activity of NK cells and suppress IL-2-stimulated NK cell growth signaling in vivo and in vitro.

IV- TDEs can also skew monocyte differentiation into DCs toward the generation of myeloid derived suppressor cells and display Transforming Growth Factor- β1 (TGF-β1) mediated suppressive activity on T Lymphocytes *in vitro*. By eeleasing of vesicular structures, tumor cells can adjust host environment for surviving and progressing in vivo. Another supporting study in mouse models demonstrated that exosomes secreted by murine mammary carcinoma cells and melanoma cells suppressed the differentiation of DCs via inducing IL-6.

V- TDEs can participate in drug resistance via several mechanisms. The first mechanism is by drug exportation through the exosome pathway. Ovarian carcinoma cells stably got resistance to the cancer chemotherapy drug cisplatin (CDDP). Exosomes snared cytoplasmic CDDP, and then exported it to exit the cell. To do it, multivesicular bodies fuse with the plasma membrane and leave their content. In addition, exosomes can nullify antibody-based drugs. Exosomes produced by HER2-overexpressing breast carcinoma cell lines that express a full-length HER2 molecule can bind to the HER2 antibody Trastuzumab. Exosomal inhibition of antibody by reducing antibody binding to cancer cells suppresses the effect of Trastuzumab on the proliferation of these cells. On the other hand, due to the similarity of Cl^- concentration within exosomes and extracellular fluids, once chemotherapy agent Cisplatin incorporated into exosomes secreted by melanoma cells, it remains in native unhydrated form.

VI- Exosomes can be used as biomarkers to monitor the emergence, progression, prognosis of cancer, and efficacy of treatment regimens. Exosomes can be detected in higher concentrations, both in tumor tissue, and the serum and plasma of cancer patients.

VII- TDEs displacing a role in tumor progression and metastatic niche formation as mediators of metastasis. They mobilize bone marrow-derived cells (BMDCs) that support tumor vasculogenesis, invasion and metastasis. Furthermore, the presence of melanoma exosomes in lymph nodes induces angiogenic growth factors necessary for melanoma growth and metastasis even in the local absence of tumor cells.

In summary, the unique character of exosomes, including their ability to induce antitumor responses, express death ligand and accommodate specific genetic materials, their participating in drug resistance, their stability in circulation, their reproducible detection and, significantly, the fact that they show the properties of cancer cells, indicate they may be used as diagnostic strategies for non-invasive and quick tracing of the pathological condition of cancer patients, as well as therapeutic agents and cancer vaccine for providing viable treatment options.

MiRNAs: Novel molecules in cancer therapy

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Extended Abstract

Introduction: MicroRNAs are a group of endogenous, non-coding RNAs which have ~22 nucleotides. MiRNAs inhibit mRNA expression in posttranscriptional manner. MicroRNAs are known as main regulatory molecules that control over half of the protein coding genes in human.

MicroRNAs recognizing key cancer molecular regulators for target therapies may specifically eliminate tumor cells. On the other hand, dysregulation of non-coding RNAs have been observed in various types of cancers. Recently, many miRNA based therapies are growing up which specifically target cancerous cells. These approaches are different based on the effects of miRNAs in tumor cells. In the following, we will overview current strategies in the field of miR therapy in cancers.

Therapeutic strategies with miRNAs: MiRNAs could be divided into two categories depends on the oncogenic function or tumor suppressor activity of them in the cells. MiRNA therapy techniques are designed for blocking of oncomiRs or increasing the expression of tumor suppressor miRNAs. So, miRNA-based therapies include blocking miRNAs and restoring miRNAs.

Blocking miRNAs: Blocking miRNAs are designed for blocking the function of oncomiRs.

Antisense oligonucleotides (ASOs): ASOs are single-stranded chemically modified RNA molecules that are complementary with target miRNAs. Antisense oligonucleotides based on the mechanism of action are divided into two categories:

I) The RNase H-dependent oligonucleotides; in this manner creation of RNA/DNA duplex leads to the degradation of the target mRNA.

