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RESEARCH ARTICLE

Targeting on the Causes as the Only Option to Solve Diseases Evolving Due to Wound Unhealing

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Abstract

To solve diseases, there are choices either to target on the causes or on the symptoms. Oriental medicine prefers to develop drugs to target on the causes to achieve long lasting therapy, whereas western medicine prefers to develop drugs to target on the symptoms to achieve faster therapeutic effects which may or may not be long lasting. It is debatable which is better to target on the causes or to target on the symptoms. On the diseases evolving due to wound unhealing such as cancer, cardiovascular diseases (CVDs) or organ failures, targeting on the causes is the only option to cure diseases. Targeting on the symptoms is incorrect for cancer or ineffective for CVDs. But the western medicine insisted on the drugs to target on the symptoms to result in these diseases as persistent top killers of humans. Health authorities have killed too many patients of diseases evolving due to wound unhealing. The objective of this article is to advice health authorities to shift exclusive attention on the targeting of symptoms to causes to save patients struggling against diseases evolving due to wound unhealing.

Cancer evolving due to wound unhealing was a valid concept introduced by Virchow in 1858. Had we followed his advice on the handling of cancer, cancer was not a difficult disease to require the attention of President Nixon to declare War on Cancer as a presidential project to solve. Virchow 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 to follow his advice to discover abnormal methylation enzymes (MEs), chemo-surveillance and the mechanism of wound healing. We, in essence, independently produced experimental data to support the validity of cancer evolving due to wound unhealing introduced by Virchow. Thus, we were also extremely talented to decode the logic of wound unhealing to the evolution of cancer. Wound healing comes naturally. So, the solution of cancer is quite easy, just to follow the natural course of wound healing to achieve perfection of wound healing to eliminate unhealed wounds. Perpetual proliferation of cancer cells (CCs) is the most outstanding symptom of cancer. Cancer authorities put most efforts on the killing of CCs to eliminate the symptoms of cancer. That was incorrect to stir up cancer as a giant killer to claim 0.61 million mortality annually in the USA and 10 million mortality annually around the world. The same mistake of health authorities to focus on the symptoms of CVDs claim even worse mortalities, 0.92 million mortality annually in the USA and 20.5 million mortality annually around the world. Health authorities are supposed to protect patients, but they in fact become the killers of patients struggling against diseases evolving due to wound unhealing for as long as these diseases became known. It must stop! Intelligent scientists like Virchow and Liau el al. cannot stop them. The survival of scientists is at the mercy of health authorities. Government officials can stop them by enacting legislatures to limit the use of legal drugs on ineligible patients to save patients from being killed by legal drugs.

Keywords: Cancer, Cardiovascular Diseases, Causes And Symptoms Of Diseases, Health Authorities, Government Officials.

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1. Introduction

Wound healing is an important health issue, so that the nature creates chemo-surveillance and immuno-surveillance to ensure perfection of wound healing to avoid disastrous consequences of wound unhealing, chemo-surveillance to heal wounds due to toxic chemicals or physical means, and immuno-surveillance to heal wounds due to infectious agents. On wound healing, chemo-surveillance and immuno-surveillance can act synergistically to heal wounds. Wound healing requires the proliferation and the terminal differentiation (TD) of progenitor stem cells (PSCs) [1]. PSCs are the most primitive stem cells to initiate the development of organs and tissues during embryonic development of the fetus. Therefore, wound healing is an extension of the embryonic program of organ and tissue development. Most primitive stem cells including totipotent stem cell and pluripotent stem cells express telomerase. MEs of telomerase expressing cells are abnormal due to a great affinity of MEs with telomerase to form complex [2]. MEs are a ternary enzyme complex consisting of methionine adenosyltransferase (MAT)-methyltransferase (MT)-S-adenosylhomocysteine hydrolase (SAHH) which plays a pivotal role on the regulation of cell growth and differentiation [3]. Thus, MEs are critically involved in wound healing and cancer which is basically a problem of growth regulation going awry. Virchow 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 [4]. He did not produce experimental data to advance his excellent concept on cancer. He was, nevertheless, respected as a great pioneer on cancer. Cancer therapy in the recent time had a bad start to rely on toxic chemicals to kill CCs. Cytotoxic chemotherapy was a tragic byproduct of World War II. During the war, toxic sulfur mustard gas bombs were employed. Victims of toxic gas all displayed depletion of leukocytes in their blood specimens, that inspired oncologists to employ toxic chemicals to treat leukemia patients. Indeed, toxic chemicals were very effective to eliminate leukemia cells to achieve immediate therapeutic effects by the elimination of the symptom of leukemia. Cytotoxic cancer therapy thus became established as the standard cancer therapy not only for hematological cancers but also for solid cancers, and the disappearance of tumor became a standard diagnosis of the success of cancer therapy. Both were wrong, because killing of CCs created wounds clearly in violation of the advice of Virchow [5, 6]. Virchow's advice was given too anciently to remain in the memory of recent authorities. His advice was brought up again by Dvorak in recent time in a very popular medical journal that ought to catch the attention of recent authorities [7]. The recent cancer authorities were unmoved to stay on their wrong course of cancer therapy. So, cancer remains a disease unsolved. Inability to solve cancer is the mistake of cancer authorities too arrogant to follow the good advice of Virchow.

