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The objective of this study is to develop effective strategies that can save cancer patients. Cancer therapy got to a bad start to rely on toxic chemicals to kill cancer cells (CCs) and to set up a rule on the reduction of tumor size to evaluate cancer drugs. These were mistakes committed by cancer establishments at a time we did not have whole knowledge of cancer to result in horrendous cancer fatality, which is still on the way to increase. In 2022, President Biden urged health profession to come up solutions to bring down cancer mortality by 50% in the following 25 years. Currently available cancer drugs, which are mostly based on the killing of CCs, are causing cancer mortality to increase by 5% annually. Health profession must get serious to develop strategies that can bring down cancer fatality. The best strategy to save cancer patients is to follow wound healing process, since cancer is caused due to wound unhealing.

Keywords: CCs; CSCs; cancer therapy; DIs; DHIs; differentiation therapy; wound healing.

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Wound Healing Process as the Best Strategy to Save Cancer Patients

Ming C. Liau[α], Christine L. Craig[σ] & Linda L. Baker[ρ]

ABSTRACT

The objective of this study is to develop effective strategies that can save cancer patients. Cancer therapy got to a bad start to rely on toxic chemicals to kill cancer cells (CCs) and to set up a rule on the reduction of tumor size to evaluate cancer drugs. These were mistakes committed by cancer establishments at a time we did not have whole knowledge of cancer to result in horrendous cancer fatality, which is still on the way to increase. In 2022, President Biden urged health profession to come up solutions to bring down cancer mortality by 50% in the following 25 years. Currently available cancer drugs, which are mostly based on the killing of CCs, are causing cancer mortality to increase by 5% annually. Health profession must get serious to develop strategies that can bring down cancer fatality. The best strategy to save cancer patients is to follow wound healing process, since cancer is caused due to wound unhealing.

Wound healing requires the proliferation and the terminal differentiation of progenitor stem cells (PSCs), which are the most primitive stem cells to give rise to the particular organ or tissue during the development of the fetus. Methylation enzymes(MEs) of PSCs are abnormal due to the association with telomerase. MEs play a pivotal role on the regulation of cell replication and differentiation. Because of this pivotal role, MEs are subject to exceptional double allosteric regulations: one on the individual enzymes and one on the enzyme complex. The association of telomerase with the enzyme complex of MEs tilts the regulation greatly in favor of cell growth, which is apparently very important for the development of fetus and the wound healing. Efficient destabilization of abnormal MEs is a critical process of wound healing. The nature creates chemo-surveillance as an allosteric regulation to ensure perfection of wound healing. Human body produces metabolites active as differentiation inducers (DIs) and differentiation helper inducers (DHIs) to keep a check on abnormal MEs. Healthy people can maintain a steady level of cell differentiation agent (CDA), which is a term to designate DIs and DHIs, to ensure perfection of wound healing to avoid disastrous consequences of wound unhealing that can be tissue fibrosis, dementia, organ failure and cancer. Wound healing is a simple matter that comes naturally. Solution of cancer should also be a simple matter as wound healing if the therapy is done right. CDA formulations are the right solution of cancer, which are preparations made up by DIs and DHIs that can direct differentiation of cancer stem cells (CSCs) and CCs, and to restore chemo-surveillance to save cancer patients.

Keywords: CCs; CSCs; cancer therapy; DIs; DHIs; differentiation therapy; wound healing.

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I. INTRODUCTION

Cancer is a fearful disease, because cancer establishments do not handle it right to let cancer mortality remains at historic high. According to NCI experts, the cancer incidence was 19 million and the cancer mortality was 10 million worldwide in 2019, which were on the way to increase at an annual increment of 5% [1]. President Biden in 2022 called for the reduction of cancer mortality by 2% annually to reach 50% reduction in 25 years [2]. Health profession must get serious to develop alternatives than those they have been relying on in the past to reduce cancer mortality. Cancer therapy got to a bad start to rely on toxic chemicals to combat cancer. Cytotoxic

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chemotherapy was a tragic byproduct of World War II. During the war, toxic sulfur mustard gas bombs were used. Victims of toxic gas all showed depletion of lymphocytes in their blood specimens, which inspired oncologists to employ toxic chemicals to treat leukemia patients.

