

Which Environment Makes Cancer?

¹Asuman Deveci, *¹Suleyman Kaleli and ¹Gamze Guney Eskiler

*¹Faculty of Medicine, Department of Medical Biology, Sakarya University, Turkey

Abstract:

Cancer occurs with uncontrolled cell growth or abnormal cell division in DNA damage. Carcinogens are the factors that cause DNA mutations and they are known to cause cancer in our body by making changes in gene level. Genetic susceptibility is also important in cancer development along with factors such as poor living conditions. Additionally, all these environmental factors such as X-rays, gamma rays, the radiation emitted from radioactive materials, aniline type dyes, cigarette, free radicals, asbestos, silica dust, air pollution, food additives, various drugs, some of the chemicals used in perfumes, oncogenic viruses and bacteria are playing an important role in cancer formation and contribute the increase of incidence of cancer. The environmental factors that cause cancer are located in air, water, soil and the food that we need to live. Consequently, human get cancer from exposure to carcinogens from the environment where they live. The cancer is a difficult disease to treat and reduces the life quality of people with cancer. Investigation of the effects of environmental factors in cancer and prevention of the cancer development by determining the factors that cause cancer are very important from this perspective.

Key words: Environment, carcinogens, cancer, DNA, mutation

1. Introduction

Cancer, which is the second leading cause of death, is a group of disease involving abnormal cell growth with the potential to invade or spread to other parts of the body. [1,2]. According to GLOBOCAN, there were 14.1 million new cancer cases, 8.2 million cancer deaths and 32.6 million people living with cancer [within 5 years of diagnosis in 2012 worldwide. On the other hand, it is estimated that 1,685,210 new cases of cancer will be diagnosed in the United States and 595,690 people will die from the disease in 2016. Thus, there is an urgent need for a new therapeutic strategy to reduce cancer-related deaths [3,4].

Cancer is a multifactorial disease and so, many genetic and environmental factors increase the risk of developing cancer, such as viruses, bacteria, radiation, genetic and eating habits and chemicals [3-8] [Figure 1]. 10-15% of all cancers are thought to be related to an inherited gene, whereas, the remaining 85-90% of cancer have their roots in the environment and lifestyle. It is known that all cancer-related deaths, almost 25–30% are due to tobacco, approximately 30–35% are linked to diet, nearly 15–20% are due to infections, and the remaining percentage is due to other factors like radiation, stress, physical activity, environmental pollutants, etc. [9]. In terms of genetic factors, mutations in a few genes, including oncogenes, tumor suppressor genes and DNA repair genes can lead to cancer formation rather than a single gene. These genes cause cancer through three main biologic pathways [cell cycle, apoptosis and differentiation], which are normally, regulate tissue

*Corresponding author: Address: ¹Faculty of Medicine, Department of Medical Biology, Sakarya University, 54187, Sakarya TURKEY. E-mail address: skaleli@sakarya.edu.tr, Phone: +902642953117

homeostasis and cell growth [9]. For this purpose, the aim of this study was to discuss the interactions of genetic factors with various environmental factors, including diet, lifestyle, metabolic alterations, and various environmental exposures.

