

Cancer Prevention versus Cure: What is our Best Option?

Petrak K*

Nangio Tx Incorporated, USA

***Corresponding author:** Karel Petrak, NangioTx Incorporated, 1180 Raymond Blvd, Newark, NJ 07102, USA, 4113, Tel: 06786131386; Email: klpetrak@gmail.com

Perspective

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Abstract

Huge resources are being expended in search of cancer therapies, with a limited success. Cancer is believed to originate from an irreversible genetic alteration which is a part of both normal and abnormal biological processes. It is questionable whether such essential biological behavior can be put under our sufficient control to cure cancer.

Given that events leading to cancer development appear to be too complex to be successfully manipulated by drug therapies, initiatives to “cure cancer” should be reevaluated and reconsidered, with a likely anticipated conclusion that taking steps to limit cancer initiation might be more cost-effective, and hence focus research efforts on measures to prevent rather than cure cancer.

Keywords: Cancer Prevention; Cancer Therapy; Cancer

Abbreviations: NCI: The National Cancer Institute.

Introduction

The rate of dying from cancer in the US has declined steadily over the past two decades. During the last ten years for which data are available, the rate of new cancer diagnoses decreased by about 2% per year in men and remained about the same in women [1]. The drop in cancer mortality is mostly due to steady reductions in smoking and not to improved early detection and treatment.

Much money and effort has been expended in the USA on fighting cancer starting with President Nixon’s War on Cancer launched in 1971. Over subsequent forty years, the country spent some \$500+ billion in supporting it [2]. The National Cancer Institute (NCI) received \$5,214 billion in 2016, and \$5,389 billion in 2017 [3]. US nonprofit organizations raised some \$2.2 billion for cancer research and treatment [4].

In his 2016 State of the Union address on 12 January 2016, United States President Barack Obama, referring to America curing cancer, stated: “Tonight, I’m announcing a new national effort to get it done. ... For the loved ones we’ve all lost, for the family we can still save, let’s make America the country that cures cancer once and for all.” Not surprisingly, no inkling was offered as to how this could be achieved, referring to the approach as a “new moonshot”.

So, what is the way forward?

Accumulated wisdom warns against activities without clearly stated directions. For example, “If you don’t know where you are going, any road will get you there.” (Lewis Carroll); “If you don’t know where you are going, you might wind up someplace else.” (Yogi Berra); “If you do not know where you come from, then you don’t know where you are, and if you don’t know where you are, then you don’t know where you’re going. And if you don’t know where you’re going, you’re probably going wrong.” (Terry Pratchett)

The last statement relates well to Precision Medicine Initiative activities given the current state of knowledge of the process by which cancer undergoes initiation, promotion, and progression. Cancer is believed to originate from an irreversible genetic alteration, such as one or more simple mutations, transversions, transitions or small deletions in DNA [5] caused by initiators. Mutations are a part of both normal and abnormal biological processes such as evolution, the development of the immune system pattern recognition, and also cancer [6]. Can such essential biological behavior be put under our sufficient control to prevent or cure cancer? Very likely not against such background it seems obvious that the heavily funded cancer research lacks an effective direction for advancing precision medicine.

Current understanding of how cancer develops [6] can be summarized very briefly as follows:

Initiation: The effects of initiators are irreversible; once a particular cell has been affected by an initiator it is susceptible to promotion until its death. Since initiation is the result of permanent genetic change, any daughter cells produced from the division of the mutated cell will also carry the mutation [7].

Promotion: Once a cell has been mutated by an initiator, it is susceptible to the effects of promoters. These compounds promote the proliferation of the cell, giving rise to a large number of daughter cells containing the mutation created by the initiator [8]. Promoters have no effect when the organism in question has not been previously treated with an initiator [9]. The effect of promoters on tumor growth is typically dose-dependent [9]. It has been shown in mice that repeated promoter applications on the skin previously exposed to initiator produces benign papillomas. Subsequent stepwise transformation generating additional, spontaneous, mutations advance a benign tumor to a neoplasm and to malignancy accompanied by an increased growth rate, invasiveness, metastasis and an alteration in biochemistry and morphology [10].

Does any of this offer a path to cure? It does not appear so.

As it is, despite new scientific knowledge being gathered at a research level, clinical progress towards developing new therapies remains fairly conventional, relying on established practices and regulatory guidelines. According to Norman E. "Ned" Sharpless, MD, director of the National Cancer Institute [11], "Clinical trials are really important. It's how we make progress

against a certain kind of cancer. We have an idea. We think a new therapy or a new way of treating a cancer will work and help the patient, but we're not sure it will yet. So, we have a means by testing new ideas and new therapies in patients through the clinical trials machinery. And that's really how we make progress in cancer." "...the idea is that by doing a clinical trial, we can do better than the standard of care or therapy for that disease." ..." So, the potential benefit for the patient is that they ... could be cured of their cancer."