Cytotoxic chemotherapy was thus established as the standard care of cancer, and the disappearance of cancer cells or the tumor was the exclusive criterion for the judgement of therapeutic efficacy. Both the selection of toxic agents and the disappearance of tumor for the evaluation of therapeutic efficacy were serious mistakes of cancer establishments to contribute the horrendous cancer mortality [3-5]. Cancer establishments were given ample opportunities including a presidential project of war on cancer during 1971-1976 to solve cancer, but they failed the challenges. The failure is attributable to the wrong approach relying on the killing of CCs [6].

Cancer is caused by wound unhealing due to the collapse of chemo-surveillance. Creating more wounds by cytotoxic agents contribute to the destruction of chemo-surveillance, clearly is contra-indication of therapy [7, 8]. This adverse effect and the ineffectiveness of cytotoxic agents against cancer stem cells (CSCs) contribute to the failure of this strategy to win the war on cancer.

CSCs are protected by drug resistance and anti-apoptosis mechanisms to resist cytotoxic agents [9]. Cytotoxic agents can only benefit a minority of early stage cancer patients whose chemo-surveillance has not yet been fatally damaged, relying on the recovery of chemo-surveillance to subdue surviving CSCs, whereas a majority of advanced cancer patients whose chemo-surveillance has been fatally damaged are either wiped out as unresponsive cancer patients, or even lucky enough to reach complete remission are eventually succumbed to recurrence [4, 5]. A drastic change of cancer establishments is necessary to save cancer patients [10]. Cancer evolves as a consequence of wound not healing properly [8]. The best strategy to save cancer patients is to follow the wound healing process [7, 11].

II. COMMENTARIES AND DISCUSSION

2.1 Failure of Cytotoxic Agents to Save Advanced Cancer Patients

Cancer is a very fearful disease, because the approved treatments are so excruciating, and the mortality is so high. This is all because of the mishandlings of cancer establishments. Cancer therapy got to a bad start. The use of toxic agents to stop fast growing CCs was acceptable at a time when we did not have full knowledge of cancer. After all, cytotoxic agents were very effective to kill CCs, the most outstanding symptom of cancer.

Cytotoxic drugs and radiation were the major drugs used in the combat of cancer during the war on cancer declared by President Nixon, but failed to achieve the goal [12]. If a treatment modality has been drilled through as a presidential project and failed, it was fair to conclude that the modality employed was not good for cancer therapy. Now we have better knowledge of cancer, and cancer establishments are still relying on these failed drugs to treat cancer patients, that is irresponsible. Cytotoxic agents can only benefit a small minority of early stage patients, but contribute to the deaths of a majority of advanced cancer patients [3-5]. President Biden lost his very accomplished son, congressman Beau, to malignant brain tumor. He was genuinely concerned with high cancer mortality. It is time for health profession to get serious to remove cytotoxic agents contributing to cancer mortality, particularly DNA reacting agents such as nucleoside analogs, platinum derivatives, intercalating agents, apoptosis inducing agents and radiation. It is also advisable to remove the use of the reduction of tumor size as a criterion for the evaluation of cancer drugs, which is a darn mistake of cancer establishments to allow only cytotoxic agents that cannot put cancer away and to block the development of good cancer drugs not based on the killing of CCs. The development of good cancer drugs is essential to save unresponsive cancer patients attributable to cytotoxic agents [4, 5, 13]. Cancer establishments are the bosses. The health professionals can do nothing. Perhaps President Jimmy Carter as a victim of toxic cancer drugs can lodge a protest and plead for the approval of good cancer drugs

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such as CDA formulations that can eliminate CSCs to come to the rescue of a lot of terminal cancer patients in the desperate situation as himself [13, 14].

