**Prospects**

# Diet and Cancer Prevention: Dietary Compounds, Dietary MicroRNAs and Dietary Exosomes†

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**Abstract**

Cancer is one of main health public problems worldwide. Several factors are involved in beginning and development of cancer. Genetic and internal/external environmental factors can be as important agents that effect on emerging and development of several cancers. Diet and nutrition may be as one of important factors in prevention or treatment of various cancers. A large number studies indicated that suitable dietary patterns may help to cancer prevention or could inhibit development of tumor in cancer patients. Moreover, a large numbers studies indicated that a variety of dietary compounds such as curcumin, green tea, folat, selenium and soy isoflavones show a wide range anti-cancer properties. It has been showed that these compounds via targeting a sequence of cellular and molecular pathways could be used as suitable options for cancer chemoprevention and cancer therapy. Recently, dietary microRNAs and exosomes have been emerged as attractive players in cancer prevention and cancer therapy. These molecules could change behavior of cancer cells *via* targeting various cellular and molecular pathways involved in cancer pathogenesis. Hence, the utilization of dietary compounds which are associated with powerful molecules such as microRNAs and exosomes and put them in dietary patterns could contribute to prevention or treatment of various cancers. Here, we summarized various studies that assessed effect of dietary patterns on cancer prevention shortly. Moreover, we highlighted the utilization of dietary compounds, dietary microRNAs and dietary exosomes and their cellular and molecular pathways in cancer chemoprevention. This article is protected by copyright. All rights reserved

**Key word**: Diet, Dietary pattern, Dietary microRNA, Dietary exosomes, Cancer, Prevention

## Introduction

Cancer is known as one of major public health problems which are associated with a public health concern worldwide (Ferlay et al., 2015). The assessing of different dimensions for this disease has led to identification of various factors involved in cancer pathogenesis. These findings could help to prevention and better treatment of various types of cancer (Mirzaei et al., 2016h; Mirzaei et al., 2016j). Various classes of factors participate in start and development of various cancers (Schottenfeld and Fraumeni Jr, 2006). Multiple lines evidences indicated that genetic and envirmental factors involved in various stages of different malignancies (Schottenfeld and Fraumeni Jr, 2006). To date, researchers with more understanding of molecular/cellular pathways involved in different cancers could design many therapies and regimen for before and after cancer. But, with growth of human knowledge in the cellular and molecular pathways involved in different stages of cancers, obtain new data that could contribute be design novel therapies (Mirzaei et al., 2016d; Mirzaei et al., 2016h; Mirzaei et al., 2016j; Salarinia et al., 2016). Moreover, using of these data could lead to development of new therapies such as gene and cell therapy for treatment of cancer (Mirzaei et al., 2016d; Mirzaei et al., 2016f; Mohammadi et al., 2016b; Saadatpour et al., 2016b; Saadatpour et al., 2017). Among of various factors involved in start and development of cancer, life style has a main role. Human dietary patterns could effect on human health in various ways. The suitable nutrition regimen has important effects on human health (Couto et al., 2011). It observed that enough uptakes of various vitamins and fats could have positive effects on various diseases such as depression and cancer (Banikazemi et al., 2016; Banikazemi et al., 2015; Chen et al., 2015b; Mayne et al., 2016). Various studies indicated that suitable diet and dietary patterns may have key roles in prevention or even treatment of cancer (Chen et al., 2015b; Rodriguez et al., 2004). The intake of various fruits and diet with many antioxidant components may help be prevention of cancer. The

inflammation is known as one of main factors for development of many cancers (Albanes et al., 1995; Catsburg et al., 2015; Marmot et al., 2007; Mayne et al., 2016; Rodriguez et al., 2004). The utilization of suitable dietary including antioxidant components may effect on development of cancer and inhibition it (Albanes et al., 1995; Marmot et al., 2007; Mayne et al., 2016). It's found that a plant-based diet that limits red meat intake could be linked with reduced risk of breast cancer (Catsburg et al., 2015).

Dietary compounds are known as one of important therapeutic agents which could affect on a variety of cellular and molecular pathways (Chen and Kong, 2005; Langner and Rzeski, 2012; Pan and Ho, 2008). A large number studies indicated that the utilization of various dietary compounds including green tea, curcumin, selenium, carotenoids and vitamins could help to cancer prevention and treatment. Hence, it seems that the utilization of them in dietary pattern could be useful for cancer prevention and therapy (Chen and Kong, 2005; Langner and Rzeski, 2012; Pan and Ho, 2008). Recently, some studies indicated that dietary microRNAs and exosomes have critical roles in change behavior various cells such as cancer cells. MicroRNAs (miRNAs) are known as small non-coding RNAs which act as epigenetic regulators (Mirzaei et al., 2016a; Mirzaei et al., 2016g; Mohammadi et al., 2016a; Rashidi et al., 2016; Salarinia et al., 2016). These molecules have critical roles in a variety of cellular and molecular pathways involved in cancer pathogenesis (Gholamin et al., 2017; Mashreghi et al., 2017; Mirzaei et al., 2017a; Moridikia et al., 2017; Ross and Davis, 2014). Hence, these molecules could be used as diagnosis, and therapeutic biomarkers (Fathullahzadeh et al., 2016). It has been showed that dietary miRNAs could be as attractive tools for cancer prevention and therapy. Moreover, it has been showed that dietary exosomes and their cargos could be used as new candidate for cancer prevention and therapy (Ju et al., 2013; Mirzaei et al., 2017b; Record, 2013). Here, we summarized the role of dietary patterns on prevention of

cancer shortly. Moreover, we highlighted the utilization of dietary compounds, dietary miRNAs and dietary exosomes as powerful candidates for cancer prevention and therapy.

**Dietary patterns and cancer**

Multiple lines evidence indicated that many factors involve in different stages of cancer (Weiderpass, 2010). These factors (including genetic and envirmental factors) play key roles in start and development of different cancers (Kolonel et al., 2004; Mayne et al., 2016; Weiderpass, 2010). Dietary patterns are probably known as one of important factors that may be associated with various cancers. Few studies have examined effect dietary patterns on cancer prevention (Chen et al., 2015b; Willett, 2000). Some evidences indicated that various dietary patterns cannot contribute to cancer prevention in different stages (Chen et al., 2015b). On the other hand, some reports revealed that a healthy diet with plenty of vegetables and fruit may decrease risk of cancer. These studies indicated that the utilizing of suitable dietary patterns and particular vitamins may contribute to cancer prevention in certain groups of patients (Weinstein et al., 2007). In a study, Rodriguez et al., found that intake of vitamin E supplements for male smokers could decrease risk of prostate cancer. Their results showed that supplementation with alpha-tocopherol (a form of vitamin E) can reduce risk of prostate cancer (Rodriguez et al., 2004). In four studies observed that vitamin E could decrease the risk of prostate cancer in past/recent and current smokers and those with low levels of this vitamin (Moyad, 2002; Weinstein et al., 2007). Moyad et al., found that selenium and vitamin E are probably 2 of the main dietary supplements which utilization of them could decrease prostate cancer risk (Moyad, 2002). Some reports revealed that there were no significant reduction between multivitamin, mineral supplementation and mortality or incidence of cancer, while some reports show a possible prevention effect in cervical cancer (Dolara et al., 2012). In 2012 a review of 9 studies assessed the effect of various vitamins and minerals on

lung cancer risk. Their results showed that there was no evidence for recommending supplements of vitamins A, C, E, selenium, either alone or in different combinations, for the prevention of lung cancer and lung cancer mortality in healthy people. Moreover, some evidence indicated that the use of beta-carotene supplements could be related with a small increase in lung cancer incidence and mortality in smokers or persons exposed to asbestos.(Cortes-Jofre et al., 2012) . Finally, there are no strong evidences that dietary supplements and dietary patterns can contribute to prevention, control and treat various cancers. But few small pilot studies have found that nutritional supplements and dietary patterns may contribute to prevention, treat and control of cancer for some subjects (Béliveau and Gingras, 2007; Chen et al., 2015b; Dolara et al., 2012). Hence, choosing suitable dietary supplements can help to prevention of cancer and effective treatment during cancer. It seems that examining of various dietary patterns on cancer patients can be contribute to identifying of new dietary patterns that are effective on the prevention, treatment and control of various cancers.

**Dietary compounds and cancer chemoprevention**

Cancer chemoprevention is known as an approach which employed natural or synthetic agents to decrease or suppress cancer development and progression (Chen and Kong, 2005; Langner and Rzeski, 2012; Pan and Ho, 2008). It has been showed that dietary compounds could be used as a suitable therapeutic agent for cancer chemoprevention. The interesting of utilization of dietary compounds due to specific properties of them such as low toxicity compared with regular drugs. Multiple lines evidence indicated that a wide range of dietary chemo-preventive agents such as long-chain polyunsaturated fatty acids, green tea polyphenols (i.e. catechins), carotenoids, curcumin, vitamins (i.e. vitamin D and folate) glucosinolates/isothiocyanates, and minerals (i.e. calcium and selenium) could be introduced

into clinical application for cancer therapy (Chen and Kong, 2005; Langner and Rzeski, 2012; Pan and Ho, 2008) (Table 1) .

