

Empowering Prevention: A Review of Modifiable Lifestyle Choices for Lowering Cancer Risk

Maryam Siahtiri¹, Zahra Rezvani^{*2}

¹ Department of Cell and Molecular Biology, Faculty of Chemistry, University of Kashan, Kashan, Iran, Maryam.siyahitiri20@gmail.com

² Department of Cell and Molecular Biology, Faculty of Chemistry, University of Kashan, Kashan, Iran rezvani@kashanu.ac.ir

* Zahra Rezvani

Abstract

Cancer remains a major global health concern, but recent research offers promising insights into preventing its development. Analyzing existing studies reveals a growing emphasis on modifiable lifestyle factors that can significantly reduce cancer risk. A key finding highlights the critical link between diet and cancer. Studies consistently warn against unbalanced diets and suggest potential benefits associated with consuming healthy, nutrient-rich foods. While research continues how dietary interventions interact with cancer, the potential of a balanced, anti-inflammatory diet as a preventative measure shows promise. Beyond diet, the analyzed studies consistently emphasize the importance of maintaining a healthy weight through regular exercise. They also reaffirm the well-established dangers of established carcinogens, such as smoking, excessive alcohol consumption, and unprotected sun exposure, as significant risk factors for various cancers. In conclusion, this analysis underscores the significant impact of modifiable lifestyle choices on cancer risk. By adopting a healthy lifestyle that incorporates a balanced diet, regular exercise, and avoiding established carcinogens, individuals can significantly reduce their risk of developing cancer. This knowledge emphasizes the need for global initiatives that promote healthy behaviors as a cornerstone strategy in cancer prevention.

Keywords: healthy lifestyle, cancer risk, cancer prevention, modifiable lifestyle factors

1- Introduction

Cancer is a complex disease characterized by uncontrolled cell growth and the ability to spread. Studies suggest that genetics play a minor role (around 5-10%) in most cancers “Fig. 1”. Most cancers are linked to environmental factors, diet, and lifestyle choices. Despite the potential for prevention through modifiable behaviors, cancer rates are rising globally, highlighting the urgent need for effective preventative strategies [1, 2]. Recent research has explored additional strategies to combat cancer, focusing on preventative measures through healthy lifestyle choices. These choices include maintaining a healthy weight, engaging in regular exercise, and avoiding established risk factors like smoking and excessive alcohol consumption [3]. Studies now demonstrate that modifying behaviors related to controllable factors, such as diet, can significantly reduce cancer incidence [4]. Despite a strong emphasis on cancer detection and treatment in research, the potential of nutrition in preventing and managing cancer has been relatively understudied.[5,6,7] This review examines how healthy lifestyle choices and various other factors can influence cancer risk and management.

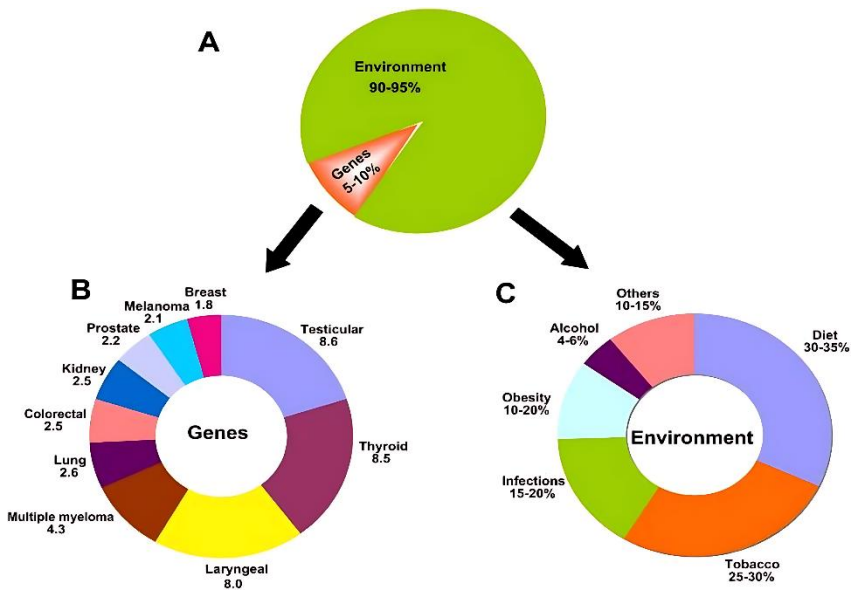


Figure 1: A explores how genes and environment influence cancer risk. It highlights the greater impact of environmental factors (90-95%), compared to genetics (5-10%). B examines familial risk, showing how having a close relative with cancer increases your own risk compared to the general population. Finally, C delves into the percentages of cancer deaths attributable to specific environmental factors[8].