2.2 Cancer Evolves as a Consequence of Wound Unhealing

The concept of cancer as wound unhealing was first introduced by the great German scientist Virchow in the 19th century [15]. It was again brought up by Dvorak in 1986 [16]. The close relationship between cancer and wound healing was noticed by MacCarthy-Morrough and Martin [17]. We provided the most important details on this subject that included abnormal MEs to block differentiation [18-20]; chemo-surveillance as the nature's creation of allosteric regulation to ensure perfection of wound healing [5, 21-23]; DIs, which are metabolites capable of eliminating telomerase from abnormal MEs, and DHIs, which are metabolites capable of inhibition of MEs, as wound healing metabolites and as the active players of chemo-surveillance [5, 21-23]; hypomethylation of nucleic acids as the most critical mechanism for the induction of terminal differentiation of cells with abnormal MEs [24]; the mechanism of wound healing to involve the proliferation and the terminal differentiation of PSCs [25-27]; and the evolution of CSCs from PSCs due to wound unhealing [9, 28, 29]. Studies above described are very convincing that cancer is caused due to the failure of wound healing.

Our carcinogenesis studies strongly supported the validity of these findings. During the challenge with hepatocarcinogen, numerous tiny hyperplastic nodules appeared before the appearance of large size carcinoma, which displayed abnormal MEs [30]. These hyperplastic nodules must represent proliferation of PSCs in the process of active repair. Most of these hyperplastic nodules disappeared, indicating completion of wound healing, and only a few large size carcinomas appeared later, which must be derived from the tiny hyperplastic nodules failed to heal. If Antineoplaston A10 was provided during the challenge with hepatocarcinogen, development of carcinomas could be prevented [31]. Antineoplaston A10 is phenylacetylglutamine which is an effective anti-cachexia agent to protect the integrity of chemo-surveillance [21]. Our carcinogenesis studies strongly support the evolution of cancer due to wound unhealing. Then the right approach of cancer therapy should employ pro-wound healing strategy. A right approach is essential to the success to put away any challenge, including illness. Cytotoxic agents create more wounds that is a wrong approach of cancer therapy. A wrong approach cannot solve anything even a very simple matter. By employing a wrong approach of anti-wound healing therapy, cancer establishments turn a simple wound unhealing problem to become an unsolvable problem.

2.3 Mechanism of Wound Healing

Wound healing comes naturally. So, nobody cares how wound is healed. Take surgical wound for example, suture and antibiotics are subsidiary to speed up the wound healing and to prevent infections that may interfere with wound healing. The treatments have nothing to do with wound healing. Wound healing requires the proliferation and the terminal differentiation of PSCs. PSCs are the most primitive pluripotent stem cells to give rise to organ or tissue during the embryonic development of the fetus. A small amount of these cells, usually less than 2% of the mass, are reserved in the organ or tissue for future expansion or repair. Wound triggers biological and immunological responses. The biological response involves the release of arachidonic acid (AA) from membrane bound phosphatidylinositol for the synthesis of prostaglandins (PGs), which are important for wound healing [32] to trigger edema for the extravasation of inhibitors such as DIs and DHIs for PSCs to proliferate. Since PGs are unstable metabolites, the final act of terminal differentiation of PSCs must be achieved by chemo-surveillance functioning as allosteric regulators to destabilize abnormal MEs. Therefore, we believe the synthesis of PGs is to facilitate the proliferation of PSCs, and the final act of wound healing is the terminal differentiation of PSCs to give rise to damaged components, which is the most critical mechanism of wound healing [24]. Terminal differentiation of PSCs depends on the integrity of

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chemo-surveillance [5, 21-23]. If the chemo-surveillance is functioning perfectly, wound healing comes naturally. If the chemo-surveillance is not functioning perfectly, then the troubles may ensue, that can be tissue fibrosis, dementia, organ failure and cancer. The nature creates chemo-surveillance to prevent such disastrous consequences from happening.