CVDs are also evolving due to wound unhealing like cancer [8], although the authors of the article did not so explicitly state. CVDs are caused by the damage to the inner lining of blood vessels, that require healing. Like cancer, the healing is not successful, most likely also due to the collapse of chemo-surveillance unable to complete terminal differentiation (TD) of progenitor stem cells (PSCs). Thus, wound unhealing is the cause responsible for the buildup of PSCs to cause the hardening of the blood vessel to lose elasticity to become easy to burst. Wound unhealing is also the cause to trigger infiltration of leukocyte and the deposit of low density lipoprotein to form plugs in the unhealed wound area to cause the blood pressure to increase. PSCs express telomerase. The association of telomerase with MEs changes kinetic properties of MEs and the regulation of MEs greatly in favor of promoting cell growth. Km values of telomerase associated isozyme pair MAT^{LT}-$SAHH^{LT}$ are 7-fold higher than the normal isozyme pair MAT^{L}-$SAHH^{L}$. The higher Km values are an indication that cells expressing telomerase have larger pool sizes of S-adenosylmethionine (AdoMet) and S-adenosylhomocysteine (AdoHcy). SAHH is an enzyme to carry out reversible reactions. Larger pool size of AdoHcy also means larger pool size of homocysteine (Hcy). High plasma level of Hcy is a risk factor of CVDs. Obviously, the metabolical activity of cells expressing abnormal MEs is the cause of CVDs, most likely PSCs unable to undergo TD. Therapy of CVDs based on the elimination of the symptom of high blood pressure is not effective, resulting in CVDs as the top killer of humans. The effective solution of CVDs is to heal the unhealed wounds.

Organ failures can also be caused by wound unhealing like cancer and CVDs. White lung of COVID-19 infection, a very outstanding organ failure, is caused by the buildup of PSCs unable to undergo TD due to the collapse of chemo-surveillance during the early phase of COVID-19 infection [5]. Renal failure is caused by the damage to glomerulus unable to perform filtration process to remove low molecular weight wastes and wound healing metabolites. So, wound healing

metabolites are enriched in renal failure patients to cause premature TD of PSCs in the attempt to heal wounds to glomerulus. It is analogous to the interference of the function of MEs by thalidomide on the development of the fetus. Thalidomide causes malformation of limbs noticeably. Malformation of limbs is non-lethal to show up in the affected babies. Malformations can also happen on vital organs such as heart and brain to result in still birth. Organ failures in the brain compartment can also be due to premature induction of TD of PSCs. Wound healing metabolites are hydrophobic metabolites that tend to accumulate in the brain compartment. Blood brain barrier functions just opposite to placenta which allow the passage of hydrophilic thalidomide and exclude hydrophobic maternal wound healing metabolites. Premature induction of TD of PSCs may be a difficult problem of wound healing like renal failure. The handling of organ failures due to premature induction of TD of PSCs must be different than the handling of wound unhealing due to the collapse of chemo-surveillance. Cell differentiation agent formulations (CDA formulations), which are preparation of wound healing chemicals, are ideal for the therapy of diseases due to wound unhealing attributable to the collapse of chemo-surveillance. Promotion of the growth of PSCs is the correct therapeutic approach for organ failures attributable to premature induction of TD of PSCs such as renal failure or Altzheimer's disease.

2. Targeting on the Causes as the Only Option to Solve Diseases Evolving due to Wound Unhealing and Discussion

2.1 Solution of Diseases: Targeting on the Causes Versus Targeting on the Symptoms

On the solution of diseases, there are three different choices: to prevent the diseases from taking place, to target on the causes which is favored by the oriental medicine that can produce long lasting therapy, or to target on the symptoms which is favored by western medicine that can produce faster therapeutic effects which may or may not be long lasting [10]. Both oriental and western medicines stress importance on the prevention of diseases. Western medicine has the edge to develop vaccines against infectious diseases. It is debatable which is better to target on the causes or to target on the symptoms to solve diseases. On some diseases evolving due to wound unhealing such as cancer and CVDs, targeting on the causes is the only option to achieve lifelong therapy. Targeting on the symptoms by killing of CCs is incorrect for cancer [5] or by hypotensive agents is ineffective for CVDs [11-15]. These diseases persistently become the top killers of humans for a very long time because of the mistake of health authorities trapped in belief that targeting on the symptoms as the best approach on the solution of diseases. Targeting on the symptoms is good for the therapy of diseases displaying pain, fever or cough as symptoms.

So far the records show that targeting symptoms by killing CCs can only benefit a small minority, roughly one quarter, of cancer patients in the early stage that include stage I and II without evidence of metastasis, CDA levels above 2.5, namely above 50% of the healthy people [16], Gleason scores of prostate cancer less than 7, 6 being the healthy score, and CSCs counts below 1% [17]. The success of cancer therapy by killing of CCs is not entirely the credit of cytotoxic drugs, the restoration of CDA levels to the functional state plays a decisive role on CSCs to dictate the success of cancer therapy [18-20], since CSCs are not responsive to cytotoxic cancer therapy [21-27]. Our studies indicated that chemo-surveillance was selective destroyed in cancer patients as shown in Table 1, which is reproduced from the reference [16].

Table 1. *Chemo-surveillance Specifically Destroyed in Cancer Patients*

Plasma/Urine Peptide Ratios	CDA Level	Patient Number	% Distribution
0.83-0.80 (Normal)	5.0	2	1.8
0.80-0.60	4.3	7	6.5
0.60-0.40 (Responsive)	3.1	18	16.5
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; Urine Peptides: nmoles/mg creatinine*