1-1-Factors related to healthy lifestyle

The World Health Organization (WHO) defines health as a state of complete physical, mental, and social well-being, not just the absence of disease. To achieve this optimal state, individuals need to take control of their behaviors and make choices that positively impact their health [9]. This proactive approach to health management is referred to as a healthy lifestyle. It goes beyond simply preventing illness and incorporates habits that enhance well-being throughout life. Some key elements of a healthy lifestyle include maintaining a balanced and appropriate diet, managing stress effectively, engaging in regular physical activity, and avoiding tobacco use [10]. In 2018, the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) joined forces to publish an updated report on cancer prevention strategies. Titled "Diet, Nutrition, Physical Activity, and Cancer: A Global Perspective," the report outlines a series of lifestyle recommendations. These recommendations emphasize maintaining a healthy diet, staying within a healthy weight range (normal Body Mass Index or BMI), and incorporating regular physical activity into your routine. The report underscores the cumulative effect of these adaptable behaviors. By consistently following a balanced diet and engaging in regular exercise, individuals can reduce their risk of developing cancer, other chronic diseases, and obesity [11]. Building on these recommendations, reducing your risk of cancer also involves avoiding both active and secondhand smoke, as well as limiting excessive sun exposure. Smoking is a significant risk factor for various cancers, particularly lung cancer. It also increases the risk of cancers in the oral cavity, pharynx, larynx, and esophagus [12]. The most crucial strategy for cancer prevention is to avoid smoking altogether. Studies have shown that individuals who never smoke or who successfully quit have a significantly lower risk of death from cancer within the next 15 years compared to those who continue to smoke [13, 14]. Researchers debate the link between sun exposure and disease risk, particularly skin cancers. Solar radiation can damage DNA and potentially lead to melanoma, squamous cell carcinoma, and basal cell carcinoma [15, 16]. Studies suggest insufficient sun exposure reduces vitamin D production, potentially increasing cancer risk. While high vitamin D levels might lower skin cancer risks, limited sun exposure creates a vitamin D deficiency dilemma. A balanced approach to sun exposure is crucial. Dietary sources like fatty fish and dairy products can also help maintain healthy vitamin D levels [17-21]. Research shows that adopting multiple healthy habits, rather than just one, improves quality and lifespan [22-25]. Studies on breast cancer survivors, for example, suggest that combining healthy behaviors is more beneficial for well-being than exercise alone [25].

2-Healthy lifestyle and risk factors of cancer

Our bodies are constantly exposed to potential carcinogens, which can cause mutations in cells. These mutations don't always lead to cancer. Brief exposures may result in limited changes that aren't enough to trigger cancerous growth. In some instances, mutations might form noncancerous benign tumors that don't spread. These tumors can remain stable for years without causing problems. However, chronic exposure to certain

carcinogens can cause more severe mutations to accumulate over time. This can lead to the development of aggressive malignant tumors, which are cancerous and pose a threat to life [26, 27].