Curcumin is one of interesting phytochemicals which shows wide ranges anti-cancer properties (Mirzaei et al., 2016b; Mirzaei et al., 2016c; Mirzaei et al., 2017d). Several studies indicated that curcumin via targeting a sequence cellular and molecular pathways exert its therapeutic effects (Mirzaei et al., 2016b; Mirzaei et al., 2016c; Mirzaei et al., 2017d). A variety of cellular and molecular targets including microRNAs (miRNAs), NF-κB, AP-1, COX-2, MMPs, cyclin D1, EGFR, Akt, β-catenin, adhesion molecules and TNF could be affected by curcumin (Mirzaei et al., 2016b; Mirzaei et al., 2016c; Mirzaei et al., 2017d; Simonian et al., 2017) (Figure 1).

Green tea is other natural components which is associated with wide ranges of therapeutic properties (Rashidi et al., 2017). It has been showed that this plant is a rich source of proteins (including enzymes), amino acids, carbohydrates, lipids, vitamins (B, C, E) and minerals (i.e. Ca, Mg, Cr, Fe, Zn, F, K) (McKay and Blumberg, 2002). Various studies indicated that is mostly therapeutic effects of Green tea is related with the abundance of polyphenols, particularly flavonoids. Catechins (flavan-3-ols) including including epicatechin (EC), epicatechin-3-gallate (ECG), gallocatechin (GC), epigallocatechin (EGC) and predominant (-)-epigallocatechin-3-gallate (EGCG) are one of important flavonoids present in green tea leaves (Langner and Rzeski, 2012). It has been that Green tea exerts its anti-cancer properties via inhibition of growth tumor via targeting cellular and molecular involved in cell proliferation, and angiogenesis. VEGFs are one of important targets which could be affected by this component (Rashidi et al., 2017).

Epigenetic mechanisms are important pathways which could be affected by dietary compounds in cancer chemoprevention (Hardy and Tollefsbol, 2011; Li et al., 2014). There

are different mechanisms including DNA methylation, histone modifications, and microRNAs (miRNAs) which act as epigenetic regulators (Mirzaei et al., 2016g; Salarinia et al., 2016). It has been indicated that dietary compounds could affect on cancer prevention via targeting of epigenetic mechanisms (Hardy and Tollefsbol, 2011; Li et al., 2014). A large number studies revealed that bioactive phytochemicals are able to change expression of a variety of oncogens and tumor suppressor genes via targeting epigenetic mechanisms involved in cancer initiation and progression (Hardy and Tollefsbol, 2011; Li et al., 2014). Moreover, the utilization of bioactive phytochemicals alone or in combination with other natural or synthetic agents could be associated with significant results against a variety of cancers (Hardy and Tollefsbol, 2011; Li et al., 2014).

Finally, it seems that the utilization of dietary compounds and put them in dietary patterns could be associated with significant results against prevention of a variety of cancers. Hence, we offer that the utilization of them could be employed as powerful candidates in dietary patterns which may contribute to new insights into cancer prevention.

**Dietary microRNA and cancer prevention**

MicroRNA (miRNA) is small noncoding RNAs which acts as epigenetic negative/positive regulators in various physiological processes (Gholamin et al., 2016; Goradel et al., 2017; Hashemi Goradel et al., 2017; Mirzaei, 2017; Simonian et al., 2017). These molecules could act as a tumor suppressor or oncogene (Keshavarzi et al., 2017a; Rabieian et al., 2017). It has been showed that these molecules are able to regulate a wide range of cellular and molecular processes such as growth, angiogenesis, cell death, invasive and metastasis (Gholamin et al., 2017; Mirzaei et al., 2016i). Multiple line evidence indicated that deregulation of them could lead to disease condition (Hoseini et al., 2017; Keshavarzi et al., 2017b; Mirzaei et al., 2017c). A variety of miRNAs could affect on initiation and development.t of various types of

cancer. Hence, identification of them could contribute to better understanding of underlying cellular and molecular pathways and could lead to better treatment for patients with various diseases such as cancer. It has been showed that a variety of dietary compounds and bioactive foods could show inhibitory effects on cancer cells and also protective effects against cancer via modulating a variety of miRNAs involved in cancer pathogenesis (Nolte-'t Hoen et al., 2015; Ross and Davis, 2011; Ross and Davis, 2014). A large number studies indicated that dietary compounds and bioactive foods could change expression of various miRNAs involved in various well known cancer processes such as angiogenesis, cell cycle regulation, apoptosis, differentiation, inflammation, metastasis and pathways involved in stress response (Cui et al., 2017; Neelakandan et al., 2012; Parasramka et al., 2012; Ross and Davis, 2011). Hence, understanding the affect of dietary compounds and bioactive foods on miRNA expression and miRNA function could provide new insight on prevention approaches to decrease the burden of cancer.

Many studies assessed effect of essential nutrients, and phytochemicals on regulation of miRNA expression in various types of cancer cells and other model systems. Few studies investigated the role of various dietary patterns (i.e. Western diet) or alterations in macronutrient content (i.e. caloric restriction) on expression of miRNAs and miRNA function (Zhu et al., 2011).

EGFR signals such as MYC and K-Ras are important signaling pathways which are associated with modulating of a variety miRNAs such as miR-143 and miR-145 in cancer tumorgensis (Dougherty et al., 2009; Zhu et al., 2011). It has been showed that Western diet (known as a diet with high levels of animal fat and low levels of cholecalciferol and calcium) could induce colonic tumorigenesis via targeting EGFR signals (Newmark et al., 2001). It has been showed that Western diet via targeting EGFR could suppress miR-143 and miR-145

(known as tumor suppressor genes) which led to increasing colonic tumorigenesis and up-regulation of miRNA targets such as MYC and K-Ras (Zhu et al., 2011).

It has been showed that Dietary folate could be associated with regulation of miRNA expression in different model systems and this could be related to the activity of folate in cancer prevention and risk. In a study, Marsit et al., indicated that deficiency of folate in growth media of human lymphoblastoid cells could induce significant changes expression levels of 24 miRNA such as miR-222 (Marsit et al., 2006). They showed that when folate was added back to the media,expression profiles of miRNAs returned to that of control cells. These findings suggested that folate and some dietary components could modulate expression of various miRNAs and deregulation of these miRNAs might be suitable biomarkers of nutritional status in humans as well as participants in cancer prevention (Marsit et al., 2006).

Vitamin E is other dietary components which could regulate miRNA expression. In a study, Gaedicke et al., indicated that utilization of diet with vitamin E deficiency (α tocopherol, < 1 mg/kg diet; γ tocopherol, < 1 mg/kg diet) for 6 month than a vitamin E-sufficient diet (α tocopherol, 12 mg/kg diet; γ tocopherol, 24 mg/kg diet) could change miRNA expression in a rat model (Gaedicke et al., 2008). They showed that vitamin E deficiency could lead to decreasing of hepatic miR-122a and miR-125b expression. These miRNAs could be involved in lipid metabolism, inflammation, and HCC. These results suggested that providing of a dietary regimen with appropriate vitamin E status could exert its prevention regulatory properties via regulating miRNA expression which involved in cancer prevention (Gaedicke et al., 2008).

MiR-21 is one of important targets of curcumin which could be involved in a wide range of cancer associated pathways (Chen et al., 2015a). Deregulation of miR-21 is associated with initiation and progression of various cancers. It has been showed that curcumin exerts anti-

cancer properties via down regulation of miR-2 in various types of cancer. It has been showed that miR-21 acts as one of important players in a variety of cancer associated processes such as proliferation, apoptosis, metastasis and drug resistance (Melnik, 2015; Mudduluru et al., 2011; Roy et al., 2013; Yang et al., 2013). A large number studies confirmed that miR-21 exerts its pathological effects via affecting various downstream pathways including phosphatase and tensin homolog (PTEN)/phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), programmed cell death protein 4 (PDCD4) and NF-κB pathways (Melnik, 2015). Moreover, It has been showed that curcumin could affect on various cancers via affecting on exosomes containing miR-21 which has critical roles in progression of cancer (Wang et al., 2017a). Hence, miR-21 is one of major targets of curcumin which curcumin and its analogs exert their therapeutic effect via modulating of it.

