

Commentary

CancerMoonshot to Bring Hope to Desperate Cancer Patients

ABSTRACT

It was very sad to learn that President Jimmy Carter and Jane Fonda have given up fights 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 a 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 a wound not healing properly. A wound creates a 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 a wound is not healed properly, the symptom created by the wound will force PSCs to keep on replicating, but the replication of PSCs is limited by the rule of contact inhibition. PSCs are normal stem cells which obey the rule of contact inhibition. They are then forced 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 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 leaderships of federal health agencies to correct the mistakes of cancer establishments to bring hope to desperate cancer patients.

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

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.

Cancer is the leading causes of death worldwide. There were 10 million deaths in 2019. Cancer mortalities are on the very top in most industrialized rich countries except USA which is second to cardiovascular diseases. Cancer incidences and mortalities are increasing, because the progress on cancer therapy is very slow. A drastic change of cancer therapies is necessary to improve the progress.

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.

Cell Differentiation Agent (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 19th 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 Bring Hope to Desperate Terminal Cancer Patients

The hopeless situation of terminal cancer patients 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 not 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 are no mechanisms to correct the mistakes they make. President Biden was genuinely committed to save cancer patients, because he lost his very accomplished son Veauto

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".

It is an immense task to correct wrong doings of cancer establishments in the past. DNA interacting toxic chemicals and radiation are wrong medicines needed to be recalled, and the disappearance of tumor is not a valid criterion for the assessment of cancer therapy. The corrective measures must be done in order first to establish CDA formulations or other drugs as effective cancer drugs to replace cytotoxic agents. The criteria of assessment of cancer therapy must also be established to replace the disappearance of tumor. CDA-2 is an approved cancer drug effective to induce terminal differentiation of CSCs and CCs, and to antagonize the effect of TNF to restore the functionality of chemo-surveillance. The induction of terminal differentiation can also put to rest difficult problems of chromosomal abnormalities to cause activation of oncogenes and inactivation of suppressor genes. Thus, CDA-2 is a perfect cancer drug. CDA formulations to pattern after CDA-2 are hopeful cancer drugs to the rescue of hopeless terminal cancer patients.

CONCLUSION

Cancer is caused by wound not healing properly due to the collapse of chemo-surveillance resulting in the loss of wound healing metabolites to promote terminal differentiation of PSCs, which are then forced to evolve into CSCs and then to progress to faster growing CCs. The perpetual proliferation of CCs is an effort to heal wound. Killing of CCs is a wrong approach of cancer therapy. Promotion of terminal differentiation of CSCs and CCs is the right approach of cancer therapy.

Cancer therapies based on killing of CCs are the choice of cancer establishments to combat cancer. Only early stage cancer patients when the functionality of chemo-surveillance is not yet fatally damaged may benefit from such therapies. The majority of cancer patients do not benefit from these therapies, because these therapies contribute to the destruction of chemo-surveillance and promote proliferation of CSCs to repair the wounds they created. At terminal stage, CSCs populations are increased to the extent unresponsive to further treatment. Obviously, the mistakes of cancer establishments create the hopeless situation of terminal cancer patients. These are also the mistakes responsible for the loss of the war on cancer.

There are no mechanisms within the health profession to correct the mistakes cancer establishments made. President Biden was genuinely committed to save cancer patients to declare cancer moonshot on Sept. 12, 2022. He has the authority to appoint leaderships at federal health organizations such as NCI and FDA to correct the mistakes made by cancer establishments in the past. We need to make a drastic change to eliminate wrong

cancer medicines and diagnostic measures previously approved, and to approve CDA formulations to replace wrong cancer medicines.

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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