2-1- Diet

Studies suggest Certain foods can help reduce inflammation, potentially lowering cancer risk. These include tomatoes, olive oil, leafy greens, citrus fruits, and healthy nuts like almonds. Conversely, some foods promote inflammation and should be limited for better health. This includes refined carbohydrates, alcohol, fried potatoes, sugary drinks, and red meat. Limiting these foods may be beneficial for both cancer prevention and management [28]. Research suggests a strong link between diet and cancer prevention [28-30]. Regularly consuming fruits and vegetables rich in bioactive compounds like polyphenols and carotenoids appears to be beneficial. Additionally, including foods rich in vitamin B12, folic acid, selenium, and fiber can further contribute to this protective effect. Interestingly, studies indicate that milk, dairy products, and omega-3 fatty acids found in oily fish and nuts may also play a role in reducing cancer risk [28-32]. Multiple studies have explored the mechanisms behind the Mediterranean diet's protective effects against cancer [33,34,35]. These studies suggest that the diet's rich content of bioactive components plays a key role. These components act as antioxidants and anti-inflammatory agents, potentially triggering apoptosis, reducing inflammation, inhibiting uncontrolled cell growth, and hindering the formation of new blood vessels and tumor cell spread. Furthermore, research indicates an inverse relationship between adherence to the Mediterranean diet and both cancer mortality and the risk of developing various cancers, including colorectal, breast, prostate, liver, stomach, and head and neck cancers [36,37,38]. This suggests that the Mediterranean diet may offer a valuable tool for cancer prevention.

2-2- Obesity

Scientific evidence shows a clear link between inflammation and the development of cancer. Interestingly, obesity is associated with a low-grade, persistent inflammatory state within the body. While the exact reasons behind this chronic inflammation aren't entirely clear, inflammation in adipose tissue likely plays a significant role [39]. Adipose tissue in a healthy state naturally harbors various immune cells, such as macrophages, B and T lymphocytes, natural killer (NK) cells, and Natural killer T (NKT) cells. However, with the onset of obesity, these cells infiltrate the tissue in greater numbers and adopt a more inflammatory profile. Macrophages, for instance, ramp up the production of tumor necrosis factor-alpha (TNF α) and other pro-inflammatory signaling molecules, often described as an "M1 state". Notably, they tend to cluster around necrotic adipocytes, sometimes forming a ring-like structure. Additionally, the number of T lymphocytes, particularly CD8+ T cells, increases alongside B cells, mast cells, and NKT cells [40]. This interplay between immune cells and enlarged obese adipocytes triggers a rise in pro-inflammatory molecules like TNF α , IL 6, IL 1 β , and plasminogen activator inhibitor 1, both locally within the tissue and throughout the body. At the same time, obese individuals exhibit lower levels of adiponectin, a molecule with anti-inflammatory properties. This

shift towards an inflammatory milieu may contribute to a heightened risk of cancer development (carcinogenesis) and potentially weaken the body's natural defenses and anticancer immunity [41]. Another important mechanism involves a buildup of oxidative stress and harmful molecules called reactive oxygen species (ROS) that damage DNA. This oxidative stress is likely worsened by a lack of antioxidant-rich healthy foods in the diet [42,43,44]. Another mechanism relates to the unregulated production of hormones, such as estrogens and androgens in postmenopausal women, leptin, and growth hormones, which can promote cancer development [45,46]. The good news is that research suggests weight loss can be a powerful tool for both preventing cancer and improving treatment outcomes [47].

2-3-Physical Activity

Regular moderate-intensity physical activity can enhance immune function, particularly within the innate immune system, which serves as our body's first line of defense against pathogens and plays a role in tissue repair [48]. This enhancement is evident in both acute and chronic exercise. For instance, studies show an increase in NK cell activity during the recovery phase following aerobic or anaerobic exercise, observed in both healthy individuals and cancer patients [49, 50]. Notably, exercise can significantly elevate circulating NK cell levels by up to fivefold compared to pre-exercise levels [50]. Conversely, a lack of physical activity (sedentary behavior) is associated with an accumulation of visceral adipose tissue and the activation of pro-inflammatory biomarkers. This chronic inflammatory state has been implicated not only in tumor growth but also in the development of other serious health conditions, including insulin resistance, atherosclerosis, and neurodegeneration – collectively referred to as the "diseases of physical inactivity" [51].