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. DIs are metabolites capable of eliminating telomerase from abnormal MEs of cells expressing telomerase and DHIs are inhibitors of MEs which can potentiate the activity of DIs. Wound healing requires the proliferation and

the TD of PSCs. Abnormal MEs are critically involved in the proliferation and TD of PSCs, therefore, MEs must have a central role to play on wound healing and cancer therapy [28-31]. Indeed, abnormal MEs are the most important issue of cancer, more important than oncogenes and suppressor genes which received many Novel prizes. After all, oncogenes and suppressor genes are cell cycle regulatory genes which have important roles to play when cells are in cell cycle replicating. But if replicating cells exit cell cycle to undergo TD, these genes have no roles to play.Therefore, destabilization of abnormal MEs to achieve TD of replicating CCs is a smart and easy way than the gene therapy the cancer authorities designated 20 years from 1976 to 1996 unsuccessfully to correct chromosomal abnormalities in an attempt to put away problems due to activation of oncogenes or inactivation of suppressor genes. Actually, it is not feasible to correct chromosomal abnormalities for cancer therapy. One chromosomal abnormality if successfully solved, there may soon pop up another chromosomal abnormality to negate the previous effort. Good thing, the development of gene therapy was not successful. If it was successful, we would be trapped in a very difficult approach of cancer therapy like we are now trapped in the unattainable cytotoxic cancer therapies based on the killing of CCs. Destabilization of abnormal MEs to focus on the cause of cancer is the most intelligent approach of cancer [28-40]. Once abnormal MEs are solved, chromosomal abnormalities and CSCs can also be put to rest. That is the ultimate solution of cancer. Cancer therapy targeting on the causes is definitely a better choice than those targeting on the symptoms which dominated cancer therapies in the past without success.

War on Cancer declared by President Nixon during 1971 to 1976 employing cytotoxic cancer therapies was a decisive failure. It was a very shameful record of health profession unable to achieve a presidential project which did not require difficult technologies. Nuclear physicists achieved Manhattan Project under President Roosevelt and rocket engineers achieved Moonshot Project under President Kennedy both of which required very difficult technologies. Mistake of cancer authorities to select an incorrect solution to target on the symptoms of cancer was to blame for the failure to achieve the president project to win the War on Cancer therapy. The ineffectiveness on CSCs, which was not known at that time and the damage to chemo-surveillance were the reasons to cause the failure of cytotoxic cancer therapies. The issue of CSCs became known in 1997 [41]. The discovery of CSCs unraveled CSCs as the initiators of cancer and the contributors of cancer fatal effects [21-27]. Fatal effects of cancer such as metastasis, drug resistance, anti-apoptosis, effective DNA repair, anti-angiogenesis, unresponsiveness and recurrence are all the making of CSCs. Cancer authorities were aware of the importance of CSCs.Approximately 19 years ago, the pharmaceutical giant GSK put up 1.4 billion to develop monoclonal antibodies against CSCs, which was the most expensive investment on cancer drugs. The development of drugs against CSCs was apparently unsuccessful, because killing of CSCs was not an option to solve the issue of CSCs which were critically linked to wound unhealing. Destabilization of abnormal MEs to achieve TD of CSCs is the only option to solve CSCs [28-40]. We are the only intelligent scientists able to handle the issue of CSCs, and therefore, we are the only intelligent scientists able to win the War on Cancer. Data presented in Table 1 are clinical data we produced to support the validity of the concept of cancer evolving due to wound unhealing. These data are quantitative analyses of plasma and urinary peptides. Peptides share physical and chemical properties similar to wound healing metabolites. Therefore, peptides can be used as the surrogate molecules to represent wound healing metabolites. As a matter of fact, acidic peptides are the major active DIs of Antineoplaston preparations Burzynski purified from urine for cancer therapy [42-44]. It is obvious that wound healing metabolites are produced in the body of healthy people as chemo-surveillance to keep cells expressing abnormal MEs under control. This safety mechanism is destroyed under pathological conditions producing tumor necrosis factor (TNF), which can induce blood vessel hyperpermeability to cause excessive excretion of low molecular weight metabolites to display cachexia symptoms [45, 46]. Wound healing metabolites are among low molecular weight metabolites excreted, resulting in the collapse of chemo-surveillance to cause wound unhealing. If the symptoms of wound unhealing are fatal like the white lung of COVID-19 infection, or heart attack and stroke of CVDs, fatality is the endpoint. But if the symptoms are non-fatal like those of carcinogens, there is a good possibility that unhealed wound will force PSCs to evolve into CSCs. It takes a single hit to silence ten-eleven translocator-1 (TET-1) to convert PSCs to become CSCs. It is an easy task for PSCs to accomplish, since these cells are equipped with exceptionally active MEs. So, CSCs are PSCs without TET-1 enzyme. The cell feature, antigenicity and cell mission of CSCs are exactly the same as those of PSCs. The only difference is the responsiveness toward contact inhibition. PSCs obey contact inhibition which has no restriction on the proliferation of CSCs. The content of PSCs to an organ

or a tissue is always less than 2% which is followed by CSCs, attributable to their progression to CCs. Malignant brain tumors are exceptional. Malignant brain tumors are either astrocytoma with CSCs counts less than 1% or glioma, glioblastoma or neuroblastoma with CSCs counts over 3% [17]. Brain compartment is unique to be protected by blood brain barrier. Hydrophobic wound healing metabolites tend to accumulate in the brain compartment. Only malignant tumors with very high CSCs counts can prevail in the brain compartment. Growth hormone is produced in the pituitary gland located in the brain compartment, which may promote the growth of benign tumor or astrocytoma with very low CSCs counts. The studies of Thon et al. [17] indicated that malignant astrocytoma with CSCs counts less than 1% was responsive to cytotoxic cancer therapies, whereas glioma, glioblastoma and neuroblastoma with CSCs above 3% were unresponsive to cytotoxic cancer therapies. These studies were very alarming. It indicates that the margin of responsiveness to cytotoxic cancer therapy is very narrow. That is the reason that cytotoxic cancer therapies can only benefit a small minority of cancer patients in the early stage, and kill the majority of cancer patients in the late stage. Thus, cancer therapies targeting on the symptoms to kill CCs did not have successful records. These therapies failed to achieve the presidential project during 1971-1976, failed to develop anti-angiogenesis therapy during 1996-2016, and is failing to develop immunotherapy during 2016-2036. There is no reason to expect immunotherapy to become successful. Cancer is basically a problem of growth regulation going awry. Immunology has nothing to do with growth regulation. Cancer authorities must have run out of choices to put the hope on immunotherapy. Immunotherapy is a better choice than cytotoxic cancer therapies to target on the programmed death antigen. It is a targeted therapy to spare adverse effects that show up in cytotoxic cancer therapies. The target of immunotherapy is the membrane antigen, which is a better choice. Targeting on DNA is a very bad choice. Cytotoxic agents can create monstrous cells nobody can handle. So, immunotherapy is a better choice than cytotoxic agents to replace cytotoxic cancer therapies, but it has the same problem of cytotoxic cancer therapies to show ineffectiveness against CSCs and to contribute to the damage of chemo-surveillance to cause the failure of cancer therapies. It appears that targeting on the cause of wound unhealing is the only intelligent solution of cancer [10-13, 18-20, 28-40].

