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The Impact of COVID-19 Pandemic on Cancer Patients

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Authors' contributions

This work was carried out in collaboration between both authors. Author MCL is an expert on wound healing and cancer who wrote the initial draft. Author LLB is a collaborator of author MCL who edited the final version of the manuscript. Both authors read and approved the final manuscript.

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Opinion Article

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ABSTRACT

The objectives of this study were to bring up chemo-surveillance as an important issue to dictate the display of a fatal symptom of pulmonary fibrosis following infection of COVID-19 that can gravely affect cancer patients and to develop CDA formulations for the therapy of pulmonary fibrosis and cancer. COVID-19 infection triggers biological and immunological responses similar to wound, resulting in the production of prostaglandins to cause symptoms of respiratory illness such as fever and cough, and tumor necrosis factor to cause cachexia symptoms leading to the collapse of chemo-surveillance which is a natural defense mechanism to ensure perfection of wound healing. The collapse of chemo-surveillance promotes the development of pulmonary fibrosis and cancer. The functionality of chemo-surveillance of cancer patients has been badly compromised. Therefore, cancer patients are particularly vulnerable to develop severe symptom of pulmonary fibrosis. Cancer therapies based on cell- killing such as chemotherapy, radiotherapy, and immunotherapy also cause the damage of chemo-surveillance to gravely enhance the development of fatal pulmonary fibrosis. Cancer patients, therefore, should be advised to avoid being infected by COVID-19, and if infected by COVID-19, targeted cancer therapy should become the priority choice to avoid the development of fatal symptom of pulmonary fibrosis.

Multiplication of the COVID-19 virus is of course the primary concern of viral infection. Vaccines, immuno-surveillance, and antiviral medicines such as interferon and nucleoside analogs can help to control COVID-19 infection and multiplication. But if the fatal symptom of pulmonary fibrosis has developed, there is no medicine available to treat this fatal symptom. The development of CDA formulations that can put out pulmonary fibrosis and Cancer Stem Cells (CSCs) is very urgent to save gravely ill patients of COVID-19 and cancer.

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1. INTRODUCTION

COVID-19 pandemic broke out in China in December of 2019, which quickly spread to other countries across the world. Up to August of 2022, it has caused 571 million confirmed cases, and 6.34 million confirmed deaths worldwide [1]. A majority of people around the world were devastated either directly by infection or indirectly through restriction of people's gatherings. The infection causes severe acute respiratory syndrome and fatal symptom of pulmonary fibrosis. The development of vaccines greatly curtailed the spread of pandemic. Yet the quick evolution of viral variants resulted in the propagation of COVID-19 pandemic one wave after another with no end in sight.

Multiplication of COVID-19 can be suppressed by vaccines, immuno-surveillance and anti-viral medicines such as interferon and nucleoside analogs. There is no medicine available for the treatment of pulmonary fibrosis which is the major cause of fatality due to COVID-19 infection. If pulmonary fibrosis can be effectively cured, COVID-19 may not be so fearful to impose people's restriction to disrupt social life. It is our intention to study the development of pulmonary fibrosis, and to seek CDA formulations as effective medicines to cure pulmonary fibrosis.

COVID-19 infection causes damages to the lung that require healing to restore lung function. Obviously, healing process is not proceeding properly to result in the development of pulmonary fibrosis [2,3]. Cancer is also evolved as a consequence of wound not healing properly [4,5]. Thus, COVID-19 infection must have a grave influence on cancer, and vice versa. Chemo-surveillance is a natural mechanism to dictate the success of wound healing [6-9]. The impact of COVID-19 infection on cancer patients would be carefully studied. We also intended to develop CDA formulations as effective medicines for the therapy of pulmonary fibrosis and cancer.

2. OPINIONS AND DISCUSSION

2.1 Chemo-Surveillance

Chemo-surveillance was brought up by Liau et al. as a natural defense mechanism against cancer [6]. It was later modified as a natural mechanism to ensure perfection of wound healing as the primary objective to avoid diseases arising as a consequence of failure to heal wound [7-9]. Diseases attributable to the failure of wound healing include tissue fibrosis, dementia, and cancer [10]. The concept of chemo-surveillance was based on the observation that healthy people were able to maintain a steady level of metabolites active as Differentiation Inducers (DIs) and Differentiation Helper Inducers (DHIs), whereas cancer patients tended to show deficiency of such metabolites due to excessive urinary excretion. DIs are chemicals capable of eliminating telomerase from abnormal Methylation Enzymes (MEs) and DHIs are inhibitors of MEs. MEs are made up by methionine adenosyltransferase-methyltransferase-S-adenosyl- homocysteine hydrolases [11]. The association of telomerase with MEs turns MEs to become exceptionally stable and active to deny hypomethylation of nucleic acids to take place, which is a critical mechanism to achieve terminal differentiation [12,13]. Progenitor Stem Cells (PSCs) are normal stem cells which also express telomerase to turn MEs abnormal like Cancer Cells (CCs). PSCs are the cells involved in wound healing. To achieve efficient wound healing, PSCs require DIs and DHIs to promote terminal differentiation. We give the mixture of DIs and DHIs the name Cell Differentiation Agents (CDAs). CDAs are wound healing metabolites to play active role in chemo-surveillance. Cancer patients have various degrees of deficiency of CDAs depending on the severity of the disease [6].