2-4-Smoking

Smoking is a major risk factor, possibly the biggest one, for developing cancer and increases mortality rates [52]. The link between smoking and lung cancer is well established [53]. Strong evidence also shows a connection between smoking and cancers of the bladder, head and neck, stomach, colon, rectum, esophagus, pancreas, kidneys, liver, and cervix [54]. Studies indicate that continuous smoking raises the risk of not only cancer but also chronic heart disease and inflammatory illnesses [55,56]. The carcinogenic effect of smoking stems from a complex mix of cancer causing compounds in cigarettes, including polycyclic aromatic hydrocarbons (PAHs), nitrosamines, and acrylamides. These damage DNA, potentially leading to mutations and cancer development. Smoke also contains free radicals (reactive oxygen and nitrogen species), creating an environment with high oxidative stress. This stress harms DNA, lipids, and proteins and promotes chronic inflammation, all of which are known to contribute to cancer [54, 57].

2-5- Alcohol

Estimates suggest alcohol is responsible for roughly 4% of global cancers, translating to over 740,000 cases annually [58]. Esophageal, liver, and breast cancers are

the most prominent types linked to alcohol use. Due to these risks, preventing alcohol consumption is a global goal. Research on alcohol consumption yields mixed results. Some studies indicate that even moderate intake (one or two drinks daily) increases the risk of breast, colorectal, liver, esophageal, and oral cavity cancers [59,60,61]. Conversely, other studies suggest moderate consumption (between 6 and 25 grams/day) reduces cancer risk [62]. For instance, a US study found lower cancer rates in light drinkers compared to non-drinkers [63]. Supporting these findings, studies in Mediterranean countries reveal that moderate red wine consumption with meals may reduce cancer risk and protect against cardiovascular diseases [64,65]. This benefit could be due to the abundance of polyphenols in red wine, which has antioxidant and anti-inflammatory properties [66,67].

Multiple studies have explored the mechanisms and molecular pathways by which alcohol consumption can lead to cancer. Alcohol appears to induce increased oxidative stress and inflammation in cancer cells, further damaging their genetic material [68].

4- Conclusions

In conclusion, a comprehensive approach to diet and lifestyle modifications is a cornerstone in the fight against cancer. Consistently adhering to a combination of healthy habits maintaining a balanced weight, engaging in regular physical activity, minimizing alcohol intake, prioritizing a nutritious diet, and most importantly, not smoking individuals can significantly reduce their risk of developing and progressing through various cancers. This underscores the crucial role of public health initiatives that create supportive environments, promoting and facilitating the adoption of these preventative measures on a global scale. While further research is necessary to fully elucidate the biological mechanisms at play, the evidence overwhelmingly points to the power of a healthy lifestyle in empowering individuals to take control of their well-being and decrease their cancer burden.

References

- [1] Anand P, Kunnumakkara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, et al. Cancer is a preventable disease that requires major lifestyle changes. *Pharm Res* 2008;25(9):2097-2116
- [2] Thun MJ, DeLancey JO, Center MM, Jemal A, Ward EM. The global burden of cancer: priorities for prevention. *Carcinogenesis* 2010;31(1):100-110
- [3] Wu, S.; Zhu, W.; Thompson, P.; Hannun, Y.A. Evaluating intrinsic and non-intrinsic cancer risk factors. *Nat. Commun.* 2018, 9, 3490
- [4] Grosso, G.; Bella, F.; Godos, J.; Sciacca, S.; Del Rio, D.; Ray, S.; Galvano, F.; Giovannucci, E.L. Possible role of diet in cancer: Systematic review and multiple meta-analyses of dietary patterns, lifestyle factors, and cancer risk. *Nutr. Rev.* 2017, 75, 405–419
- [5] Bahrami H, Tafrihi M, Mohamadzadeh S. Reversing the Warburg effect to control cancer: a review of diet-based solutions. *J Curr Oncol Med Sci* 2022;2(3):234-248

