

RESEARCH ARTICLE

Putting aside Ideological Disputes to Focus on the Rescue of President Biden, an Exceptional President to Save Cancer Patients

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Abstract

President Biden is an exceptional political leader to show enthusiastic concern of the welfare of ordinary people to bring up Cancer Moonshot Initiative save cancer patients in 2022. He was diagnosed to suffer from cancer in advanced stage in 2025. The purpose of this article is to call for the health profession to put aside ideological disputes to focus on the rescue of President Biden who has put up so much efforts to benefit health profession. In return, the health profession is obliged to come up a solution to save him. On cancer, solutions can be based on the elimination of causes or symptoms. Elimination of symptoms including cytotoxic cancer therapies, anti-angiogenesis, and immunotherapy dominates the field of cancer therapies, which is not very effective to achieve lifelong survival. Elimination of causes that includes cell differentiation agent (CDA) formulations and targeted therapies to achieve differentiation therapy is a better choice to achieve lifelong survival. Tumor shrinkage is a rule set up by cancer establishments as a condition to qualify for cancer drugs. CDA formulations cannot satisfy this requirement, thus, are excluded as acceptable cancer drugs for the therapy of solid cancers. Tumor shrinkage was the most grave mistake of cancer establishments to account for the failure to achieve cancer therapy. It blocked the acceptance of CDA formulations which provided the only intelligent solution of cancer stem cells (CSCs), thus, also blocked their mission to win the war on cancer, which required the elimination of CSCs to success. Since President Biden did so much to benefit health profession, the health profession is obliged to approve CDA formulations to save his life.

Keywords: Cancer Therapies, CDA Formulations, Cytotoxic Cancer Therapies, President Biden.

1. Introduction

President Nixon and President Biden are the two exceptional Presidents to show genuine concern of the welfare of ordinary people. President Nixon declared War on Cancer in 1971 trying to put away cancer, a major killer of American people [1], and President Biden put up Cancer Moonshot Initiative in 2022 trying to follow the successful moonshot to save 50% of cancer patients in 25 years [2-4]. War on Cancer was a presidential project. Presidential projects are specific projects to solve monumentally important issues of the nation, which carry a time limit of 5 years with unlimited support from the national resources. War on Cancer was the third presidential project in the history of USA, which

was not successful. It was a very shameful record of health profession to fail an important presidential assignment which did not require difficult technology. The previous two presidential projects required very difficult technology. Nuclear physicists achieved Manhattan Project under President Roosevelt and rocket engineers achieved Moonshot Project under President Kennedy. Cancer actually is a medical problem that can be solved easily if the solution is right [5, 6]. But if the solution is not right, it becomes a giant killer of cancer patients [7]. Solution of giant killing diseases is an important issue of national interest. President Nixon was an exceptional president to pay attention to top killing diseases. Cardiovascular diseases were the top killers of American people. But

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heart attack and stroke were too difficult to overcome. So, he picked the easier cancer which was the second top killer as his presidential project. Unfortunately, the inept cancer establishments failed to achieve the most easy presidential project which did not require difficult technology [1]. Health profession is an authoritarian profession very much like communist regimes. The big bosses set up policies for the entire profession to follow. Intelligent bosses can set up good policies of vaccinations and antibiotics to enhance the reputation of the health profession and to benefit patients. But inept bosses can set up bad policies of cytotoxic agents and hypotensive agents to damage the reputation of health profession and to hurt patients. The health profession has a peculiar tradition to protect policies put up by big bosses. Once a policy is adopted, there is a great resistance to change. The protection of good policy is laudable. But the protection of bad policy is rotten. The mistake of cytotoxic cancer therapy carries on to result in huge casualty of 10 million annual deaths around the world and with an annual increment of 5% to go along with 5% annual increment of cancer incidence according to the experts of Nation Cancer Institute [8]. Other professions can achieve difficult presidential projects in 5 years, but the health profession cannot achieve a very easy War on Cancer in 50 years [1]. The reason cancer establishments fail to solve cancer is because they do not have a valid concept of cancer. They are misguided by the symptoms of cancer and pursue solution of cancer based on the elimination of symptoms. Elimination of symptoms is the favorite of western medicine that can produce immediate effect to achieve short term therapeutic efficacy that may not last lifelong. Therapy that can achieve lifelong survival is the real good therapy. Only early stage cancer patients can benefit from cytotoxic cancer therapy to achieve lifelong survival, that include stage I and II without metastasis, Gleason scores below 7 of prostate cancer, CSCs count less than 1% [9], and CDA levels above 2.5 [10]. Cancer patients in the early stage responsive to cytotoxic therapies are approximately 25% of all cancer patients [10]. So, cytotoxic cancer therapies can only save 25% of cancer patients, but contribute to the deaths of 75% cancer patients. President Biden when diagnosed to suffer from cancer in 2025 was in advanced stage with Gleason score of 9.0 and distant bone metastasis. He was beyond the help of cytotoxic cancer therapies, immunotherapy and surgery favored by cancer establishments [11-13]. CDA formulations are the only drugs to the rescue of President Biden [4, 14-18]. President Biden has put up so much efforts to help health profession to solve cancer [2-4]. He

even personally raised 100 million to support the oncology surgical project of Tulane University. The health profession ought to do everything possible to save him in return. It is evil to kill him with cytotoxic agents, immunotherapy or surgery. Save him with CDA formulations!

