A TREATISE ON A PHILOSOPHY OF CANCER

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How sensible is it to try and link human behavior to the way cancer cells conduct themselves?

"Flower in the Crannied Wall"

Flower in the crannied wall,
I pluck you out of the crannies,
Hold you here, root and all, in my hand,
Little flower—but if I could understand
What you are, root and all, and all in all,
I should know what God and man is.
— Alfred, Lord Tennyson

The premise of a philosophy of cancer

A century after the birth of Tomizō Yoshida—the renowned cancer pathologist—I was immersed in an event to commemorate his achievements. In 1929, at 26 years of age, Dr. Yoshida induced liver cancer in laboratory animals, a discovery of central importance to the investigation of chemical carcinogenesis. By age 40, he had discovered a cancer cell line in rats (the so-called Yoshida ascites sarcoma), which has its own characteristic chromosome constitution and multiplies by regular mitosis. It, too, yielded information that is fundamental to our understanding of cancer. His demonstrations of the individuality of cancer cells within populations of cancer cells, regardless of the tumor line, led to a new way of thinking about cancer and to what was, at that time, a new therapy for killing cancer: chemotherapy.

So moved was Dr. Yoshida by his observations of the behavior of cancer at the cellular level that he began to preach about the individuality and diversity of cancer cells. Dr. Yoshida eventually added a philosophical dimension to his thinking, and used eloquent analogies with cancer to explain his outlook on life.

As a pathologist who has peered through a microscope at cancer for more than 40 years, I, too, have witnessed the individuality and diversity of which Dr. Yoshida spoke—and more. Our treatise draws, in part, from Dr. Yoshida's scientific and philosophical standpoint. We also draw from a political philosophy by Shigeru Nanbara, the first post-war president of the University of Tokyo, summarized as: we depend on what the nation addresses by having pursued the validity of it ourselves. Each of us can fathom how we affect our fellow man in society.

How does pathologist become philosopher, beyond just calling himself one? On what grounds should a pathologist think that he could wander into philosophy and make pronouncements about it? Is it somehow any more credible (or any less ridiculous) than a philosopher, after having examined a sample of biopsied tissue under a microscope for ten minutes, issuing a diagnosis to a patient?

At first consideration, the "communities" or "societies" of human cells under the microscope have nothing to do with those of humans, no more than a Petri dish of bacteria apparently has to do with a hive of bees. But there is, in fact, a correspondence between the goings-on at the microscopic, cellular level of our bodies and those on the macroscopic scale of human activity. The correspondence is bounded by constraints and assumptions, but the correspondence has been scientifically established nevertheless.

The pathologist is well-suited to investigate the correspondence because he is one of the few organisms from either world that can "move between" and "live within" both worlds to study them. By "move between," I mean that the pathologist is able to shift his observational frame of reference back and forth, from the human scale to the cellular scale (and at even the smaller, molecular scale) at will, with the aid of his microscope and other instruments. "Live within" means that the pathologist sees more than cellular structures and processes; he observes cellular behaviors and their consequences, as he does with human behaviors.

Pathology is predicated on trying to understand phenomena at the cellular level. The pathologist sometimes uses his understanding of human behavior to analyze aspects of such phenomena. But the reverse is also true; he notices aspects of cellular behavior that might give him insight into human behavior and philosophical matters thereof: implications of sentience, consciousness, existence, thought, and so on. And this, in large part, is the simplest answer to "How does pathologist become philosopher?"

So, what are the so-called cellular behaviors, and how could they have anything to do with human behavior?

Until recently, physicians and scientists had been grossly underestimating the staggering complexity, tenacity, and intelligence of the cell, be it normal or cancerous. The confounding matter of how a normal cell transforms into an oncogenic "immortal cell" that proliferates prodigiously has to do with the essence of human existence and longevity, if not immortality. Whereas the mechanics of how cancer cells come into being are still under investigation, where they come from, what they want, and how they get it are not mysteries. Cancer cells come from normal cells. Cancer cells want to live no less than any other life form. As for how they get what they want—their behavior—I will now explain, which leads to the premise for a philosophy of cancer.

The impetus of cancer cells

Just like a normal cell, an individual cancer cell is sentient and conscious.[1,2] It communicates with other cells, be they cancerous or normal, or from the large category of the bizarre and unclassifiable "in between" cells, as well as with pathogens. It eavesdrops on the intercellular chatter, then determines if, when, and how it should act upon the intelligence that it gleans. When it does decide to communicate, the messages are filled with lies or espionage-like misinformation, unless when replying, of course, in code to its own kind. The cancer cell has the equivalent of a photographic memory and learns quickly; it can store and recall all of its conversations and, by doing so, has the ability to anticipate.[3]