- [6] Johnson SB, Park HS, Gross CP, Yu JB. Complementary Medicine, Refusal of Conventional Cancer Therapy, and Survival Among Patients With Curable Cancers. *JAMA Oncol* 2018;4(10):1375-1381
- [7] Jones E, Nissen L, McCarthy A, Steadman K, Windsor C. Exploring the Use of Complementary and Alternative Medicine in Cancer Patients. *Integr Cancer Ther* 2019;18:1534735419846986
- [8] Anand P, Kunnumakkara AB, Sundaram C, et al. Cancer is a preventable disease that requires major lifestyle changes [published correction appears in *Pharm Res.* 2008 Sep;25(9):2200. Kunnumakara, Ajaikumar B [corrected to Kunnumakkara, Ajaikumar B]]. *Pharm Res.* 2008;25(9):2097-2116. doi:10.1007/s11095-008-9661-9
- [9] Bostan N, Beser A. Factors affecting the healthy lifestyle behaviors of nurses/Hemsirelerin saglikli yasam bicimi davranislarini etkileyen faktorler. *Journal of Education and Research in Nursing.* 2017 Jan 1;14(1):38-45
- [10] Çetinkaya S, Sert H. Healthy lifestyle behaviors of university students and related factors. *Acta Paulista de Enfermagem.* 2021 May 5;34:eAPE02942
- [11] World Cancer Research Fund/American Institute for Cancer Research. Diet, Nutrition, Physical Activity and Cancer: A Global Perspective. Continuous Update Project Expert Report 2018. Available online: <http://dietandcancerreport.org> (accessed on 25 October 2023)
- [12] Zhu M, Wang T, Huang Y, Zhao X, Ding Y, Zhu M, Ji M, Wang C, Dai J, Yin R, Xu L. Genetic risk for overall cancer and the benefit of adherence to a healthy lifestyle. *Cancer research.* 2021 Sep 1;81(17):4618-27
- [13] Jacob L, Freyn M, Kalder M, Dinas K, Kostev K. Impact of tobacco smoking on the risk of developing 25 different cancers in the UK: a retrospective study of 422,010 patients followed for up to 30 years. *Oncotarget.* 2018 Apr 4;9(25):17420
- [14] Alshammari FD, Ahmed HG, Alshammari D, Alharbi AM, Alsaedi AS, Elsbaly A. Population insight of the relationship between lifestyle and cancer: A population-based survey. *AIMS Public Health.* 2019;6(1):34
- [15] Schmalwieser, A.W. Possibilities to estimate the personal UV radiation exposure from ambient UV radiation measurements. *Photochem. Photobiol. Sci.* 2020, 19, 1249–1261
- [16] Lucas, R.M.; Yazar, S.; Young, A.R.; Norval, M.; de Gruijl, F.R.; Takizawa, Y.; Rhodes, L.E.; Sinclair, C.A.; Neale, R.E. Human health in relation to exposure to solar ultraviolet radiation under changing stratospheric ozone and climate. *Photochem. Photobiol. Sci.* 2019, 18, 641–680
- [17] Scott, J.F.; Lu, K.Q. Vitamin D as a therapeutic option for sunburn: Clinical and biologic implications. *DNA Cell Biol.* 2017, 36, 879–882
- [18] Scott, J.F.; Das, L.M.; Ahsanuddin, S.; Qiu, Y.; Binko, A.M.; Traylor, Z.P.; Debanne, S.M.; Cooper, K.D.; Boxer, R.; Lu, K.Q. Oral vitamin D rapidly attenuates inflammation from sunburn: An interventional study. *J. Investig. Dermatol.* 2017, 137, 2078–208
- [19] Alfredsson, L.; Armstrong, B.K.; Butterfield, D.A.; Chowdhury, R.; de Gruijl, F.R.; Feelisch, M.; Garland, C.F.; Hart, P.H.; Hoel, D.G.; Jacobsen, R.; et al. Insufficient sun exposure has become a real public health problem. *Int. J. Environ. Res. Public Health* 2020, 17, 5014
- [20] Carlberg, C.; Muñoz, A. An update on vitamin D signaling and cancer. In *Seminars in Cancer Biology*; Elsevier: Amsterdam, The Netherlands, 2022
- [21] Crowe, F.L.; Steur, M.; Allen, N.E.; Appleby, P.N.; Travis, R.C.; Key, T.J. Plasma concentrations of 25-hydroxyvitamin D in meat eaters, fish eaters, vegetarians and vegans: Results from the EPIC–Oxford study. *Public Health Nutr.* 2011, 14, 340–346
- [22] Hawkes, A.L.; Chambers, S.K.; Pakenham, K.I.; Patrao, T.A.; Baade, P.D.; Lynch, B.M.; Aitken, J.F.; Meng, X.; Courneya, K.S. Effects of a telephone-delivered multiple health behavior

