癌症化学预防在中国——代专辑前言

余四旺[1] 杨中枢[2]
(1. 北京大学药学院 北京 100191; 2. Department of Chemical Biology and Center for Cancer Prevention Research, Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey, Piscataway, NJ 08854-8020, USA)

中图分类号：R730.1; 06-1 **文献标识码**：A **文章编号**：1005-281X(2013)09-1411-04

当前，全球的癌症负担持续增加，是世界范围内对人类健康的主要威胁之一。根据 GLOBOCAN 2008 提供的数据，癌症在发达国家居民死因中占据首位，而在发展中国家居民死因中占第二位。癌症发病率和死亡率在美国及部分国家已经开始下降，但在发展中国家中仍在上升[1]。中国作为最大的人口最多的发展中国家，正面临着更为严峻的来自癌症的挑战[2]。

尽管部分癌症的早期诊断和治疗已经取得了显著进展，但对于大多数中晚期癌症仍然治疗乏术；癌症生存率，尤其是已发生转移的癌症，近几十年来都没有显著提高[3]。因此，为了应对癌症日益增长的威胁，需要加强对预防的投入。“化学预防”是指利用天然的或者合成的化学物质来预防、减缓或逆转癌症发生发展的策略，是重要的癌症预防策略之一[4]。在认识到这种需求之后，美国国立卫生研究所（NIH）设立了“化学 / 食物预防”评审组来评审这个领域内的研究基金申请。随着对癌症发生机制的深入了解，越来越多的化学预防分子靶标被发现，而一些重要的分子靶标如 Nrf2 在癌症防治中的作用也被更全面地阐明[5—8]。许多天然的或合成的化合物、食物成分乃至全食物都被作为化学预防试剂进行了研究，并获得了很多有意义的结果[8—11]。其中一些化合物，例如阿司匹林、选择性雌激素受体调控剂和选择性 COX-2 抑制剂等的化学预防作用也在临床上得到了验证[12, 13]。值得注意的是，这些化学预防试剂的效用和人体自身以及体内微生物群的代谢密切相关，而如何提高它们的生物利用度是关键问题之一[14, 15]。然而，在实验室研究中发现的许多化学预防试剂还没有被证明在人体中也有效，一些化学预防的临床试验结果也令人失望。如何解读这些研究成果，对于中国乃至世界范围的癌症化学预防研究都有重要意义[10]。

在感染相关的癌症方面，基于疫苗的癌症预防研究取得了突出成就。人类乳头状瘤病毒（HPV）疫苗已被证明可有效预防宫颈癌，而四价 HPV 疫苗已经被美国 FDA 批准并被引介到包括中国在内的多个国家[16]。肝细胞癌的发生在很大程度上与乙肝（HBV）或丙肝（HCV）感染相关，针对乙肝的疫苗可以显著降低肝细胞癌的发生，这对中国的肝癌预防尤其重要[16]。此外，幽门螺旋杆菌感染是胃癌发生的重要危险因子，清除幽门螺旋杆菌感染也可以有效地预防胃癌的发生[17]。

中国曾经对癌症预防研究作出了重要贡献。早在 1973 年，中国启动了有史以来最大规模的癌症发生和死亡的流行病学调查，揭示了中国多种癌症特有的分布模式，并在 1980 年首次发表了《中国癌症地图》。随后，中国和美国以及其它国家的研究者们联合在中国的癌症高发现场开展了一系列的癌症化学预防和干预研究，包括河南林县的食管癌、山东临朐的胃癌和江苏启东的肝癌等研究[17—19]。这些现场研究已经成为国际上癌症预防研究的重要里

程碑。与此同时，“癌症化学预防”的概念在中国理应有较好的接受度。“上医治未病”是中医数千年来的重要理念，而中医药或其它民族医药长期运用的许多药物或其成分则是很有价值的化学预防药物重要来源[20]。

