

Micro Environmental Modulators: Enhancing the Tumor Response to Radiation Therapy

Yogini Qiu*

Department of Radiation Oncology and Image-applied Therapy, Graduate School of Medicine, Kyoto University, Japan

Abstract

This tumor stroma, comprised of various cells, and extracellular matrix (ECM), has been shown to aid in suppressing host immune responses against tumor cells. Through immunosuppressive cytokine secretion, metabolic alterations, and other mechanisms, the tumor stroma provides a complex network of safeguards for tumor proliferation. With recent advances in more effective, localized treatment, radiation therapy (XRT) has allowed for strategies that can effectively alter and ablate tumor stromal tissue. Hypoxia-inducible factor 1 (HIF-1) is a transcription factor that is activated by hypoxia and induces the expression of various genes related to the adaptation of cellular metabolism to hypoxia, invasion and metastasis of cancer cells and angiogenesis, and so forth. HIF-1 is a potent target to enhance the therapeutic effects of radiation therapy. Another approach is antiangiogenic therapy. The combination with radiation therapy is promising, but several factors including surrogate markers, timing and duration, and so forth have to be optimized before introducing it into clinics.

Introduction

The stromal microenvironment of a tumor presents an underlying challenge to the efficacy of cancer immunotherapy. In their seminal review, Hanahan and Weinberg named evading immune destruction as an emerging hallmark of cancer among other related activities, such as metabolic reprogramming and induction of angiogenesis within the TME. For cytotoxic T cells and other immune cells to kill cancer cells, physical cell-to-cell contact is necessary. However, stromal cells actively orchestrate resistance to antitumor immunity by restricting T cells from making physical contact with cancer cells [1]. The stroma surrounding tumor islets of solid malignancies consists of a myriad of molecular and cellular components: immune cells, including myeloid-derived suppressor cells, tumor-associated macrophages, and regulatory T cells; fibroblasts; epithelial cells; extracellular matrix proteins; blood and lymphatic vessels; and various metabolites, chemokines, and cytokines [2].

Radiation therapy shows antitumor effects is important in understanding the relationship between the microenvironment and radiation therapy [3]. Cytotoxicity due to radiation is primarily attributed to damage to genomic DNA which contains all the genetic instructions for the development and functions of all living organisms. Radiation can affect atoms and/or molecules in the cells and produce free radicals. Because free radicals are highly reactive, they damage genomic DNA, resulting in cell death. This is a so-called indirect action of radiation [4].

Tumor microenvironments that affect the therapeutic effect of radiation therapy

The microenvironment of malignant solid tumors is totally different from that of normal tissues, being characterized by marked diversities in pH, the distribution of nutrients, and oxygen concentrations, and so forth [5]. To understand this heterogeneity is important in cancer radiation therapy because it influences the effect of ionizing radiation through various mechanisms as described in the following. Since the tumor microenvironment is a unique feature, it can be a potent target for cancer therapy.

Mechanism behind radio resistance of cancer cells under hypoxia

Extensive research in the field of radiation biology and radiation

oncology has revealed that cancer cells become approximately 2-3 times more radio resistant under hypoxic conditions than under normoxic conditions. This phenomenon is known as the oxygen effect. The mechanism behind the oxygen effect has not yet been fully elucidated [6]. However, it is widely believed that oxygen acts at the level of the generation of free radicals. Ionizing radiation literally induces ionization of target genomic DNA or intracellular molecules such as water, and produces highly reactive radicals. Under oxygen-available conditions, molecular oxygen oxidizes the DNA radicals, leading to the formation of irreparable DNA damage [7]. Tumor vasculature may play a strong role in the stromal mechanisms of immune exclusion. The migration of T cells through the endothelium, which is often dysregulated as a result of vasculature remodeling, is another challenge to antitumor immunity. For T cells to migrate to the tumor bed, they must adhere to the endothelium. However, expression of various endothelial adhesion molecules, such as intercellular adhesion molecule (ICAM)-1 and vascular cell adhesion protein (VCAM)-1, is down regulated in endothelial cells surrounding solid tumors. Recently, Motz and colleagues have described a mechanism by which the tumor endothelial barrier regulates T cell migration into tumors [8]. In human and mouse tumor vasculature, the expression of Fas ligand, which induces apoptosis, was detected, but it was not detected in normal vasculature. Additionally, the expression of FasL on endothelium was associated with decreased CD8+ infiltration and accumulation of Tregs, which were resistant to FasL due to higher c-FLIP expression.