2.2 Perfection of Wound Healing as the only Intelligent Solution of Diseases Evolving Due to Wound Unhealing

Wound healing comes naturally, because the nature put up chemo-surveillance to ensure perfection of wound healing [16, 18, 47, 48]. Wound healing is a simple matter unable to attract attention. We are the only few scientists to consider wound healing as an important health issue. It is indeed a very important health issue, because top killers are diseases evolving due to wound unhealing such as CVDs, cancer, and organ failures. Unfortunately, wound unhealing is often neglected by health authorities [15], diseases evolving due to wound unhealing are badly handled by health authorities to stir up these diseases as the top killers of humans. Western medicine tends to focus the attention on the solution of symptoms. It is totally unprepared to solve diseases evolving due to wound unhealing. Diseases evolving from wound unhealing can only be solved by the elimination of causes. Chemo-surveillance selectively destroyed in cancer patients we discovered was an important finding [16]. Chemo-surveillance can be destroyed by immunological disorder that produces TNF to initiate the incidence of myelodysplastic syndromes (MDSs) [49].

Boula et al. confirmed that TNF was indeed responsible to initiate the incidence of MDSs, since antibody of TNF was effective to halt the progression of MDSs [50]. Thus, immunological response producing TNF can also act antagonistically to chemo-surveillance to prevent wound healing. Immunological response is commonly associated with wounds [1], and is very closly associated with cancer, since CCs are marked with programmed death antigen to provoke immune response. Therefore, unhealed wounds and the progression of cancer are very damaging to chemo-surveillance which plays a very important defensive role to prevent the buildup of cells expressing abnormal MEs.

Protection of the function of chemo-surveillance is very important to prevent diseases evolving due to wound unhealing. Antineoplaston A10, which is a code name of phenylacetylglutamie by Burzynski, was found effective to antagonize TNF to prevent the loss of wound healing metabolites [16]. By protection of the integrity of chemo-surveillance, Antineoplaston could effectively prevent hepatocarcinogenesis induced by potent hepatocarcinogen aflatoxin B1 as shown in Fig. 1, which is reproduced from the reference [16]. Antneoplaston A10 is biologically inactive.

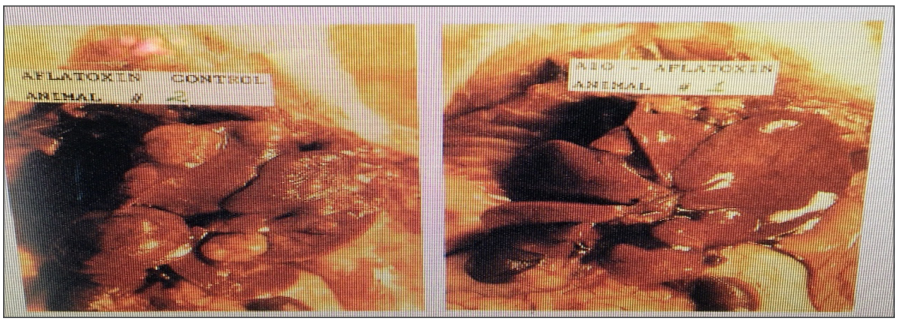

Figure 1. *Effective Prevention of Hepatocarcinogenesis by Antineoplaston A10*

It is remarkable that a biologically inactive chemical can prevent hepatocarcinogenesis challenged with a potent hepatocarcinogen. Drugs that can prevent diseases from taking place are valued by oriental and western medicines. Antineoplaston A10 should be acceptable as an excellent cancer drug. Phenyacetylglutamine is a major metabolite present in the plasma and urine, which is a major chemical composition of Antineoplaton preparations purified from urine by Burzynski [42-44] and also is a major chemical composition of CDA-2 purified from urine by Liau [51-53], which played an important role on the success of therapy of cancer by Antineoplastons and CDA-2. Of course, perfection of wound healing through DIs and DHIs as the active anticancer components of Antineoplastons and CDA-2 was decisive on the success of cancer therapy. Chemo-surveillance is the prescription of the nature for the perfection of wound healing and cancer therapy. The success of cancer therapy is expected. Antineoplastons were successful employed by Burzynski during 1976 to1990 to display a very impressive success on cancer therapy that attracted the 20/20 national broadcasting coverage. The success story alerted cancer authorities to enact legislature to limit the use of only FDA approved drugs for cancer therapy. Antineoplastons were blocked, which were unable to cause the shrinkage of tumor to qualify as a cancer drug.The therapeutic endpoint of Antineoplastons is TD of CSCs and CCs unable to cause the tumor to disappear. TD of PSCs is a critical mechanism of wound healing [1], and TD of CSCs is the only option for the eradication of CSCs which are critically linked to unhealed wounds [20]. Cancer authorities successfully blocked Antineoplastons. They also successfully blocked the solution of cancer, because the success of cancer therapy required the eradication of CSCs [10-13, 18-20]. CDA-2 also displayed impressive success on cancer therapy to be approved by the Chinese FDA [52, 53]. It was approved as an adjuvant agent to supplement cytotoxic cancer therapy because the shrinkage of tumor by CDA-2 alone was not acceptable. It was approved as a mono-therapeutic agent for MDSs. On the therapy of MDSs, tumor shrinkage was not a concern. Tumor shrinkage is a very bad diagnosis standard for the evaluation of cancer therapy, because creation of wounds by killing of CCs is incorrect for cancer therapy [5, 6]. Creation of wounds tend to promote the proliferation of CSCs to heal the wounds to increase the content of CSCs which are unresponsive to cytotoxic agents [21-27]. When the content reaches a level above 3%, the tumor becomes unresponsive to further treatment [17], eventually resulting in the failure of cancer therapy. Therefore, requirement of tumor shrinkage as a cancer drug is a grave mistake of cancer authorities. Induction of TD of CCs can achieve cancer therapy by turning replicating CCs into terminally differentiated cells to carry out specific function of the affected organs. Treatment of human Smmu7721 xenografted into athymic nude mice with CDA-2 could convert malignant tumor into histology very much like normal liver as shown in Fig. 2, which is reproduced from the reference [28].