Wound healing is an important health issue, so that the nature creates chemo-surveillance to ensure perfection of wound healing. Chemo-surveillance was a term we created to describe a natural defense mechanism against cancer, which was based on the observation that healthy people could maintain a steady level of metabolites active as DIs and DHIs, whereas cancer patients tended to show deficiency of such metabolites [21]. We have identified acidic peptides, AA, membrane fragments containing AA as the major DIs [33-37], and uroerythrin, pregnenolone, steroid metabolites, amino acid derivatives and fatty acid derivatives as the major DHIs [35, 38-41]. Active DIs and DHIs are degradative products of erythrocytes and metabolites of organs involved in steroid metabolism. Healthy people can maintain a steady level of DIs and DHIs. The steady level of DIs and DHIs may be disrupted under pathological conditions which trigger the production of TNF to display cachexia symptom. A manifestation of cachexia symptom is excessive urinary excretion of low molecular weight metabolites due to membrane hyperpermeability caused by TNF [42, 43]. DIs and DHIs are among low molecular weight metabolites excreted. In general, pathological conditions resulting from wound, toxic chemicals, infections and inflammatory responses are at a risk of causing damage to chemo-surveillance. The collapse of chemo-surveillance is a contributing factor of wound unhealing. The host will respond by forcing PSCs to proliferate. The contact inhibition prohibits the proliferation of PSCs beyond the damaged space. The pressure will be put on PSCs to evolve into CSCs to escape contact inhibition. It takes a single hit to silence TET-1 enzyme to turn PSCs into CSCs that is within the reach of PSCs equipped with abnormally active MEs. The problem of wound unhealing is due to the collapse of chemo-surveillance. The proliferation of CSCs still cannot heal the wound. More pressure will set in to force slow growing CSCs to progress to faster growing CCs by chromosomal translocations to activate oncogenes, or deletions to inactivate suppressor genes. The build up of PSCs unable to undergo terminal differentiation is the cause of tissue fibrosis, such as white lung due to COVID-19 infection, or hepatic cirrhosis due to hepatitis. Dementia is caused by toxic peptide amyloid beta, analogous to TNF to result in wound unhealing. For the therapy of tissue fibrosis, application of suitable amount of phenylacetylglutamine, which is an effective anti-cachexia chemical [21], and a preparation of CDA-CSC made up by ED_{50} of AA and $2xRI_{0.5}$ pregnenolone [11, 13, 35] can be very effective. Dementia is a tough medical problem as difficult as cancer. More studies will be needed to come up a good solution. For the therapy of cancer, an additional CDA-CC made up by ED_{50} of BIBR1532 and $2xRI_{0.5}$ of pyrvinium pamoate [11, 13, 35] may be needed to provide a satisfactory result. Natural DIs and DHIs are good for the therapy of PSCs and CSCs since they are the partners of PSCs and CSCs to carry out wound healing. PSCs and CSCs are protected by drug resistance mechanism, non-natural chemicals may be rejected. Fast growing CCs are known to express a high level of degradative enzymes to salvage natural metabolites as the substrates for macromolecular syntheses in order to support their faster growth. Natural metabolites may be rapidly degraded to lose biological activities. Non-natural drugs are a better choice for the therapy of CCs.

2.4 Restoration of Chemo-surveillance as a Top Priority to Save Cancer Patients

DIs and DHIs are wound healing metabolites and are also the active players of chemo-surveillance. Cancer evolves as a consequence of the collapse of chemo-surveillance. DIs and DHIs are hydrophobic metabolites that can be retained by C18 and eluted from C18 with 80% methanol. Acidic peptides are very active DIs. Not all peptides are active as DIs. But peptides share physical-chemical properties similar to most active DIs and DHIs. Therefore, peptides can be used as surrogate molecules to represent CDA, a

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term to designate DIs and DHIs, levels of plasma and urine. We have carried out quantitative analyses of plasma and urinary peptides of healthy people and cancer patients by initial peptide purification through C18 cartridge as above described, and then resolved peptide profile through HPLC on a column of sulfonated polystyrene and ninhydrin reaction. Quantitative data were computed by integrator. As presented in Table 1, Only 2% of cancer patients showed CDA level as high as 5.0 as the healthy people, and only 25% of cancer patients showed CDA levels above 3.0. We assume CDA 3 is a critical level to account for the responsiveness to cytotoxic therapy. Above CDA3, patients may have chance to be cured. Below CDA3 patients may not have chance to be cured. But if the therapy is carried out by CDA formulations, all patients can respond positively to a full recovery. Evidently, the progression of cancer drives CDA levels to decline, since cancer growth and inflammatory conditions contribute to cachexia symptom to cause the decline of CDA levels. Therapy with cytotoxic agents accelerates the decline of CDA levels. We believe boosting CDA levels can benefit cancer therapy, even the therapy is carried out with cytotoxic agents [5]. CDA -2 was a preparation of wound healing metabolites purified from freshly collected urine [44], which was approved for cancer therapy by the Chinese FDA based on its ability to boost CDA levels to enhance therapeutic efficacy of cytotoxic chemotherapy and to greatly improve quality of life of cancer patients [45]. CDA-2 is a drug effective to eliminate CSCs by induction of terminal differentiation, the critical mechanism of wound healing. The ability to eliminate CSCs is an absolute requirement of good cancer drugs.