- change intervention (CanChange) on health and behavioral outcomes in survivors of colorectal cancer: A randomized controlled trial. *J. Clin. Oncol.* 2013, 31, 2313–2321
- [23] Spring, B.; Moller, A.C.; Coons, M.J. Multiple health behaviours: Overview and implications. *J. Public Health* 2012, 34 (Suppl. S1), i3–i10
- [24] Tollosa, D.N.; Tavener, M.; Hure, A.; James, E.L. Adherence to multiple health behaviours in cancer survivors: A systematic review and meta-analysis. *J. Cancer Surviv.* 2019, 13, 327–343
- [25] Dalla Via, J.; Daly, R.; Fraser, S. The effect of exercise on bone mineral density in adult cancer survivors: A systematic review and meta-analysis. *Osteoporos. Int.* 2018, 29, 287–303
- [26] Alberts B, Johnson A, Lewis J, et al. *Molecular biology of the cell*. 4th ed. New York: Garland Science; 2002
- [27] Ledford H. The human body is a mosaic of different genomes. *Nature news.* 2019
- [28] Scheiber A, Mank V. *Anti-Inflammatory Diets*. Treasure Island (FL): StatPearls Publishing; 2023
- [29] Solans M, Castelló A, Benavente Y, Marcos-Gragera R, Amiano P, Gracia-Lavedan E, Costas L, Robles C, Gonzalez-Barca E, de la Banda E, Alonso E. Adherence to the Western, Prudent, and Mediterranean dietary patterns and chronic lymphocytic leukemia in the MCC-Spain study. *haematologica.* 2018 Nov;103(11):1881
- [30] Fliss-Isakov, N.; Kariv, R.; Webb, M.; Ivancovsky, D.; Margalit, D.; Zelber-Sagi, S. Mediterranean dietary components are inversely associated with advanced colorectal polyps: A case-control study. *World J. Gastroenterol. WJG* 2018, 24, 2617
- [31] Farràs Mañé, M.; Almanza-Aguilera, E.; Hernández, Á.; Agustí, N.; Julve, J.; Castañer, O. Beneficial effects of olive oil and Mediterranean diet on cancer physio-pathology and incidence. In *Seminars in Cancer Biology*; Elsevier: Amsterdam, The Netherlands, 2021
- [32] Morze, J.; Danielewicz, A.; Przybyłowicz, K.; Zeng, H.; Hoffmann, G.; Schwingshackl, L. An updated systematic review and meta-analysis on adherence to mediterranean diet and risk of cancer. *Eur. J. Nutr.* 2021, 60, 1561–1586
- [33] Goñi, I.; Hernández-Galiot, A. Intake of nutrient and non-nutrient dietary antioxidants. contribution of macromolecular antioxidant polyphenols in an elderly Mediterranean population. *Nutrients* 2019, 11, 2165
- [34] De Matteis, C.; Crudele, L.; Gadaleta, R.M.; Di Buduo, E.; Novielli, F.; Petruzzelli, S.; Cariello, M.; Moschetta, A. Low Adherence to Mediterranean Diet Characterizes Metabolic Patients with Gastrointestinal Cancer. *Nutrients* 2024, 16, 630
- [35] Agaj, A.; Peršurić, Ž.; Pavelić, S.K. Mediterranean Food Industry By-Products as a Novel Source of Phytochemicals with a Promising Role in Cancer Prevention. *Molecules* 2022, 27, 8655
- [36] Kuan, A.S.; Green, J.; Kitahara, C.M.; De González, A.B.; Key, T.; Reeves, G.K.; Floud, S.; Balkwill, A.; Bradbury, K.; Liao, L.M.; et al. Diet and risk of glioma: Combined analysis of 3 large prospective studies in the UK and USA. *Neuro-Oncol.* 2019, 21, 944–952
- [37] Hashemian, M.; Farvid, M.S.; Poustchi, H.; Murphy, G.; Etemadi, A.; Hekmatdoost, A.; Kamangar, F.; Sheikh, M.; Pourshams, A.; Sepanlou, S.G.; et al. The application of six dietary scores to a Middle Eastern population: A comparative analysis of mortality in a prospective study. *Eur. J. Epidemiol.* 2019, 34, 371–38
- [38] Schwingshackl, L.; Schwedhelm, C.; Galbete, C.; Hoffmann, G. Adherence to Mediterranean diet and risk of cancer: An updated systematic review and meta-analysis. *Nutrients* 2017, 9, 1063
- [39] Hanahan D, Weinberg RA. 2000. The hallmarks of cancer. *Cell* 100:57–70
- [40] Anderson EK, Gutierrez DA, Hasty AH 2010. Adipose tissue recruitment of leukocytes. *Curr. Opin. Lipidol.* 21:172–77