Multiple lines evidence indicated that dietary factors may have adverse effects on microRNA signaling and could induce various types tumor (Melnik, 2015). For example, some studies indicated that there are significant relation between melanoma incidence and BMI (Calo et al., 2016; Candido et al., 2014). Among of various cellular and molecular targets which involved in BMI, MiR-21 is one of important players in this area. It has been showed that miR-21 could be involved in adipocyte differentiation and up regulation of it could be associated with obesity in obese subjects (Chartoumpekis et al., 2012; Kang et al., 2013; Keller et al., 2011). In the other hand, inhibition of miR-21 could be associated with reduction of obesity in db/db mice (Seeger et al., 2014). In a study, Pandey et al., indicated that HFD-induced obesity could be related with increasing of melanoma progression via targeting Cav-1 and FASN expression in tumors from HFD mice (Pandey et al., 2012). Moreover, adipocytes could release exosomes containing various miRNAs which could affect on various pathways (Ferrante et al., 2015; Muller et al., 2011). These findings suggested

that dietary miRNAs and dietary exosomes containing miRNAs may have critical roles in progression of various types of cancer.

**Dietary effects on exosomal microRNAs and their role in cancer prevention**

Exosomes are known as nano vesicles with 50–100 nm in diameter. Exosomes consist of a lipid bilayer membrane and a variety of proteins (Wagner et al., 2015). Moreover, it has been showed that these nano-criers could carry a variety of molecules such as DNAs, small non-coding RNAs( i.e. microRNAs) and various proteins(Mirzaei et al., 2016e; Saadatpour et al., 2016a). It has been showed that exosomes play critical roles in cell-to-cell communication. These vehicles via targeting their cargos could change behaviors recipient cells. Multiple lines evidence indicated that exosomes have important roles in initation and progression of a variety of diseases such as cancer (Mirzaei et al., 2016e; Saadatpour et al., 2016a). These vehicles via targeting their cargos to recipient cells could lead to activation/inhibition of a sequence of cellular and molecular pathways involved in cancer (Mirzaei et al., 2016e; Saadatpour et al., 2016a). Recently, few studies indicated that dietary exosomes could be used as effective tools for cancer therapy. In a study, Ju et al., indicated that grape exosome-like nanoparticles (GELNs) could induce intestinal stem cells and protect mice from DSS-induced colitis (Ju et al., 2013). They results indicated that GELNs are able to travel within the gut and migrate through the intestinal mucus. They could be taken up by mouse intestinal stem cells and could induce the proliferation of intestinal stem cells. These finding suggested that edible exosomes could be used as effective candidates for prevention and treatment of a variety of diseases (Ju et al., 2013).

One of important exosomes cargos are miRNAs. It has been showed that a variety of dietary components are able to modulate expression of miRNAs in various models (Wagner et al., 2015). These regulations could lead to decreasing of cancer risk. Hence, it seems that dietary exosomes via introducing various cargos such as miRNAs could exert their therapeutic. It seems that future studies could open new windows in this area.

It has been showed that only viable cells are able to synthesize and release exosomes that could carry miRNAs to recipient cells. Dietary factors with nutrigenomic effects may modify the miRNA composition and content of cell-derived exosomes (Cui et al., 2017; Neelakandan et al., 2012; Parasramka et al., 2012).

Recent efforts have been undertaken to use milk-derived exosomes foe the encapsulation curcumin which could enhance curcumin transport and drug effects. These results suggested that using milk-derived exosomes containing curcumin could induce therapeutic effects of curcumin in the better way than using curcumin alone (Vashisht et al., 2017).

**Dietary exosomes and cancer promotion**

Various types of cells such as Somatic cells, immune cells, tumor cells, and mammary gland epithelial cells especially during lactation could release abundant exosomes for mRNA-, protein- and miRNA-mediated cell-cell communication, which has favorable (breastfed infant) or adverse effects on human health (Melnik, 2015). Numerous studies indicated that bovine milk could provide various bioactive exosomal miRNAs (Reinhardt et al., 2012; Sun et al., 2013). MiR-29b is one of exosomal miRNAs which could be absorbed by humans in biologically meaningful amounts. The uptake of this could be associated with increasing its systemic circulation and leads to alteration of gene expression of the milk consumer (Baier et al., 2014; Melnik et al., 2013). It has been showed that almost 245 miRNAs could be

presented in cow's milk. These miRNAs could affect on 11,000 human genes in the human (Baier et al., 2014). Hence, Milk could be suggested as an epigenetic transfection system that could promote postnatal growth via transferring a variety of miRNAs involved in various cellular and molecular pathways (Melnik et al., 2013). Moreover, bovine miRNAs of cow's milk could be survived in various processing such as pasteurization, homogenization and refrigerated storage for over 2 weeks (Howard et al., 2015).

Exosomal miR-21 is one of major miRNAs present in cow's milk (Chen et al., 2010; Sun et al., 2013). It has been showed that increasing of milk consumption could be associated with progression of hepatocellular carcinoma (Duarte-Salles et al., 2014). It has been showed that interleukin 6 (IL-6) is able to induces STAT3-dependent miR-21 transcription in hepatocellular carcinoma (Loffler et al., 2007). In a study, Michaëlsson et al., indicated that there are a positive correlation between milk intake and high levels of IL-6 (Michaelsson et al., 2014). The increasing of serum IL-6 levels has been related with a worse prognosis of melanoma (Hoejberg et al., 2012; von Felbert et al., 2005). Milk exosomal miR-155 is other important molecules which could be inovolved in STAT3-mediated tumorigenesis (Cao et al., 2013). It has been showed that miR-155 could induce STAT3 expression via inhibition of cytokine signaling 1 (SOCS1) which is known as a target of miR-155 (Cao et al., 2013; Zhao et al., 2013). Up regulation of miR-21 and miR-155 could be related with progression of melanocytic lesions. Exosomal TGFβ is other proteins which could be transmited by commercial milk (Pieters et al., 2015). It has been showed that TGFβ signaling induces up regulation of miR-21 via stimulating the processing of primary transcripts of miR-21 (pri-miR-21) into precursor miR-21 (pre-miR-21) by the DROSHA complex (Davis et al., 2008). Hence, milk exosomes could be associated with progression of cancer via targeting various miRNAs and proteins such as miR-21, miR-155 and TGFβ.

## Conclusion

Dietary patterns are known as one of main risk factors for various cancers. It has observed that various dietary patterns such as meat (red meat, processed meat, fish and processed fish) or sugary-diet pattern are associated with risk of various cancers. In addition, multiple lines evidences indicated that plant dietary patterns have many antioxidant and anti-inflammatory components such as vitamin E that may be suitable for prevention or treatment of various cancers. The effect of various dietary patterns for prevention or treatments of different cancer remains unclear yet. Hence, more studies for showing positive or negative roles of them in cancer prevention are still required to be done. Moreover, a large numbers studies indicated that dietary compounds, dietary microRNAs and dietary exosomes could have critical roles in cancer prevention and therapy. Dietary compounds including curcumin, greet tea components, carotenoids, minerals and vitamins could affect on a variety of cellular and molecular targets which are involved in cancer initiation and progression. Hence, it seems that the applying of them in various dietary patterns could be useful for cancer prevention and therapy.

## References


Albanes D, Heinonen OP, Huttunen JK, Taylor PR, Virtamo J, Edwards B, Haapakoski J, Rautalahti M, Hartman A, Palmgren J. 1995. Effects of alpha-tocopherol and beta-carotene supplements on cancer incidence in the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study. The American journal of clinical nutrition 62(6):1427S-1430S.

Annabi B, Lachambre MP, Bousquet-Gagnon N, Page M, Gingras D, Beliveau R. 2002. Green tea polyphenol (-)-epigallocatechin 3-gallate inhibits MMP-2 secretion and MT1-MMP-driven migration in glioblastoma cells. Biochim Biophys Acta 30:1-3.

Baier SR, Nguyen C, Xie F, Wood JR, Zempleni J. 2014. MicroRNAs are absorbed in biologically meaningful amounts from nutritionally relevant doses of cow milk and affect gene expression in peripheral blood mononuclear cells, HEK-293 kidney cell cultures, and mouse livers. J Nutr 144(10):1495-1500.

Banikazemi Z, Mirzaei H, Mokhber N, Mobarhan MG. 2016. Selenium Intake is Related to Beck's Depression Score. Iranian Red Crescent Medical Journal 18(3).

Banikazemi Z, Mokhber N, Safarian M, Mazidi M, Mirzaei H, Esmaily H, Azarpazhooh MR, Ghafouri-Taleghani F, Ghayour-Mobarhan M, Ferns GA. 2015. Dietary vitamin E and fat intake are related to Beck's depression score. Clinical Nutrition ESPEN 10(2):e61-e65.

Bartsch H, Nair J, Owen RW. 1999. Dietary polyunsaturated fatty acids and cancers of the breast and colorectum: emerging evidence for their role as risk modifiers. Carcinogenesis 20(12):2209-2218.

