Curing Cancer – Part 3 – Curative cancer treatment based on complexity theory

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This is my third essay about curing cancer using the principles of complexity theory. It outlines my recommendations for curative treatment for advanced adult cancers with a poor prognosis, such as lung and pancreatic cancer.

Curative treatment should address the following principles:

I. Network medicine. Adult cancer is a systemic disease. It arises and is maintained due to dysfunctional cellular networks, not just mutated genes. Advanced disease is due to an altered systems biology (**Koutsogiannouli 2013**) with changes in networks beyond the tumor that typically will not revert to normal if the tumor is destroyed. Thus, focusing on "network medicine" is mandatory (**Barabási 2011**).

In contrast, cancer in children and young adults may not be a systemic disease because it is due to inherited or developmental mutations that primarily affect only the tumor cells (**Kentsis 2020**). Unlike adult cancer, it is not due to risk factors and there may be minimal involvement of the inflammatory system, immune system and hormonal pathways (**Curing Cancer – Part 2**).

II. Blocking multiple pathways. Disabling the activity of a dysfunctional network often requires drug combinations because networks interact in a weblike manner and can readily bypass a single block in a particular pathway. For cancers of children and young adults, curative treatment typically requires at least 3 to 5 drugs to block pathways sufficiently to disrupt the cancer network (**Mukherjee: The Emperor of All Maladies 2010**).

III. Combinations of combinations of treatment. Since adult tumors are due to dysfunction in many key systemic networks (see below), each often requiring a different set of combinatorial therapies, curative therapy may involve combinations of combinations of treatment.

IV. Monitoring key networks. To optimize treatment, it is important to monitor the status of these key networks as treatment is given: the inflammatory process in general, the immune system's antitumor capabilities, the tumor's microenvironment, unicellular type networks that promote malignant properties, embryonic networks that promote lack of cell differentiation, hormonal expression that promotes tumor growth and inherited changes that promote malignant behavior. For each of these networks, we must determine what biological molecules to monitor, how best to do so, how changes in their expression should affect treatment and how these values will impact long term survival rates.

V. Clinical trials. Extensive clinical trials will be needed to determine the effectiveness of individual treatments, combinations of treatments and combinations of combinations of treatments against these key networks, as well as their effect on tumor growth and long term survival rates. Additional studies will determine how to reduce side effects and what adjustments to make for particular patients. Towards this end, every cancer patient should be enrolled in a clinical trial, a major change in the status quo.

VI. Public health and preventative programs. A curative treatment program should attempt to reduce personal behavior that promotes malignancy, such as tobacco use, excess weight and alcohol abuse; develop better screening programs to identify premalignant or malignant lesions in both high risk patients and current cancer patients being monitored for relapse; and promote strong public health programs that encourage risk factor reduction and ensure that all patients get adequate medical care.

Key network issues to be addressed by curative treatment are:

1. Kill as many tumor cells as possible.

2. Attack multiple targets within local tumor cell networks.

3. Move local tumor cell networks into less lethal pathways.

4. Disrupt the inflammatory process, which plays a central role in promoting and sustaining carcinogenesis.

5. Disrupt the microenvironment that nurtures tumor cells at primary and metastatic sites.

6. Disrupt the microenvironment that promotes an embryonic phenotype in some tumors, which is associated with aggressive tumor behavior.

7. Repair immune system dysfunction that coevolves with carcinogenesis.

8. Promote the activation of gene networks supporting stable, multicellular processes and suppress networks promoting unicellular processes that support malignant type behavior.

9. Antagonize hormonal expression that promotes tumor growth.

10. Antagonize inherited genetic changes that promote malignant behavior.

Future essays will discuss these principles and network issues in depth.