

Cancer is One Disease



It is commonly stated that cancer is hundreds or even thousands of different diseases. Each major type of cancer has its own experts, advocates, organizations, funding and dogmas. At one level, there is no doubt that every patient's cancer is different. It is probable that every cancer cell is different from all other cancer cells at the genetic and epi-genetic level. However, the widely accepted assumption that cancer is hundreds of different diseases is false. The widely accepted notion that a unique set of drugs will be required for each patient's cancer is false. [i]

Tumor cell evolution implies that cancer is essentially one disease.

All types of cancer involve evolutionary populations of malignant cells

The starting point for tumor cell evolution varies depending upon the origin of the tumor stem cell. It is different for breast versus prostate cancer. However, the set of all malignant cells that could potentially evolve in a patient with breast cancer is almost identical to that for prostate cancer. The normal cellular machinery that potentially can carry out malignant behavior, proliferation and invasiveness is essentially the same for all cancers.

If we ask the question what can be known about the sets all malignant cells that could evolve in a patient with breast cancer and in a patient with prostate cancer, the answers would be almost exactly identical. [ii] This holds true for all solid cancers. In this respect cancer is one disease.

This does not imply that the normal cellular machinery actually expressed by all cancers is identical. It is not. Differences are well known and commonly observed. The normal cellular machinery that carries out proliferation and invasiveness varies between different cancer cells within a patient. In addition there are differences between different types of cancer.

For example, some cancers strongly express urokinase, a protein involved in invasiveness. Others do not. However, on closer analysis, urokinase "positive" cancers will generally be

found to have malignant cells that lack urokinase. In addition, urokinase “negative” cancers can evolve urokinase positive malignant cells. Under the appropriate selective pressures traits expressed by one cell out of billions can become dominant in the cancer cell population.

If a particular set of normal proteins can carry out malignant behavior in one type of cancer, in general this implies a clinically significant probability that malignant cells can evolve that use the same set of proteins to carry out malignant behavior in any type of cancer.

The genes that encode normal proteins are ordinarily present in all cells of the body [iii] Genetic and epi-genetic alterations that turn on or off existing genes are relatively common in cancer. By relatively common we mean the probability is greater than one out of every trillion cell divisions (10^{-12}). Your chances of winning the state lottery are about a million times greater. However, when thinking about cancer you need to re-calibrate your idea of what is probable. A patient with cancer can have a trillion cells, so extremely rare events can matter. If genetic and epi-genetic alterations can turn on a particular gene in prostate cancer, it is likely that the same can occur in breast cancer cells or any other type of cancer cell.

There is extensive data on aberrant expression of proteins in cancer cells. For example, breast cancer cells have been described that produce significant levels of prostate specific antigen (PSA), [1] while the production of high levels of the hormone prolactin have been described by prostate cancer. [iv] [2] The evolution of new functional machinery is an extremely low probability event. By contrast, turning on the production of cellular machinery that is already encoded with the human genome is a high probability event.

Objection:

Granted, excluding the genetic alterations, the DNA of all cells in the body is ordinarily the same. However, there are big **epigenetic** differences.

Response

That is true. However, the aberrant expression of normal proteins is commonly seen in cancer cells. But this misses the point. The point is that we cannot know exactly which proteins are used by *all* cancer cells to carry out malignant behavior. This would require either the examination of *all* cancer cells in the patient, or comprehensive knowledge of the pathways of tumor cell evolution, which is generally not possible.

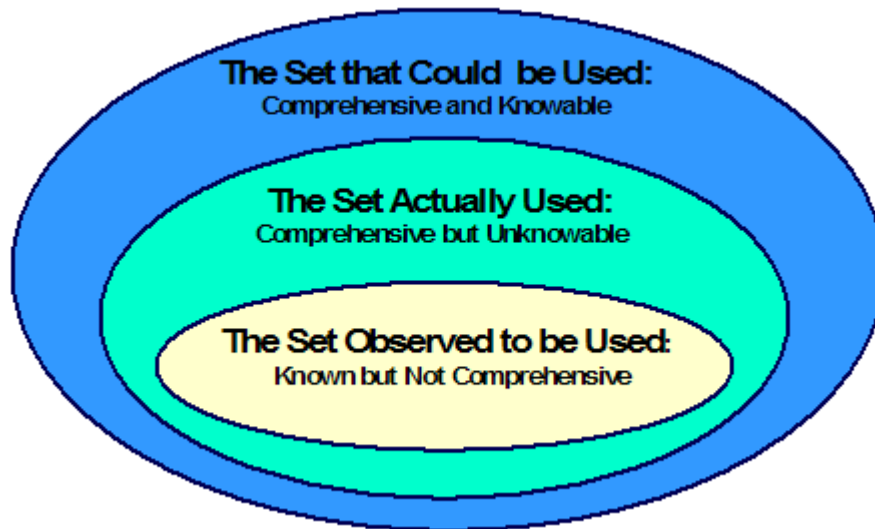
The observation that a *particular* normal protein is present in a sample of a patient’s cancer provides an incomplete and often misleading picture. Since cancer is a diverse evolutionary process, we cannot generalize to all cancer cells in the patient. It is likely that some malignant cells are present, or will evolve in the patient that lack the *particular* protein.