2. Putting aside Ideological Disputes to Focus on the Rescue of President Biden and Discussion

2.1 Cancer Therapies: The Elimination of Symptoms Versus the Eliminations of Causes

Solution of disease can be based on the elimination of symptoms or causes. Western medicine likes to develop drugs to eliminate symptoms to produce immediate therapeutic effects that may not last lifelong. Elimination of causes is the choice of oriental medicine [19]. Oriental medicine considers the drugs that can prevent disease from taking place as the best drugs, and the drugs to target on the cause of disease as the next to the best drugs. The drugs to target on the symptoms are the worst kind, which are the most favored drugs of western medicine. There are disputes on the solution of disease. In view of the fact that President Biden was an exceptional president to put up great efforts to help health profession to solve cancer, the health profession is obliged to put aside ideological disputes to focus on the solution best to save his life. He introduced Cancer Moonshot Initiative in 2022 to encourage health profession to follow the success of Moonshot Project to come up an equal success to save 50% of cancer patients in 25 years. That was a much modest request than the War on Cancer project of President Nixon. He even personally raised 100 million to support the oncology surgical project of Tulane University. The health profession benefited so much from his presidency. We ought to put aside disputes to save him.

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 all displayed deficiency of leukocytes in their blood specimens, which inspired oncologists to employ toxic chemicals to treat leukemia patients. Indeed, toxic chemicals were very effective to eliminate leukemia cells to achieve immediate short term therapeutic efficacy. Cytotoxic chemotherapy thus became the standard cancer therapy not only for hematological cancers but also for solid cancers, and the disappearance of tumor became the standard evaluation on the success of cancer therapy of solid cancers. Both were wrong, because cancer evolved due to wound unhealing,

creation of wound was incorrect for cancer therapy [13]. Consequently, disappearance of tumor was also wrong for the evaluation of the success of cancer therapy [20, 21]. Cancer evolving due to wound unhealing was a concept introduced by Virchow in 1858 [22], which may be too ancient to remain in the memory of recent authorities. It was again brought up by Dvorak in 1986 in the most popular medical journal that ought to catch the attention of recent authorities [23]. Recent cancer establishments were not moved to continue on their wrong approaches of cancer therapies, stirring up cancer as a giant killer of cancer patients. The inability to solve cancer is the fault of cancer establishments who direct cancer therapies in the battle ground of cancer cells (CCs) which are the most abundant cells of cancer but are not very critical to the solution of cancer. CSCs became known in 1997 [24]. The discovery of CSCs unraveled CSCs as the cells to initiate tumor growth and the cells responsible for the fatal effects of cancer [25-31]. Fatal effects of cancer such as metastasis, drug resistance, anti-apoptosis, angiogenesis, unresponsiveness and recurrence are all the making of CSCs. Therefore, elimination of CSCs is far more important than the elimination of CCs to achieve cancer therapy [32]. Of course, cancer establishments were aware of CSCs as the more troublesome cells. Approximately 19 years ago, the pharmaceutical giant GSK put up an outrageous 1.4 billion, the most expensive investment on a cancer drug, to develop monoclonal antibodies against CSCs invented by the scientists of Stanford University, which was not successful because killing of CSCs was not an option to solve the issue of CSCs. Cancer establishments were aware of the important cancer issues. But they always selected the wrong approaches to fail the solution of important issues. They neglected to pay attention to the advice of Virchow and Dvorak to let cancer to become a giant killer [22, 23]. They focused the attention on CCs to miss the important target of CSCs [32]. They focused the attention on aberrant tRNA methylation around 1966 and DNA methylation around 1985 to miss the important target of abnormal MEs to let the solution of cancer to slip away [33]. Cancer establishments are able to identify the important issues of cancer, but tend to miss the most critical point to fail to solve the problems. The problem of cancer unable to solve is the fault of cancer establishments, who are so dumb not able to understand the logic of wound unhealing to the evolution of cancer at a time when both cancer and wound healing become known completely. They are not only unable to solve the problem, but also to block the solution. Yet, they are very powerful to control the

lifelines of health professionals. Worse yet, the health profession has a rotten tradition to protect inept cancer establishments to resist correction. This rotten tradition is exactly the display of evil genes of communist regimes to carry on bad policies. Secretary of Health Robert Kennedy Jr appears to be a political leader willing to challenge the health establishments. But he is doing the opposite. He challenges the good policy of vaccination, but neglects to challenge the bad policy of cytotoxic cancer therapy that killed his uncle Edward Kennedy. It would be nice if he leaves good policy of vaccination alone and challenges the bad policy of cytotoxic cancer therapy to save President Biden. Cancer evolving due to wound unhealing was a valid concept on cancer introduced by Virchow in 1858 [22]. He was extremely talented to comprehend the logic of wound unhealing to the evolution of cancer at a time neither cancer nor wound healing was completely known. He did not produce experimental data to advance his excellent concept on cancer. We pursued cancer therapy unknowingly following his guidance to discover abnormal MEs [34-36], chemo-surveillance [10, 37, 38], and the mechanism of wound healing [39-42]. Our studies provided experimental data to strongly support the validity of Virchow's concept of cancer evolving due to wound unhealing. So, Liao et al. are also extremely talented to comprehend the logic of cancer evolving due to wound unhealing. The alliance of Virchow and Liao et al. becomes the only intelligent solution of cancer and other fatal diseases evolving due to wound unhealing [43]. The only intelligent solution to cancer, cardiovascular diseases and a series of fatal diseases was blocked by health establishments because of ideological disputes. Health establishments are always the winners of ideological disputes, because they control the lifelines of health professionals. The challengers may win the arguments but are certainly to lose the livelihood. That is why health professionals are afraid to challenge big establishments. The bad policies put up by big establishments can never be rectified within the health profession. Secretary Kennedy is the right government officer to shape up health profession that requires a drastic change of health leaders and therapeutic approaches [18, 32, 44]. Wound healing comes naturally. It is a very simple matter unable to attract attention. But if wound is not healed, it can be troublesome, often fatal. Evidently, wound healing is an important health issue, so that the nature creates chemo-surveillance and immuno-surveillance to ensure perfection of wound healing, chemo-surveillance to heal wounds caused by