Table 1: Plasma/Urine Peptide Ratios of Cancer Patients

Plasma/Urine	CDA Peptide Ratios	No. of Patients Levels	% Distribution
0.8 - 0.83	5.0	2 (Normal)	1.8
0.6 - 0.8	4.3	7	6.5
0.4 - 0.6	3.1	18	16.7
0.2 - 0.4	1.8	38	35.2
0.1 - 0.2	0.9	24	22.2
0.02 - 0.1	0.4	19	17.6

Plasma Peptides: nmoles/ml; Urine Peptides: nmoles/mg creatinine

2.5 Abnormal MEs as the Most Critical Issue of Cancer

Perpetual proliferation of CCs is the most outstanding feature of cancer. Abnormal MEs and the collapse of chemo-surveillance resulting in the blockade of differentiation is an important factor.

Another important factor is the activation of oncogenes or the inactivation of suppressor genes. Abnormal MEs is due to the association of telomerase with MEs [20], that happens on PSCs, the precursors of CSCs, and passes on to CSCs and then to CCs. This abnormality is universal to all cancers [19]. The activation of oncogenes or the inactivation of suppressor genes happens quite late during the evolution of cancer. The abnormalities are variable among different cancers. A solution of abnormal MEs is applicable to all cancers. Once abnormal MEs is solved, the solution can also put to rest chromosomal abnormalities which are otherwise very difficult to solve. Oncogenes and suppressor genes are cell cycle regulatory genes, which have very important roles to play when cells are in cell cycle replicating. If the replicating cell is diverted to undergo terminal differentiation through destabilization of abnormal MEs to exit cell cycle, then abnormal chromosomal abnormalities have no roles to play. Chromosomal abnormalities are variable and the solution is extremely difficult. Even a difficult chromosomal abnormality is solved, there may soon pop up another chromosomal abnormality. Development of unresponsiveness is a frequent problem of

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targeted therapy. It is an endless efforts trying to put away all chromosomal abnormalities. Even all chromosomal abnormalities can be put away, the problem of abnormal MEs remains unsolved. We considered abnormal MEs as the most critical issue of cancer [46], which are the bullseye for targeted therapy [47]. If the problem of abnormal MEs is fixed by CDA formulaions, the remission can last life time. Remission achieved by cytotoxic agents frequently recurs in a short while.

MEs are a ternary enzyme complex consisting of methionine adenosyltransferase (MAT) methyl-transferase (MT) - S-adenosylhomocysteine hydrolase (SAHH) [48]. MEs maintain enzyme complex on gel filtration and sucrose density sedimentation, but dissociate into individual enzymes upon DEAE-agarose chromatography. Individual enzymes display sedimentation values as 4S for SAHH, 5.5S for MT and 6S for MAT.

SAHH is a steroid hormone receptor, which is the most unstable enzyme of the three, requiring steroid hormone or related molecules to assume stable configuration to form dimeric enzyme complex with MT, MT-SAHH dimer displays a sedimentation of 6S similar to that of MAT. A ternary enzyme complex is formed between MAT and MT-SAHH dimer. Thus, MEs are under the allosteric regulation of steroid hormone to form stable and active ternary enzyme complex and become inactive as dissociated individual enzymes in the absence of allosteric regulators. MTs in the individual enzyme state have the tendency to be modified to become nucleases which can trigger apoptosis to cause organ involution.