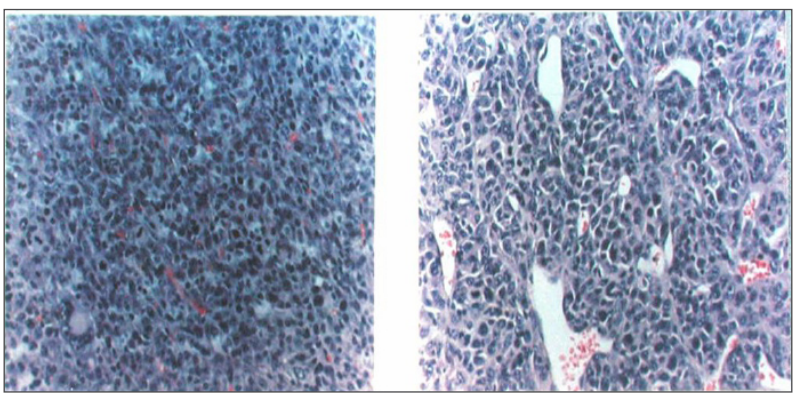

Figure 2. *Induction of Histological Change of Malignant Tumor by CDA-2*

Hematological oncologists can recognize the differences between malignant cells and terminally differentiated cells. Oncologists of solid tumors should also be trained to recognize the difference between malignant tumor and terminally differentiated tumor. Radiological image can tell the tumor size, but cannot reveal the detail of histology. That is too crude a method for the evaluation of cancer therapy. Oncologists of solid tumors should be trained like hematological oncologists to distinguish the difference between malignant tumor and terminally differentiated tumor to make a more precise judgement on the success of cancer therapy. CDA-2 could be a standard care as a mono-therapeutic agent for the breast, non-small cell lung cancer and hepatoma if the shrinkage of tumor was not a factor in the consideration of cancer therapy [54].

MDSs are classical diseases to support the validity of the concept of cancer evolving due to wound unhealing introduced by Virchow [4]. TNF that causes the collapse of chemo-surveillance is responsible for MDSs to get started [49, 50]. TNF is a toxic cytokine produced by immune competent leukocytes to kill pathological cells targeted to be removed such as CCs marked with programmed death antigen. TNF can also kill normal unipotent stem cells (UPSCs) to cause excessive apoptosis of bone marrow stem cells, thus severely affecting the ability of the patient to produce hematopoietic cells such as erythrocytes, platelets or neutrophils. The apoptosis of bone marrow stem cells triggers the proliferation of PSCs to replenish stem cells wiped out by TNF to start the process of wound unhealing and cancer evolution [1]. MDSs are at the stage of PSCs becoming forced to evolve into CSCs and before CSCs progressing to CCs to become full blown cancer. The propagating pathological cells of MDSs have been identified as CSCs [55]. The only option of the therapy of MDSs is the TD of CSCs to become functional erythrocytes, platelets or neutrophils. That is exactly the critical mechanism of wound healing [1]. CSCs can be induced to undergo TD by CDA-2 to eliminate telomerase associated with abnormal MEs of CSCs [2, 28, 51, 56, 57], or by Vidaza and Decitabine to eliminate methyltransferase (MT) by forming covalent bond between MT and azacytosine incorporated into DNA [58].

The inactivation of MEs by CDA-2 is selective that does not affect normal UPSCs, whereas the inactivation of MEs by Vidaza and Decitabine is non-selective that can also affect UPSCs. Professor J. Ma, the Director of Harbin Institute of Hematology and Oncology, was instrumental in carrying out clinical trials of all three MDSs drugs for the approval by the Chinese FDA for the therapy of MDSs. Vidaza and Decitabine were also approved by the US FDA for MDSs therapy. According to the assessments of Professor Ma based on two cycles of treatment protocols each 14 days, CDA-2 had a noticeable better therapeutic efficacy based on the cytological evaluations, although slower to reach complete remission and a markedly better therapeutic efficacy based on hematological improvement evaluations, meaning becoming independent on blood transfusion to stay healthy as shown in Fig. 3, which is reproduced from the refence [53]. CDA-2 is obvious the best drug for the therapy of MDSs with better therapeutic efficacy and without adverse effects, whereas Vidaza and Decitabine are worse on therapeutic efficacy and demonstrated unacceptable adverse effects as carcinogens [59, 60], and very toxic to DNA, particularly toward cardiac DNA [61-63]. We have predicted that the winner of the contest to eradicate CSCs won the contest of cancer therapies [64]. Fig. 3 clearly shows that we are the clear winner of the contest to eradicate CSCs. Our winner's status was denied by cancer authorities because CDA-2 was unable to cause the tumor to disappear. Cancer authorities put up a wrong rule to deny the best cancer drug. CDA-2 is acceptable in China which practice oriental medicine oriented toward therapeutic efficacy while chemical compositions can be largely unknown. Drugs with compositions unknown are not acceptable in western medicine. Antineoplastons and CDA-2 showing excellent therapeutic effects on cancer are not acceptable in western medicine.