Basak SK, Zinabadi A, Wu AW, Venkatesan N, Duarte VM, Kang JJ, Dalgard CL, Srivastava M, Sarkar FH, Wang MB, Srivatsan ES. 2015. Liposome encapsulated curcumin-difluorinated (CDF) inhibits the growth of cisplatin resistant head and neck cancer stem cells. Oncotarget 6(21):18504-18517.

Béliveau R, Gingras D. 2007. Role of nutrition in preventing cancer. Canadian Family Physician 53(11):1905-1911.

Boudreau MD, Sohn KH, Rhee SH, Lee SW, Hunt JD, Hwang DH. 2001. Suppression of tumor cell growth both in nude mice and in culture by n-3 polyunsaturated fatty acids: mediation through cyclooxygenase-independent pathways. Cancer Res 61(4):1386-1391.

Calo N, Ramadori P, Sobolewski C, Romero Y, Maeder C, Fournier M, Rantakari P, Zhang FP, Poutanen M, Dufour JF, Humar B, Nef S, Foti M. 2016. Stress-activated miR-21/miR-21* in hepatocytes promotes lipid and glucose metabolic disorders associated with high-fat diet consumption. Gut 65(11):1871-1881.

Candido S, Rapisarda V, Marconi A, Malaponte G, Bevelacqua V, Gangemi P, Scalisi A, McCubrey JA, Maestro R, Spandidos DA, Fenga C, Libra M. 2014. Analysis of the B-RafV600E mutation in cutaneous melanoma patients with occupational sun exposure. Oncol Rep 31(3):1079-1082.

Cao Q, Li YY, He WF, Zhang ZZ, Zhou Q, Liu X, Shen Y, Huang TT. 2013. Interplay between microRNAs and the STAT3 signaling pathway in human cancers. Physiol Genomics 45(24):1206-1214.

Catsburg C, Kim RS, Kirsh VA, Soskolne CL, Kreiger N, Rohan TE. 2015. Dietary patterns and breast cancer risk: a study in 2 cohorts. The American journal of clinical nutrition 101(4):817-823.

Chalabi N, Delort L, Satih S, Dechelotte P, Bignon YJ, Bernard-Gallon DJ. 2007. Immunohistochemical expression of RARalpha, RARbeta, and Cx43 in breast tumor cell lines after treatment with lycopene and correlation with RT-QPCR. J Histochem Cytochem 55(9):877-883.

Chartoumpekis DV, Zaravinos A, Ziros PG, Iskrenova RP, Psyrogiannis AI, Kyriazopoulou VE, Habeos IG. 2012. Differential expression of microRNAs in adipose tissue after long-term high-fat diet-induced obesity in mice. PLoS One 7(4):4.

Chen C, Kong AN. 2005. Dietary cancer-chemopreventive compounds: from signaling and gene expression to pharmacological effects. Trends Pharmacol Sci 26(6):318-326.

Chen J, Xu T, Chen C. 2015a. The critical roles of miR-21 in anti-cancer effects of curcumin. Ann Transl Med 3(21):2305-5839.

Chen X, Gao C, Li H, Huang L, Sun Q, Dong Y, Tian C, Gao S, Dong H, Guan D, Hu X, Zhao S, Li L, Zhu L, Yan Q, Zhang J, Zen K, Zhang CY. 2010. Identification and characterization of microRNAs in raw milk during different periods of lactation, commercial fluid, and powdered milk products. Cell Res 20(10):1128-1137.

Chen Y, Zaman MS, Deng G, Majid S, Saini S, Liu J, Tanaka Y, Dahiya R. 2011. MicroRNAs 221/222 and genistein-mediated regulation of ARHI tumor suppressor gene in prostate cancer. Cancer Prev Res 4(1):76-86.

Chen Z, Wang PP, Woodrow J, Zhu Y, Roebothan B, McLaughlin JR, Parfrey PS. 2015b. Dietary patterns and colorectal cancer: results from a Canadian population-based study. Nutrition journal 14:8.

Chyou P-H, Nomura AM, Hankin JH, Stemmermann GN. 1990. A case-cohort study of diet and stomach cancer. Cancer research 50(23):7501-7504.

Cortes-Jofre M, Rueda JR, Corsini-Munoz G, Fonseca-Cortes C, Caraballoso M, Bonfill Cosp X. 2012. Drugs for preventing lung cancer in healthy people. The Cochrane database of systematic reviews 10:CD002141.

Couto E, Boffetta P, Lagiou P, Ferrari P, Buckland G, Overvad K, Dahm C, Tjønneland A, Olsen A, Clavel-Chapelon F. 2011. Mediterranean dietary pattern and cancer risk in the EPIC cohort. British journal of cancer 104(9):1493-1499.

Cui J, Zhou B, Ross SA, Zempleni J. 2017. Nutrition, microRNAs, and Human Health. Adv Nutr 8(1):105-112.

Davis BN, Hilyard AC, Lagna G, Hata A. 2008. SMAD proteins control DROSHA-mediated microRNA maturation. Nature 454(7200):56-61.

Dhar S, Hicks C, Levenson AS. 2011. Resveratrol and prostate cancer: promising role for microRNAs. Mol Nutr Food Res 55(8):1219-1229.

Dolara P, Bigagli E, Collins A. 2012. Antioxidant vitamins and mineral supplementation, life span expansion and cancer incidence: a critical commentary. European journal of nutrition 51(7):769-781.

Dougherty U, Cerasi D, Taylor I, Kocherginsky M, Tekin U, Badal S, Aluri L, Sehdev A, Cerda S, Mustafi R, Delgado J, Joseph L, Zhu H, Hart J, Threadgill D, Fichera A, Bissonnette M. 2009. Epidermal growth factor receptor is required for colonic tumor promotion by dietary fat in the azoxymethane/dextran sulfate sodium model: roles of transforming growth factor-{alpha} and PTGS2. Clin Cancer Res 15(22):6780-6789.

Duarte-Salles T, Fedirko V, Stepien M, Trichopoulou A, Bamia C, Lagiou P, Lukanova A, Trepo E, Overvad K, Tjonneland A, Halkjaer J, Boutron-Ruault MC, Racine A, Cadeau C, Kuhn T, Aleksandrova K, Trichopoulos D, Tsiotas K, Boffetta P, Palli D, Pala V, Tumino R, Sacerdote C, Panico S, Bueno-de-Mesquita HB, Dik VK, Peeters PH, Weiderpass E, Torhild Gram I, Hjartaker A, Ramon Quiros J, Fonseca-Nunes A, Molina-Montes E, Dorronsoro M, Navarro Sanchez C, Barricarte A, Lindkvist B, Sonestedt E, Johansson I, Wennberg M, Khaw KT, Wareham N, Travis RC, Romieu I, Riboli E, Jenab M. 2014. Dairy products and risk of hepatocellular carcinoma: the European Prospective Investigation into Cancer and Nutrition. Int J Cancer 135(7):1662-1672.

Fathullahzadeh S, Mirzaei H, Honardoost MA, Sahebkar A, Salehi M. 2016. Circulating microRNA-192 as a diagnostic biomarker in human chronic lymphocytic leukemia. Cancer Gene Ther 23(10):327-332.

Fedirko V, Bostick RM, Flanders WD, Long Q, Sidelnikov E, Shaukat A, Daniel CR, Rutherford RE, Woodard JJ. 2009. Effects of vitamin d and calcium on proliferation and differentiation in normal colon mucosa: a randomized clinical trial. Cancer Epidemiol Biomarkers Prev 18(11):2933-2941.

Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. 2015. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. International journal of cancer 136(5):E359-E386.

Ferrante SC, Nadler EP, Pillai DK, Hubal MJ, Wang Z, Wang JM, Gordish-Dressman H, Koeck E, Sevilla S, Wiles AA, Freishtat RJ. 2015. Adipocyte-derived exosomal miRNAs: a novel mechanism for obesity-related disease. Pediatr Res 77(3):447-454.

Fimognari C, Nusse M, Iori R, Cantelli-Forti G, Hrelia P. 2004. The new isothiocyanate 4-(methylthio)butylisothiocyanate selectively affects cell-cycle progression and apoptosis induction of human leukemia cells. Invest New Drugs 22(2):119-129.

Foley NH, Bray I, Watters KM, Das S, Bryan K, Bernas T, Prehn JH, Stallings RL. 2011. MicroRNAs 10a and 10b are potent inducers of neuroblastoma cell differentiation through targeting of nuclear receptor corepressor 2. Cell Death Differ 18(7):1089-1098.

Gaedicke S, Zhang X, Schmelzer C, Lou Y, Doering F, Frank J, Rimbach G. 2008. Vitamin E dependent microRNA regulation in rat liver. FEBS Lett 582(23-24):3542-3546.

