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A Brief Outlook on Cancers and Preventive Methods

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Abstract

Cancers are a group of diseases and one of the leading causes of death worldwide as per the recent reports of World Health Organization. In the article, a concise account on etiology of cancers, abnormal molecular mechanisms of cancerous cells, various stages of cancers and simple preventive methods for cancers have been brought into fore in a forthright manner. Moreover, strategies for designing small molecular anti-cancer compounds have also been discussed from standpoints of an integrated approach comprising of experimental and computational methods.

Keywords: Cancers, Chemotherapy, Drug Design and Phytochemicals.

CANCER INCIDENCE

Cancer is a group of diseases affecting almost any part of the human system. Depending on the organs/tissues/cells where the cancers form, the cancers are named like lung cancer, blood cancer, epithelial carcinoma and so on. Accordingly, more than 100 types of cancers have been distinctly authenticated to date. As per the recent reports of World Health Organization (WHO, 2018), cancers accounted about 8.8 million deaths in 2015 and about 50% of the cancer deaths were due to five types of the following cancers: lung cancer, liver cancer, colorectal cancer, stomach cancer and breast cancer. A recent report from the National Cancer Institute (NIH, 2018) alerts that about 1.73 million new cancer cases would be diagnosed in USA itself in the year of 2018 and it also alarmed that the cancer cases at global level may rise to 23.6 million by 2030. Meanwhile, the cancer burden can be reduced through early detection and subsequently adequate treatments. In addition, avoiding tobacco and alcohol consumption, eating healthy diet foods, engaging to more physical activities and taking vaccinations against infections due to viruses such as Hepatitis B/C, HIV and HPV would also significantly reduce the cancer burden.

CANCEROUS CELLS VS. HEALTHY CELLS

Cancers are characterized as uncontrolled cell proliferation of abnormal cells owing to genetic disorders and various environmental factors (physical, chemical and biological carcinogens). In general, the cancerous cells are differing from the normal healthy cells in the following salient cellular features: sustaining proliferative signaling, evading growth suppressors, activating invasion and metastasis, enabling replicative immortality, inducing angiogenesis and resisting programmed cell death or apoptosis [Fig.1, 1]. As mentioned above, uncontrolled proliferation is one of the fundamental traits of cancerous cells. While normal cells control the production of growth promoting signals and also maintain defined architectures and functions of the cells, cancerous cells deregulate these signals and have ill-defined organization of cells. Another important hallmark of cancer is evading growth suppressor. Quite a number of studies carried out on various types of cancers showed that growth suppressor genes were found to be inactivated in cancerous cells [2]. Cancerous cells develop into macroscopic tumors by enabling replicative immortality to its cells and telomeres proved to be played an important role in unlimited proliferation [3]. Since formation of new blood vessels is essential to evacuate metabolic wastes and carbon dioxide and as well for the intake of nutrients and oxygen, angiogenic switch is always 'ON' during tumor progressions. Invasion and metastasis are another complex hallmarks leading cancerous cells to move nearby blood and lymphatic vessels and as well to distant tissues.

RISK FACTORS FOR CANCERS

The cell proliferation processes are tightly regulated by oncogenes and tumor suppressor genes. The homeostasis of the functions of these genes are affected through mutations, which may be caused either by hereditary genetic factors and/or environmental factors such as exposure to mutagens, carcinogens, radiations, infections and imbalanced diet habits [4]. For instance, the positive correlations between high salt diet and gastric cancer [5], betel nut chewing and oral cancer [6], tobacco smoke and lung cancer [7] and inhalation of benzene and leukemia [8] are reported in the literature. It has been also shown that exposure to UV radiations (from sources like laminar-flow) and radio-waves (from sources like mobile phones) may induce melanoma [9, 10]. Furthermore, oncovirus (hepatitis B/C) and helicobacter pylori bacteria are main causes to hepatocellular carcinoma and gastric carcinoma, respectively [11, 12].