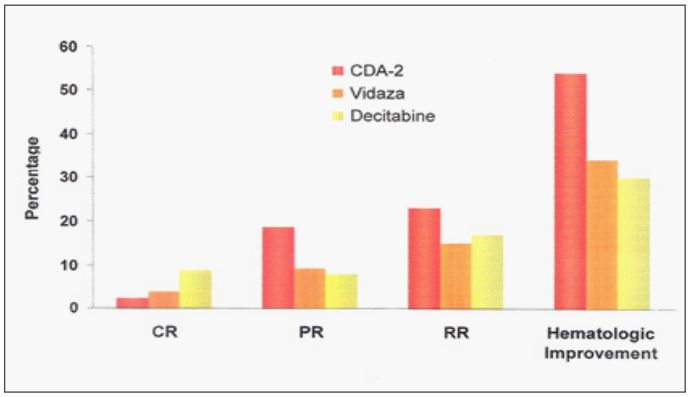

Figure 3. *CDA-2 as the Best Drug for the Therapy of MDSs*

We have carried out extensive studies on the active components of Antienoplastons , CDA-2, natural sources and synthetic drugs for the manufacture of CDA formulations with defined chemical compositions [28, 43, 44, 51, 65-70], which should be acceptable by the western medicine. We are in a unique position to provide intelligent solution to win the war on cancer, on CVDs, and on a series of fatal diseases evolving due to wound unhealing [12].

2.3 Wound Unhealing Can be Due to Too Little Wound Healing Metabolites or Too Much Wound Healing Metabolites.

Immunological disorder triggering the production of TNF to cause excessive excretion of wound healing metabolites is to blame for the collapse of chemo-surveillance to result in wound unhealing. Phenylacetylglutamine that can antagonize TNF and CDA formulations made up by DIs and DHIs that can destabilize abnormal MEs are the best solution for diseases such as cancer and CVDs. Wound unhealing can also be caused by too much wound healing metabolites to induce premature TD of PSCs. Renal failure is caused by the injury to glomerulus to damage filtration process for the removal of low molecular weight wastes including wound healing metabolites. Wound unhealing in the case of renal failure is due to premature TD of PSCs. Wound healing metabolites are hydrophobic metabolites tended to accumulate in the brain compartment. Wounds happen in the brain compartment have the same problem of premature TD of PSCs due to too much wound healing metabolites. Wound unhealing due to premature TD of PSCs must be handled differently from that due to the collapse of chemo-surveillance. Wound triggers biological and immunological responses [1]. The biological response involves the synthesis of prostaglandins (PGs) from arachidonic acid released from membrane bound phosphatidyl-Inositol. PGs play a role to promote the replication of PSCs. So, the application of PGs or PSCs is the right solution to heal wound due to too much wound healing metabolites to cause premature TD of PSCs.

3. Conclusion

Diseases can be solved by targeting on the causes or on the symptoms. Oriental medicine likes to focus on the causes, whereas western medicine prefers to focus on the symptoms. Western medicine is totally unprepared to handle diseases evolving due to wound unhealing which can only be solved by targeting on the causes. These diseases become the top killers for a very long time. Western medicine must shift attention from symptoms to causes in order to cure diseases evolving due to wound unhealing. Wound unhealing can be caused by too little or too much wound healing metabolites. CDA formulations are perfect for the solution of diseases due to the collapse of chemo-surveillance. Wound unhealing due to too much wound healing metabolites may have to rely on PGs or PSCs.

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Consent and Ethical Approval

It is not applicable.

Competing Interests

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4. References

1. 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.

2. Liau MC, Zhuang P, Chiou GCY. Identification of the tumor factor of abnormal methylation enzymes as the catalytic subunit of telomerase. Clin Oncol Cancer Res.2010; 7(2): 86-96.

3. 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.

4. Virchow R. Die Cellular Pathologie in Ihrer Begrundung auf Physiologische und Pathologische Gewebelehve. Hirschwald. 1858; 16: 440.

5. Liau MC, Craig CL, Baker LL. Creation of wounds is incorrect for cancer therapy. J Cancer Res Rev Rep. 2025; 7(6): 1-8.

6. Liau MC, Craig CL, Baker LL. Cytotoxic agents can cure cancer, but can also kill cancer patients. Intl J Clin Oncol Cancer Res. 2025; 10(1):27-35.

7. Dvorak HF. Tumors: Wounds that do not heal. N Engl J Med. 1986; 315(26): 1650-1659.

8. Johnson AA, Akman K, Calimport SRG, Wuttke D, Stozing A, de Magalhaes JP. The role of DNA methylation in aging, rejuvenation, and age-related diseases.Http://doi.org/10.1089/REJ.2012.1324.

9. Liau MC, Baker LL. The impact of COVID-19 pandemic on cancer patients. Intl Res J Oncol. 2022; 6(4): 13-17.

10. Liau MC, Craig CL, Baker LL. CDA formulation as superb and excellent cancer drugs to save cancer patients. J Cancer Res Rev Rep. 2025; 7(2): 1-9.

11. Liau MC, Craig CL, Baker LL. CDA formulations to remove cancer and cardiovascular diseases as the top killers of humans. Arch Oncol Cancer Ther. 2025; 5(2): 20-32.

12. Liau MC, Craig CL, Baker LL. The alliance of Virchow and Liau et al. to offer the only intelligent solution to win the war on cancer, on cardiovascular diseases and on a series of fatal diseases evolving due to wound unhealing. Arch Oncol Cancer Ther.2026; 6(1): 13-26.

13. Liau MC, Craig CL, Baker LL. Tearing down cytotoxic agents and ineffective hypotensive agents to give desperate cancer and cardiovascular patients the access to life saving CDA formulations. Arch Oncol Cancer Ther. 6(1): 27-41.