Garzon R, Pichiorri F, Palumbo T, Visentini M, Aqeilan R, Cimmino A, Wang H, Sun H, Volinia S, Alder H, Calin GA, Liu CG, Andreeff M, Croce CM. 2007. MicroRNA gene expression during retinoic acid-induced differentiation of human acute promyelocytic leukemia. Oncogene 26(28):4148-4157.

Gholamin S, Mirzaei H, Razavi SM, Hassanian SM, Saadatpour L, Masoudifar A, ShahidSales S, Avan A. 2017. GD2-targeted immunotherapy and potential value of circulating microRNAs in neuroblastoma. J Cell Physiol 1(10):25793.

Gholamin S, Pasdar A, Khorrami MS, Mirzaei H, Mirzaei HR, Salehi R, Ferns GA, Ghayour-Mobarhan M, Avan A. 2016. The potential for circulating microRNAs in the diagnosis of myocardial infarction: a novel approach to disease diagnosis and treatment. Curr Pharm Des 22(3):397-403.

Goradel NH, Hour FG, Negahdari B, Malekshahi ZV, Hashemzehi M, Masoudifar A, Mirzaei H. 2017. Stem Cell Therapy: A New Therapeutic Option for Cardiovascular Diseases. J Cell Biochem 25(10):26169.

Hardy TM, Tollefsbol TO. 2011. Epigenetic diet: impact on the epigenome and cancer. Epigenomics 3(4):503-518.

Hashemi Goradel N, Ghiyami Hoor F, Jahangiri S, Negahdari B, Sahebkar A, Masoudifar A, Mirzaei H. 2017. Nanoparticles as new tools for inhibition of cancer angiogenesis. J Cell Physiol 25(10):26029.

Hoejberg L, Bastholt L, Schmidt H. 2012. Interleukin-6 and melanoma. Melanoma Res 22(5):327-333.

Hoseini Z, Sepahvand F, Rashidi B, Sahebkar A, Masoudifar A, Mirzaei H. 2017. NLRP3 inflammasome: Its regulation and involvement in atherosclerosis. J Cell Physiol 27(10):25930.

Howard KM, Jati Kusuma R, Baier SR, Friemel T, Markham L, Vanamala J, Zempleni J. 2015. Loss of miRNAs during processing and storage of cow's (Bos taurus) milk. J Agric Food Chem 63(2):588-592.

Hsing AW, McLaughlin JK, Schuman LM, Bjelke E, Gridley G, Wacholder S, Chien HTC, Blot WJ. 1990. Diet, tobacco use, and fatal prostate cancer: results from the Lutheran Brotherhood Cohort Study. Cancer Research 50(21):6836-6840.

Hu S, Dong TS, Dalal SR, Wu F, Bissonnette M, Kwon JH, Chang EB. 2011. The microbe-derived short chain fatty acid butyrate targets miRNA-dependent p21 gene expression in human colon cancer. PLoS One 6(1):0016221.

Ivanov NI, Cowell SP, Brown P, Rennie PS, Guns ES, Cox ME. 2007. Lycopene differentially induces quiescence and apoptosis in androgen-responsive and -independent prostate cancer cell lines. Clin Nutr 26(2):252-263.

Ju S, Mu J, Dokland T, Zhuang X, Wang Q, Jiang H, Xiang X, Deng ZB, Wang B, Zhang L, Roth M, Welti R, Mobley J, Jun Y, Miller D, Zhang HG. 2013. Grape exosome-like nanoparticles induce intestinal stem cells and protect mice from DSS-induced colitis. Mol Ther 21(7):1345-1357.

Kang M, Yan LM, Zhang WY, Li YM, Tang AZ, Ou HS. 2013. Role of microRNA-21 in regulating 3T3-L1 adipocyte differentiation and adiponectin expression. Mol Biol Rep 40(8):5027-5034.

Keller P, Gburcik V, Petrovic N, Gallagher IJ, Nedergaard J, Cannon B, Timmons JA. 2011. Gene-chip studies of adipogenesis-regulated microRNAs in mouse primary adipocytes and human obesity. BMC Endocr Disord 11(7):1472-6823.

Keshavarzi M, Darijani M, Momeni F, Moradi P, Ebrahimnejad H, Masoudifar A, Mirzaei H. 2017a. Molecular Imaging and Oral Cancer Diagnosis and Therapy. J Cell Biochem 8(10):26042.

Keshavarzi M, Sorayayi S, Jafar Rezaei M, Mohammadi M, Ghaderi A, Rostamzadeh A, Masoudifar A, Mirzaei H. 2017b. MicroRNAs-Based Imaging Techniques in Cancer Diagnosis and Therapy. J Cell Biochem 29(10):26012.

Kolonel LN, Altshuler D, Henderson BE. 2004. The multiethnic cohort study: exploring genes, lifestyle and cancer risk. Nature Reviews Cancer 4(7):519-527.

Kvåle G, Bjelke E, Gart JJ. 1983. Dietary habits and lung cancer risk. International Journal of Cancer 31(4):397-405.

Lamprecht SA, Lipkin M. 2001. Cellular mechanisms of calcium and vitamin D in the inhibition of colorectal carcinogenesis. Ann N Y Acad Sci 952:73-87.

Langner E, Rzeski W. 2012. Dietary derived compounds in cancer chemoprevention. Contemp Oncol 16(5):394-400.

Li Y, Saldanha SN, Tollefsbol TO. 2014. Impact of epigenetic dietary compounds on transgenerational prevention of human diseases. Aaps J 16(1):27-36.

Li Y, VandenBoom TG, 2nd, Kong D, Wang Z, Ali S, Philip PA, Sarkar FH. 2009. Up-regulation of miR-200 and let-7 by natural agents leads to the reversal of epithelial-to-mesenchymal transition in gemcitabine-resistant pancreatic cancer cells. Cancer Res 69(16):6704-6712.

Liu G, Xiang T, Wu QF, Wang WX. 2016. Curcumin suppresses the proliferation of gastric cancer cells by downregulating H19. Oncol Lett 12(6):5156-5162.

Loffler D, Brocke-Heidrich K, Pfeifer G, Stocsits C, Hackermuller J, Kretzschmar AK, Burger R, Gramatzki M, Blumert C, Bauer K, Cvijic H, Ullmann AK, Stadler PF, Horn F. 2007. Interleukin-6 dependent survival of multiple myeloma cells involves the Stat3-mediated induction of microRNA-21 through a highly conserved enhancer. Blood 110(4):1330-1333.

Lu Y, Wang J, Liu L, Yu L, Zhao N, Zhou X, Lu X. 2017. Curcumin increases the sensitivity of Paclitaxel-resistant NSCLC cells to Paclitaxel through microRNA-30c-mediated MTA1 reduction. Tumour Biol 39(4):1010428317698353.

Marmot M, Atinmo T, Byers T, Chen J, Hirohata T, Jackson A, James W, Kolonel L, Kumanyika S, Leitzmann C. 2007. Food, nutrition, physical activity, and the prevention of cancer: a global perspective.

Marsit CJ, Eddy K, Kelsey KT. 2006. MicroRNA responses to cellular stress. Cancer Res 66(22):10843-10848.

Mashreghi M, Azarpara H, Bazaz MR, Jafari A, Masoudifar A, Mirzaei H, Jaafari MR. 2017. Angiogenesis biomarkers and their targeting ligands as potential targets for tumor angiogenesis. J Cell Physiol 13(10):26049.

Mayne ST, Playdon MC, Rock CL. 2016. Diet, nutrition, and cancer: past, present and future. Nature Reviews Clinical Oncology.

McKay DL, Blumberg JB. 2002. The role of tea in human health: an update. J Am Coll Nutr 21(1):1-13.

Melnik BC. 2015. MiR-21: an environmental driver of malignant melanoma? J Transl Med 13(202):015-0570.

Melnik BC, John SM, Schmitz G. 2013. Milk is not just food but most likely a genetic transfection system activating mTORC1 signaling for postnatal growth. Nutr J 12(103):1475-2891.

Michaelsson K, Wolk A, Langenskiold S, Basu S, Warensjo Lemming E, Melhus H, Byberg L. 2014. Milk intake and risk of mortality and fractures in women and men: cohort studies. Bmj 28(349).

Mirzaei H. 2017. Stroke in women: Risk factors and clinical biomarkers. J Cell Biochem 12(10):26130.

Mirzaei H, Fathullahzadeh S, Khanmohammadi R, Darijani M, Momeni F, Masoudifar A, Goodarzi M, Mardanshah O, Stanveng J, Jaafari MR, Mirzaei HR. 2017a. State of the Art in MicroRNA as Diagnostic and Therapeutic Biomarkers in Chronic Lymphocytic Leukemia. J Cell Physiol 13(10):25799.

