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EDITORIAL

Cancer, Mankind's Challenge

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Cancer, or malignant tumour, is a group of diseases defined by the uncontrollable growth of the transformed cells, and their capabilities of invasion into surrounding healthy tissues and metastasis to remote sites in the body of organisms[1,2]. According to different origins, it can be further divided into five subtypes: carcinoma, adenocarcinoma, sarcoma, lymphoma/leukemia and myeloma. Cancer is the second leading cause of death worldwide after cardiovascular disease (GBD 2013 Mortality and Causes of Death Collaborators 2015)[3]. Usually, scientists attribute tumorigenesis to the control loss of cell proliferation, inhibition of cell differentiation and blockade of cell senescence and death at cellular level; chromosome aneuploidy[4,5] and hyperactive telomerase[6] at sub-cellular level; excessive activation of oncogenes and excessive inhibition of anti-oncogenes, gene mutation and epigenetic modification (DNA methylation and histone acetylation, *etc*.)[7] at molecular level, respectively. Mutagens in *in vitro* environment, including physical carcinogens (UV, X-rays, *etc*.), chemical carcinogens (Benzopyrene, Aflatoxin B1, *etc*.) and biological carcinogens (DNA viruses, RNA retroviruses) can promote the transformation of benign tumours to malignant tumours with the help of factors in *in vivo* environment (*e.g.* hormone secretion disorder[8], immune dysfunction[9], chronic inflammation[10,11] and excessive oxygen radicals[12]). Recent years, the relationships between various viruses, bacteria and malignant tumours have aroused concerns of cancer researchers, e.g. Human papillomavirus (HPV) & cervical cancer, head and neck cancer, Hepatitis B/C virus (HBV, HCV) & liver cancer, Epstein-Barr virus (EBV) & various lymphoma and nasopharyngeal carcinoma, Human T-cell lymphotropic virus type-1 (HTLV-1) & adult T-cell leukemia (ATL), Human immunodeficiency virus (HIV) & lymphoma, Human herpesvirus 8 (HHV-8) & kaposi sarcoma, Helicobacter pylori (HP) & gastric cancer, and Porphyomonas gingivalis (PG) & esophageal cancer, *etc*. All these indicate a complex relationship between viruses, bacteria, malignant tumours and immunity.

Genetically, carcinogenesis usually results from DNA point mutations and alterations of larger amounts of DNA (including chromosome translocation, inversion, duplication/deletion and aneuploidy, *etc*.)[13,14], not only because all these changes can possibly lead to gene amplification and/ or loss of heterozygosity (LOH) of tumour suppressor genes (anti-oncogenes)[15], but also bring about overexpression of oncoproteins, further activate the signalling pathway to carcinogenesis.

"Is cancer inherited?" is another topic of general public concern, because there is a high incidence of certain cancers in some places, and presenting a familial character. For example, nasopharyngeal carcinoma is highly prevalent in

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Guangzhou, Dongguan and Zhanjiang, Guangdong province; hepatocellular carcinoma prevalent in Qidong, Jiangsu Province; and laryngeal cancer prevalent in Linzhou, Henan Province, *etc*. in China. Usually, most geneticists believe that tumours and cancers originate from malignant transformation of somatic cells and are rooted in gene mutations. And cancer is just genic disease instead of genetic disease. Cancer shows familial characteristics in some areas just because cancer susceptibility genes[16,17] can be transmitted in the family and their mutations make cancers seem inheritable in the same living environment. Therefore, isolation and identification of candidate tumour or cancer susceptibility genes are also worthwhile to explore and report.

It is not possible to overstate cancer is the fatal disease human being have to face at present, because it is very hard for the detection and diagnosis of cancer at early stage in clinic. Once diagnosed, it is in the middle and late stages. Protein biomarker (e.g. alpha fetoprotein AFP, carcinoembryonic antigen CEA, *etc*.) detection, imaging techniques and tissue biopsy are successively and widely used to detect and diagnose cancer in clinic, however, these methods still fail to detect early cancerous cells on account of sensitivity deficiency, false negative or even false positive. Recently, oncogene expression pattern detection at RNA level seems ready to come out at one's call[18]. More optimal biomarkers for tumour or cancer diagnosis need exploring and developing for early genetic test of cancer.

