

## Commentary

### Cancer Moonshot to Bring Hope for Desperate Cancer Patients

#### ABSTRACT

It was very sad to learn that President Jimmy Carter and Jane Fonda have given up fight to battle cancer. Terminal stage cancer patients all end up like these two very distinguished figures hopeless to carry on fighting. At terminal stage, patient's cancer cells (CCs) are loaded with cancer stem cells (CSCs) unresponsive to therapies currently in practice, which are actually responsible for the creation of hopeless situation. Perpetual replication of CCs is the most outstanding feature of cancer. Naturally, killing of replicating CCs becomes the top choice of cancer establishments to combat cancer. Killing of replicating CCs is actually a wrong approach of cancer therapy, because cancer is caused by wound not healing properly. Wound creates symptom, and healing is an effort to eliminate the symptom created by the wound. Wound healing requires the proliferation and the terminal differentiation of progenitor stem cells (PSCs) [1-3]. Terminal differentiation of PSCs is the most important mechanism of wound healing, because only terminally differentiated cells can restore biological function damaged by the wound. Thus, terminal differentiation of PSCs is the critical mechanism to dictate the success of wound healing. If wound is not healed properly, the symptom created by the wound will force PSCs to evolve into CSCs to escape contact inhibition, and then to progress to faster growing CCs. Henceforth, the replication of CSCs and CCs is an effort to heal the wound. Promotion of terminal differentiation of CSCs and CCs is, therefore, the right approach of cancer therapy [4].

The hopeless situation of terminal cancer patients is the result of wrong therapies put forth by cancer establishments. Cancer arises due to the collapse of chemo-surveillance which is a mechanism created by the nature to ensure perfection of wound healing to avoid cancer. The functionality of chemo-surveillance has been badly damaged for the symptom of cancer to show up. Cytotoxic agents further aggravate the already badly damaged chemo-surveillance by creating more wounds. Killing of CCs also triggers CSCs to proliferate to heal the damages created by cytotoxic agents. In the end, CCs are replaced by CSCs which are not responding to cytotoxic agents, because these cells are protected by drug resistance and anti-apoptosis mechanisms. Restoration of chemo-surveillance is an effective measure to limit the build up of CSCs [5]. Development of CDA formulations to restore the functionality of chemo-surveillance is a right remedy to correct the mistakes created by cancer establishments [6-12]. Cancer establishments were definitely not doing the things right to fail the challenge of war on cancer. They continued to use the failed strategy on killing of CCs to cause deaths of cancer patients [13, 14]. There is no mechanism within the health profession to correct the mistakes made by cancer establishments. President Biden was genuinely committed to save cancer patients to declare cancer moonshot initiative. He has the authority to replace leadership of federal health agencies to correct the mistakes of cancer establishments to bring hope to desperate cancer patients.

#### Comment [a1]:

Abstract can be limited to 250 to 300 words

#### Comment [a2]: It can be discussed in Introduction

Key words: cancer moonshot; wound healing; CSCs; PSCs; cancer therapy.