In its battle for survival, the cancer cell negotiates strategic and opportunistic alliances with other cancer cells, normal cells, the "in between" cells, and even the pathogens to wage hot wars…and cold ones. It presents fake identification to dupe agents of the immune system that otherwise would execute it on the spot. And if those agents manage to tease forth one truth from the cancer cell's tangle of lies, the cancer cell knows how to formulate quickly a new deception and survive another round. The cancer cell also can send false instructions to entire communities (tissues) of unsuspecting normal cells nearby or in faraway regions of the body. In this way, normal cells undertake changes that are beneficial to the cancer cell, such as allowing cancerous tissue to plug into the body's infrastructure (e.g., a blood vessel) for nourishment. In addition to being a master communicator and deceiver, it has the power of movement. Unlike most normal cells, once a cell becomes cancerous it can move to other parts of the body in a bid to maximize the survival and growth of its communities. But the cancer cell is far from perfect. It can miscalculate and wind up being executed, or simply die of battle fatigue or starvation.

Cancer cells exist, as do all living things, by one impetus: survive long enough to reproduce. In doing so, they become clever, even wise. But something more startling than individuality arises. At every turn, *the cancer cell conspicuously displays cognizance of its own sovereignty.*[4]

It has been hypothesized, and credibly defended in the scientific literature, that our consciousness and sentience are derived from those of all of our constituent, individual cells.[6] As part of this, I refer the reader to the well-known "binding problem" of phenomenal objects (e.g., a building-block component of a human thought), a problem that exists at the intersection of neuroscience, cognitive science and philosophy of mind. In total, all the cells and pathogens in a body store within themselves, and communicate between themselves, at least 4 quintillion bytes of data. Many of the conversations and chatter at the microscopic scale are parsed, mixed and matched, and smashed together—in other words, the process of "binding"—to create phenomenal objects for our use at our macroscopic scale. Yet, the cells and pathogens at the microscopic scale that are collecting and processing data, and exchanging data between themselves in these intercellular conversations, apparently are oblivious to the phenomenal object to which they are contributing.

There is a correspondence between the nature and behavior of normal cells, cancer cells, and tissues on the microscopic scale to that of humans and our communities on our macroscopic scale. This is my premise for a philosophy of cancer.

The utility of a philosophy of cancer

The most obvious use of the correspondence between the microscopic and macroscopic behaviors is for improving our understanding of cancer cells and of their relationship to their communities—different kinds of malignant tissues—as well as of the nature and relationship of normal cells to their communities. But there also might be potential for improving our understanding of ourselves and of our relationships to our communities.

As individuals (analogous to cells, be they normal or cancerous), are we unknowingly contributing data from our everyday conversations and behaviors to the creation of objects, about which we know nothing? Are there objects that operate on a scale that is larger than the individual, such as on the scale of our communities, tribes, societies, countries, or even that of all living organisms? There is evidence of neural synchronization, for example, between leaders and followers, for which the parties are unaware because the synchrony is happening on the biological level at the junction between their left temporal and parietal lobes. Social synchrony, moreover, is disturbed when people are threatened.

A caveat: a philosophy of cancer is in its infancy, and with it comes many unknowns, assumptions, and limitations. If you have the chance to observe the microscopic world of normal cells, cancer cells, and their communities, you might find yourself projecting phenomena from our macroscopic world to what you wish to see on their microscopic world, and vice versa. Without proper experimental validation, one risks mistaking coincidence for correspondence, correlation for causation. Humans are excellent at pattern recognition: seeing pockets of order in totally random things. We tend to see more than what is there; we jump to conclusions, then to the fanciful, and then to the ideological. How many times have we heard of cancer cures, ranging from the medical to the magical, and about people claiming special knowledge about cancer? Yet here I am, in 2019, writing about a disease that still does a great job of flummoxing everyone: scientist, seer, and everyone in between. I try my utmost to be objective and scientific, as a physician. But my biases will seep in, try as I might to prevent them.

Do not expect to find any propositions, theorems, proofs, or a cure for cancer in this treatise. I am putting forth the scientific basis for a premise for a philosophy of cancer, not a full philosophical exposition.

En route to developing that exposition, however, I have found that creating thought problems about what we observe clinically is a good way to start pondering possible hypotheses. And thought problems have practical value in the clinical setting by helping physician and patient to improve their communication, especially about the big questions: "Will I live?", "What are my options?", "What is the meaning of it all?" My medical colleagues in Japan have been keen to use it like this, and approximately 170 clinics in Japan are doing so today. I will now give several examples of thought problems. Some have a rigorous scientific basis; others, less so, being more like reflections or musings on some predicaments of man.

"Here I am, in 2019, writing about a disease that still does a great job of flummoxing everyone: scientist, seer, and everyone in between."

Thought problem: Are you the unwitting progenitor of a new species?