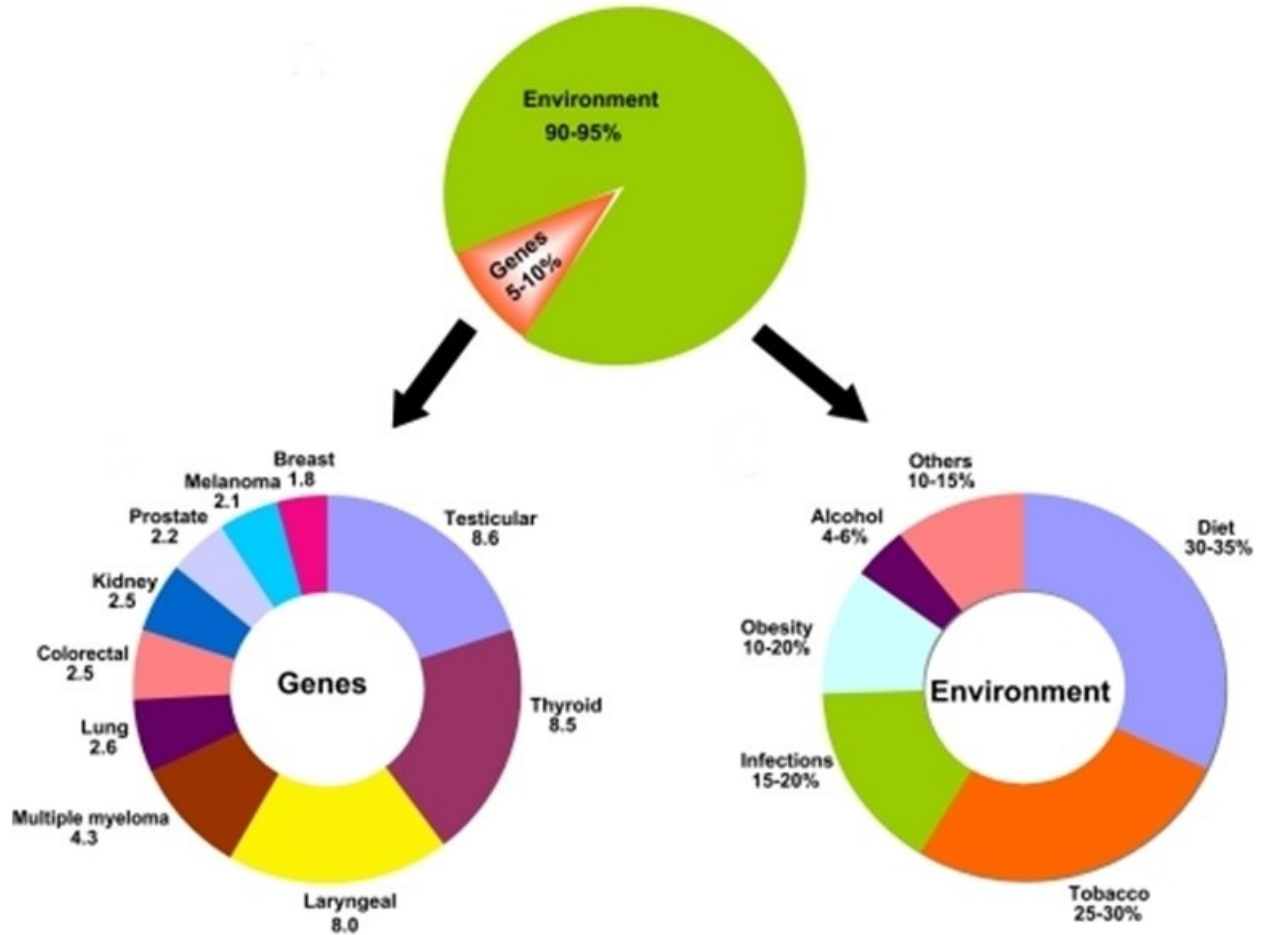


Figure 1. The role of genes and environment in the development of cancer [9].

2. The relationship between cancer and genetics

Inherited genetic factors play an important role in cancer development. The mutation of critical genes, including tumor-suppressor genes, oncogenes and genes involved in DNA repair, leads to genetic instability and cancer development. Several genes related to inherited cancers have been identified on leukemia, certain childhood tumors, colon and especially breast and ovarian cancer. [10]. For example, germline mutations in breast cancer gene 1 [BRCA1] represent a predisposing genetic factor in 15-45% of hereditary breast cancers. Female mutation carriers have a 60-80% lifetime risk for developing breast cancer [11,12] and a 20-40% lifetime risk of developing ovarian cancer [13-15]. Furthermore, mutations in APC gene or mismatch DNA repair genes lead to two

different types of inherited colon cancer familial adenomatous polyposis [FAP] and hereditary non-polyposis colorectal cancer [HNPCC], respectively [16].

3. The relationship between cancer and carcinogens

Environmental factors such as X-rays, gamma rays, radiation emitted from radioactive materials, aniline type dyes, cigarette, free radicals, asbestos, silica dust, air pollution, food additives, various drugs, some of the chemicals used in perfumes, oncogenic viruses and bacteria play an important role in the risk of cancer. [10].