toxic chemicals or physical means, and immuno-surveillance to heal wounds caused by infectious agents. Chemo-surveillance and immuno-surveillance can act synergistically on wound healing to prevent disastrous consequence of wound unhealing. Chemo-surveillance was a terminology we created to describe an 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 as shown in Table 1, which is reproduced from the reference [10].

Table 1. Chemo-surveillance Selectively Destroyed in Cancer Patients

Plasma/Urine Peptide Ratios	CDA Levels	Number of Patients	% Distribution
0.83 – 0.80 (Normal)	5.0	2	1.8
0.80 – 0.60	4.3	7	16.7
0.60 – 0.40 (Responsive)	3.1	18	16.7
0.40 – 0.20	1.8	38	35.2
0.20 – 0.10	0.9	24	22.2
0.10 – 0.02 (Unresponsive)	0.37	19	17.6

Plasma Peptides : nmoles/ml ; **Urinary Peptides :** nmoles/mg creatinine

DIs are metabolites capable of eliminating telomerase from abnormal methylation enzymes (MEs) and DHIs are inhibitors of MEs capable of potentiating the activity of DIs. DIs and DHIs are actually wound healing metabolites to direct terminal differentiation of progenitor stem cells (PSCs). Wound healing requires the proliferation and the terminal differentiation of PSCs [40]. PSCs are the most primitive stem cells to initiate the development of organ or tissue during embryonic stage of fetal development. A small number of these cells, usually less than 2% of the organ or tissue mass, are preserved in the organ or tissue for future expansion or repair. Wound healing is actually an extension of embryonic program of organ or tissue development. MEs are a ternary enzyme complex consisting of methionine adenosyltransferase (MAT)-methyltransferase (MT)-S-adenosylhomocysteine hydrolase (SAHH) [45], which play a pivotal role on the regulation of cell replication and differentiation. In cells expressing telomerase such as PSCs of embryonic stem cells, MEs become associated with telomerase [36]. The association with telomerase changes kinetic properties of MAT-SAHH isozyme pair and the regulation of MEs greatly in favor of promoting cell growth. The K_m values of telomerase associated MAT^{LT}-SAHH^{LT} isozyme pair are 7-fold higher than the K_m values of normal MAT^L-SAHH^L isozyme pair. The higher K_m values are an indication that abnormal MEs are far more stable, since the study of Prudova et al. showed that S-adenosylmethionine (AdoMet) could protect associated protein against protease digestion [46]. The higher K_m values are also an indication that larger pool sizes of AdoMet, S-adenosylhomocysteine (adoHcy) and homocysteine (Hcy) are needed to promote the growth of cells expressing

telomerase, since the study of Chiba et al. showed that when HL-60 cancer cells were induced to undergo terminal differentiation, the pool sizes of AdoMet and AdoHcy shrank greatly. Abnormal MEs are a shared feature of cancer cells and primitive embryonic stem cells. It appears that the seed of cancer is sown at the very beginning of life, namely the fertilization of egg with a sperm to activate totipotent stem cell which expresses telomerase. The expression of telomerase spreads through pluripotent stem cells, but secedes when pluripotent stem cells undergoing lineage transitions to reach unipotent stem cells (UPSCs). Telomerase is a recognized oncogenic protein. The association with MEs to promote exceptional growth is the most important factor to contribute to telomerase as an oncogenic protein. Data presented in Table 1 strongly support the concept of cancer evolving due to wound unhealing introduced by Virchow [22]. The break down of chemo-surveillance is the reason unable to promote terminal differentiation of PSCs to heal the wound. PSCs are then forced to evolve into CSCs, and then to progress to faster growing CCs. The breakdown of chemo-surveillance is most likely due to immunological disorder producing too much tumor necrosis factor (TNF), just like the incidence to contribute to myelodysplastic syndromes (MDSs) [48]. TNF is capable of creating blood vessel hyperpermeability to cause excessive excretion of low molecular weight metabolites to result in the collapse of chemo-surveillance [49, 50]. TNF is responsible for the initiation as well as the progression of MDSs, since antibody to TNF can halt the progression of MDSs [51]. It is very likely that immunological disorder producing TNF is responsible for the collapse of chemo-surveillance for the initiation of cancer, and