DIs and DHIs are all low molecular weight metabolites. Organic acids and acidic peptides are major DIs. We have identified arachidonic acid and its metabolites as organic acids of major DIs [14,15] and uroerythrin [16] and pregnenolone [17] as major DHIs. Inhibitors of methyltrasferase and S-adenosylhomocysteine hydrolase are in general excellent DHIs [16-18]. The identity of acidic peptides as the surveillance DIs remains unknown. Erythrocyte breakdown products contribute a great proportion of CDAs that include arachidonic acid and its metabolites, acidic peptides and uroerythrin. Pregnenolone and steroid metabolites are contributed by organs actively involved in steroid metabolism

such as the adrenal gland, liver, and organs of the reproductive system.

Evidently maintenance of a steady level of CDAs is important for the perfection of wound healing [4-10]. Since wounds are always healed naturally without having to put up any effort. Nobody cares to study wound healing and chemo-surveillance. Nature creates chemo-surveillance for a good reason to avoid devastating diseases like cancer, pulmonary fibrosis and Alzheimer's disease. Cancer is the top killer in most countries. Pulmonary fibrosis contributes to the major fatality of COVID-19 infection, and Alzheimer's disease remains untreatable. These diseases remain untreatable if the health establishments keep on ignoring the importance of wound healing and chemo-surveillance.

2.2 The Impact of COVID-19 Pandemic on Cancer Patients

COVID-19 infection causes damage to the lung to trigger wound healing responses that produce PGs and TNF [19]. PGs are good for wound healing to boost CDA content. But TNF is bad for wound healing to reduce CDA content. TNF is also named cachectin after its effect to cause cachexia symptoms. A manifestation of cachexia is the excessive excretion of low molecular weight metabolites due to the effect of TNF to induce vascular hyperpermeability [20,21]. Active CDA components are among low molecular weight metabolites excreted resulting in the collapse of chemo-surveillance. Without sufficient CDA components to induce terminal differentiation of PSCs is the cause of pulmonary fibrosis.

Cancer is also evolved due to the collapse of chemo-surveillance to affect induction of terminal differentiation of PSCs [19]. The concept of cancer as a non-healing wound was first introduced by the great German scientist Virchow in the 19th century [22]. It was again brought up by Dvorak in 1986 [23]. The close relationship between cancer and wound healing was noticed by MacCarthy-Morrough and Martin [24]. We provided the most important details on this subject that included abnormal MEs to block differentiation [12], DIs and DHIs as wound healing metabolites and also as active players of chemo-surveillance [4-10,14-18], hypomethylation of nucleic acids as the most critical mechanism to accomplish terminal differentiation of PSCs, CSCs, and CCs [13] the evolution of CSCs from PSCs due to the collapse of chemo-surveillance [8,9] and the mechanism of wound healing [19]. The functionality of chemo-surveillance is obviously badly compromised for the symptom of cancer to show up. Therefore, cancer patients are particularly vulnerable to develop fatal symptom of pulmonary fibrosis if infected by COVID-19. They are advised to receive the vaccination to prevent infection. If infected, they are advised to switch therapies from cell killing agents such as cytotoxic agents, radiotherapy, or immunotherapy to targeted therapies such as inhibitors of growth factors or signal transductions [10]. Cell killing creates damage like a viral infection to cause the collapse of chemo-surveillance that can aggravate COVID-19 infection. Targeted therapeutic agents are excellent DIs or DHIs that can prevent the development of fatal pulmonary fibrosis.