- [41] Berg AH, Scherer PE. 2005. Adipose tissue, inflammation, and cardiovascular disease. *Circ. Res.* 96:939–49
- [42] Maiuolo, J.; Gliozzi, M.; Carresi, C.; Musolino, V.; Oppedisano, F.; Scarano, F.; Nucera, S.; Scicchitano, M.; Bosco, F.; Macri, R.; et al. Nutraceuticals and cancer: Potential for natural polyphenols. *Nutrients* 2021, 13, 3834
- [43] Włodarczyk, M.; Nowicka, G. Obesity, DNA damage, and development of obesity-related diseases. *Int. J. Mol. Sci.* 2019, 20, 1146
- [44] Hayes, J.D.; Dinkova-Kostova, A.T.; Tew, K.D. Oxidative Stress Cancer. *Cancer Cell* 2020, 38, 167–197
- [45] Almdendros, I.; Martinez-Garcia, M.A.; Farré, R.; Gozal, D. Obesity, sleep apnea, and cancer. *Int. J. Obes.* 2020, 44, 1653–1667
- [46] Spyrou, N.; Avgerinos, K.I.; Mantzoros, C.S.; Dalamaga, M. Classic and novel adipocytokines at the intersection of obesity and cancer: Diagnostic and therapeutic strategies. *Curr. Obes. Rep.* 2018, 7, 260–275
- [47] Harris, B.H.L.; Macaulay, V.M.; Harris, D.A.; Klenerman, P.; Karpe, F.; Lord, S.R.; Harris, A.L.; Buffa, F.M. Obesity: A perfect storm for carcinogenesis. *Cancer Metastasis Rev.* 2022, 41, 491–515
- [48] Wang Q., Zhou W. Roles and Molecular Mechanisms of Physical Exercise in Cancer Prevention and Treatment. *J. Sport Health Sci.* 2021;10:201–210. doi: 10.1016/j.jshs.2020.07.008
- [49] Bigley A.B., Spielmann G., LaVoy E.C.P., Simpson R.J. Can Exercise-Related Improvements in Immunity Influence Cancer Prevention and Prognosis in the Elderly? *Maturitas.* 2013;76:51–56. doi: 10.1016/j.maturitas.2013.06.010
- [50] Timmons B.W., Cieslak T. Human Natural Killer Cell Subsets and Acute Exercise: A Brief Review. *Exerc. Immunol. Rev.* 2008;14:8–23
- [51] Pedersen B.K. The Disease of Physical Inactivity-and the Role of Myokines in Muscle-Fat Cross Talk. *J. Physiol.* 2009;587:5559–5568. doi: 10.1113/jphysiol.2009.179515
- [52] Inoue-Choi M, Liao LM, Reyes-Guzman C, Hartge P, Caporaso N, Freedman ND. Association of long-term, low-intensity smoking with all-cause and cause-specific mortality in the National Institutes of Health–AARP Diet and Health Study. *JAMA internal medicine.* 2017 Jan 1;177(1):87–95
- [53] Adams SJ, Stone E, Baldwin DR, Vliegenthart R, Lee P, Fintelman FJ. Lung cancer screening. *The Lancet.* 2023 Feb 4;401(10374):390-408
- [54] Caliri AW, Tommasi S, Besaratinia A. Relationships among smoking, oxidative stress, inflammation, macromolecular damage, and cancer. *Mutation Research/Reviews in Mutation Research.* 2021 Jan 1;787:108365
- [55] Krutz M, Acharya P, Chissoe G, Raj V, Driskill L, Krempf G, Zhao D, Mhaweji R, Queimado L. Tobacco cessation after head and neck cancer diagnosis is an independent predictor of treatment response and long-term survival. *Oral oncology.* 2022 Nov 1;134:106072
- [56] Wills L, Ables JL, Braunscheidel KM, Caligiuri SP, Elayouby KS, Fillinger C, Ishikawa M, Moen JK, Kenny PJ. Neurobiological mechanisms of nicotine reward and aversion. *Pharmacological reviews.* 2022 Jan 1;74(1):271-310
- [57] Münzel T, Hahad O, Kuntic M, Keaney Jr JF, Deanfield JE, Daiber A. Effects of tobacco cigarettes, e-cigarettes, and waterpipe smoking on endothelial function and clinical outcomes. *European heart journal.* 2020 Nov 1;41(41):4057-70
- [58] Runggay, H.; Shield, K.; Charvat, H.; Ferrari, P.; Sornpaisarn, B.; Obot, I.; Islami, F.; Lemmens, V.E.P.P.; Rehm, J.; Soerjomataram, I. Global burden of cancer in 2020 attributable to alcohol consumption: A population-based study. *Lancet Oncol.* 2021, 22, 1071–1080