Apoptosis is another tightly regulated cellular process by proteins of Bcl-2 family in order to maintain homeostasis [13,14]. The Bcl-2 family proteins are generally classified into three types: pro-apoptotic proteins, anti-apoptotic proteins and BH3-only proteins [15-17]. While pro-apoptotic proteins such as Bax, Bak and Bok are promoting apoptotic process, the anti-apoptotic proteins such as Bcl-2, Bcl-XL, Bcl-B, Bcl-W, Bfl-1 and Mcl-1 are retarding the apoptotic process. The BH3-only proteins play essential roles either to activate the pro-apoptotic proteins (through Bid, Bim and Puma) or to inactivate (through Bad, Bik, Hrk, Bmf and Noxa) the anti-apoptotic proteins in order to maintain the homeostasis [18-21]. In this background, it has been suggested that small chemical molecules that are capable of antagonizing the anti-apoptotic proteins would act as promising molecules to be developed as anti-cancer

compounds. Similarly, designing chemical inhibitors to proteins that are abnormally playing roles in inducing angiogenesis or in evading tumor suppressor events or in activating metastasis has become an important strategy in chemotherapy treatments of cancers.

CANCER LEVELS

At first instant, whether the cells taken from a particular body part are cancerous or not can be examined through histopathology methods. The cancerous cells would be graded on the basis of their degree of differentiation and organizations: the cancerous cells are graded as 'low grade', 'intermediate grade' and 'high grade', when they are 'well differentiated', 'moderately differentiated' and 'poorly differentiated', respectively. The burden of cancers can also be classified into four stages: stage 0 represents the pre-cancerous condition; stages 1-3 represent the tumor spreading to lymph nodes; stage 4 represents metastatic levels of the cancer conditions posing unfavorable prognosis in the course of medical treatments.

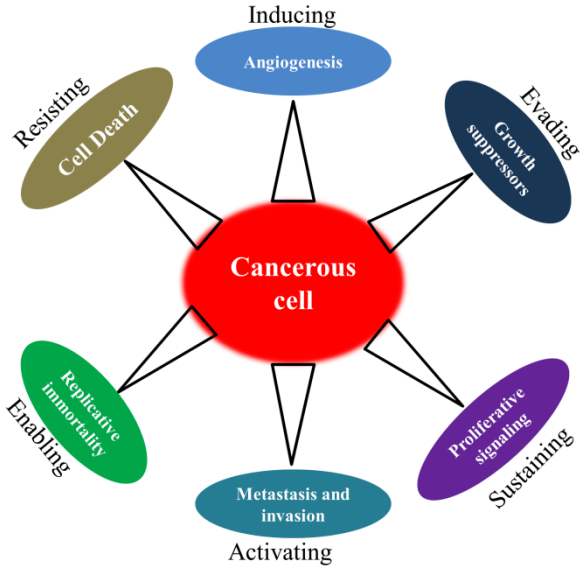

Figure 1: Schematic illustration of six hallmarks of cancer cells as documented in the literature (Hanahan D, Weinberg RA. Hallmarks of Cancer: The Next Generation. Cell. 2000; 100: 57–70).

CANCER PREVENTIONS

Fortunately, eating right foods and maintaining standard hygienic environments can simply keep us healthy as well as away from these types of cancer diseases. Recently, it has been shown that an extract obtained from dried papaya leaves promotes the production of cytokines, anti-tumor (solid neoplasm) molecules, in 10 different types of cancer cell cultures, when the cell cultures were treated with the extract [22]. Blue color fruits such as blueberries, plums, pomegranate and purple grapes contain anthocyanin, which is an anti-oxidant and shows anti-cancer activities [23]. Green color vegetables like broccoli, cabbage, cucumbers, sprouts etc. are rich in isothiocyanates, which have anti-cancer properties [23, 24]. Lycopene, an anti-oxidant that may act against prostate cancer, is present in reddish fruits and veggies [23, 24].

In reality, receiving optimal benefits from these natural sources is obviously depending upon their preservation methodologies and cooking procedures. In other hand, the phytochemicals present in the natural sources can be extracted, fractionated, purified at high quality and structurally characterized. The small natural molecules can then be subjected to high-throughput virtual screening against all possible target molecules under considerations followed by 'bioavailability filter' and 'toxicity filter' paving way to identify of 'lead molecules'. In this context, it is worthy of mentioning herein that *de novo* lead molecules can also be generated using an array of computation approaches [25-29]. The subsequent pre-clinical studies on the 'lead molecules' would facilitate to discover 'drug-likeness' molecules from which 'drugs' (entering into market) can be distinguished through systematic 'clinical studies'. It will be quite redeeming to have a smart hybrid approach integrating computational methods and experimental techniques in an organized manner and acting as beacons for the drug designing in an unequivocally manner in the near future.

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