You have cancer. We all do. More precisely, at any given time, all of us have cancer cells in our body. They pop in and out of existence all the time. They are inside you now as you read this treatise, even if your annual check-up "found" no cancer. If the result of a diagnostic is negative, it simply means that the diagnostic has not been able to detect cancer cells within its limits of its sensitivity and specificity. The cells are there, but there are too few of them, at least in one place, so the diagnostic cannot "see" them. Blood tests, biomarkers, and radiological imaging equipment do not have the resolution to detect a few hundred, or even a few hundred-thousand, cancer cells. It is accurate to describe people as "otherwise not known to have a detectable cancer" rather than being "cancer free."

When our immune system cannot destroy the cancer cells, or when the cancer cells do not self-destruct according to a predestined, programmed cell death (apoptosis) as do normal cells, they differentiate and specialize. These specialized cancer cells gather into communities (tissues) analogous to normal tissues composed of specialized normal cells. If the cancerous tissue is unable to plug into part of the body's infrastructure (e.g., a nearby blood vessel) to draw nourishment, it probably will reach only a static spherical limit of approximately 2 mm in diameter (approximately one million cells). The inner cells will die at the rate at which the outer cells are produced: an equilibrium. If, however, the cancerous tissue is successful in finding a blood pipeline from which to draw additional nourishment, it will grow big enough for us to detect. Such growing cancerous tissue is detectable when it reaches 5 to 7 mm in diameter. We might call such a thriving community of cancerous cells a malignant tumor or a malignant lesion, or if it grows big enough, a mass. "So and so has cancer" is the vernacular expression for someone having enough cancerous tissue to be detectable.

How do patients die from cancer? Cancer cells, under their impetus to survive and reproduce, attempt to develop their own version of organs, entirely from cancer cells. These abnormal organs neither regulate their impetus nor cooperate with the rest of the body to achieve mutually beneficial goals. According to Eglebad et al:

> Solid tumors are not simply clones of cancer cells. Instead, they are abnormal organs composed of multiple cell types and extracellular matrix. Some aspects of tumor development resemble processes seen in developing organs, while others are more akin to tissue remodeling. Cancer cells can also instruct surrounding tissues to undergo changes that promote malignancy. Understanding the complex ways in which cancer cells interact with their surroundings, both locally in the tumor organ and systemically in the body as a whole, has implications for effective cancer prevention and therapy.[7]

There is evidence to suggest that this is the first of a new species (albeit a short-lived one) and this is a topic of scientific debate.[8]

Whether or not it is a new species, the practical problem is that this kind of origination of a new organism (abnormal organ(s) and its constituent cancer cells) entirely within an organism (you) frequently ends up killing the host and, ironically, the new organism with him. The patient dies when cancerous tumors consume resources in his body to the point of depriving normal cells and tissues of what they need to function properly. The other mechanism for death is when the cancerous tissue (and/or its ancillary affects, such as pleural effusions) occupies so much physical space in the body such that the normal tissues and organs cannot function properly. One mechanism seldom appears without the other.

Despite the efficacy of our latest technologies such as immunotherapy, it remains unlikely that we will be able to eliminate cancer in the foreseeable future. Some species, such as elephants, whales, and certain kinds of moles, rarely get cancer. But humans did not evolve to have the same checks and balances in their cellular governance as the cancer-free species. The processes that sustain our lives and carry us through life also happen to be the ones that push us resolutely along the path to cancer. Cancer cells will forever be popping up inside us or rather, I should say, for as long as we live. Many will be eradicated by the body's natural defenses, therapies, or cellular self-destruction. Others will not.

If a patient has a malignancy that cannot be eradicated, the ideal situation is for the patient to die with cancer, not from cancer. This can be achieved by means of therapeutic strategies that aim to retard severely the malignancy's growth. If successful, the result is a malignancy that co-exists in an asymptomatic state with the rest of the patient's normal cells, tissues, organs, and all the life processes of the body. Natural causes would be the first to claim the patient, not cancer. This approach has the ancillary benefit of eliminating the symptoms of cancer, at least the ones that hurt the quality of the patient's life. The cancer becomes a chronic (ongoing) illness, much the same as diabetes or heart disease or high blood pressure. It has not gone away, but it is managed. Its lethality is kept in check. Depending on the type and stage of cancer, such as thyroid cancer or prostate cancer, such outcomes are now routine. Radiation, hormones, and/or surgery are used to hammer prostate cancer so far into submission that the time required for it to bounce back is longer than the remaining natural lifespan of the patient.

Neither side desires this arrangement, the cancer cells nor the normal cells, but it is one that allows both sides to live. The disease concedes to an opportunistic coexistence with all the normal parts of the body. It is allowed to live. The deal? Don't suck the body's resources dry or else there will be mutual assured destruction. A détente at the cellular level. But both sides monitor each other scrupulously. The moment that one side catches so much as a whiff of vulnerability in the other side, perhaps in a therapy or among the countless intercellular deceptions, it will charge headlong to exploit it in a cellular blitzkrieg to eradicate its enemy.