- [59] McNabb, S.; Harrison, T.A.; Albanes, D.; Berndt, S.I.; Brenner, H.; Caan, B.J.; Campbell, P.T.; Cao, Y.; Chang-Claude, J.; Chan, A.; et al. Meta-analysis of 16 studies of the association of alcohol with colorectal cancer. *Int. J. Cancer* 2020, 146, 861–873
- [60] Klein, W.M.; Jacobsen, P.B.; Helzlsouer, K.J. Alcohol and cancer risk: Clinical and research implications. *JAMA* 2020, 323, 23–24
- [61] Shield, K.; Manthey, J.; Rylett, M.; Probst, C.; Wettlaufer, A.; Parry, C.D.H.; Rehm, J. National, regional, and global burdens of disease from 2000 to 2016 attributable to alcohol use: A comparative risk assessment study. *Lancet Public Health* 2020, 5, e51–e61
- [62] Bagnardi, V.; Rota, M.; Botteri, E.; Tramacere, I.; Islami, F.; Fedirko, V.; Scotti, L.; Jenab, M.; Turati, F.; Pasquali, E.; et al. Alcohol consumption and site-specific cancer risk: A comprehensive dose–response meta-analysis. *Br. J. Cancer* 2015, 112, 580–593
- [63] Li, Y.; Pan, A.; Wang, D.D.; Liu, X.; Dhana, K.; Franco, O.H.; Kaptoge, S.; Di Angelantonio, E.; Stampfer, M.; Willett, W.C.; et al. Impact of healthy lifestyle factors on life expectancies in the US population. *Circulation* 2018, 138, 345–355
- [64] Ventriglio, A.; Sancassiani, F.; Contu, M.P.; Latorre, M.; Di Slavatore, M.; Fornaro, M.; Bhugra, D. Mediterranean diet and its benefits on health and mental health: A literature review. *Clin. Pract. Epidemiol. Ment. Health: CP EMH* 2020, 16 (Suppl. S1), 156–164
- [65] Jani, B.D.; McQueenie, R.; Nicholl, B.I.; Field, R.; Hanlon, P.; Gallacher, K.I.; Mair, F.S.; Lewsey, J. Association between patterns of alcohol consumption (beverage type, frequency and consumption with food) and risk of adverse health outcomes: A prospective cohort study. *BMC Med.* 2021, 19, 1–14
- [66] Pavlidou, E.; Mantzourou, M.; Fasoulas, A.; Tryfonos, C.; Petridis, D.; Giaginis, C. Wine: An aspiring agent in promoting longevity and preventing chronic diseases. *Diseases* 2018, 6, 73
- [67] Martínez-González, M.A.; Gea, A.; Ruiz-Canela, M. The Mediterranean diet and cardiovascular health: A critical review. *Circ. Res.* 2019, 124, 779–798
- [68] Barbería-Latasa, M.; Gea, A.; Martínez-González, M.A. Alcohol, drinking pattern, and chronic disease. *Nutrients* 2022, 14, 1954