Comment [a3]: Can be avoided in keywords

## INTRODUCTION

President Jimmy Carter and Jane Fonda have recently announced giving up their fights to battle cancer. It was unfortunate that such distinguished figures would give up hope to stay alive. In fact all terminal cancer patients are in the same desperate situation to stay alive. It is the mistakes of cancer establishments employing wrong medicines to treat cancer, thus creating hopeless situation to give up struggles. Cancer moonshot initiative announced by President Biden on Sept. 12, 2022 offered hope to save lives of desperate cancer patients. The inability to save lives of cancer patients was due to the execution of therapies based on killing of CCs [13, 14]. The adaption of cytotoxic cancer therapy was a tragic byproduct of World War II. During the war, toxic sulfur mustard gas bombs were used. Victims of toxic gas bombs all showed depletion of lymphocytes in their blood specimens, which inspired oncologists to employ toxic chemicals to treat leukemia patients. The successful elimination of leukemic cells with toxic chemicals established cytotoxic chemotherapy of cancer. Cytotoxic agents and the disappearance of cancer cells in hematological cancers and the disappearance of tumor in solid cancers became the established standards of cancer therapy. When President Nixon declared war on cancer in 1971, cytotoxic chemotherapy and radiotherapy based on killing of CCs were the top choice of cancer establishments to wage the war on cancer. But the battle failed because the mortalities of cancer remained the same despite intensive effort to execute killing of CCs. Cancer establishments shifted the focus from cytotoxic agents to gene therapy and targeted therapy during 1976-1996, and then to anti-angiogenesis during 1996-2016, and now to immunotherapy from 2016 [15]. Obviously, cancer establishments were making efforts to win the war on cancer. They were, however, trapped in unwinnable killing of CCs, because they have set up rules of cancer therapies all based on the killing of CCs. It is not possible to rely on them to find solutions of cancer. Health profession does not have a mechanism to correct the mistakes made by cancer establishments. The President has the authority to replace important cancer establishments such as directors of NCI and FDA to offer the hope to desperate terminal cancer patients.

## COMMENTARIES AND DISCUSSIONS

### Desperate Situation of Terminal Cancer Patients

Perpetual proliferation of CCs is the most outstanding feature of cancer. Killing of CCs or

induction of terminal differentiation of CCs are two options to stop proliferation of CCs. Killing is the choice of cancer establishments and induction of terminal differentiation is the choice of the nature, namely the creator of the nature. The same creator also creates photosynthesis we all depend to stay alive, and immuno-surveillance to resist diseases caused by microbes such as COVID-19. Chemo-surveillance the creator created to stop cancer was not recognized by the cancer establishments because this creation revealed the wrongdoings of cancer establishments on cancer. The two choices to stop proliferation of CCs are contradictory to each other, one anti-wound healing and the other pro-wound healing. Only one of these two approaches is the right approach of cancer therapy. Killing of CCs definitely is not a right approach of cancer therapy, because cancer is caused by wound unhealing due to the collapse of chemo-surveillance [1-3]. Killing of CCs creates wound to the tumor to trigger CSCs to proliferate in order to heal the wound. Dead CCs are gradually replaced by CSCs to increase the proportion of CSCs from less than 2% in the primary tumor to become a very large percentage at terminal stage. When a tumor has an enrichment of CSCs around 10% like primary malignant brain tumor, it becomes untreatable [16]. Enrichment of CSCs is a major factor to cause unresponsiveness to the treatment of terminal cancer patients. Cytotoxic agents have other undesirable adverse effects. By slowing down DNA replicating activity, they increase the opportunity for DNA methyltransferases to introduce aberrant DNA methylations [17, 18] to result in creation of vicious cancer cells often seen in terminal cancer patients. DNA interacting agents have the risk to turn cancer cells to become untreatable cells. Cytotoxic agents have been drilled through as a presidential project during 1971-1976, but failed to achieve the goal to put cancer away. It was fair to conclude that these agents were not good for cancer therapy.

Early stage cancer may benefit from cytotoxic cancer therapy when the functionality of chemo-surveillance is not yet fatally damaged. The recovery of the functionality of chemo-surveillance can subdue surviving CSCs to prevent recurrence [5]. If the damage to chemo-surveillance has reached the point of no return, the treatment with cytotoxic agents may result in patients becoming hopelessly resistant to further treatment. Even the treatment is successful to reach complete response. The fortunate patients are eventually succumbed to recurrence sooner or later, because the functionality of chemo-surveillance is totally destroyed by cytotoxic agents and CSCs remain unaffected. That is the reason cancer mortalities remain at historical high. President Biden wished to bring cancer mortality down 50% in the following 25 years. A drastic change of therapeutic approaches away from killing of CCs is necessary to achieve his goal. It is also needed to bring the hope to desperate terminal cancer patients.