the progression of cancer triggering immunological response further to deteriorate the collapse of chemo-surveillance. The application of cytotoxic agents to create wound also contribute to the deterioration of chemo-surveillance. CDA level of 2.5 presented in the Table 1 is most likely the threshold level, above 2.5 chemo-surveillance can restore to the functional level to subdue surviving CSCs which are not responsive to cytotoxic therapy [25-31]. The success of cytotoxic cancer therapy on early stage patients is not entirely the credit of cytotoxic agents. The restoration of chemo-surveillance plays a decisive role to subdue surviving CSCs. Below 2.5, chemo-surveillance has no chance to restore to the functional level to subdue surviving CSCs. The inability of cytotoxic cancer therapy to put away cancer is attributable to ineffectiveness against CSCs and the contribution to damage chemo-surveillance. Immunotherapy has the same problem of cytotoxic cancer therapy to show ineffectiveness against CSCs, and the contribution to damage chemo-surveillance. CSCs are PSCs without ten-eleven translocator-1 (TET-1). Cell feature, antigenicity and cell mission of CSCs are exactly the same as those of PSCs. PSCs are tolerable to natural immune mechanisms, so are CSCs. Immunotherapy is not likely to put away cancer despite the award of Nobel Prize in 2025. CDA formulations are the only intelligent solution to win the war on cancer [43] and to save President Biden. Cancer is basically a problem of growth regulation going awry. Abnormal MEs and the activation of oncogenes or the inactivation of suppressor genes are the most critical factors to contribute to the development of cancer, abnormal MEs to block differentiation and the activation of oncogenes or the inactivation of suppressor genes to speed up replication. The activation of oncogenes or the inactivation of suppressor genes attracted the

most attention to receive many Nobel prizes. Cancer establishments designated gene therapy to replace cytotoxic cancer therapy was a right move to solve the cause of cancer. They should select abnormal MEs to attack the cause of cancer, because it is not feasible to pursue gene therapy. One gene therapy is successfully executed, there may soon put up another gene abnormality to negate the previous effort. After all, oncogenes and suppressor genes are cell cycle regulatory genes. These genes have important roles to play when cells are in cell cycle replicating. But if cells exit cell cycle to undergo terminal differentiation these genes have no roles to play. Therefore, the solution of abnormal MEs is a smarter attempt to remove the cause of cancer. Once abnormal MEs is solved by CDA formulations, the problems of chromosomal abnormalities will also be eliminated. The solution of abnormal MEs is very easy, whereas the solution of chromosomal abnormalities is immensely difficult. The failure to develop gene therapy during 1976-1996 was a good thing. If it was successful like the success of cytotoxic cancer therapy on early stage cancer patients, we will be trapped in a very difficult gene therapy like we are now trapped in unattainable cytotoxic cancer therapies. Telomerase is a recognized oncogenic protein to make MEs abnormal. TNF is also a recognized oncogenic protein responsible for the initiation and the progression of MDSs [48-51]. Phenylacetylglutamine, which is the major chemical composition of Antineoplastons purified from urine by Burzynski for cancer therapy [10, 52-54] and CDA-2 purified from urine by Liau for cancer therapy [55-57]. Phenylacetylglutamine is biologically inactive, but it is effective to antagonize TNF to protect chemo-surveillance.



Figure 1. Effective Prevention of Hepatocarcinogenesis by Antineoplaston A10

The figure on the left is the control liver receiving aflatoxin B₁ only, and the figure on the right is the liver receiving Antineoplaston A10 after the administration of aflatoxin B₁.

By the protection of chemo-surveillance, phenylacetylglutamine can effectively prevent hepatocarcinogenesis induced by potent

hepatocarcinogen aflatoxin B₁ as shown in Fig. 1, which is reproduced from the reference [58]. It is remarkable that a biologically inactive chemical

can prevent crinotenesis induced by potent hepatocarcinogen aflatoxin B₁. So, Antineoplaston A10, the code name for phenylacetylglutamine by Burzynski, is the best cancer drug that can prevent the disease from taking place according to oriental medicine [19]. The nature creates chemo-surveillance to ensure perfection of wound healing. Protection of chemo-surveillance becomes the most intelligent solution to prevent fatal diseases evolving due to wound unhealing [5, 6, 10, 14-19]. Perfection of wound healing and creation of wounds make a great difference on the therapy of cancer. Perfection of wound healing can easily put cancer away and creation of wounds are difficult to put cancer away, it can only make cancer worse, particularly in the situation of advanced stage like President Biden. Solution of CSCs is the key to the success of cancer therapy. Cancer establishments knew that, so, they put up an outrageous 1.4 billion to develop monoclonal antibodies against CSCs above mentioned to scare off competitors on CSCs. It does not need that much to solve CSCs. CDA-2, a preparation of wound healing metabolites purified from urine [57] can handle CSC satisfactorily. MDSs are classical cases to illustrate the evolution of cancer due to wound unhealing. Immunological disorders producing too much TNF are responsible for the development of MDSs [48-51]. Wound unhealing in most cases is due to the build up of PSCs unable to undergo terminal differentiation due to the collapse of chemo-surveillance caused by TNF. Chemo-surveillance is always operating at the maximus capacity. When it is destroyed by excessive