Mirzaei H, Khataminfar S, Mohammadparast S, Sales SS, Maftouh M, Mohammadi M, Simonian M, Parizadeh SM, Hassanian SM, Avan A. 2016a. Circulating microRNAs as Potential Diagnostic Biomarkers and Therapeutic Targets in Gastric Cancer: Current Status and Future Perspectives. Curr Med Chem 23(36):4135-4150.

Mirzaei H, Khoi MJ, Azizi M, Goodarzi M. 2016b. Can curcumin and its analogs be a new treatment option in cancer therapy? Cancer Gene Ther 23(11):47.

Mirzaei H, Masoudifar A, Sahebkar A, Zare N, Nahand JS, Rashidi B, Mehrabian E, Mohammadi M, Mirzaei HR, Jaafari MR. 2017b. MicroRNA: A Novel Target of Curcumin in Cancer Therapy. J Cell Physiol 15(10):26055.

Mirzaei H, Momeni F, Saadatpour L, Sahebkar A, Goodarzi M, Masoudifar A, Kouhpayeh S, Salehi H, Mirzaei HR, Jaafari MR. 2017c. MicroRNA: Relevance to Stroke Diagnosis, Prognosis and Therapy. J Cell Physiol 9(10):25787.

Mirzaei H, Naseri G, Rezaee R, Mohammadi M, Banikazemi Z, Mirzaei HR, Salehi H, Peyvandi M, Pawelek JM, Sahebkar A. 2016c. Curcumin: A new candidate for melanoma therapy? Int J Cancer 139(8):1683-1695.

Mirzaei H, Sahebkar A, Avan A, Jaafari MR, Salehi R, Salehi H, Baharvand H, Rezaei A, Hadjati J, Pawelek JM, Mirzaei HR. 2016d. Application of Mesenchymal Stem Cells in Melanoma: A Potential Therapeutic Strategy for Delivery of Targeted Agents. Curr Med Chem 23(5):455-463.

Mirzaei H, Sahebkar A, Jaafari MR, Goodarzi M, Mirzaei HR. 2016e. Diagnostic and Therapeutic Potential of Exosomes in Cancer: The Beginning of a New Tale? J Cell Physiol 14(10):25739.

Mirzaei H, Sahebkar A, Jaafari MR, Hadjati J, Javanmard SH, Mirzaei HR, Salehi R. 2016f. PiggyBac as a novel vector in cancer gene therapy: current perspective. Cancer Gene Ther 23(2-3):45-47.

Mirzaei H, Shakeri A, Rashidi B, Jalili A, Banikazemi Z, Sahebkar A. 2017d. Phytosomal curcumin: A review of pharmacokinetic, experimental and clinical studies. Biomed Pharmacother 85:102-112.

Mirzaei H, Yazdi F, Salehi R, Mirzaei HR. 2016g. SiRNA and epigenetic aberrations in ovarian cancer. J Cancer Res Ther 12(2):498-508.

Mirzaei HR, Mirzaei H, Lee SY, Hadjati J, Till BG. 2016h. Prospects for chimeric antigen receptor (CAR) gammadelta T cells: A potential game changer for adoptive T cell cancer immunotherapy. Cancer Lett 380(2):413-423.

Mirzaei HR, Sahebkar A, Mohammadi M, Yari R, Salehi H, Jafari MH, Namdar A, Khabazian E, Jaafari MR, Mirzaei H. 2016i. Circulating microRNAs in Hepatocellular Carcinoma: Potential Diagnostic and Prognostic Biomarkers. Curr Pharm Des 22(34):5257-5269.

Mirzaei HR, Sahebkar A, Salehi R, Nahand JS, Karimi E, Jaafari MR, Mirzaei H. 2016j. Boron neutron capture therapy: Moving toward targeted cancer therapy. J Cancer Res Ther 12(2):520-525.

Mohammadi M, Goodarzi M, Jaafari MR, Mirzaei HR, Mirzaei H. 2016a. Circulating microRNA: a new candidate for diagnostic biomarker in neuroblastoma. Cancer Gene Ther 23(11):371-372.

Mohammadi M, Jaafari MR, Mirzaei HR, Mirzaei H. 2016b. Mesenchymal stem cell: a new horizon in cancer gene therapy. Cancer Gene Ther 23(9):285-286.

Moridikia A, Mirzaei H, Sahebkar A, Salimian J. 2017. MicroRNAs: Potential candidates for diagnosis and treatment of colorectal cancer. J Cell Physiol 16(10):25801.

Moyad MA. 2002. Selenium and vitamin E supplements for prostate cancer: evidence or embellishment? Urology 59(4 Suppl 1):9-19.

Mudduluru G, George-William JN, Muppala S, Asangani IA, Kumarswamy R, Nelson LD, Allgayer H. 2011. Curcumin regulates miR-21 expression and inhibits invasion and metastasis in colorectal cancer. Biosci Rep 31(3):185-197.

Muller G, Schneider M, Biemer-Daub G, Wied S. 2011. Microvesicles released from rat adipocytes and harboring glycosylphosphatidylinositol-anchored proteins transfer RNA stimulating lipid synthesis. Cell Signal 23(7):1207-1223.

Neelakandan K, Babu P, Nair S. 2012. Emerging roles for modulation of microRNA signatures in cancer chemoprevention. Curr Cancer Drug Targets 12(6):716-740.

Newmark HL, Yang K, Lipkin M, Kopelovich L, Liu Y, Fan K, Shinozaki H. 2001. A Western-style diet induces benign and malignant neoplasms in the colon of normal C57Bl/6 mice. Carcinogenesis 22(11):1871-1875.

Niu T, Tian Y, Mei Z, Guo G. 2016. Inhibition of Autophagy Enhances Curcumin United light irradiation-induced Oxidative Stress and Tumor Growth Suppression in Human Melanoma Cells. Sci Rep 6(31383).

Nolte-'t Hoen EN, Van Rooij E, Bushell M, Zhang CY, Dashwood RH, James WP, Harris C, Baltimore D. 2015. The role of microRNA in nutritional control. J Intern Med 278(2):99-109.

Palozza P, Serini S, Boninsegna A, Bellovino D, Lucarini M, Monastra G, Gaetani S. 2007. The growth-inhibitory effects of tomatoes digested in vitro in colon adenocarcinoma cells occur through down regulation of cyclin D1, Bcl-2 and Bcl-xL. Br J Nutr 98(4):789-795.

Pan MH, Ho CT. 2008. Chemopreventive effects of natural dietary compounds on cancer development. Chem Soc Rev 37(11):2558-2574.

Pandey V, Vijayakumar MV, Ajay AK, Malvi P, Bhat MK. 2012. Diet-induced obesity increases melanoma progression: involvement of Cav-1 and FASN. Int J Cancer 130(3):497-508.

Parasramka MA, Ho E, Williams DE, Dashwood RH. 2012. MicroRNAs, diet, and cancer: new mechanistic insights on the epigenetic actions of phytochemicals. Mol Carcinog 51(3):213-230.

Peng X, Vaishnav A, Murillo G, Alimirah F, Torres KE, Mehta RG. 2010. Protection against cellular stress by 25-hydroxyvitamin D3 in breast epithelial cells. J Cell Biochem 110(6):1324-1333.

Pieters BC, Arntz OJ, Bennink MB, Broeren MG, van Caam AP, Koenders MI, van Lent PL, van den Berg WB, de Vries M, van der Kraan PM, van de Loo FA. 2015. Commercial cow milk contains physically stable extracellular vesicles expressing immunoregulatory TGF-beta. PLoS One 10(3).

Pisano M, Palomba A, Tanca A, Pagnozzi D, Uzzau S, Addis MF, Dettori MA, Fabbri D, Palmieri G, Rozzo C. 2016. Protein expression changes induced in a malignant melanoma cell line by the curcumin analogue compound D6. BMC Cancer 16(317):016-2362.

Qin J, Xie LP, Zheng XY, Wang YB, Bai Y, Shen HF, Li LC, Dahiya R. 2007. A component of green tea, (-)-epigallocatechin-3-gallate, promotes apoptosis in T24 human bladder cancer cells via modulation of the PI3K/Akt pathway and Bcl-2 family proteins. Biochem Biophys Res Commun 354(4):852-857.

Rabieian R, Boshtam M, Zareei M, Kouhpayeh S, Masoudifar A, Mirzaei H. 2017. Plasminogen activator inhibitor type-1 as a regulator of fibrosis. J Cell Biochem 18(10):26146.

Rashidi B, Hoseini Z, Sahebkar A, Mirzaei H. 2016. Anti-Atherosclerotic Effects of Vitamins D and E in Suppression of Atherogenesis. J Cell Physiol 14(10):25738.

Rashidi B, Malekzadeh M, Goodarzi M, Masoudifar A, Mirzaei H. 2017. Green tea and its anti-angiogenesis effects. Biomed Pharmacother 89:949-956.