3.1. Radiation

Radiation is classified into two fundamental categories, non-ionizing and ionizing radiation. Ionizing radiation is defined as X-rays, which forms electrically charged particles or ions [17] X- and gamma rays are especially used for medical imaging [16,19]. Computed tomography [CT] is a radiological method that generates a three-dimensional image for the diagnosis of various diseases [20]. It has been described in several studies that diagnostic X-rays lead to cause mutations and up to 10% of invasive cancers are related to radiation exposure [21-26]. With regard to this concern, large cohorts of patients treated with radiotherapy for cervical cancer, breast cancer, Hodgkin lymphoma, testicular cancer, and childhood cancer have been followed for decades. Increased levels of screening in a radiation-exposure is known of the risk of cancer incidence. In this respect, the biological impact can change according to the dose equivalent of radiation [27-30].

3.2. Heavy Metals

Exposure to various chemicals and heavy metals depending on exposed dose, genetics, people's immune resistance and overall health status, age, the level of nutrition has been associated with risk of different cancers, including breast cancer, pancreatic, lung cancer, and gallbladder cancer etc. [10]. When metals get into the body through air, food, water, or dermal exposure, they exert their enzymatic and genotoxic effects on different organs [31]. Some heavy metals such as arsenic, cadmium, chromium, nickel, and zinc are known as developing cancer. They bind to vital cellular components, such as structural proteins, enzymes, and nucleic acids [32]. For instance, the effect of cadmium on the lung and prostate cancer has been definitely determined [33]. The toxicological effects of zinc were determined in experimental animals [34]. Additionally, there may be a relationship between exposure to certain metal compounds and the risk of breast cancer [35]. However, there is urgently needed the experimental animal studies, and also epidemiologic studies associated metals with cancer.

3.3. Cigarette

Chemicals in cigarette smoke cause DNA damage and have been increasing the risk of various cancers, particularly primary lung cancer [3-10]. It is known that nearly 9 out of 10 lung cancers

are caused by cigarette smoking. Cigarettes cause about 1.5 million deaths from lung cancer per year and it is estimated that a number will rise to nearly 2 million per year by the 2020s or 2030s [6].

3.4. Foods and Nutrition

Dietary factors have been associated with 30% of cancers in Western countries. In fact, making diet is a second factor after tobacco as a preventable cause of cancer. The effects diet on cancer risk in developing countries has been considered around 20% [37]. On the other hand, some parts of additives have carcinogenic effects. For example, the dulce, cinnamyl anthranilate and thiourea like synthetic additives, which cause liver cancer, have been identified in some experiments and thus, they are forbidden to use these substances in foods [38-40]. However, some substances, including nitrite salts, sodium nitrite [E250] or potassium nitrite [E249] have been used despite of increasing the risk of cancer. Meat products such as sausage as antibacterial and color holder include these substances. This type of processed meat products increases the risk of bowel cancer by 21% [41]. Unfortunately, an excess of consumption of sugar and salt, which are the two main foods, causes obesity and an increase in insulin and so, higher level of these substances indirectly increase the risk of cancer [42]. Besides, aflatoxins are found in the groundnut, pulses, oilseeds and grains and they increase the risk of hepatocellular carcinoma [11].

3.5. Free Radicals and ROS

Free radicals and ROS have been associated with the increased risk of cancer [12]. Particularly free radicals cause cancer and atherosclerosis diseases. The free radicals lead to cancer initiation and promotion by chromosomal defects and oncogene activation. On the other hand, ROS, such as super oxide anion, hydrogen peroxide, hydroxyl radical, and nitric oxide and their biological metabolites also play an important role in carcinogenesis. ROS induce DNA damage including double strand break, base modification and DNA protein cross-links [43].