II) The steric-blocker oligonucleotides; these oligonucleotides only bind to the 5 or AUG initiation codon region and inhibit the production of proteins.

In the following, some strategies of ASOs methods are introduced briefly:

LNA anti-miRs

LNA anti-miRs are partially modified antisense oligonucleotides. These molecules have 13-22 ribonucleotides. The methylene bridge between 2′ oxygen and 4′ carbon causes greater target specificity and great nuclease stability.

Tiny LNA anti-miRs

They are fully modified ASOs with 8 nucleotides that target miRNAs seed region. These molecules can be used for suppressing miRNAs with the same seed sequence and consequently increase expression of related protein coding genes.

Antagomirs

Antagomirs are single-stranded RNAs which are conjugated with cholesterol. They have 23 ribonucleotides with 2′ O methoxyethyl group modification and partial phosphorothioate backbone. Conjugated cholesterol makes Antagomirs easily transfer to the cells. Antagomirs complement to the whole sequence of mature target miRNAs, so they are very specific.

miR sponges

Sponges contain multiple tandem repeat of certain miRNA seed region that would be suppressed. These sequences are expressed under strong promoters such as CMV promoter. miR sponges have a great potential for targeting miRNA families with the same seed region.

Small molecule inhibitors (SMIRs)

SMIRs are chemical component that interfere with miRNAs, furthermore they could be used as an important tools for identifying the mechanism of miRNAs function and offering new therapeutic approaches. For example, azobenzene acts as a specific inhibitory molecule for miRNA-21. These molecules cause an increased chemotherapy response and also act as an anti-cancer drug. However, they

have some problems such as low specificity, unexpected effects and complex design compared to blocking techniques.

miRNA masking

The sequence of these oligonucleotides are complement to the binding sites of miRNAs in the target mRNA which creats a high affinity duplex. The effectiveness of this strategy in cancer treatment methods depends on the function of miRNA target gene. MiRNA functions decrease without complications caused by degradation, however, miRNA masking may have toxicity and undesirable effects.

Restoring miRNAs

MiRNA replacement therapy or restoring miRNAs are strategies for retrieving and activating miRNAs with tumor suppressor features.

Small molecules

Small molecules which act by hypomethylating could be used for the removal of epigenetic silencing of miRNAs with tumor suppressor manner, such as decitabine (5-Aza-2′ deoxycytidine).

miRNA mimics

Mimics are one of the techniques for adjusting miRNA level. In this method, miRNA duplex is transferred to the cells and processed into the mature miRNA. For increasing the stability and efficiently action of miRNA mimics, proper transfer systems are required.

miRNA expression vectors

Using vectors for restoring miRNAs is a simple method to increase desired miRNA in the cells. In this method vectors containing miRNA gene sequence produce mature miRNA in certain tissue after processing.

Perspective: Nowadays, developments of creative strategies for using miRNA in cancer therapy are growing up rapidly and introduction of new delivery systems make them easy to targeted cancerous cells. It seems that different therapeutic approaches based on miRNAs have great promising way for cancer treatment.