面对中国癌症等重大慢性疾病控制的严峻形势，中国国务院发布的《国家中长期科技发展规划纲要（2006—2020）》强调了“疾病防治重心前移，坚持预防为主、促进健康和防治疾病结合”的战略方针。自 2012 年起，国家自然科学基金委员会在肿瘤预防学科下面设置了“化学预防”等具体研究方向，对相关研究的资助力度逐年增加。尽管如此，中国的癌症化学预防研究还是远远落后于国际研究前沿和中国人口健康需要。

总的看来，癌症化学预防应有很好的前景，但也在实验室研究成果的临床转化方面遭遇了一些障碍和挫折。在本期专辑中，来自美国和中国的癌症化学预防研究者们针对癌症化学预防在实验室研究临床试验中的最新进展，尤其是与中国相关的内容，进行了较为全面的综述和展望。同时，也期望通过本期专辑来增强中外学者的交流，以促进国际国内的癌症化学预防研究。

Cancer Prevention in China: Introduction to the Special Issue on Cancer Chemoprevention

Siwang Yu[1]　*Chung S. Yang*[2]

(1.School of Pharmaceutical Sciences, Peking University, Beijing 100191, China; 2. Department of Chemical Biology and Center for Cancer Prevention Research, Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey, Piscataway, NJ 08854-8020,USA)

The global cancer burden keeps increasing and continues to pose a major threat to human health worldwide. According to the GLOBOCAN 2008 data, cancer is the leading cause of death in developed countries and is the second leading cause of death in developing countries. While cancer incidence and mortality rates in the United States and some other countries have started to decrease, those in developing countries keep increasing [1]. China, the largest developing country with a vast population, is facing a even more serious challenge from cancer [2].

Although significant progress has been made in the early detection and treatment of certain cancers, effective treatments of most cancers in advanced stages are limited. The survival rate of cancer, especially of metastatic cancers, has not been improved significantly during the past decades [3]. To deal with the increasing threat from cancer, more efforts need to be put into prevention. “Chemoprevention” refers to the strategy to prevent, delay or reverse the development of cancer by using natural or synthetic chemicals, and should be an important cancer prevention strategy [4]. Recognizing the need, the U.S. National Institute of Health established the Study Section of “chemo-/dietary prevention” to review grant applications in this area. With better understanding of the mechanisms of carcinogenesis, more and more molecular targets of chemopreventive agents have been identified, and their roles in cancer prevention and treatment are revealed in greater detail [5—8]. Many natural or synthetic compounds, dietary factors and even whole foods have been investigated as chemopreventive agents and interesting results have been well documented [8—11]. Some of these agents such as aspirin, selective estrogen receptor modulators and selective cox-2 inhibitors have been shown to be clinically effective [12,13]. It is noteworthy that the efficacy of these agents could be profoundly influenced by metabolisms as well as intestinal microbiota, and how to improve their bioavailability is important for successful chemoprevention [14,15]. Nevertheless, the effectiveness of many laboratory chemopreventive agents has not been demonstrated in humans, and the results from some human cancer chemoprevention studies have been disappointing. The interpretation of these results is very important for future cancer chemoprevention studies [11].

Another significant success in cancer chemoprevention arose from vaccine-based approaches, which focused on infection-related cancers. Human papilloma virus (HPV) vaccine has been shown to be effective at preventing cervical cancers, and the quadravalent HPV vaccine has been approved by the FDA and introduced into many countries including China [16]. Hepatocellular carcinoma (HCC) incidence is largely attributable to hepatitis B virus (HBV) or hepatitis C infection, and vaccination against HBV has been shown to significantly reduce the incidence of HCC; this is extremely important for prevention of HCC in China [16]. In addition, Helicobacter pylori (H. pylori) infection has been associated with increased risk of stomach cancer; therefore, elimination of H. pylori infection has been shown to effectively prevent stomach cancer in China [17].

China has made significant contributions to cancer prevention research. As early as 1973, China initiated the largest ever epidemiological investigation of

cancer incidence and mortality, which revealed distinct distribution patterns of various cancers in China, and in turn led to the publication of "The Chinese Cancer Atlas" in 1980. Subsequently, there were a series of chemoprevention and intervention studies in the high incidence sites, conducted by Chinese researchers in collaboration with scientists from the United States and other countries. These include studies on esophageal cancer in Linxian, Henan; gastric cancer in Linqu, Shandong; and hepatocellular carcinoma in Qidong, Jiangsu [17—19]. These field studies have set landmarks in cancer prevention research internationally.