However, the set of normal proteins encoded within the human genome that potentially could carry out proliferation and invasiveness is both limited in size and knowable. All cancer cells that evolve will use elements of this set of normal machinery to carry out malignant behavior. The problem is that we can't know exactly which proteins in the set all malignant cells in the patient will use.

It is important to emphasize that whether or not a particular protein is observed in a patient's cancer cells is totally irrelevant to the specific cure of cancer, unless all cancer cells in the patient are examined. There is no way logically valid way to generalize to unobserved cancer cells.

It is instructive to consider sets and sub-sets of normal proteins that can carry-out malignant behavior as shown in the diagram below:

Sets and Sub-sets of Normal Proteins that Carry Out Malignant Behavior in a Patient



Knowledge of the set of normal proteins that is **Observed to be Used** by cancer cells in the patient is generally incomplete, except in the case of localized disease.

The set of normal proteins that is **Actually Used** in a given patient is comprehensive, but is in general unknowable. This set is a function of the pathways of tumor cell evolution in a patient, which as previously discussed are unknowable.

By contrast the set of proteins that **Could be Used** is both comprehensive and knowable by means of a well-corroborated scientific theory.

To achieve comprehensiveness, it is necessary to target cancer cells based on the set of normal cellular machinery that potentially could carry-out malignant behavior . This set is essentially the same for all solid cancers.

As a consequence cancer is essentially one disease is essentially one disease" .

One set of curative drugs for all cancers

It is difficult to overestimate the practical significance of a unifying theory of cancer in which all solid cancers are the same disease. Tumor cell evolution implies that for a therapy to be able to consistently and specifically cure one type of solid cancer it must be able to cure all types of solid cancer. Models that view cancer as multiple diseases are logically inconsistent with the reality of tumor cell evolution and cannot provide a basis for the consistent and specific cure or control of cancer.

Objection:

"There can be no single cure to cancer because there is no single cause to cancer. In fact, cancer is not a specific disease. It is a sprawling family of altered body states whose members demonstrate so many different traits, backgrounds, and behavior patterns they scarcely seem related." [3]

Response

It is true that there are many different causes for cancer. However, this does not mean that there cannot be a single cure for cancer. Cancer is like a forest fire. Many things can cause a forest fire: lightning; embers from a campfire; an improperly discarded cigarette; spontaneous combustion; a spark; arson. Once the fire is burning it becomes self-propagating. The initial cause is irrelevant to the techniques used to extinguish a forest fire. Similarly, the causes of cancer are irrelevant to the cure cancer. Even if we did know the initial cause of cancer in a patient this would be of little help. We are dealing with a stochastic evolutionary process. Comprehensive knowledge of the causal lesions in a patient with metastatic disease is generally not possible. This means that any therapy that can consistently and specifically cure cancer must be independent of the causes of the disease. Indeed, therapy targeted to specific causes of cancer is destined to fail as new causes evolve in the patient.

Objection:

Testicular cancer is curable 96% of the time, then how come the same drugs don't cure lung cancer?

Response

Current cures for testicular cancer are non-specific. The drugs are extremely toxic. The drugs just happen to be more toxic to testicular cancer cells than to lung cancer cells. This is not at all what we are talking about. We are talking about a set of drugs that could cure testicular cancer without toxicity to normal cells, i.e., a set that achieves both specificity and comprehensiveness. The same set of drugs would also cure lung cancer and all other forms of solid cancers. What could evolve in each case is basically the same.

Footnotes

[i] The leukemias, lymphomas, and so-called "liquid cancer" are different from the solid cancers and will require different drugs to cure. The technology of PRTT can be used to this end.

[ii] This is not exactly true. The normal DNA is different between males and females. Females lack a Y chromosome.

[iii] Unless the genes are lost due to genetic alterations

[iv] Prolactin is normally made in significant amounts by the pituitary gland, breast and uterus.

References

[1] Sauter ER, Klein G, Wagner-Mann C, Diamandis EP; "Prostate-specific antigen expression in nipple aspirate fluid is associated with advanced breast cancer.";Cancer Detect Prev. 2004;28(1):27-31.

[2] Lissoni P, Bignami A, Frontini L, Manganini V, Dapretto E, Gardani GS, Vigano P, Strada G.; "Possible involvement of prolactin in endocrine-resistant metastatic prostate cancer."; Int J Biol Markers. 2005 Apr-Jun;20(2):123-5

[3] Edelhart, M.; Lindenmann, J.; Interferon: The New Hope for Cancer"; 1981, Addison Wesley Publishing Co. Reading, MA.; P.28