Keywords: miRNA, Cancer, Therapeutic approaches

Dietary factors and cancer prevention

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Extended Abstract

Introduction: 90-95% of cancer cases are due to environmental risk. So, cancer is a preventable disease. Although, all environmental causes are not controllable, such as naturally occurring background radiation. many cancers can be prevented by not smoking, maintaining a healthy weight , not drinking too much alcohol, eating plenty of vegetable, fruits and whole grains, not eating too much red meat and avoiding too much exposure to sunlight. Tobacco use is the single greatest avoidable risk factor for cancer mortality worldwide. Tobacco smoking causes many types of cancer, including cancers of the lung, esophagus larynx, mouth, throat, kidney, bladder, pancreas, stomach and cervix. Antioxidants are chemicals that interact with and neutralize free radicals, thus preventing them from causing damage. Many observational studies have been conducted to investigate whether the use of dietary antioxidant supplements is associated with reduced risk of cancer in humans. So, fresh, organic, preferably locally grown foods may prevent cancer if you should eat at least one − third of your food raw. Avoiding frying or charbroiling, boil, poach or steam your food instead. Some specific foods are linked to specific cancers. A high-salt diet is linked to gastric cancer. Aflatoxin B1, a frequent food contaminates causes liver cancer. Betel-nut chewing causes oral cancer. Normalize your ratio of omega-3 to omega − 6 fats by taking a high − quality krill oil and reducing your intake of processed vegetable oils. Fish and vegetable oils are rich in omega − 3, so they can reduce the risk of cancer, including prostate cancer. Adding naturally fermented food to your daily diet is an easy way to prevent cancer or speed recovery. Cereal consumptions may increase the amount of fiber, selenium and vitamin E and also phyto-chemical compounds in the body which is useful in the prevention of cancer. You can always add a high − quality probiotic supplement as well, but naturally fermented foods are the best. Some plants that can be useful in cancer prevention include: Basil, Clove, Coriander, Cumin, Garlic, Ginger, Saffron, … compounds in these plants have anti-cancer agents. Recent researches has shown that sulfide in raw garlic has anti- cancer properties. And also has shown the people who consume more garlic are less likely to develop cancer of the stomach and large intestine. Gingerols that is the most important ingredient of ginger responsible for taste in this plant, prevent the growth of cancer cells, particularly colon cancer in humans. Saffron is the most precious plant as food and medicine as an anti-cancer agent and its main metabolite, especially carotenoids like crocin, picrocricin, monoterpene aldehyde, has anti-cancer properties. Selenium is a mineral salt that found in walnut, fruits of the sea, some meat, fish, cornflower, wheat, brown rice, and prevents cancer. Recent studies have shown that cloves can prevent skin, lungs and gastrointestinal cancers. Therefore, the use of botanicals including those mentioned in the diet can partly be effective for cancer prevention. Making regular exercise a priority in order to reduce the risk of cancer can help to prevent cancer. In our previous studies, we showed that silibinin can probably inhibit metastasis in prostate cancer.

Results: Dietary fibers, folic acid, Vitamin D, Vitamin C, Vitamin E, antioxidant , tea and soy isoflavones can reduce the risk of colorectal, pancreas, breast, prostate, cervix and lung cancers. Antioxidants such as beta − carotene and lycopene have great influence on prostate and breast cancer cells death. Lycopene found in red fruits and vegetables such as tomatoes, grapefruit, watermelon etc and also Beta - carotene found in vegetables that are dark green and orange such as carrots, mango, orange, peach can prevent cancer. Research has shown that blueberries and grapes of coarse purple have elements inside them that cause liver cancer cells disappear. Cranberry can help prevent ovarian cancer in women. As well, research has shown that men who are at risk for prostate cancer tumor benefite from by taking broccoli 4 servings per week. Spinach also has anti-cancer properties and prevents bladder cancer. So the dark green leaves of this plant reduces the risk of liver cancer. Today, some vaccines can be useful in the prevention of cancer. Vaccines have been developed that prevent infection by some carcinogenic viruses. A virus that can cause cancer is called an onco-virus. Human papillomavirus vaccine decreases the risk of developing cervical cancer. The hepatitis B vaccine prevents infection with hepatitis B virus and thus decreases the risk of liver cancer.

Conclusion: Finally, cancer is a class of diseases; it is unlikely that there will ever be a single “cure for cancer”. Because of numerous favorable and preventive effects of antioxidants and botanicals, these groups of food have been suggested in many dietary plans for cancer prevention.

Keywords: Cancer prevention, Antioxidant; Dietary factors, Botanicals