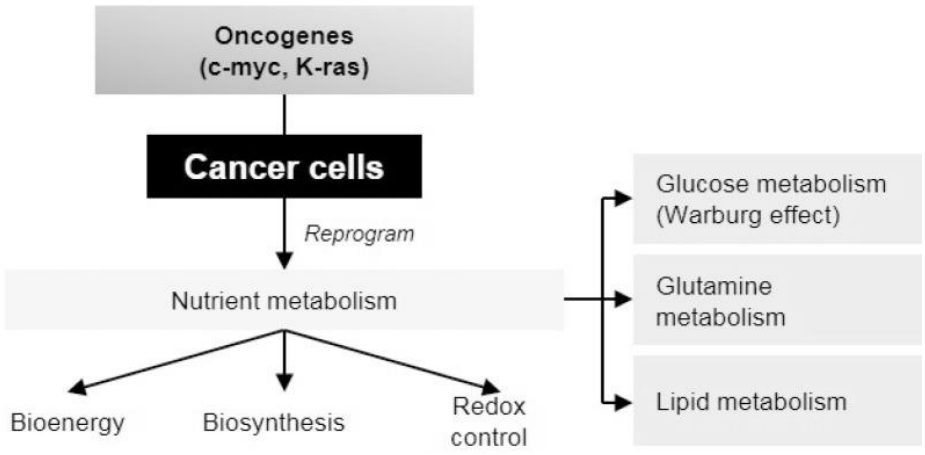





Fig. 2 Metabolic reprogramming in cancer cells involves a distinct process where oncogenes, unlike in normal cells, have the ability to dictate the metabolic phenotype of cancer cells. This reprogramming is aimed at meeting the increased requirements of cancer cells for bioenergy, biosynthesis, and redox control.

The Warburg Effect, discovery, has shed light on the significance of glucose metabolism in cancer development. Unlike normal cells, which primarily rely on glycolysis in the absence of oxygen, cancer cells exhibit aerobic glycolysis. This metabolic shift allows for faster carbon incorporation into biomass, facilitating rapid cell division. Additionally, aerobic glycolysis eliminates oxidative phosphorylation, the main source of reactive oxygen species (ROS), thereby protecting cells from excessive oxidative stress during proliferation. While most cells require aerobic glycolysis for survival, certain cancer cells also depend on

glutamine, the most abundant amino acid in the blood and muscle. These cancer cells express high levels of glutamine transporters to meet their increased demand for glutamine. Once inside the cells, glutamine is metabolized into glutamate and then α-ketoglutarate, fueling the TCA cycle for energy production and macromolecule biosynthesis. Moreover, glutamine serves as a nitrogen source for non-essential amino acids and nucleotide synthesis, and provides glutamate for the production of glutathione, an important regulator of intracellular ROS levels. In some tumors with defective mitochondria, glutamine can be utilized via reductive carboxylation, providing citrate derived from glutamine for both lipid synthesis and intermediates needed for the remaining TCA cycle metabolites. In addition to glucose and glutamine metabolism, lipid metabolism is also altered in cancer cells. While normal cells typically rely on exogenous fatty acids, cancer cells can uptake and synthesize fatty acids de novo by upregulating key enzymes.



Fatty acids not only serve as a highly efficient source of ATP production, but also play important roles as signaling molecules and contribute to membrane components. Excess fatty acids can be stored as lipid droplets, which cancer cells can utilize for energy during nutrient deprivation or metabolic stress. Overall, cancer cells reprogram their metabolism to adapt to harsh tumor environments characterized by limited nutrients and oxygen. Mitochondria, as the central regulators of metabolism, play a crucial role in tumor development. They generate ATP and building blocks, produce ROS, and regulate apoptosis.

Both nuclear DNA and mitochondrial DNA are essential for proper mitochondrial function, and mutations in mitochondrial genes have been observed in many cancer cell lines, illustrating the impact of mitochondrial alterations on metabolic reprogramming. For example, germline mutations in mitochondrial complex II succinate dehydrogenase have been identified in patients with paragangliomas and phaeochromocytomas [28], and somatic missense mutations in isocitrate dehydrogenase can induce metabolic changes that

promote tumor growth.

Therefore, mitochondrial dysfunction is associated with malignant transformation and contributes to tumorigenesis.

Cancer arises from alterations in oncogenes or tumor suppressor genes, such as the amplification of growth factor receptors or inactivation of the important tumor suppressor p53. While many mechanisms have been identified, the role of oncogenes in shaping the metabolic phenotype has only recently received attention. For instance, the well-known oncogene c-myc regulates key enzymes in glycolysis, supporting the Warburg Effect. Similarly, Kras mutation reprograms glutamine metabolism by upregulating aspartate transaminase and suppressing glutamate dehydrogenase in pancreatic cancer. Understanding the relationship between oncogenes and metabolic regulation provides valuable insights into the underlying mechanisms that can be further explored for the development of cancer therapies.