CDA Formulations as the Right Medicines for Cancer Therapy, and to the Rescue of Hopeless

Terminal Cancer Patients

Induction of terminal differentiation of CCs is the right approach of cancer therapy, because cancer is caused by wound unhealing and induction of terminal differentiation of stem cells involved in wound healing is the most critical mechanism of wound healing [1-3]. The concept

of cancer as an unhealing wound was first introduced by the great German scientist Virchow in the 19<sup>th</sup> century [19]. It was again brought up by Dvorak in 1986 [20]. The close relationship between cancer and wound healing was noticed by MacCarthy-Morrrough and Martin [21]. We provided the most important details on this subject that included abnormal methylation enzymes (MEs) to block differentiation [22-24]; chemo-surveillance as the creation of the nature (our creator) to ensure perfection of wound healing to avoid cancer [5,, 25-27]; differentiation inducers (DIs) which are chemicals capable of eliminating telomerase from abnormal MEs, and differentiation helper inducers (DHIs), which are inhibitors of MEs, as the wound healing metabolites and as the active players of chemo-surveillance [25-27]; hypomethylation of nucleic acids as the most critical mechanism to achieve terminal differentiation of cells with abnormal MEs [28]; the mechanism of wound healing to involve the proliferation and the terminal differentiation of PSCs [1-4]; and the evolution of CSCs from PSCs due to wound unhealing [7, 29, 30]. Our studies strongly indicate that cancer is closely related to wound healing. Cancer arises as a consequence of wound unhealing. Therefore, wound healing process is the most appropriate modality of cancer therapy [4, 15]. Indeed, CDA-2 which was a preparation of wound healing metabolites purified from freshly collected urine we created. CDA-2 has been proved as the drug of choice for the therapy of myelodysplastic syndrome (MDS) [4, 7, 8, 15, 31]. MDS is a disease attributable entirely to CSCs [32]. Wound healing metabolites are obviously the best medicines to eliminate CSCs. The ability to eliminate CSCs is very important for the success of cancer therapy [6, 9, 10]. Untreatable cancers are loaded with CSCs such as primary brain tumors and terminal cancer patients above described. CDA formulations are the best medicines to solve such desperate cases [4, 6-12, 15, 31].

#### Cancer Moonshot to Inspire Hope for Desperate Terminal Cancer Patients

The hopelessness situation of cancer is attributable to high percentage of CSCs unresponsive to treatments based on killing of CCs. CDA formulations are the best medicines to solve CSCs, which were allowed by cancer establishments as cancer drugs because CDA formulations could not make tumor to disappear. Cancer establishments created the problems of desperate cancer patients, and blocked the development of medicines capable of solving the hopeless situation they created. Cancer establishments are very powerful. When they make mistakes, there is no mechanisms to correct the mistakes they make. President Biden was genuinely committed to save cancer patients, because he lost his very accomplished son Veau to malignant brain tumor. He can, and only he can shake up the unshakable health profession to make a drastic change to save cancer patients. He can install leadership who are willing to make the change for good at federal health agencies. When he makes such change, we can then rise and yell God blesses America.

## CONCLUSION

Cancer is a simple matter as wound healing. Healing wound is not a big deal. It comes naturally without having to put up any effort. Cancer arises due to wound unhealing. Wound healing process offers the best modality of cancer therapy. This approach of cancer therapy is the choice our creator who creates chemo-surveillance to ensure perfection of wound healing to avoid cancer.

Cancer establishments took exactly opposite anti-wound healing approach for cancer therapy. They lost the war on cancer during 1971-1976 when the USA committed unlimited resources to fight cancer. The war on cancer is still not over half a century later, leaving a lot of patients in desperate hopeless situation. Cancer establishments made cancer impossible to solve. Only the President has the authority to install leadership at federal agencies who are willing to make the change to correct the mistakes made by cancer establishments in the past. When that happens, we can all rise and yell God blesses America!

## COMPETING INTERESTS DISCLAIMER:

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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