In some specific areas of cancer treatment, good progress has been made, for example in treating breast tumours and hematological malignancies. However, the field of cancer research needs to start paying attention to obvious conclusions that can be drawn from the lack of progress in developing new, effective therapies. As observed by Park [12], money spent on cancer research is largely going towards a worthy cause; however, is that money being converted into effective cancer treatments? In his view, the field have made great strides in understanding the nature and behavior of cancer cells, but using that information to design and validate effective and reliable treatments is proving to be much more difficult than expected. Reality remains that, despite receiving billions of dollars in funding and after conducting countless expensive and lengthy drug clinical trials, scientists have yet to develop anything that can even get close to curing the disease. A 2017-published report [13] informs that two-thirds of all cancer drugs that were approved in the past two years showed no evidence of extending survival at all; if true, this is very disappointing. In comparison, the death toll from heart disease has decreased significantly over the past several decades; during the time between 1950 and 2005, the death rate of heart disease dropped by 64%. In contrast, during the same time period, the death rate for cancer fell by only 5% [14].

There has been too much hype featuring heartwarming stories of cancer patients being saved miraculously by revolutionary new treatments that will stop cancer in its tracks. Such as CAR-T therapy; it is not often mentioned that it can be incredibly dangerous as it "needs to bring your body to the brink of death in order to save you" [15].

Perhaps there is a lesson to be learned from this. Less hype, more specific research directions, more academic collaboration than competition, better validation of early, preliminary results, and more focus on precision drugs might be considered, with and an extensive use of hyperintelligent digital intelligence being employed. And here is an idea: treating cancer is a complicated and expensive business. Why not introducing an approach

that the charge made to patients is scaled accordingly to how well the drug has worked? As Dr. Otis Brawley, the chief medical officer at the American Cancer Society, explained, "We have a lot of patients who spend their families into bankruptcy getting a hyped therapy that [many] know is worthless... [Some choose a medicine that] has a lot of hype around it and unfortunately lose their chance for a cure" [16]. Many scientists have adopted the hype mindset, often inflating the successes of their research so that it appeals to investors. In 2003, Dr. Andrew von Eschenbach, the director of the National Cancer Institute, announced the possibility of "eliminating suffering and death due to cancer by 2015" [17-19]. MD Anderson logo on buses and buildings, with "Cancer" crossed out in red, and claiming to be "Making cancer history", is another example of a conveniently adjusted truth.

Precision Medicine and Precision Drugs

I argued on several previous occasions that unique molecular structures associated with a given disease need to be identified to which precision drugs could be targeted [20-22]. This approach is likely relevant for many diseases, but could it ever work for cancer? The whole approach to precision medicine and its expected and desired outcomes needs to be reviewed [23]. Several technical terms, formerly personalized medicine, now precision medicine, or theranostics are being used currently in healthcare that refer to practice of tailoring disease treatment to each individual patient. The idea is apparently not that new as it dates back to Hippocrates [24]. The difference is that today we have much more information including that of genetic nature to collect from individuals to create an extensive database on the basis of which to make medical-treatment decisions. How exactly is such information to be used without having new, more effective treatment approaches also available has not yet been made clear.

Calling an initiative a different name helps it to start afresh (just like calling drug-delivery macromolecules and particles "nanomaterials". Because of another hype, it somehow makes an unfamiliar reader more likely to believe that a "nanomaterials" will in themselves solve the old problems [25]. Precision medicine faces the same numerous obstacles that personalized medicine did not overcome in the past [26,27]. There is a long list of items to consider and put in place: insufficient clinicians' knowledge; lack of funding to develop diagnostics, therapies, and drugs; training of test providers; education of payers about the data; intellectual property protection; incentives for reimbursement structure; appropriate

regulatory framework; manufacturing readiness; lack of data demonstrating clinical efficacy, safety and reliability, etc. It is not clear how information alone gathered by precision-medicine efforts would cure cancer.

Conclusion

Given that events leading to the initiation and subsequent development of cancer appear to be too complex to be successfully manipulated by drug therapies, initiatives to "cure cancer" should be reevaluated and reconsidered, with a likely anticipated conclusion that taking steps to limit cancer initiation might be more cost-effective, and hence focus on measures to prevent rather than cure cancer. Appropriate steps should be taken vigorously and effectively to remove from our environment (the air, water, food supply, etc.) pollutant that have been identified as initiators and promoters of biological pathways that lead to cancer.

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