excretion. It cannot be replenished through body metabolisms. The pressure is building up for PSCs to replicate. But the replication is limited by contact inhibition. So, PSCs are forced to evolve into CSCs to escape contact inhibition. It takes a single hit to silence TET-1 to convert PSCs to become CSCs [59, 60], that is an easy task of PSCs to accomplish, because these cells are equipped with exceptionally active MEs. But the conversion of PSCs to become CSCs is still unable to solve the problem of wound unhealing which requires the terminal differentiation of PSCs to become functional cells. The pressure is than building up to force the progression of CSCs to become faster growing CCs. So, the cause of cancer is wound unhealing, and the replication of CCs is the symptom of cancer. The smart alliance of Virchow and Liau et al. knew to solve cancer by the employment of CDA formulations to eliminate the cause of cancer [44], and the dumb cancer establishments were trapped in belief that elimination of CCs could solve cancer, resulting in ever escalation of cancer mortality. The evolution of cancer starts from excessive production of TNF due to wounds that trigger the production of TNF to cause the breakdown of chemo- surveillance to allow CSCs to become established, and the propagation of CSCs is the cause of MDSs [61]. The production of TNF is also responsible for the apoptosis of bone marrow stem cells to affect the production of erythrocytes, platelets or neutrophils. The solution of MDSs requires the inactivation of abnormal MEs to achieve terminal differentiation of CSCs to furnish erythrocytes, platelets or neutrophils.

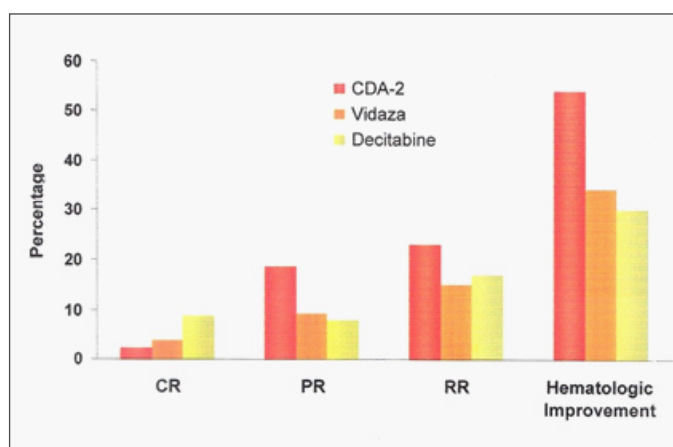


Figure 2. CDA-2 as the Best Drug for the Therapy of MDSs

Inactivation of abnormal MEs can be done by CDA formulations to destabilize abnormal MEs [34, 36, 56, 62] or by Vidaza and Decitabine to get incorporated into cellular DNA to trap MT [63]. CDA formulations offer a smart approach to eliminate the tumor factor telomerase from abnormal MEs, whereas Vidaza and Decitabine are a stupid approach to get incorporated

into DNA that can eliminate abnormal MEs but can also cause cancer [64, 65], and damage DNA of cancer cells and normal unipotent stem cells (UPSCs)[66-68]. Professor Ma, the Director of the Harbin Institute of Hematology and Oncology, was instrumental to carry out clinical trials for the approval of Vidaza, Decitabine and CDA-2 for the therapy of

MDSs by the Chinese FDA. CDA-2 was the drug of wound healing metabolites we purified from urine [56] which was also approved for the therapy of breast cancer, non-small cell lung cancer and primary hepatoma [55]. Vidaza and Decitabine were also approved for the therapy of MDSs by the US FDA. According to the assessments of Professor Ma based on two cycles of treatment protocols, each 14 days, CDA-2 had a noticeably better therapeutic efficacy based on cytological evaluation, although slower to reach complete remission, and a markedly better therapeutic efficacy based on hematological evaluation, meaning becoming independent on blood transfusion to stay healthy as shown in Fig.2, which is reproduced from the reference 57. CDA-2 is the drug to eliminate the cause of cancer which is evidently the drug of choice for the therapy of CSCs, the pathological cells of MDSs. We have predicted that the winner of the contest to win the eradication of CSCs won the contest of cancer therapies [69]. We were the clear winner, but our winner's status was denied by cancer establishments who put up a rule of tumor shrinkage as a condition to qualify for cancer drugs. The rule of tumor shrinkage was the most grave mistake of cancer establishments to block the acceptance of Antineoplaston preparations initiated by Burzynski during 1976-1990 to display excellent cancer therapy which caught the attention of 20/20 news reporting program [20]. The blockade

of Antineoplaston preparations which were similar preparations of wound healing metabolites as CDA-2 also blocked their mission to win the war on cancer, because the elimination of CSCs was essential to the success to win the war on cancer [5, 6, 11, 14-19, 32]. It is incredible that cancer establishments put up a rule to defeat themselves to win the war on cancer. The rule is based on radiological image. Radiological image can only provide crude judgement on the size of tumor, but cannot reveal detail histology of tumor. Hematological cancer cells and terminally differentiated hematological cancer cells display different morphology that can be distinguished by pathologist to make intelligent judgement on the success of cancer therapy. Solid cancer and terminally differentiated solid cancer also display distinctly different histology as shown in Fig. 3, which is reproduced from the reference [70]. Cancer establishments should use more elaborate evidence like hematological oncologist on the morphological examination to make important judgement on the success of cancer therapy. Histological examination as shown in Fig. 3 clearly show the effectiveness of CDA-2 to achieve terminal differentiation of human Smmn7721 hepatocarcinoma cells to heal the wound. The healed wound displays the histology of normal liver.