2.3 Development of CDA Formulations to Combat COVID-19 and Cancer

Pulmonary fibrosis is the most feared symptom of COVID-19 infection, because it contributes the major fatality of COVID-19 infection. Pulmonary fibrosis is caused by the build-up of PSCs unable to undergo terminal differentiation because of the collapse of chemo-surveillance. The situation is quite similar to MyeloDysplastic Syndrome (MDS) which is caused by the build up of CSCs unable to undergo terminal differentiation [8]. CSCs are derived from PSCs by a single hit to silence the TET-1 enzyme [25]. Thus, the problem of pulmonary fibrosis is exactly the same as that of MDS. The only solution is to induce terminal differentiation of pathological cells to become functional cells, which is the critical mechanism of wound healing. Induction of terminal differentiation is, therefore, the most appropriate strategy for the therapy of pulmonary fibrosis and MDS. PSCs and CSCs are protected by drug resistance and anti-apoptosis mechanisms. Toxic chemicals cannot access these cells, and radiation is also ineffective. Wound healing metabolites are the partners of their natural missions to heal a wound. Therefore, wound healing metabolites can easily access these cells to achieve induction of terminal differentiation. Consequently, wound healing metabolites are the most appropriate choice of medicines to solve the problem of pulmonary fibrosis and MDS [5,10,17,25]. CDA-2 was a preparation of wound healing metabolites purified from freshly collected urine [26], which has been approved for the therapy of cancer and MDS by the Chinese FDA [27,28]. Evidently CDA-2

was the drug of choice for the therapy of MDS [10]. We have carried out intensive studies of DIs and DHIs to make effective CDA formulations for the therapy of pulmonary fibrosis and cancer [10,14-18,28]. If pulmonary fibrosis can be effectively cured, the virulence of COVID-19 can be reduced to that comparable to influenza virus. Then restriction of people's gatherings is not necessary. We can return to the normal life. The development of CDA formulations can also allow us to win the war on cancer [29-31] and possibly on Alzheimer's disease [10].

3. CONCLUSION

COVID-19 pandemic has devastated the entire world for almost three years causing 6.34 million deaths. The development of pulmonary fibrosis due to the breakdown of chemo-surveillance is the major cause of fatality. Cancer is also evolved due to the breakdown of chemo-surveillance. Cancer patients are particularly vulnerable to develop fatal symptom of pulmonary fibrosis if Infected by COVID-19. Therefore, cancer patients are advised to receive vaccination to prevent Infection by COVID-19. Cancer therapies based on cell-killing such as cytotoxic agents, radiotherapy, and Immunotherapy also contribute to the breakdown of chemo-surveillance. It is advisable for cancer patients to switch therapies to targeted therapies which are DIs or DHIs good for healing wound to avoid development of pulmonary fibrosis if they are infected by COVID-19.

Development of medicines effective for pulmonary fibrosis is urgent to remove the menace of COVID-19 pandemic. Pulmonary fibrosis is caused by the build-up of PSCs unable to undergo terminal differentiation, which is similar to MDS due to build-up of CSCs unable to undergo terminal differentiation. CDA-2 is a preparation of wound healing metabolites purified from urine, which was the drug of choice for the therapy of MDS. Development of CDA formulations similar to CDA-2 is urgent to put out pulmonary fibrosis, cancer, and possibly Alzheimer's disease.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Yahoo. COVID-19 pandemic. Yahoo Search; 2022.
2. Wynn TA. Cellular and molecular mechanism of fibrosis. J Pathol. 2008;214 (2):199-210.
3. Rybinski B, Cukieman E. The wound healing, chronic fibrosis and cancer progressing triad. Physiol Genomics. 2014; 46(7):223-244.
4. Liau MC, Baker LL. Wound healing, evolution of cancer and war on cancer. Intl Res J Oncol. 2021;4(3):13-20.
5. Liau MC, Baker LL. Cancer arises as a consequence of wound not healing properly. Thus, perfection of wound healing must be the most appropriate strategy to win the war on cancer. Adv Complement Alt Med. 2021;6(3):584-586.
6. Liau MC, Szopa M, Burzynski B, Burzynski SR. Chemo-surveillance: A novel concept of the natural defense mechanism against cancer. Drug Exptl Clin Res. 1989;13 (5):72-82.
7. Liau MC, Craig CL. Chemo-surveillance as a natural mechanism to ensure perfection of wound healing to avoid cancer evolution and to cure cancer. In: New Horizons in Medicine and Medical Research. 2022;6(3). Print ISBN: 978-93-5547-607-4
8. Liau MC, Baker LL. Destruction promotes the proliferation of progenitor stem cells and cancer stem cells. Therefore, non-destruction strategy is a better choice for cancer therapy. J Pharmacol Pharmaceu Pharmacovigi. 2020;4:029. DOI:10.24966/PPP-5649/100029
9. Liau MC, Baker LL. The functionality of chemo-surveillance dictates the success of wound healing as well as cancer therapy. Nov Res Sci. 2021;7(2):1-3.
10. Liau MC, Craig CL. Wound healing metabolites to heal cancer and unhealed wounds. Intl Res J Oncol. 2022;6(3):8-20.
11. Liau MC, Chang CF, Saunder GF, Tsai YH. S-Adenosylhomocysteine hydrolases as the primary target enzymes in androgen regulation of methylation complexes. Arch Biochem Biophys. 1981;208(1):261-272.
12. Liau MC, Zhuang P, Chiou GCY. Identification of the tumor factor of abnormal methylation enzymes as the catalytic subunit of telomerase. Chin Oncol Cancer Res. 2010;7(2):86-96.
13. Liau MC, Lee SS, Burzynski SR. Hypomethylation of nucleic acids: A key to