Combination of radiation therapy and antiangiogenic therapy

The synergistic effects of the combination of radiation therapy and

***Corresponding author:** Yogini Qiu, Department of Radiation Oncology and Image-applied Therapy, Graduate School of Medicine, Kyoto University, Japan, E-mail:YonQiu847@gmail.com

Received: 1-May-2023, Manuscript No: jham-23-99125, **Editor assigned:** 3-May-2023, Pre QC No: jham-23-99125 (PQ), **Reviewed:** 17-May-2023, QC No: jham-23-99125, **Revised:** 23-May-2023, Manuscript No: jham-23-99125 (R), **Published:** 29-May-2023, DOI: 10.4172/2573-4555.1000379

Citation: Qiu Y (2023) Micro environmental Modulators: Enhancing the Tumor Response to Radiation Therapy. J Tradit Med Clin Natur, 12: 379.

Copyright: © 2023 Qiu Y. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

antiangiogenic agents have been reported in several preclinical studies that an anti-VEGF antibody alone did not suppress the growth of U87 glioblastomas, but when it was combined with radiation [9]; it showed a significant improvement in terms of antitumor effects. Kozin. an anti-VEGFR2 antibody enhanced the effects of radiation therapy in 54A non-small cell lung cancer and U87. Several tyrosine kinase inhibitors were developed to block the VEGF receptor and other receptors that are proangiogenic. Although many preclinical studies showed enhanced antitumor effects in the combination of antiangiogenic agents and radiation therapy, this study indicated the possibility that a schedule of both radiation therapy and antiangiogenic therapy could influence the therapeutic outcome [10].

Conclusion

Radiation's ability to eradicate areas of gross disease provides a strong rationale for its use with systemic agents, which would eradicate remaining circulating microscopic disease. Systemic agents are much more effective against the microscopic disease for many reasons, as they no longer face the hypoxic and metabolic changes associated with gross tumor deposits, providing much greater access to target tissues and improving T-cell functionality. Since radiation therapy itself has a great impact on host cells like vascular endothelial cells, it has become clear that changes in the tumor microenvironment during therapy and the optimal timing of the combination is a key to achieving maximal therapeutic effects in the combination therapy of radiation and microenvironment targeting. However, we still have further challenges to incorporate targeting therapy for the microenvironment to improve the effects of radiation therapy in clinics, and this will lead to greater knowledge about how radiation therapy works in cancer therapy and thus further improvements in radiation therapy.

References

1. Mabaera R, West RJ, Conine SJ (2008) A cell stress signaling model of fetal hemoglobin induction: what doesn't kill red blood cells may make them stronger. *Exp Hematol* 36:1057-1072.
2. El-Beshlawy A, Hamdy M, Ghamrawy M (2009) Fetal globin induction in β -thalassemia. *Hemoglobin* 33:197-203.
3. Bhatia M, Walters MC (2008) Hematopoietic cell transplantation for thalassemia and sickle cell disease: Past, present and future. *BMT* 41:109-117.
4. Khelil AH, Denden S, Leban N (2010) Hemoglobinopathies in North Africa: A review. *Hemoglobin* 34:1-23.
5. Aidoo M, Terlouw DJ, Kolczak MS (2002) Protective effects of the sickle cell gene against malaria morbidity and mortality. *The Lancet* 359:1311-1312.
6. Lindberg J, Padyukov L, Lundberg K, Engstrom A, Venables PJ, et al. (2000) Multiple antibody reactivities to citrullinated antigens in sera from patients with rheumatoid arthritis: Association with HLA-DRB1 alleles. *Ann Rheum Dis* 68:736-743.
7. Alamanos Y, Drosos AA (2005) Epidemiology of adult rheumatoid arthritis. *Autoimmun Rev* 4:130-136.
8. Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, et al. (2008) Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. *Arthritis Rheumatol* 58:15-25.
9. Makrygiannakis D, Hermansson M, Ulfgren AK, Nicholas AP, Zendman AJ, et al. (2008) Catrina AI Smoking increases peptidylarginine deiminase 2 enzyme expression in human lungs and increases citrullination in BAL cells. *Ann Rheum Dis* 67:1488-1492.
10. Hootman JM, Helmick CG, Barbour KE, Theis KA, Boring MA, et al. (2016) Updated projected prevalence of self-reported doctor-diagnosed arthritis and arthritis-attributable activity limitation among US adults, 2015-2040. *Arthritis Rheumatol* 68:1582-1587.