MEs play a pivotal role on the regulation of cell replication and differentiation by virtue of the fact that DNA methylation controls the expression of tissue specific genes [49], and pre-rRNA methylation controls the production of ribosome [50], which in turn dictates the commitment of cell to initiate cell replication [51]. If enhanced production of ribosome is locked in place, it becomes a factor to drive carcinogenesis [52].

Because of such pivotal role, MEs are subject to exceptional double allosteric regulations: one on the individual enzymes and one on the enzyme complex. On the individual enzymes, SAHH is allosteric regulated by steroid hormones or related allosterically regulators as above described. In telomerase expressing cells, MEs become associated with telomerase [20]. The association with telomerase changes kinetic properties of MEs and the regulation to tilt in favor of growth. K_m values of the telomerase associated MAT-SAHH isozyme pair are 7-fold higher than the normal isozyme pair. The increased K_m values suggest that telomerase expressing cells have much larger pool sizes of S-adenosylmethionine (AdoMet) and S-adenosylhomocysteine (AdoHcy). A larger pool sizes of AdoMet and AdoHcy is important for the build up of cells with abnormal MEs to conduct their biological functions. It has been shown by Prudova et al. [53] that AdoMet could protect protein from protease digestion. Chiba et al. [54] found that pool sizes of AdoMet and AcoHcy shrunk greatly when HL-60 cells were induced to undergo terminal differentiation. Obviously, abnormal MEs play an important role for the build up of cells with abnormal MEs. The build up of normal stem cells with abnormal MEs such as embryonic stem cells and PSCs is important for the development of the fetus or for wound healing. MEs turn abnormal do not seem to create problems for normal primitive cells, because there are mechanisms to limit the build up to become problematic, mechanisms such as contact inhibition, TET-1 enzyme to direct lineage transitions, and chemo-surveillance to keep a check on abnormal MEs. Problems arise when these safety mechanisms become dysfunctional [21, 23, 25-27, 55, 56]. Restoring the safety mechanisms on abnormal MEs is obviously the best strategy to save cancer patients.

2.6 Screening of Good Cancer Drugs via MDS

MDS are diseases to display the evolution of CSCs from PSCs by a single hit to silence TET-1 enzyme to allow building up of CSCs unable to undergo terminal differentiation. They are a typical case of intermediary cancer, namely cancer at the stage of CSCs.

MDS often start with a display of an immunological disorder [57], which prompts the production of immunological cytokines. Among

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such cytokines, TNF is the most critical factor related to the development of MDS [58]. It causes excessive apoptosis of bone marrow stem cells, thus severely affecting the ability of the patient to produce hematopoietic cells such as erythrocytes, platelets and neutrophils. TNF is also named cachectin after its effect to cause cachexia which is responsible for the collapse of chemo-surveillance to result in the evolution of CSCs from PSCs. The propagating cells of MDS have been identified as human CSCs [59]. So, MDS are diseases due to wounds triggering immunological disorder which are not healed to result in the evolution of PSCs to become CSCs. The therapy of MDS is obviously to turn CSCs to functional erythrocytes, platelets and neutrophils, that requires the critical mechanism of wound healing to efficiently promote terminal differentiation of PSCs and CSCs. The killing of CSCs, which is the choice of cancer establishments, cannot cure MDS. Besides, killing of CSCs is a task that cannot be easily done. So far, Vidaza, Decitabine and CDA-2 are the three drugs approved for the therapy of MDS. Professor Jun Ma, Director of Harbin Institute of Hematology and Oncology, was instrumental to conduct clinical trials of these three drugs for the Chinese FDA to approve. Vidaza and Decitabine were also approved by the US FDA. According to Professor Ma, based on two cycles of treatment protocols, CDA-2 had a slightly better efficacy based on cytological evaluation, and a markedly better efficacy based on hematological improvement efficacy, namely no longer dependent on blood transfusion to stay heathy, as shown in Figure 1 [60]. The therapy of MDS by these three drugs is based on the inactivation of abnormal MEs, CDA-2 by the elimination of telomerase from abnormal MEs, and Vidaza and Decitabine by inducing covalent bond formation between methyltransferase and 5-azacytosine incorporated into DNA [61]. CDA-2 exercises a selective action on cancer MEs, whereas Vidaza and Decitabine titrate out MEs non-selectively. Adverse effects of Vidaza and Decitabine include induction of cancer [62, 63], and toxicities to DNA [64-66]. CDA-2 is devoid of serious adverse effects. Drugs effective against MDS are good cancer drugs that can induce CSCs to undergo terminal differentiation