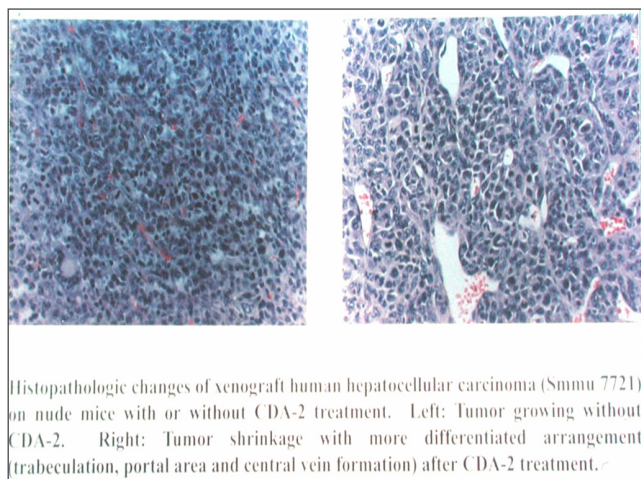


Figure 3. Histological Changes of Solid Hepatoma Smmu 7721 Included by CDA-2

In summary, the disputes on cancer therapies based on the perfection of wound healing to induce terminal differentiation of both CSCs and CCs and the creation of wounds to kill CCs to result in the disappearance of tumor is presented in Table 2. It is clear only therapies that can eradicate CSCs are able to achieve lifelong survival. Targeted therapy cannot eradicate CSCs, but it can improve chemo-surveillance to restore it to the functional state to subdue surviving CSCs like

the early stage cancer patients undergoing therapies based on the creation of wounds. Induction of terminal differentiation can achieve lifelong survival better than the killing of CCs. Vidaza and Decitabine although can achieve eradication of CSCs, but their adverse effects on UPSCs cut down their ability to achieve lifelong survival. Improvement of chemo-surveillance can result in lifelong survival. CDA and targeted therapies are the only therapies to achieve

improvement of chemo-surveillance. Immunotherapy is great to remove pathological CCs marked with programmed death antigen. Inability to eradicate CSCs

and the contribution to damage chemo-surveillance contribute to its failure to put cancer away just like cytotoxic cancer therapies.

Table 2. Summary of Disputes on the Therapy of Cancer

Cancer Therapies	CSCs	CCs	UPSCs	Chemo-surveillance	Inimmuno-surveillance	Tumor Shrinkage	Lifelong Survival
Therapies Based on the Perfection of Wound Healing:							
CDAs	+	A	-	+	0	-	+
Vidaza Decitabine	+	A	+	-	-	-	-
Targeted	-	A	-	+	0	-	+
Therapies Based on the Creation of Wounds:							
Chemo	-	B	+	-	-	+	+ Early - Late
Radio	-	B	+	-	-	+	+ Early - Late
Immuno	-	B	-	-	+	+	+ Early - Late
Surgery	+ -	B	-	-	0	+	+ Early - Late

Therapeutic effects on CSCs: + means can eliminate and – means cannot eliminate, on surgery + means can eliminate CSCs of tumor removed and – means cannot eliminate CSCs of metastatic tumors; on CCs: A means induction of terminal differentiation of CCs and B means killing of CCs; on UPSCs: - means does not affect and + means does cause damage; on chemo-surveillance: + means can improve and – means can damage; on immuno-surveillance: 0 means no effect, - means damaging effect and + means improving effect; on tumor shrinkage: - means cannot cause tumor to shrink and + means can cause tumor to shrink; on lifelong survival: + means patient’s death is not related to cancer or its treatments and – means patient’s death is related to cancer or its treatments.

In final analysis, CDA formulations and targeted cancer therapies are the only therapies that can save President Biden. Immunotherapy and surgery can also be considered to help President Biden if CDA formulations are included as combination therapy to eradicate CSCs.

2.2 Perfection of Wound Healing to Save President Biden

It appears that perfection of wound healing is the only option to save President Biden. We need to know how wound is healed. Wound healing requires the proliferation and the terminal differentiation of PSCs [40]. Wound usually triggers biological and immunological responses. The biological response involves the release of arachidonic acid (AA) from membrane bound phosphatidylinositol by phospholipase A2 for the synthesis of prostaglandins (PGs) by cyclooxygenases and PG synthases [71, 72]. Although AA and PGs are active DIs [73, 74], the induction of terminal differentiation of PSCs at the initial phase of wound is not the primary objective of PGs. Rather, the localized inflammation caused by PGs [71] is responsible for the increase of membrane permeability to facilitate the extravasation of plasma proteins and regulatory factors into the wound area

resulting in edema response, which is the primary objective of PGs to orchestrate the healing process. PGs are responsible for the promotion of proliferation of PSCs to produce enough cells to heal the wound. Chemo-surveillance mediated through DIs and DHIs is responsible for the induction of terminal differentiation (TD) at the final stage of wound healing. PGs are metabolically unstable [71]. Their biological effects are most likely brief and confined to the wound area. Thus, the promotion of the proliferation of PSCs is the primary objective of PGs on wound healing, whereas the induction of TD is accomplished by chemo-surveillance. The stable end products of PGs may participate in the final stage of wound healing, which are also active as DIs, although not as active as PGs [74]. The immunological response triggered by wound is not good for wound healing. Immunological response tends to trigger the production of cytokines which are toxic proteins to assist immunotherapy. These proteins will create wounds to aggravate the already bad situation of wound unhealing. TNF among cytokines produced is particularly bad for wound healing as above described. Thus, immunological response can act antagonistically to chemo-surveillance to prevent wound healing. It is the balance of biological response