## IMPLICATION FOR CANCER TREATMENT AND PREVENTION:

Consistent physical activity plays a crucial role in cancer prevention. Participating in moderate to vigorous exercise for a minimum of150 minutes weekly can aid in weight management, enhance immune function, balance hormone levels, and decrease inflammation.

Research indicates that regular physical activity can reduce the likelihood of developing several types of cancer, such as breast, colon, lung, and endometrial cancers. Integrating activities like brisk walking, jogging, cycling, or swimming into everyday schedules can greatly support cancer prevention efforts.

The use of tobacco stands out as a primary contributor to preventable cancer cases. Smoking is closely associated with various cancers, including those affecting the lungs, mouth, throat, esophagus, and bladder. Ceasing smoking and steering clear of secondhand smoke are vital measures in mitigating cancer risk. Likewise, excessive alcohol consumption is linked to a heightened risk of specific cancer types, such as breast, liver, colorectal, and oral cancers. Moderating alcohol consumption or abstaining entirely can reduce the likelihood of developing these cancers.

Prolonged exposure to ultraviolet (UV) radiation from the sun or indoor tanning devices significantly increases the risk of skin cancer, including melanoma, which is the most lethal type of skin cancer. Safeguarding the skin against UV radiation plays a crucial role in cancer prevention.



This involves seeking shade during peak sunlight hours, donning protective attire like broad-brimmed hats and long-sleeved clothing, and consistently applying sunscreen with a high sun protection factor (SPF). Metabolic reprogramming in cancer cells presents a promising target for cancer treatment due to the reliance of cancer cells on specific metabolic pathways, rendering them vulnerable to metabolic disruption. For instance, the glycolysis inhibitor2-deoxyglucose (2-DG) is a widely recognized anticancer therapy effective against most cancer cells.

Additionally, statins, inhibitors of cholesterol synthesis, have been shown to inhibit RAS and growth factor receptor signaling pathways crucial for tumor growth.

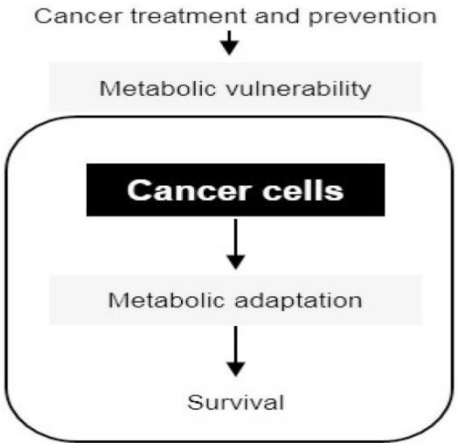
Targeting cancer through metabolite depletion, such as using recombinant arginine deiminase and arginase I to reduce arginine levels, or L-asparaginase for hematopoietic tumors, has also shown promise. Metformin, a medication for type2 diabetes, has demonstrated the ability to inhibit tumor growth either alone or in combination with other treatments, currently undergoing clinical trials.

Understanding cancer metabolism not only provides valuable targets for cancer therapy but also informs dietary strategies for cancer patients. For example, red meat and processed meat consumption have been linked to an increased risk of colorectal cancer, while calcium, fiber, milk, and whole grains have been associated with lower cancer risks. This can be attributed to the modulation of immune response, inflammation, and excess nutrient intake, all of which are risk factors for colorectal cancer development.



The ketogenic diet (KD), characterized by high fat, low carbohydrate, and adequate protein intake, aligns with the Warburg effect observed in many cancer cells that heavily rely on glycolysis for survival. By restricting carbohydrates, the KD can deplete ATP sources in cancer cells, while normal cells can utilize ketone bodies for sustenance. Furthermore, the KD reduces blood glucose levels and insulin production, both crucial for cancer growth. Clinical trials have demonstrated the potential of the KD in suppressing tumor growth in various cancers such as glioblastoma, prostate, colon, pancreatic, and lung cancer, suggesting its role as an adjunct therapy in cancer treatment.

Fig. 3 Metabolic vulnerability as the promising therapeutic target in cancer treatment and prevention




## MODIFICATION OF LIFESTYLE BEHAVIORS FOR CANCER RISK REDUCTION:

Understanding the connection between nutrient metabolism and cancer risk is essential for implementing lifestyle medicine in cancer patients. Research, as depicted in Figure 4, has revealed that adopting a low-fat diet post-diagnosis can lower the chances of breast cancer recurrence and enhance survival rates. Given the direct association between overweight/obesity and breast cancer development, it is imperative to instigate significant lifestyle changes, including regular physical activity and a diet rich in fruits, vegetables, whole grains, and low in red meat and saturated fats. Since cancer cells thrive on abundant nutrients to fuel their rapid growth, calorie restriction (CR) has been proposed as a strategy to reduce cancer risk. CR involves a chronic decrease in energy intake by approximately30% without causing malnutrition. This practice has been linked to extending lifespan and reducing age-related illnesses, including cancer.

