Preface

Fazlul H. Sarkar

Published online: 12 August 2010
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Nutraceutical research including those of “natural agents” has been the subject of intense investigation in the last decade compared to previous decades. Although the field is still suffering from controversies as to the role of nutraceuticals in the prevention and treatment of cancer, encouraging results especially from pre-clinical studies are beginning to show some promise. Thus, it is hoped that cutting-edge innovative research especially well-designed clinical trials would help the field in order for nutraceuticals to be realized as novel therapeutic agents for the prevention of tumor recurrence and/or treatment of human malignancies.

Keeping abreast with emerging and rapid advances in nutraceutical research especially those focusing on “natural agents” is becoming important. In an attempt to report recent advances in nutraceutical research in cancer and metastasis, we have compiled a series of review articles for this theme issue on “Nutraceutical and Cancer” for the journal of *Cancer and Metastasis Reviews*. These articles are focused on specific and novel classes of agents derived from both “natural” resources as well as from the tables of synthetic medicinal chemists, targeted at multiple signaling pathways, and as such could become a new resource for rapid development and for novel design of clinical trials. Therefore, emerging evidence together with evidence presented in these review articles suggests that nutraceuticals alone or in combination with conventional therapeutics could become a superior strategy for the management of human malignancies, which will result in the improve-

ment of overall survival of patients diagnosed with what we know as the beast of humanity.

This special thematic volume of *Cancer and Metastasis Reviews* is composed of 12 review articles focusing on the theme “Nutraceutical and Cancer,” starting with the premier article written by Dr. Sarkar entitled “The role of nutraceuticals in the regulation of Wnt and Hedgehog signaling,” describing how nutraceuticals could target important genes that are developmentally regulated and whose expression is re-activated during the development and progression of cancer. This article is followed by an article by Dr. Majumdar, documenting evidence in support of the title of his article “Do nutraceuticals play a role in prevention and treatment of colorectal cancer?” The next article is a comprehensive review article focusing on many nutraceuticals contributed by Dr. Aggarwal entitled “Regulation of survival, proliferation, invasion, angiogenesis and metastasis of tumor cells through modulation of inflammatory pathways by nutraceutical.” This article also links inflammation-regulated genes in the development and progression of cancer and how these genes could be targeted by multiple nutraceuticals. This article is followed by two specific articles focusing specifically on two different classes of “natural agents” and compounds—one is contributed by Dr. Mukhtar entitled “Cancer and metastasis: Prevention and treatment by green tea,” on cancer cell invasion and metastasis, documenting how these compounds could be useful for the prevention and/or treatment of human cancers. The other is contributed by Dr. Agarwal entitled “Anti-metastatic efficacy of silibinin: molecular mechanisms and therapeutic potential against cancer” where the role of nutraceutical has been proposed to affect the biology of epithelial–mesenchymal transition (EMT) phenotypic cells that are considered to be reminiscent of cancer stem-like cells. Next, three articles are

F. H. Sarkar (✉)
Department of Pathology, Karmanos Cancer Institute,
Wayne State University,
Detroit, MI, USA
e-mail: fsarkar@med.wayne.edu

focused on multiple “natural agents,” starting with the article contributed by Dr. Bergan entitled “The inhibition of cancer cell invasion and metastasis by genistein,” the agent that is readily available through foods enriched with soy bean products, followed by an article contributed by Dr. Kong entitled “Phytochemical: Cancer chemoprevention and suppression of tumor onset and metastasis” and Dr. Wargovich entitled “Nutraceutical use in late stage cancer,” describing the role of phytochemicals in early and late stages of cancer, respectively. Next three articles are focused on the role of nutraceutical peptides (Dr. Gonzalez de Mejia), micronutrient synergy (Dr. Niedzwiecki), and lipid replacement therapy (Dr. Nicolson). Nutraceutical proteins and peptides in addition to small molecules are becoming important, which is summarized by Dr. Gonzalez de Mejia in the article entitled “Nutraceutical proteins and peptides in apoptosis, angiogenesis and metastasis of cancer cells.” Since humans usually consume multiple nutraceuticals (micronutrients) and since there is no clear documentation on how these nutraceuticals may cause either antagonistic or synergistic health effects, an article on this topic was considered essential for this theme issue, and such an article has been contributed by Dr. Niedzwiecki entitled “Micronutrient synergy: A new tool in effective control of metastasis and other key mechanisms of cancer.” Moreover, a new area is emerging on the role of lipid replacement therapy in attenuating cancer-associated adverse effects, which is contributed by Dr. Nicolson entitled “Lipid replacement therapy: A nutraceutical approach for reducing cancer-associated fatigue and adverse effects of cancer therapy while restoring mitochondrial function.” The final concluding article is contributed by Dr. Clinton, focusing on the clinical utility of nutraceuticals, especially tomato-based food products, for the prevention of prostate

cancer entitled “Tomato-based food products for prostate cancer prevention: What have we learned?” All these articles are very timely, which clearly suggests that disease-specific clinical trials are warranted because it is now ready for primetime in order to fully appreciate the value of nutraceuticals in cancer prevention and therapy.

In concluding the preface for this theme issue, it is important to note that emerging evidence are beginning to suggest that novel therapeutic strategies must be developed for the killing of cancer cells that are the “root” cause of tumor recurrence, invasion, and metastasis. Therefore, focused research on elucidating the expanding role of nutraceuticals not only for primary prevention of cancer but also for the prevention of tumor recurrence and further assessment of the role of these nutraceuticals for sensitization of cancer cells to conventional therapeutics are warranted. If we succeed, then we may witness the application of nutraceuticals for the treatment of human malignancies with better survival outcome and as such would be useful for improving the overall health of cancer patients. Such strategies would be able to eliminate not only tumor cells but also tumor-initiating cells or the cells that are resistant to therapy often found in the remnants of tumors after conventional therapies and could be defined as EMT-type cells or cancer stem-like cells. In conclusion, nutraceuticals may play a dominant role in the design of future clinical trials and together with our emerging knowledge in “omics” and “systems biology” would revolutionize personalized medicine for the treatment of human malignancies; however, much remains to be done in order to fully appreciate the value of nutraceuticals not only for cancer patients but also for serving the humanity at large.