14. Liau MC, Craig CL, Baker LL. Legal drugs that consistently kill advanced cancer and cardiovascular patients are worse than illegal drugs that occasionally kill abusers.Arch Oncol Cancer Ther. 2026; 6(2): 1-12.

15. Liau MC, Craig CL, Baker LL. Negligence on unhealed wounds is a grave mistake of health profession. Arch Oncol Cancer Ther. 2026; 6(2): 13-23.

16. Liau MC, Szopa M, Burzynski B, Burzynski SR. Chemo-surveillance: A novel concept of the natural defense mechanism against cancer. Drugs Exptl Clin Res. 1989;13(Suppl. 1): 72-82.

17. Thon N, Damianoff K, Hegermann J, Gran S, Krebs B, Schnell O, et al. Presence of pluripotent CD133+ cells correlates with malignance of glioma. Mol Cell Neurosci.2010; 43(1): 51-59.

18. Liau MC, Craig CL. Baker LL. Restoration of chemo-surveillance as a top priority to save cancer patients. Intl Res J Oncol. 2023; 6(2): 227-237.

19. Liau MC, Craig CL, Baker LL. Development of good cancer drugs effective against cancer stem cells. Intl Res J Oncol. 2023; 6(2): 238-247.

20. Liau MC, Craig CL, Baker LL. Decoding cancer stem cells: A game change in oncology therapeutics. Arch Oncol Cancer Ther. 2025; 5(1): 25-33.

21. Zhou S, Schuetz JD, Bunting KD, Colapietro AM. The ABC transporter Bcrp ABCG2 is expressed in a wide variety of stem cells and is a molecular determinant of the side population phenotype. Nature Medicine. 2001; 7(9): 1028-1034.

22. Zhang M, Atkinson RJ, Mosen JM. Selective targeting of radiation resistant tumor initiating cells. Proc Natl Acad Sci USA. 2010; 107(8): 3522-3527.

23.Moitra K, Lou H, Dean M. Multidrug efflux pumps and cancer stem cells. Insight into therapy resistance and therapeutic development. Clin Pharmacol Ther. 2011; 89(4):491-502.

24. Frame FN, Maitland NJ. Cancer stem cells, model of study and implication of therapy resistance mechanisms. Adv Exp Med Biol. 2011; 720(2): 105-118.

25. Kim YI, Siegler FJ, Siriwon N, Wenig P. Therapeutic strategies for targeting cancer stem cells. J Cancer Metasta Treat. 2016; 2: 233-242.

26. Bartato L, Boccetti M, DiBisae A, Regat T. Cancer stem cells and targeting strategies.Cells. 2019; 9: 926.

27. Aromimi B, Masciale V, Grisendi G, Bertrikubu F, Maur M, Guaitoli G, et al. Disecting tumor growth: The role of cancer stem cells in drug resistance and recurrence. Cancers. 2022; 14: 974.

28. Liau MC, Kim JH, Fruehauf JP. Destabilization of abnormal MEs to combat cancer: The nature's choice to win the war on cancer. Lamber Academic Publishing. 2020;ISBN: 978-620-2-66889-7.

29. Liau MC, Craig CL. Baker LL. Exceptional allosteric regulation of methylation enzymes. In: Saraydin Su (ed), Novel Research Aspects in Medicine and MedicalResearch. 2023; Vol 4: 39-56.

30. Liau MC, Craig CL, Baker LL. Destabilization of abnormal methylation enzymes as the only viable option for the elimination of cancer stem cells to save cancer patients.Intl Res J Oncol. 2024; 7(1): 142-152.

31. Liau MC, Craig CL, Baker LL. Targeting abnormal methylation enzymes: A new approach of cancer therapy. J Cancer Tumor Intl. 2025; 15(2): 97-110.

32. Liau MC, Baker LL. Destruction promotes the proliferation of progenitor stem cells and cancer stem cells. Therefore, non-destruction is a better strategy for cancer Therapy: A commentary. J Pharmacol Pharmaceu Pharmacovigi. 2020; 4: 029.

33. Liau MC, Baker LL. Abnormal methylation enzymes as the bullseye of targeted cancer therapies. Nov Res Sci. 2021; 7(4): 1-3.

34. Liau MC, Craig CL, Baker LL. Wound healing process as the most appropriate modality of cancer therapy. Eur J Applied Sci. 2023; 11(1): 463-471.

35. Liau MC, Craig CL, Baker LL. Wound healing process as the best strategy to save cancer patients. London J Med Health Res. 2023; 23(13): 1-11.

36. Liau MC, Craig CL, Baker LL. Healing the unhealed wound as the top priority to save cancer patients. Intl J Res Oncol. 2025; 4(1): 1-10.

37. Liau MC, Craig CL, Baker LL. Perfection of wound healing to win the war on cancer. J Cancer Rev Rep. 2025; 7(5): 1-10.

38. Liau MC, Craig CL, Baker LL. CDA formulations as the best drugs to turn around cancer mortality from escalation to deceleration. J Cancer Res Rev Rep. 2025; 7(2):1-9.

39. Liau MC, Craig CL. Baker LL. Perfection of wound healing to the rescue of patients struggling against fatal diseases evolving due to wound unhealing. Arch OncolCancer Ther. 2026; 6(1): 1-12.

40. Liau MC, Craig CL, Baker LL. CDA formulations to make health profession great again. Arch Oncol Cancer Ther. 2026; 6(1): 56-68.

41. Bonnet D, Dick JE. Human acute myeloid leukemia is organized as a hierarchy that originate from a primitive hematopoietic cells. Nature Medicine. 1997; 3: 730-737.

42. Burzynski SR. Isolation, purification andsynthesis of Antineoplastons. Adv Exptl Clin Chemother. 1988; 88/6: 1-8.

43. Liau MC, Burzynski SR. Separation of active anticancer components of Antineoplaston A2. A3 and A5. Intl J Tiss React Extl Clin Aspects. 1990; 12(Suppl.): 1-18.