At present, surgery, radiation therapy, chemotherapy, Chinese medicine treatment and targeted therapy are the major methods for cancer treatment in clinic. However, none of these methods can cure cancer fundamentally. Surgery may increase the risk of cancer cell invasion and metastasis; radiotherapy and chemotherapy not only kill cancer cells, but also damage normal cells; Chinese medicine treatment cure symptoms instead of root causes; and targeted therapy is so expensive that common civilians cannot afford it. In addition, resistance to chemotherapeutic drugs is currently a major problem in cancer therapy, accounting for treatment failure in over 90% of human patients with metastatic or recurrent cancer[19]. In response to this situation, some scientists put forward hypothesis that cancer consists of a larger number of cancer cells and a few of cancer stem cells[20,21], the former with the characteristics of uncontrollable proliferation and metastasis, and the latter with ATP-binding cassette transporters to remove drugs from the cells[22], further lead to the resistance to anti-cancer drugs. All these remind us that we can screen anti-cancer drugs from natural products targeting the signalling pathways controlling proliferation, metastasis and invasion of cancer cells[23–28], and targeting ATP-binding cassette transporters[22] of cancer stem cells, respectively. Recent years, new strategies for cancer treatment have been proposed and developed, including starvation of cancer cells by inhibiting angiogenesis[29,30], gene therapy, immunotherapy via chimeric antigen receptor- T cell (CAR-T)[31] and integrated Chinese and Western medicine therapy[32], *etc*. A good case in point is the 2018 Nobel Prize in Physiology or Medicine was awarded to James P. Allison and Tasuku Honjo for their discovery of cancer therapy by inhibition of negative immune regulation (via CTLA-4)[33,34]. Despite the potential limitations of immunotherapy[35], its novel development may bring hope to the treatment of malignant tumours in the future[36].

Considering the heterogeneity of tumour[37,38] and multiple stages of carcinogenesis[39,40], even patients with the same cancer have different therapeutic effects on the same anticancer drug, and precision medicine was put forward to satisfy the needs of personalized therapy of patients with the same disease (e.g. cancer)[41]. However, as far as current technological progress is concerned, there is still a long way to go.

Just as every coin has two sides, cancer is also thought a normal form of life by some scientists, not only because cancer cell surely exists in nearly everybody of human, but also cancer patients who have a 5-year survival rate after surgery are usually considered to be cured in clinic. What's more, there is no shortage of cancer-bearing survivors to old age and death. In other words, under physiological homeostasis, everyone can live with the transformed cells, just when appropriate and necessary, the cells can be removed by apoptosis and phagocytosis without any side effects (e.g. inflammation) in human body. Once their surroundings (microenvironments) deteriorated, the balance broken, the transformed cell growth and proliferation will predominate over its surrounding somatic cells, gradually through hyperplasia, dysplasia, tumour in situ, and metastatic tumour stages finally develop into malignant tumours, or cancers. Recently, tumour angiogenesis, cancer invasion, metastasis and cancer interaction with its surroundings (microenvironments)[42,43] have become hot spots in the fields of cancer research. Therefore, all factors that lead to microenvironment deterioration, including abnormal lifestyles (e.g. smoking, alcoholism, high-fat, and high-salt diet, *etc*.) and irregular way of working & sleeping (e.g. long-term overnight work, sedentariness & less movement, and bad mental condition, *etc*.), should arouse people's attention. In one word, cancer has become the common challenge of mankind, needing us to work together in the same boat, concentrate and defeat it in the coming future.

Current cancer reports (CCR) (ISSN: 2661-3166) is a new born academic journal, a platform aiming to provide doctors, researchers, physicians, pharmacists and healthcare professionals all over the world to communicate their latest research progress,[44,45] novel ideas[46], technique innovations[47–49] and candidate anti-cancer drug leads[50] in the fields of cancer-related research, prevention and treatment. As we know, the first year of a newborn is always a challenge, as it was the case with a journal. Sincerely wish you and your colleagues to submit manuscripts of high quality and support her growth. Let's witness her healthy growth with the process of human conquering cancer together.

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