3.6. Air Pollution

Emissions from motor vehicles, industrial processes, power generation, the household combustion of solid fuel, and other sources pollute the ambient air across have global effect in the world. The chemical and physical features of ambient air pollution can vary according to sources of pollution, climate, and meteorology. However, the specific chemicals in the air pollution are known to be carcinogenic to humans. In 1971, the US Clean Air Act was established and ozone, particulate matter, sulfur dioxide, nitrogen dioxide, carbon monoxide and lead were defined as air pollutants. Furthermore, 189 toxic and hazardous air pollutants have been identified [44]. Exposure to ambient fine particles [PM_{2.5}] was recently estimated to have contributed 3.2 million premature deaths worldwide in 2010, due largely to cardiovascular disease, and 223 .000 deaths from lung cancer [45, 46].

These air pollutants cause to acute illness such as vomiting, chronic diseases such as cancer, as well as immunologic, neurologic, reproductive, developmental and respiratory diseases. Exposure

of these chemicals increases the risk of pleural and peritoneal tumors and also lung cancer incidence [47-50].

3.7. Oncogenic Viruses

Oncoviruses or tumor viruses are a general term used for viruses. This term began to use in 1950-60 years to show acute conversion. Nowadays, it means any virus containing DNA or RNA genome and thus, it is synonymous with "tumor virus" or "cancer virus". However, the majority of viruses does not cause cancer in humans or animals [51]. Oncoviruses such as Hepatitis viruses [HBV, HCV], Human papilloma viruses [HPV], Kaposi sarcoma-associated herpesvirus [HHV-8], Human T-Lymphotropic Virus [HTLV] and Epstein-Barr virus [EBV] have been associated with the risk of cancer [13]. It is estimated that viral infections contribute to 15–20% of all human cancers [52]. Thus, these cancers [e.g. Papillomavirus vaccines] can be prevented by vaccination and can be detected with a simple blood test and can be treated with antiviral compounds.

4. Discussion

New areas of cancer research are focusing on the potential for pollutants to interact with one another and with genetic factors. The exact cause or causes of cancer have not known exactly. However, certain genes that tend to cancer interact with some environmental factors such as viruses, exposure to radiation, various chemicals and pollutants are related to increasing the risk of cancer. Carcinogens have an effect on damaging DNA, disrupting hormones, inflaming tissues, or switching genes on or off [53]. On the other hand, there is substantial evidence that synergism between two different exposures can cause some cancers. Asbestos, for example, enhances the carcinogenicity of tobacco smoke, so the rate of lung cancer was especially high among people who smoked and were exposed to asbestos in their workplaces [53]. Consequently, the environment is often used with a broad scope in the medical literature and it is known that the environmental factors have been increased the risk of cancers [54]. Thus, more detailed studies are needed to determine the exact effects of environmental factors on cancer development.

5. Conclusion

People can avoid some cancer-causing exposures, such as tobacco smoke and the sun rays. However, other environmental risk factors including air, water, food pollutants can not be prevented due to consisting of normal life. It is known that environmental factors may cause or contribute to the development of cancer. However, studies that are more detailed are needed to determine the exact cause of a health effect. As a result, when a large number of studies have been performed, association the actual risk of cancer with the environmental risk factors can be clearer.

References

[1] Futreal PA, Kasprzyk A, Birney E, Mullikin JC, Wooster R, Stratton M. Cancer and genomics. Nature 2001;6822: 850-2

[2] Kanser. <https://tr.wikipedia.org/wiki/Kanser> (accessed March 3, 2016).