Record M. 2013. Exosome-like nanoparticles from food: protective nanoshuttles for bioactive cargo. Mol Ther 21(7):1294-1296.

Reinhardt TA, Lippolis JD, Nonnecke BJ, Sacco RE. 2012. Bovine milk exosome proteome. J Proteomics 75(5):1486-1492.

Rodriguez C, Jacobs EJ, Mondul AM, Calle EE, McCullough ML, Thun MJ. 2004. Vitamin E supplements and risk of prostate cancer in U.S. men. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology 13(3):378-382.

Rose DP, Cohen LA. 1988. Effects of dietary menhaden oil and retinyl acetate on the growth of DU 145 human prostatic adenocarcinoma cells transplanted into athymic nude mice. Carcinogenesis 9(4):603-605.

Ross SA, Davis CD. 2011. MicroRNA, nutrition, and cancer prevention. Adv Nutr 2(6):472-485.

Ross SA, Davis CD. 2014. The emerging role of microRNAs and nutrition in modulating health and disease. Annu Rev Nutr 34:305-336.

Roy S, Yu Y, Padhye SB, Sarkar FH, Majumdar AP. 2013. Difluorinated-curcumin (CDF) restores PTEN expression in colon cancer cells by down-regulating miR-21. PLoS One 8(7).

Saadatpour L, Fadaee E, Fadaei S, Nassiri Mansour R, Mohammadi M, Mousavi SM, Goodarzi M, Verdi J, Mirzaei H. 2016a. Glioblastoma: exosome and microRNA as novel diagnosis biomarkers. Cancer Gene Ther 23(12):415-418.

Saadatpour Z, Bjorklund G, Chirumbolo S, Alimohammadi M, Ehsani H, Ebrahiminejad H, Pourghadamyari H, Baghaei B, Mirzaei HR, Sahebkar A, Mirzaei H, Keshavarzi M. 2016b. Molecular imaging and cancer gene therapy. Cancer Gene Ther 18(10):62.

Saadatpour Z, Rezaei A, Ebrahimnejad H, Baghaei B, Bjorklund G, Chartrand M, Sahebkar A, Morovati H, Mirzaei HR, Mirzaei H. 2017. Imaging techniques: new avenues in cancer gene and cell therapy. Cancer Gene Ther 24(1):1-5.

Salarinia R, Sahebkar A, Peyvandi M, Mirzaei HR, Jaafari MR, Riahi MM, Ebrahimnejad H, Nahand JS, Hadjati J, Asrami MO, Fadaei S, Salehi R, Mirzaei H. 2016. Epi-Drugs and Epi-miRs: Moving Beyond Current Cancer Therapies. Curr Cancer Drug Targets 16(9):773-788.

Sartippour MR, Shao ZM, Heber D, Beatty P, Zhang L, Liu C, Ellis L, Liu W, Go VL, Brooks MN. 2002. Green tea inhibits vascular endothelial growth factor (VEGF) induction in human breast cancer cells. J Nutr 132(8):2307-2311.

Sarveswaran S, Liroff J, Zhou Z, Nikitin AY, Ghosh J. 2010. Selenite triggers rapid transcriptional activation of p53, and p53-mediated apoptosis in prostate cancer cells: Implication for the treatment of early-stage prostate cancer. Int J Oncol 36(6):1419-1428.

Schottenfeld D, Fraumeni Jr JF. 2006. Cancer epidemiology and prevention: Oxford University Press.

Seeger T, Fischer A, Muhly-Reinholz M, Zeiher AM, Dimmeler S. 2014. Long-term inhibition of miR-21 leads to reduction of obesity in db/db mice. Obesity 22(11):2352-2360.

Simonian M, Mosallayi M, Mirzaei H. 2017. Circulating miR-21 as novel biomarker in gastric cancer: diagnostic and prognostic biomarker.

Steinmetz KA, Kushi LH, Bostick RM, Folsom AR, Potter JD. 1994. Vegetables, fruit, and colon cancer in the lowa women's health study. American journal of epidemiology 139(1):1-15.

Sun M, Estrov Z, Ji Y, Coombes KR, Harris DH, Kurzrock R. 2008. Curcumin (diferuloylmethane) alters the expression profiles of microRNAs in human pancreatic cancer cells. Mol Cancer Ther 7(3):464-473.

Sun Q, Chen X, Yu J, Zen K, Zhang CY, Li L. 2013. Immune modulatory function of abundant immune-related microRNAs in microvesicles from bovine colostrum. Protein Cell 4(3):197-210.

Tajbakhsh A, Hasanzadeh M, Rezaee M, Khedri M, Khazaei M, Sales SS, Ferns GA, Hassanian SM, Avan A. 2017. Therapeutic potential of novel formulated forms of curcumin in the treatment of breast cancer by the targeting of cellular and physiological dysregulated pathways. J Cell Physiol 17(10):25961.

Tsang WP, Kwok TT. 2010. Epigallocatechin gallate up-regulation of miR-16 and induction of apoptosis in human cancer cells. J Nutr Biochem 21(2):140-146.

Vaisman N, Arber N. 2002. The role of nutrition and chemoprevention in colorectal cancer: from observations to expectations. Best Pract Res Clin Gastroenterol 16(2):201-217.

Vashisht M, Rani P, Onteru SK, Singh D. 2017. Curcumin Encapsulated in Milk Exosomes Resists Human Digestion and Possesses Enhanced Intestinal Permeability in Vitro. Appl Biochem Biotechnol 2(10):017-2478.

Vinciguerra M, Sgroi A, Veyrat-Durebex C, Rubbia-Brandt L, Buhler LH, Foti M. 2009. Unsaturated fatty acids inhibit the expression of tumor suppressor phosphatase and tensin homolog (PTEN) via microRNA-21 up-regulation in hepatocytes. Hepatology 49(4):1176-1184.

von Felbert V, Cordoba F, Weissenberger J, Vallan C, Kato M, Nakashima I, Braathen LR, Weis J. 2005. Interleukin-6 gene ablation in a transgenic mouse model of malignant skin melanoma. Am J Pathol 166(3):831-841.

Wagner AE, Piegholdt S, Ferraro M, Pallauf K, Rimbach G. 2015. Food derived microRNAs. Food Funct 6(3):714-718.

Wang X, Gocek E, Liu CG, Studzinski GP. 2009. MicroRNAs181 regulate the expression of p27Kip1 in human myeloid leukemia cells induced to differentiate by 1,25-dihydroxyvitamin D3. Cell Cycle 8(5):736-741.

Wang X, Hang Y, Liu J, Hou Y, Wang N, Wang M. 2017a. Anticancer effect of curcumin inhibits cell growth through miR-21/PTEN/Akt pathway in breast cancer cell. Oncol Lett 13(6):4825-4831.

Wang Y, Ying X, Xu H, Yan H, Li X, Tang H. 2017b. The functional curcumin liposomes induce apoptosis in C6 glioblastoma cells and C6 glioblastoma stem cells in vitro and in animals. Int J Nanomedicine 12:1369-1384.

Weiderpass E. 2010. Lifestyle and cancer risk. J Prev Med Public Health 43(6):459-471.

Weinstein SJ, Wright ME, Lawson KA, Snyder K, Mannisto S, Taylor PR, Virtamo J, Albanes D. 2007. Serum and dietary vitamin E in relation to prostate cancer risk. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology 16(6):1253-1259.

Willett WC. 2000. Diet and cancer. The oncologist 5(5):393-404.

Yang CH, Yue J, Sims M, Pfeffer LM. 2013. The curcumin analog EF24 targets NF-kappaB and miRNA-21, and has potent anticancer activity in vitro and in vivo. PLoS One 8(8).

Yang J, Cao Y, Sun J, Zhang Y. 2010. Curcumin reduces the expression of Bcl-2 by upregulating miR-15a and miR-16 in MCF-7 cells. Med Oncol 27(4):1114-1118.

Zhang J, Feng Z, Wang C, Zhou H, Liu W, Kanchana K, Dai X, Zou P, Gu J, Cai L, Liang G. 2017. Curcumin derivative WZ35 efficiently suppresses colon cancer progression through inducing ROS production and ER stress-dependent apoptosis. Am J Cancer Res 7(2):275-288.

Zhao XD, Zhang W, Liang HJ, Ji WY. 2013. Overexpression of miR -155 promotes proliferation and invasion of human laryngeal squamous cell carcinoma via targeting SOCS1 and STAT3. PLoS One 8(2):20.

Zhou S, Li J, Xu H, Zhang S, Chen X, Chen W, Yang S, Zhong S, Zhao J, Tang J. 2017. Liposomal curcumin alters chemosensitivity of breast cancer cells to Adriamycin via regulating microRNA expression. Gene 18(17):30277-30279.