and immunological response to dictate the outcome of wound healing. If biological response prevails, wound is healed. But if immunological response prevails, wound is not healed to produce clinical symptoms. If clinical symptoms are fatal as the white lung of COVID-19 infection or heart attack and stroke of cardiovascular diseases, the fatality is the end point, but if clinical symptoms are not fatal such as those caused by carcinogens, there is a good possibility that wound unhealing will be forced to evolve into cancer as the occurrence of hepatoma presented in Fig. 1 and the occurrence of MDSs presented in Fig. 2. So, we have presented data to describe how wound is healed and how cancer evolves due to wound unhealing. It is too bad that cancer establishments are unable to understand cancer evolving due to wound unhealing. They have their choices of solving cancer, which do not seem to work because cancer mortalities keep on escalating. Cancer establishments are the bosses. Health profession has a rotten tradition to go along with the inept bosses to make top killing diseases such as cardiovascular and cancer diseases unable to solve. Now we are facing with the rescue of President Biden who has done very much to help health profession to solve cancer. Are cancer establishments evil enough

to kill him with cytotoxic agents, immunotherapy and surgery they preferred, or can they put the disputes aside to approve CDA formulations to save him?

2.3 Development of CDA Formulation to Save President Biden

Development of CDA formulations is very important to solve cancer. The cancer establishments put up 1.4 billion for the development of cancer drugs to eliminate CSCs, which were not successful. We have developed CDA formulations that can take care of CSCs, which should worth more than 1.4 billion. It is essential to develop CDA formulations to save patients struggling against fatal diseases evolving due to wound unhealing [5, 6, 14-19, 32]. We are very concerned to help patients struggling against fatal diseases evolving due to wound unhealing like President Biden. Save him at all cost since he has done so much to help health profession. We have carried out extensive studies on natural DIs and DHIs, and non-natural DIs and DHIs for the manufacture of CDA formulations [1-6, 11, 14-19, 32, 33, 53-57, 73-76].

Table 3. Active DIs

DIs	ED25 (µM)	ED50 (µM)	ED75 (µM)
ATRA	0.18	0.36	0.75
PGJ2	7.9	13.8	20.5
PGE2	20.6	32.0	40.5
DicycloPGE2	21.0	43.5	-
AA	21.0	42.0	-
BIBR1532	32.3	43.7	55.1
Boldine	60.1	78.8	94.2

Active DIs and DHIs are presented in Table 3 and 4, which are summarized from references above cited. ED_{25, 50, 75} of DIs and reductive index 0.5 (RI_{0.5}) of DHIs are included to facilitate manufacturing of CDA formulations. RI_{0.5} is equivalent to ED₂₅ of a DI, which can be determined by the procedure previously reported [75]. DIs and DHIs can be excellent cancer drugs. ATRA, a DI, is the standard care of acute promyelocytic leukemia [77] and gleebec, a DHI, is the standard care of chronic myeloid leukemia [78]. It has to demonstrate an excellent therapeutic efficacy to be designated as a standard care of particular cancer. ATRA requires the expression of the receptor of ATRA, namely RAR, to achieve the therapeutic efficacy. RAR is the repressor of the gene coding for oligoisoadenylate synthetase. The association

of RAR with ATRA activates the transcription of oligoisoadenylate synthetase. The product of this enzyme, oligoisoadenylate, is the active DI to destabilize MEs [79]. ATRA is actually an indirect DI. Oligoisoadenylate has to be synthesized inside the cell to function. The triphosphate structure of oligoisoadenylate prevents it from entering into cells from outside. The rest of DIs listed in Tale 3 are direct DIs to act on abnormal MEs to achieve induction of TD of cells with abnormal MEs. PGs are drugs approved for the delivery. BIBR1532 and boldine are telomerase inhibitors approved for cancer therapy. Change of indication does not take long clinical trial as the application of new drug which usually requires 10 years. Effective CDA formulations can be developed quickly with approved drugs active as DIs and DHIs.

Table 4. Active DHIs

SAHH Inhibitors	RI0.5 (μM)	Signal Transduction Inhibitors (STIs)	RI0.5 (μM)
Pyrvinium Pamoate	0.012	Sutent	0.28
Vitamin D3	0.61	Berberine	1.62
Dexamethasone	0.75	Vorient	10.1
Beta-Sitosterol	1.72	Gleevec	11.9
Dihydroepiandrosterone	1.79	Selenite	19.7
Prenisolone	2.22		
Hydrocortisone	4.59	Polyphenols	RI0.5 (μM)
Pregnenolone	7.16		
		Tannic Acid	0.37
MT Inhibitors	RI0.5 (μM)	EGCG	0.62
		Resveratrol	1.16
Uroerythrin	1.9	Curcumin	1.24
Hycanthone	2.1	Kuromanin	1.43
Riboflavin	2.9	Coumestrol	1.95
		Genisteine	2.19
MAT Inhibitors	RI0.5 (μM)	Pyrogallol	3.18
		Silibinine	3.80
Indol Acetic Acid	220	Caffeic Acid	3.87
Phenylacetylvaline	500	Ellagoc Acid	4.45
Phenylacetylleucine	780	Gallic Acid	5.35
Butyric Acid	850	Ferulic Acid	7.41
Phenylbutyric Acid	970	Phloroglucinol	38.82