- [3] Williams GM. Mechanisms of chemical carcinogenesis and application to human cancer risk assessment. *Toxicology* 2001;14: 3-10.
- [4] Williams GM. Review of in vitro test systems using DNA damage and repair for screening of chemical carcinogens. *J. Assoc. Official Anal. Chemists* 1979;62: 857–63.
- [5] Williams GM. Genotoxic and epigenetic carcinogens. In: Homburger F, editors. *Safety Evaluation and Regulation of Chemicals 2. Impact of Regulations-Improvement of Methods*, Basel: Karger; 1985, p. 251–6
- [6] Williams GM. DNA reactive and epigenetic carcinogens. In: Barrett JC, ed. *Mechanisms of Environmental Carcinogenesis, Vol 1: Role of Genetic and Epigenetic Changes*, Boca Raton, FL: CRC Press, Inc; 1987, p. 113–27.
- [7] Williams GM. Definition of a human cancer hazard. In: *Nongenotoxic Mechanisms in Carcinogenesis*. New York: Banbury Report 25, Cold Spring Harbor Laboratory. 1987; 367–80.
- [8] Williams GM. DNA reactive and epigenetic carcinogens. *Experimental and Toxicologic Pathology* 1992; 44: 457– 64.
- [9] Early diagnosis of cancer. <https://sanjivharibhakti.wordpress.com/tag/early-diagnosis-of-cancer/> (accessed May 11, 2016).
- [10] Yokus B, Ülker DU. Kanser Biyokimyası. *Dicle Üniv Vet Fak Derg* 2012: 1(2): 7-18
- [11] Aksoy U, Eltem R, Meyvacı KB, Altındisli A, Karabat S. Five-year survey of ochratoxin A in processed sultanas from Turkey. *Food Addit Contam* 2007; 24: 292-6.
- [12] Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacognosy Reviews*. 2010;4(8):118-126.
- [13] Bougie O, Weberpals JI. Clinical Considerations of BRCA1 - and BRCA2 -Mutation Carriers: A Review. *Int J Surg Oncol* 2011;2011:1–11.
- [14] King MC, Marks JH, Mandell JB, New York Breast Cancer Study G. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. *Science* 2003;302(5645):643–6.
- [15] Antoniou A, Pharoah PDP, Narod S, Risch H a, Eyfjord JE, Hopper JL, et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case Series unselected for family history: a combined analysis of 22 studies. *Am J Hum Genet*. 2003;72(5):1117–30.
- [16] Vogelstein A, Kinzler KW. The multistep nature of cancer. *Trends Genet* 1993;9: 138–41.

- [17] Dasdag S. Elektromanyetik Kirlilik ve Sağlık. Kent ve Elektromanyetik Dalga Kirliliği Sempozyumu Bildiri Kitabı, Antalya, 2010; 15-22.
- [18] Valentin J, editor. Annals of ICRP, Publication 103. The 2007 recommendation of the international Commission on Radiologic Protection.
- [19] ICRP Publication 105. Radiation protection in Medicine. Annals of ICRP 2007; 37:1-5.
- [20] Radiation protection, X-rays. <http://www.arpansa.gov.au/radiationprotection/Basics/xrays.cfm> (accessed May 29, 2016).
- [21] Huang BS, Law MWM, Khong PL. Whole-Body PET/CT Scanning: Estimation of Radiation Dose and Cancer Risk. Radiology 2009;251:166-74.
- [22] U.S. Department of Health and Human Services, 11th Report on Carcinogens. 2005, Public Health Service - National Toxicology Program.
- [23] Dedic S, Pranjić N. Lung cancer risk from exposure to diagnostic x-rays. Health Med 2009;3:307-13.
- [24] Herfarth H, Palmer L. Risk of Radiation and Choice of Imaging. Digest Dis 2009;27:278-84.
- [25] Heyes GJ, Mill AJ, Charles MW. Mammography-oncogenicity at low doses. J Radiol Protect 2009;29: A123-A132.
- [26] Gilbert ES. Radiation-related risk of solid cancers appears to persist throughout life. Int J Radiation Biol 2009;85:467-82.
- [27] Dawson P, Punwani S. The thyroid dose burden in medical imaging A re-examination. Eur J Radiol 2009;69:74-9.
- [28] Wakeford R, Childhood leukaemia following medical diagnostic exposure to ionizing radiation in utero or after birth. Radiation Protect Dosimetry 2008;132:166-74.
- [29] Myles P, Evans S, Lophatananon A, et al. Diagnostic radiation procedures and risk of prostate cancer. British J Cancer 2008;98:1852-6.
- [30] Gilbert ES. Ionizing Radiation and Cancer Risks: What Have We Learned From Epidemiology? Int J Radiat Biol 2009;85(6): 467–482.
- [31] Chhabra D, Oda K, Jagannath P, Utsunomiya H, Takekoshi S, Nimura Y. Chronic Heavy Metal Exposure and Gallbladder Cancer Risk in India, a Comparative Study with Japan. Asian Pacific J Cancer Prev, 2012;13: 187-190.