Zhu H, Dougherty U, Robinson V, Mustafi R, Pekow J, Kupfer S, Li YC, Hart J, Goss K, Fichera A, Joseph L, Bissonnette M. 2011. EGFR signals downregulate tumor suppressors miR-143 and miR-145 in Western diet-promoted murine colon cancer: role of G1 regulators. Mol Cancer Res 9(7):960-975.

Table 1. A variety of dietary compounds which are associated with anti-cancer properties

| **Dietary compound (s)** | **Cancer** | **Target gene (s)** | **Effect (s)** | **Citation** |
|---|---|---|---|---|
| Green tea | Bladder | PI3K/Akt, Bcl-2 family | The enhancing of apoptosis | (Qin et al., 2007) |
| | Glioblastoma | MMP-2 , MT1-MMP | Inhibition of tumor growth | (Annabi et al., 2002) |
| | Breast | VEGF | Inhibition of angiogenesis | (Sartippour et al., 2002) |
| Polyunsaturated fatty acids | Colon | COX-1 or COX- | Inhibition of tumor growth | (Boudreau et al., 2001) |
| | Breast | - | Inhibition of tumor growth | (Bartsch et al., 1999) |
| | Prostate | - | Inhibition of tumor growth | (Rose and Cohen, 1988) |

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| Glucosinolates/isothiocyanates | Lung | - | Inhibition of growth tumor | (Kvåle et al., 1983) |
| | Stomach | - | Inhibition of growth tumor | (Chyou et al., 1990) |
| | Colon | - | Inhibition of growth tumor | (Steinmetz et al., 1994) |
| | Prostate | - | Inhibition of growth tumor | (Hsing et al., 1990) |
| Carotenoids | Colon | cyclin D1, Bcl-2 and Bcl-xL | Induce apoptosis and inhibition of tumor growth | (Palozza et al., 2007) |
| | Prostate | AKT, cyclin D1 | inhibition of tumor growth | (Ivanov et al., 2007) |
| | Breast | RARalpha and Cx43 | inhibition of tumor growth | (Chalabi et al., 2007) |
| Vitamin D | Colon | p21, MIB-1 | inhibition of tumor growth | (Fedirko et al., 2009; Lamprecht and Lipkin, |

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|---|---|---|---|---|
| | | | | 2001) |

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| Folate | Colon | COX2 | inhibition of tumor growth | (Vaisman and Arber, 2002) |
| Selenium | Leukemia | cyclin B1 | Inhibition of cell proliferation | (Fimognari et al., 2004) |
| Calcium | Colon | COX2 | inhibition of tumor growth | (Vaisman and Arber, 2002) |
| Curcumin | Melanoma | COX-2 | Inhibition of cell proliferation | (Niu et al., 2016; Pisano et al., 2016) |
| | Colon | - | Inducing apoptosis , ROS, and ER stress | (Zhang et al., 2017) |
| | Glioblastoma | - | Inducing apoptosis | (Wang et al., 2017) |
| | Gastric | p53, Bcl-2, Bax and c-Myc | Inhibition of cell proliferation, | (Liu et al., 2016) |

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|---|---|---|---|---|
| | | | Inducing apoptosis | |
| | Breast | miR-29b-1-5p, PPARG, RRM2, SRSF1and EPAS1 | Inhibition of tumor growth | (Tajbakhsh et al., 2017; Zhou et al., 2017) |
| | Head and neck | | Inhibition of tumor growth | (Basak et al., 2015) |
| | Lung | miR-30c | Increasing the sensitivity of Paclitaxel-resistant , Inhibition of tumor growth | (Lu et al., 2017) |

**Table 2. Dietary microRNA involved in cancer prevention**

| Dietary component | Cell line | MicroRNA | Expression in cancer | Citation |
|---|---|---|---|---|
| Folate | TK-6 | miR-222 | Up regulation | (Marsit et al., 2006) |
| RA | NB4 | miR-15a | Up regulation | (Garzon et al., 2007) |
| | | miR-15b | Up regulation | (Garzon et al., 2007) |
| | | miR-16–1 | Up regulation | (Garzon et al., 2007) |
| | | let-7a-3 | Up regulation | (Garzon et al., 2007) |
| | | let-7c | Up regulation | (Garzon et al., 2007) |
| | | let-7d | Up regulation | (Garzon et al., 2007) |
| | | miR-223 | Up regulation | (Garzon et al., 2007) |
| | | miR-342 | Up regulation | (Garzon et al., 2007) |
| | | miR-107 | Up regulation | (Garzon et al., 2007) |
| | | miR-181b | Down | (Garzon et |

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|---|---|---|---|---|
| | | | regulation | al., 2007) |
| RA | SK-N-BE, LAN5 and SHSY-5Y | miR-10a | Up regulation | (Foley et al., 2011) |
| | | miR-10b | Up regulation | (Foley et al., 2011) |
| 1,25(OH)$_2$D | HL60 and U937 | miR181a | Down regulation | (Wang et al., 2009) |
| | | miR181b | Down regulation | (Wang et al., 2009) |
| 1,25(OH)$_2$D | MCF12F | miR-26b | Down regulation | (Peng et al., 2010) |
| | | miR-200c | Down regulation | (Peng et al., 2010) |
| | | miR-200b | Down regulation | (Peng et al., 2010) |
| | | miR-182 | Down regulation | (Peng et al., 2010) |
| | | Let-7b | Up regulation | (Peng et al., 2010) |
| Sodium selenite | LNCaP | miR-34b | Up regulation | (Sarveswaran et al., 2010) |
| | | miR-34c | Up regulation | (Sarveswaran et al., 2010) |
| EGCG | HepG2 | miR-18a | Down regulation | (Tsang and Kwok, 2010) |

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| | | miR-34b | Down regulation | (Tsang and Kwok, 2010) |
| | | miR-193b | Down regulation | (Tsang and Kwok, 2010) |
| | | miR-222 | Down regulation | (Tsang and Kwok, 2010) |
| | | miR-342 | Down regulation | (Tsang and Kwok, 2010) |
| | | let-7a, | Up regulation | (Tsang and Kwok, 2010) |
| | | miR-16 | Up regulation | (Tsang and Kwok, 2010) |
| | | miR-221 | Up regulation | (Tsang and Kwok, 2010) |
| Curcumin | BxPC-3 | miR-22 | Up regulation | (Sun et al., 2008) |
| | | miR-199a | Down regulation | (Sun et al., 2008) |
| Curcumin | MCF-7 | miR-15a | Up regulation | (Yang et al., 2010) |
| | | miR-16 | Up regulation | (Yang et al., 2010) |
| DIM | MiaPaCa-2, Panc-1 and L3.6pl | miR-200b | Up regulation | (Li et al., 2009) |
| | | miR-200c | Up regulation | (Li et al., |

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|---|---|---|---|---|
| | | | | 2009) |
| | | let-7b | Up regulation | (Li et al., 2009) |
| | | let-7e | Up regulation | (Li et al., 2009) |
| Isoflavones | MiaPaCa-2, Panc-1 and L3.6pl | miR-200b | Up regulation | (Li et al., 2009) |
| | | miR-200c | Up regulation | (Li et al., 2009) |
| | | let-7b | Up regulation | (Li et al., 2009) |
| | | let-7e | Up regulation | (Li et al., 2009) |
| Genistein | PC-3 | miR-221 | Down regulation | (Chen et al., 2011) |
| | | miR-222 | Down regulation | (Chen et al., 2011) |
| Resveratrol | LNCaP | miR-150 | Up regulation | (Dhar et al., 2011) |
| | | miR-296–5p | Up regulation | (Dhar et al., 2011) |
| | | miR-7 | Down regulation | (Dhar et al., 2011) |
| | | miR-17 | Down regulation | (Dhar et al., 2011) |

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| | | miR-20a | Down regulation | (Dhar et al., 2011) |
| | | miR-18b | Down regulation | (Dhar et al., 2011) |
| | | miR-20b | Down regulation | (Dhar et al., 2011) |
| | | miR-92b | Down regulation | (Dhar et al., 2011) |
| | | miR-106a | Down regulation | (Dhar et al., 2011) |
| | | miR106b | Down regulation | (Dhar et al., 2011) |
| SCFA butyrate | HCT-116 | miR-17 | Down regulation | (Hu et al., 2011) |
| | | miR-20a | Down regulation | (Hu et al., 2011) |
| | | miR-20b | Down regulation | (Hu et al., 2011) |
| | | miR-93 | Down regulation | (Hu et al., 2011) |
| | | miR-106a | Down regulation | (Hu et al., 2011) |
| | | miR-106b | Down regulation | (Hu et al., 2011) |
| Oleic acid | HepG2 | miR-21 | Up regulation | (Vinciguerra |

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| | | | | et al., 2009) |

Figure 1. Various cellular and molecular targets which regulated by curcumin and its analogs