Combinations of therapy to substantially reduce cancer deaths

natpernickshealthblog.wordpress.com/2021/06/23/combinations-of-therapy-to-substantially-reduce-cancer-deaths/

June 23, 2021

23 June 2021

Our **strategic plan** aims to reduce annual US cancer deaths from 600,000 projected in 2021 to 100,000 by 2030. The war on cancer, now 50 years old, needs a specific goal and time frame to focus our efforts. This echoes the challenge in 1961 from President John F. Kennedy to land a man on the moon by the end of that decade (**President Kennedy Challenges NASA to Go to the Moon**, 1961 at 1:09).

The “moonshot” is often used as an inspiration to utilize our collective brainpower and other talents to find a “cure” for cancer:

The time has come in America when the same kind of concentrated effort that split the atom and took man to the moon should be turned toward conquering this dread disease. Let us make a total national commitment to achieve this goal. **President Nixon’s 1971 State of the Union at 15:03**.

Successful cancer treatment may be analogous to the moon landing, but only if we consider that the moon landing was due not to a single breakthrough, but combinations of technological and scientific advances related to all aspects of the flight. Similarly, success at reducing cancer deaths will require a range of therapies directed at all aspects of the malignant process, as well as efforts to reduce risk factor exposure and improve screening.

This essay introduces our strategy of using combinations of therapies directed at all aspects of the malignant process, appropriate for each cancer type, to substantially reduce cancer related deaths. This strategy is based on the understanding that cancer is the result of intersecting webs of biological activity for the cancer cells, their microenvironment and systemic networks affecting the cancer. Effective treatment must damage the end result of these webs sufficiently so that their overall malignant properties cannot continue. This typically cannot be achieved by a single drug, for several reasons. First, one drug may break only one strand of one web and can be readily bypassed through alternative pathways. For example, childhood cancers have an uncomplicated origin due to inherited or constitutional cancer predisposition or developmental mutations that may only activate a single pathway. Yet single drug treatment for childhood leukemia invariably fails – it initially kills most cancer cells but they return through activation of alternative pathways. Successful therapy requires combinations of 3-5 drugs with different mechanisms of action (**Curing Cancer Blog – Part 2 – Adult versus childhood cancer, 2020**). Second, adult cancers have a complicated origin because they originate from mutations in many cells caused by multiple risk factors

acting over long periods. Thus, adult cancers need additional combinations of treatment that target the more diverse primary cancer, the cancer cell microenvironment and the systemic networks that nurture and promote cancer growth.

For each specific cancer type, we propose that successful treatment is possible using combinations of therapies with some demonstrated impact on the attributes of the malignant process listed below. Although no therapy may individually eradicate the cancer, combinations of these partially effective therapies may damage the related biologic webs sufficiently to lead to prolonged patient survival. Subsequently, we can refine these preliminary successes to further improve survival and reduce side effects (see **Curing Cancer Blog – What will success look like in the war on cancer? 2021**). We propose creating a summary for each cancer type of its cancer related attributes and known therapies for use by oncologists to create combinations to test – click **here** for the current summary for pancreatic adenocarcinoma.

These are the general malignant attributes to target, which must be refined for each cancer type:

Malignant attributes of the primary cancer, including rapid cell growth, cell migration, resistance to apoptosis, immature phenotypes; driver mutations and their networks, networks promoting unicellular type programming; resistance to disruptions to their cancer attractor states that prevent changes to their malignant phenotypes.

Features of the microenvironment that sustain the cancer, including inflammation, vasculature, stroma and the extracellular matrix.

Associated systemic networks which promote cancer growth, including chronic inflammation, immune system dysfunction and hormonal production (estrogens, androgens and insulin) (**Curing Cancer Blog – Part 8 – Strategic Plan, 2021**).

Germline variations of genes promoting the above features.

Patients can only tolerate a limited number of therapies at one time. Determining which combinations of therapies work optimally together and how to administer them will require extensive clinical trials, although deep learning and other computational approaches may be helpful (**How Pancreatic Cancer Arises, Based on Complexity Theory, 2021**).

We also need to better understand, treat and minimize **cancer deaths occurring shortly after diagnosis**, whether due to treatment side effects, infections or severe disruptions to important physiologic systems (**Curing Cancer blog – part 9 – How cancer kills, 2021**).

To improve survival for cancer types typically associated with longer survival, we should also promote behavior changes in patients to reduce risk factors for additional cancers. To reduce the incidence of cancer in general and promote better patient care, we need to optimize our public health system. A well run public health system acts as a behavioral immune system to

prevent many lethal cancers from arising through risk factor reduction and earlier detection (**How Pancreatic Cancer Arises, Based on Complexity Theory, 2021**). It also optimizes patient health through equitable and adequate access to medical care.

To have the greatest impact on reducing cancer deaths, we should initially focus on lung cancer, pancreatic cancer and advanced cancers of the colon and breast, which are the leading causes of US cancer death (**Curing Cancer blog – What will success look like in the war on cancer? 2021**).

This strategic plan focuses on the common goal of physicians and scientists worldwide to substantially reduce cancer deaths. Its implementation will take continued hard work, the ability to admit our failures and learn from them and the need to overcome the limitations of institutional thinking. But we can succeed:

“We choose to go to the moon. We choose to go to the moon in this decade and do the other things, not because they are easy, but because they are hard, because that goal will serve to organize and measure the best of our energies and skills, because that challenge is one that we are willing to accept, one we are unwilling to postpone, and one which we intend to win, and the others, too. (“**Why go to the moon?” – John F. Kennedy at Rice University**, at 9:38).