As listed in Table 4, inhibitors of SAHH and MT are better DHIs than inhibitors of MAT. The stability of three MEs is proportional to the mass [45]. SAHH is the smallest of the three and is the most unstable enzyme that requires steroid hormone to assume a stable configuration for the formation of MT-SAHH dimer to become stable. MAT has a mass similar to the MT-SAHH dimer. MAT can form the ternary complex with MT-SAHH dimer, but cannot form dimeric complex with MT or SAHH. MAT is the most stable enzyme of the three MEs. The association with telomerase further increases its stability. It takes large amounts of inhibitors to function as DHIs. Inhibitors of SAHH and MTs are better DHIs. Although pregnenolone is not the most active DHI, we consider it as a very valuable DHI. It is the master substrate for all biologically active steroids. It is also a single steroid to have profound influence on the development of cancer. According to Moreley, the production of pregnenolone is bell shape in relation to ages with a peak daily production of around 50 mg at the ages of 20-25 [80]. The youngest and oldest people produce the least amounts of pregnenolone, and these are the two age groups most vulnerable to develop cancer. It is our choice to make CDA-CSC.

DI is more important than DHIs for the induction of TD. But DI alone cannot achieve differentiation to reach completion, because elimination of telomerase from abnormal MEs tends to cause the dissociation of MEs into individual enzymes. MT as a monomer has a tendency to be modified by protease to become nuclease, which can create damage to disrupt differentiation process. The damage can be repaired to cause recurrence. The therapy of acute promyelocytic leukemia with ATRA was excellent, reaching above 90% complete remission, but most patients recurred within one year [77]. The inclusion of SAHH or MT inhibitors can keep MT-SAHH dimer intact to prevent modification of MT to become nuclease to disrupt differentiation process. It is a good idea to include DI and DHI to make CDA formulations. The finding of signal transduction inhibitors (STIs) as excellent DHIs is expected, since STIs always lead to the production of factors to inhibit the activity of MEs. STIs are tyrosine kinase inhibitors, but the inhibition of the activity of MEs is the consequence. STIs and inhibitors of MT become synonyms. The finding of polyphenols as excellent DHIs is unexpected. Epigallocatechi-3-gallic acid (EGCG) has been found as a good STI to inhibit MT [81-82]. It is possible that

all polyphenols act via inhibition of tyrosine kinase to result in inhibition of MEs like EGCG. Vital Reds is a food supplement produced by the famed cardiologist Steven Gundry, which contains polyphenols as the major active ingredients. It was found effective to clear the blocked blood vessel [83]. So, Gundry found an intelligent solution of cardiovascular diseases (CVDs) just like the intelligent CDA formulations we have found for the solution of cancer. The intelligent solution is to promote perfection of wound healing. Evidently, both cancer and CVDs evolve due to wound unhealing, and CDA formulations are the only intelligent solution [16, 18, 44, 84], which were unfortunately blocked by the inept health establishments. Polyphenols are generally considered as healthy foods. The finding of polyphenols as excellent DHIs adds the credibility of polyphenols as healthy foods.

The manufacture of CDA formulations can be the following formula to reach plasma concentrations as ED_{25} of a DI + $3xRI_{0.5}$ of a DHI, or ED_{50} of a DI + $2xRI_{0.5}$ of a DHI, or ED_{75} of a DI + $RI_{0.5}$ of a DHI [87]. We recommend to make two sets of CDA formulations: one set CDA-CSC consisting of AA + pregnenolone to get access to CSCs and PSCs, and another set CDA-CC consisting BIBR1532 + pyrvinium pamoate to resist enzymatic degradation of natural active ingredients by faster growing cancer cells. The application of phenylacetylglutamine is also recommended to antagonize TNF, which can be administered independently as a capsule preparation and monitor independently through quantitative assay of plasma and urinary peptides [10, 52]. The therapeutic endpoint of phenylacetylglutamine can be the restoration of CDA to reach the healthy level of 5.0 of the Table 1. The therapeutic endpoint of cancer can be the drop of carcinoembryonic antigens to reach the normal levels.

3. Conclusion

President Biden when first diagnosed to suffer from prostate cancer in 2025 was in advanced state with Gleason score of 9.0 and distant bone metastasis beyond the help of cytotoxic cancer therapies, immunotherapy and surgery favored by cancer establishments. Cytotoxic cancer therapy and immunotherapy can only save cancer patients in the early stage with Gleason score below 7.0 and without metastasis. Surgery also can only save cancer patients in the early stage without metastasis. Surgery will promote dissemination of metastasis if metastasis has been detected. So, CDA formulations are the only

option to save President Biden, which were blocked by cancer establishments. In view of the fact that President Biden has done so much to help health profession to solve cancer, the health profession is obliged to save him. Put aside ideological disputes to approve CDA formulation to save him.

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