Drugs ineffective against CSCs are bad cancer drugs. MDS can be used to screen good cancer drugs. Evidently, CDA-2 is a perfect good cancer drug. Vidaza and Decitabine are imperfect good cancer drugs because of toxicities as nucleoside analogs.

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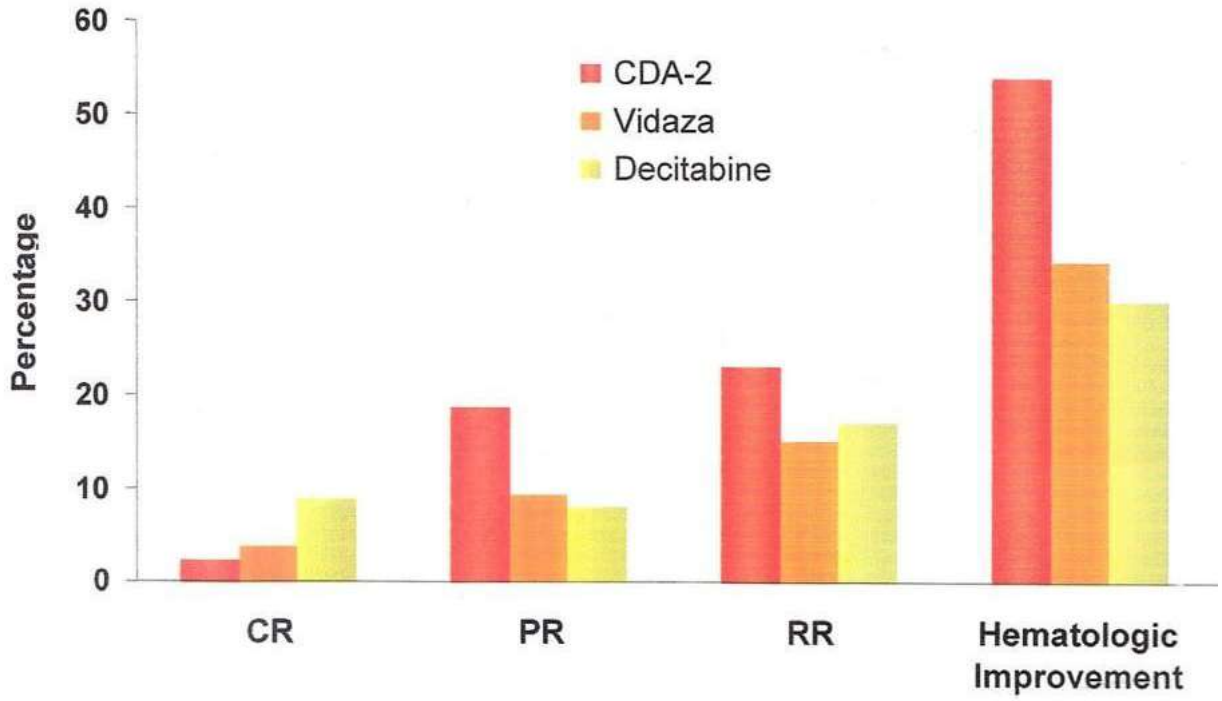

Figure 1: A Comparison of Therapeutic Efficacy of CDA-2, Vidaza and Decitabine on MDS

III. CONCLUSION

A good cancer drug must be able to take out both CSCs and CCs, and to restore chemo-surveillance. MDS are diseases attributable entirely to the propagation of CSCs, which are ideal for the screening of good cancer drugs. Only drugs able to inactivate abnormal MEs can offer therapeutic effects on MDS. CDA formulations are the best choice as good cancer drugs.

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