44. Liau MC, Burzynsk SR. Differentiatiion inducing components of Antinwoplaston A5.Adv Exptl Clin Chemther. 1988; 88/6: 9-26.

45. Itkin T, Rafii S. Luekemia cells “gas up” leaky bone marrow blood vessels. Cancer Cell. 2017; 32(3): 276-278.

46. Passaro D, Di Tullio A, Abarrategi A, Rousault-Pierre K, Foster K, Ariza-McNaughton L,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.

47. Liau MC, Baker LL. The functionality of chemo-surveillance dictates the success of wound healing as well as cancer therapy. Novel Res Sci. 2021; 7(2): 1-3.

48. 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: Pietro Scicchitano (ed), New Horizons in Medicine and Medical Research. 2022; Vol 6: 21-28.

49. Williamson PJ, Kruger AR, Renolds PJ, Hamlin TJ, Oscier DG. Establishing the incidence of myelodysplastic syndromes. Br J Haemato. 1994; 87(4): 743-745.

50. Boula A, Vougarelis M,Giannouli S, Katrinakis G, Psyllaki M, Pontikoglou C, et al. Effect of CA2 of antitumor necrosis factor-alpha antibody therapy on hematopoiesis of patients with myelodysplastic syndromes. Clin Cancer Res. 2006; 12(10): 3099-3108.

51. Liau MC. Pharmaceutical composition inducing cancer cell differentiation and the use for treatment and prevention of cancer thereof. US Patent. 2007; 7232578.B2.

52. 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.

53.Ma J. Differentiation therapy of malignant tumor and leukemia. In: Treaties of Chinese Society of Clinical Oncology on the Education of Clinical Oncology. 2007; pp 480-486.

54. Liau MC, Craig CL, Baker LL. CDA formulations: Potentially the standard care of breast, lung and liver cancer. Intl J Clin Oncol Cancer Res. 2024; 9(3): 44-51.

55. Woll PS, Kjallquist U, Chowdhurdy O, Doolittle H, Wedge DC, Thongjuea S, et al.Myelodysplastic syndromes are propagated by rare and distinctly human cancer stem cells in vivo. Cancer Cell. 2014; 25(6): 794-808.

56. Liau MC, Lin GW, Hurlbert RB. Partial purification and characterization of tumor and liver S-adenosylomethionine synthetases. Cancer Res. 1977; 37(2): 427-435.

57. Liau MC, Chang CF, Giovanella BC. Demonstration of an altered synthetase in human malignant tumors xenografted into athymic nude mice. J Natl Cancer Inst. 1980; 64(5): 1071-1075.

58. Santi DV, Norment A, Garret CE. Covalent bond formation between DNA-cytosine methyltransferase of DNA containing 5-azacytosine. Proc Natl Acad Sci USA. 1984;81(22): 6993-6997.

59. Prassana P, Shack S, Wilson VL, Samid D. Phenylacetate in chemoprevention of 5-aza-2’-deoxycytidine-induced carcinogenesis. Clin Cancer Res. 1995; 1(18): 865-871.

60. Gaudet F, Hodgson JG, Eden A, Jackson-Grusby L, Dausman J, Gray JW, et al.Induction of tumor in mice by genomic hypomethylation. Science. 2003; 300(5618):489-492.

61. Palii SS, van Emgurgh BO, Sankpal UT, Brown KD. Robertson KD. DNA methylation inhibitor 5-aza-2’-deoxycytidine induces reversible DNA damage that is distinctly influenced by DNA-methyltransferase 1 and 3B. Mol Cell Biol. 2008; 28(2): 752-771.

62. Kizietepe T, Hideshima T, Catley L, Raje N, Yasue H, Shiraishi N, et al. 5-Azacytidine, a methyltransferase inhibitor, induces ATR-mediated DNA-double strand break response, apoptosis, and synergistic cytotoxicity with doxorubicine and bortezomib against multiple myeloma cells. Mol Cancer Ther. 2007; 6(6): 1718-1727.

63. Yang Q, Wu F, Wang F, Cai K, Zhang Y, Sun Q, et al. Impact of DNA methyltransferase inhibitor 5-azacytidine on cardiac development of zebrafish in vivo and cardiomyelocyte proliferation, apoptosis, and the homeostasis of gene expression in vitro. J Cell Biochem. 2019; 120(10); 17459-17471.

64. Liau MC, Fruehauf JP. The winner of the contest to eradicate cancer stem cells wins the contest of cancer therapies: The winner is cell differentiation agent formulations.Adv Complement Alt Med. 2020; 5(4): 476-478.

65. Liau MC, Huang LJ, Lee DH, Chen SC, Kuo SC. Development of differentiation helper inducers for the differentiation therapy of cancer. Chin Pharma J. 1998; 50(5): 299-303.

66. Liau MC, Liau CP. Methyltransferase inhibitors as excellent differentiation helper inducers for differentiation therapy of cancer. Bull Chin Cancer. 2002; 11: 166-168.

67. Liau MC, Fruehauf PA, Zheng ZH, Fruehauf JP. Development of synthetic cell differentiation agent formulations for the prevention and therapy of cancer via targeting of cancer stem cells. Cancer Stu Ther J. 2019; 4(1): 1-15.

68. Liau MC, Kim JH, Fruehauf JP. Potentiation of ATRA activity in HL-60 cells by targeting methylation enzymes. J Pharmacol Pharmaceu Pharmacovigi. 2019; 3: 009.

69. Liau MC, Kim JH, Fruehauf JP. In pursuance of differentiation inducers to combat cancer via targeting of abnormal methylation enzymes. J Cancer Tumor Intl. 2020;10(2): 39-47.

70. 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.