- [32] Antwi SO, Eckert EC, Sabaque CV, Leof ER, Hawthorne KM, Bamlet WR, Chaffee KG, Oberg AL, Petersen GM. *Cancer Causes Control* 2015;26(11):1583-91
- [33] Verougstraete V, Lison D, Hotz P. Cadmium, Lung and Prostate Cancer: A Systematic Review of Recent Epidemiological Data, *Journal of Toxicology and Environmental Health, Part B* 2003;6:3, 227-256
- [34] Vural, H., Ağır metal iyonlarının gıdalarda oluşturduğu kirlilikler. *Çevre Dergisi* 1993;8: 3 8.
- [35] Florea AM, Büsselberg D. Metals and Breast Cancer: Risk Factors or Healing Agents?, *Journal of Toxicology* 2011; 8:1-8.
- [36] Proctor NR. The history of the discovery of the cigarette lung cancer link: evidentiary traditions, corporate denial, global toll. *Tobacco Control* 2012;21:87-91.
- [37] KeyTJ, Schatzkin A, Willett WC, Allen NE, Spencer EA, Ruth C Travis¹ Diet, nutrition and the prevention of cancer. *Public Health Nutrition*: 7(1A), 187–200.
- [38] Czene K, Lichtenstein P, Hemminki K. Environmental and heritable causes of cancer among 9.6 million individuals in the Swedish Family-Cancer Database. *Int J Cancer* 2002; 99: 260-6.
- [39] Anand P, Kunnumakara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, et al. Cancer is a preventable disease that requires major lifestyle changes. *Pharmaceutical Res* 2008; 25: 2097-116.
- [40] Boffetta P, Nyberg F. Contribution of environmental factors to cancer risk. *Br Med Bull* 2003; 68: 71-94.
- [41] Irigaray P, Newby JA, Clapp R, Hardell L, Howard V, Montagnier L, et al. Lifestyle-related factors and environmental agents causing cancer: An overview. *Biomed Pharmacother* 2007; 61: 640-58.
- [42] Kushi LH, Byers T, Doyle C, Bandera EV, McCullough M, McTiernan A, et al. American Cancer Society 2006 Nutrition and Physical Activity Guidelines Advisory Committee. American Cancer Society guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin* 2006; 56: 254-81.
- [43] Hussain SP, Hofseth LJ, Harris CC. Radical causes of cancer. *Nature* 2003; 3:276-285
- [44] Clean Air Act, 33 United States Code Sec. 1241 Et Esq., 1971.
- [45] Air pollution and cancer. <https://www.iarc.fr/en/publications/books/sp161/AirPollutionandCancer16.pdf> (accessed May 18, 2016).

- [46] Paolo Boffetta P, Nyberg F. Contribution of environmental factors to cancer risk. *British Medical Bulletin* 2003; 68: 71–94.
- [47] Brown RC, Hoskins JA, Miller K, Mossman BT. Pathogenetic mechanisms of asbestos and other mineral fibres. *Mol Aspects Med* 1990; 11: 325-349
- [48] Peto J, Seidman H, Selikoff IJ. Mesothelioma mortality in asbestos workers: Implications for models of carcinogenesis and risk assessment. *Br J Cancer* 1982; 45: 124-132.
- [49] Maghissi AA, Seiler MA. Enhancement of exposure to radon progeny as a consequence of passive smoking. *Environ Int* 1989; 15: 261-264.
- [50] Kunz E, Serc J, Placek V, Horacek L. Lung cancer in man in relation to different time distribution of radiation exposure. *Health Phys* 1979; 36: 699-706.
- [51] Onkovirüs. <https://tr.wikipedia.org/wiki/Onkovir%C3%BCs> (accessed May 20, 2016).
- [52] Margaret EM, Munger K. Viruses associated with human cancer. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease* 2008;1782: 127-150
- [53] How Many Cancers Are Caused by the Environment? <http://www.scientificamerican.com/article/how-many-cancers-are-caused-by-the-environment/> (accessed May 13, 2016).
- [54] Tomatis L, Aitio A, Day NE et al. *Cancer: Causes, Occurrence and Control* (IARC Scientific Publications No 100). Lyon: International Agency for Research on Cancer, 1990