the induction of terminal differentiation. Intl J Exptl Clin Chemotherapy. 1989;2(2): 187-199.
14. Liau MC, Kim JH, Fruehauf JP. In pursuance of differentiation inducers for the differentiation therapy of cancer. J Cancer Tumor Intl. 2020;10(2):29-47.
15. Liau MC, Kim JH, Fruehauf JP. Arachidonic acid and its metabolites as the surveillance differentiation inducers to protect healthy people from becoming cancer patients. Clin Pharmacol Toxicol Res. 2021;4(1):7-10.
16. Liau MC, Liau CP. Methyltransferase inhibitors as excellent differentiation helper inducers for differentiation therapy of cancer. Bull Chin Cancer. 2002;11(3): 166-168.
17. Liau MC, Fruehauf PA, Zheng ZH, Fruehauf JP. Development of synthetic differentiation agent formulations for the prevention and therapy of cancer via targeting of cancer stem cells. Cancer Stud Ther J. 2019;4(1):1-15.
18. Liau MC, Kim JH, Fruehauf JP. Potentiation of ATRA activity in HL-60 cells by targeting of methylation enzymes. J Pharmacol Pharmaceu Pharmacovigi. 2019;3(1):009.
DOI:10.24966/PPP-5649/100009
19. Liau MC, Craig CL. On the mechanism of wound healing, and the impact of wound on cancer evolution and cancer therapy. Intl Res J Oncol. 2021;5(3):25-31.
20. Itkin T, Rafii S. Leukemia cells "gas up" leaky bone marrow blood vessels. Cancer Cell. 2017;32(3):276-278.
21. Passaro D, Di Trullo A, Abarrategi A, Rouault-Pierre K, Foster K, et al. Increased vascular permeability in the bone marrow microenvironment contributes to disease progression and drug response in acute myeloid leukemia. Cancer Cell. 2017;32 (3):324-341.
22. Virchow R. Die cellular pathilogie in ihrer begrundung auf physiologische und pathologische gewebelehve. Hirschwald. 1858;16:440.
23. Dvorak HF. Tumors: Wound that do not heal. N Engl J Med. 1986;315(26): 1650-1659.
24. MacCarthy-Morrough L, Martin P. The hallmarks of cancer are also the hallmarks of wound healing. Science Signaling. 2020;13:648.
25. Liau MC, Kim JH, Fruehauf JP. Destabilizaion of abnormal methylation enzymes: Nature's way to eradicate cancer stem cells. Online J Complement Alt Med. 2019;2(5): OJCAM.MS.ID.000546.
DOI:10.33542/OJCAM.2019.02.000546
26. Liau MC. Pharmaceutical composition inducing cancer cell differentiation and the use for treatment and prevention of cancer thereof. US Patent. 2007;7232578:82.
27. Feng F, Li Q, Ling CQ, Zhang Y Qin F, Wang H, et al. Phase III clinical trials of the cell differentiation agent-2 (CDA-2): Therapeutic efficacy on breast cancer, non-small cell lung cancer and primary hepatoma. Chin J Clin Oncol. 2005;2(4): 706-716.
28. Liau MC, Kim JH, Fruehauf JP. Destabilization of abnormal methylation enzymes to combat cancer: The nature's choice to win the war on cancer. Lambert Academic Publishing. 2020;978-620-2-66889-7.
29. Liau MC, Fruehauf JP. It has been half a century since President declared war on cancer: Destabilization of abnormal methylation enzymes has the blessing of the nature to win the war on cancer. Adv Complement Alt Med. 2020;6(3):538-539.
30. Liau MC, Baker LL. Eradication of cancer stem cells to win the war on cancer. Nov Res Sci. 2021;6(5):1-3.
31. Liau MC, Baker LL. Cell differentiation agent formulations to win the war on cancer. Cancer Sci Res. 2022;5(2):1-4.

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