A systematic review indicated a 75.5% decrease in tumor incidence across various tumor models with CR. While implementing chronic CR in cancer patients may be challenging, intermittent CR, CR mimetic drugs,

or alternative dietary plans can be considered. Intermittent CR has been suggested to enhance the efficacy of chemotherapy and radiation therapy in cancer treatment, hinting at its potential as an adjunct therapy. CR mimetics, such as metformin and resveratrol, have shown promise in sensitizing cancer cells to traditional anti-cancer treatments. Additionally, dietary approaches like the ketogenic diet, which is high in fat, low in carbohydrates, and adequate in protein, have demonstrated benefits in combination therapies for cancer patients.

The ketogenic diet can lower blood glucose and insulin levels, crucial factors for inhibiting cancer growth. Clinical trials have indicated the efficacy of the ketogenic diet in suppressing tumor growth in various cancer types, suggesting its potential as an adjuvant therapy. Alongside dietary interventions, physical activity plays a significant role in reducing cancer risk across multiple cancer types.



Regular exercise can help maintain muscle mass, reduce fat mass, and lower the risk of breast cancer by 25-30%. Therefore, promoting and sustaining an individual's motivation for consistent physical activity, such as jogging, walking, or gym workouts, is paramount in cancer prevention and treatment.

Fig. 4 Lifestyle behavior modification for cancer prevention.

The association between smoking and the risk of numerous cancer types, including lung, oral, pharyngeal, laryngeal, esophageal, bladder, kidney, and pancreatic cancer, as well as implications of tobacco as a risk factor for colon, stomach, cervical cancer, and leukemia, underscores the critical importance of smoking prevention in cancer prevention strategies; however, current smokers diagnosed with cancer are strongly advised to cease smoking not only for cancer risk mitigation but also for reducing the likelihood of developing other diseases, with evidence suggesting that individuals who quit smoking tend to live longer than those who continue the habit, particularly highlighted by the significant decrease in mortality risk within 15 years for individuals who quit before the age of 50 compared to persistent smokers, and the immediate and lasting reduction in mortality risk observed shortly after quitting and extending for at least a decade and a half, emphasizing the pivotal role of education in promoting smoking cessation and emphasizing the imperative of maintaining a smoke-free lifestyle to mitigate the risks associated with various forms of cancer.



In conjunction with the aforementioned crucial elements, embracing additional healthy lifestyle practices plays a significant role in cancer prevention. These encompass:

**Sustaining a healthy weight**: Obesity is linked to heightened risks of various cancers, including breast, colon, kidney, and pancreatic cancers. Attaining and upholding a healthy weight through a well-rounded diet and consistent physical activity is pivotal in diminishing the likelihood of cancer.

**Undergoing regular screenings**: Routine screenings like mammograms, Pap smears, colonoscopies, and skin examinations can identify cancer in its early stages, enhancing the effectiveness of treatment. Adhering to recommended screening protocols based on age, gender, and individual risk profiles is vital for early detection and prevention.



**Managing stress:** Persistent stress can compromise the immune system and foster unhealthy behaviors. Engaging in stress-alleviating practices such as exercise, meditation, mindfulness, and seeking social support can aid in stress management and bolster overall well-being.

## CONCLUSION:

Healthy lifestyle choices are paramount in cancer prevention, encompassing aspects such as maintaining a nutritious diet, participating in consistent physical activity, abstaining from tobacco and excessive alcohol consumption, shielding the skin from UV radiation, managing weight effectively, undergoing routine screenings, and effectively managing stress.

Equipping individuals with information on healthy lifestyle practices is key to empowering them to proactively mitigate their cancer risk. Cancer pathology involves changes in molecular biology and metabolic characteristics. While traditional views emphasize the disruption of signaling pathways, the focus has shifted to metabolic reprogramming as a key hallmark of cancer. Extensive research has been conducted to unravel the mechanisms, biological implications, and clinical relevance of cancer metabolism. This review consolidates perspectives on common themes in cancer pathology.

Firstly, alterations in both molecular traits and nutrient metabolism, such as glucose, glutamine, and fatty acid metabolism, can promote tumor growth. Secondly, metabolic reprogramming is linked not only to impaired mitochondria but also to the activation of oncogenes.



Lastly, the varied metabolic profiles in cancer cells suggest that modifying lifestyle habits can be advantageous for cancer prevention and treatment. In conclusion, comprehending cancer development offers valuable insights for targeting this formidable disease, which ranks among the most lethal illnesses.

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