The concept of cancer chemoprevention should be readily acceptable in China. "To cure the disease before it happens" has been a motto of traditional Chinese medicine (TCM) for thousands of years, and many herbs/constituents that have been utilized in TCM and other ethnopharmacies could be valuable sources of chemopreventive agents [20].

In response to the urgent needs in major chronic disease control, the "National Medium- and Long-term Program for Science and Technology Development (2006—2020)", published by the State Council of China, specifically emphasized the principle of "prevention-first" and the "earlier-stage disease control" strategy. "Chemoprevention" has been set up as a sub-field of "cancer prevention" by the Natural Science Foundation of China (NSFC) since 2012, and the financial support of cancer chemoprevention research has been steadily increasing. Nevertheless, cancer chemoprevention studies in China are still lagging behind international research communities and the health demands of Chinese population.

Cancer chemoprevention should have high potential to reduce the cancer burden, but also encountered major obstacles in translating laboratory results into clinical outcomes. This Special Issue on Cancer Chemoprevention intends to present reviews of recent progresses in cancer chemoprevention research, in both laboratory studies and human trials, that are particularly relevant to the situation in China. It is the goal of this Special Issue to enhance international communication, thus promoting more effective cancer chemoprevention studies in China and the rest of the world.

Reference

[1] Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. CA Cancer J. Clin., 2011, 61(2): 69—90

[2] 曾红梅 (Zeng H M), 陈万青 (Chen W Q). 化学进展 (Prog. Chem.), 2013, 25(9): 1415—1420

[3] Howe G K, Clapp R W. New Solut., 2004, 14(2): 109—124

[4] Sporn M B, Suh N. Nat. Rev. Cancer, 2002, 2(7): 537—543

[5] Xiong D, Osarogiagbon R U, Wang Y, You M. 化学进展 (Prog. Chem.), 2013, 25(9): 1517—1525

[6] 王秀君 (Wang X J), 李欣 (Li X), 唐修文 (Tang X W). 化学进展 (Prog. Chem.), 2013, 25(9): 1544—1552

[7] Bode A M, Dong Z. 化学进展 (Prog. Chem.), 2013, 25(9): 1501—1516

[8] Su Z Y, Shu L, Lee J H, et al. 化学进展 (Prog. Chem.), 2013, 25(9): 1526—1543

[9] Sporn M B, Liby K T. 化学进展 (Prog. Chem.), 2013, 25(9): 1421—1428

[10] Stoner G D. 化学进展 (Prog. Chem.), 2013, 25(9): 1480—1491

[11] Yang C S. 化学进展 (Prog. Chem.), 2013, 25(9): 1492—1500

[12] Chan A T. 化学进展 (Prog. Chem.), 2013, 25(9): 1450—1453

[13] Dunn B K. 化学进展 (Prog. Chem.), 2013, 25(9): 1429—1449

[14] Gao S, Basu S, Yang G, Deb A, Hu M. 化学进展 (Prog. Chem.), 2013, 25(9): 1553—1574

[15] Niu T, Hu M. 化学进展 (Prog. Chem.), 2013, 25(9): 1601—1612

[16] 王少明 (Wang S M), 乔友林 (Qiao Y L). 化学进展 (Prog. Chem.), 2013, 25(9): 1583—1587

[17] You W, Zhang L, Pan K, Ma J. 化学进展 (Prog. Chem.), 2013, 25(9): 1575—1582

[18] Egner P A, Wang J B, Zhu Y R, et al. 化学进展 (Prog. Chem.), 2013, 25(9): 1454—1461

[19] 黎均耀 (Li J Y). 化学进展 (Prog. Chem.), 2013, 25(9): 1462—1479

[20] Wang Y, You M. 化学进展 (Prog. Chem.), 2013, 25(9): 1594—1600