Given the possibility of an opportunistic coexistence, is it possible to use the consciousness and sentience of cancer cells to our advantage, rather than seeing cancer as "the other" that must be eradicated? Imagine if both organisms, the one composed of normal cells and the one of cancerous cells, could be induced into a long-term truce, the term being the natural life of the patient if he did not have cancer. The death of the cancerous organism may or may not cause the death of the normal organism (i.e., the patient —the host). But the reverse is certainly not true in humans. Though the cancerous organism produces nothing of apparent benefit to the host, it is allowed to live in exchange for not killing the host: a trade-off.

Taken one step further, is it possible for the cancer to be viable after the host dies? Unlike the case with humans, there is evidence to the effect that a certain species of parasite that infects a species of mollusk may actually have originated as cancer in those mollusks millions of years ago. At some point, after many generations of the mollusk dying from its cancer and, therefore, the cancer along with it, the mollusk and the cancer evolved eventually to the point that the cancer could become viable and independent of the mollusk after the mollusk's death. So, when the mollusk died, unlike in previous generations, the cancer not only survived but also separated from the dead mollusk to become a new species with its own reproductive cycle, organs, and so forth.

Could cancer be the next step toward new life forms in a new evolutionary branch?

Thought problem:
How "human" is the cancer inside you?

The nature of cancer tissue varies within individuals and from one individual to the next because of the genetic changes that arise within cancer cells that comprise the tissue. This is what is meant when one hears, "Cancer is not one disease, but many… hundreds of diseases." To understand what is meant by "cancer cells differing by their genetics," it is necessary to first understand what is a gene, a protein, and their relationship:

> Proteins are the doers of the human body. They build things and break things down. They shuttle things around. They play major roles in the complicated dance the cell performs to read instructions from its own DNA. They're also the primary products of the DNA.[4]

Cells use them, for example, as the means to encode and transmit messages for intra-cellular and intercellular communications. But where do the proteins come from?

Each cell makes the proteins that it and, thereby, the entire body needs to survive. The human body uses approximately 87,000 different types of proteins. To make any one protein, the cell needs an "instruction guide" to build the protein. The instructions are written using "letters" made from molecules, and there are only four letters in the cell's alphabet: adenine (A), thymine (T), guanine (G) and cytosine (C). Using these letters, the cell can form only four "words" (base pairs) for its vocabulary according to the following rule: an A must always pair with a T (i.e., AT or TA), and a C always with a G (i.e., CG or GC). Six "grammar" rules have been found to date. This is everything that is required for a cell to read and understand an instruction guide for how to make a protein.

The instruction guide to make one protein is commonly 27,000 words long, but can be up to 2,000,000. Again, to avoid confusion, there are not 27,000 different words. There are only four different words, namely AT, TA, CG, and GC. The instruction guide has 27,000 of those four words in a certain sequence. The instruction guide has one "page" that is very, very long. That page is called DNA, which is a long strand of the words, like ticker tape.

The cell bundles the instruction guides in groups of three, on average, and each bundle is kept in a library called a "gene." But the cell (including cancer cells) needs to know how to make approximately 87,000 proteins to do its job. So, 10,000 instruction guides are required to make all of the 87,000 proteins, which means that all of the instruction guides are stored in approximately 30,000 genes. The genes are also bundled in groups—from hundreds to thousands in each group—called chromosomes. Humans have 23 chromosomes. All the chromosomes and the all genes that comprise them are called a "genome" (gene + chromosome). The human genome has all the lines in all the instruction guides for all the proteins: approximately three billion words in total. Finally, a proteome is the entire complement of proteins that can be created by a cell from all those instruction guides.

All cells in all organisms use the very same method of encoding instructions to make all of their proteins, too. And the outcomes are, not surprisingly, consistent within and among all life forms. But if any given cancer cell's genome is different from a human genome, how "human" (or "non-human") is cancer? As you will now see, one might first need to ask "How 'human' is a human?"

All humans have 99.9% of the same genome. In other words, each human is 99.9% similar to every other human; 99.9% of the four words are in the same sequence for all humans. The 0.1% difference expresses itself in many recognizable ways, everything from eye color to whether one is predisposed to certain diseases. Likewise, chimpanzees, our closest living non-human relatives, are 96% genetically the same as humans. Cats: 90%. Mice: 86%. Domestic Cows: 80%. Chickens: 60%. This last percent also happens to be the same as bananas and fruit flies. As for cancer, two-thirds of human genes known to be involved in cancer have counterparts in the fruit fly.

How 'human' is a human? The "1,000 Genomes Project," one of the greatest scientific projects that humanity has ever undertaken, found the answer. In a study of 2,504 people from 26 world regions, researchers found that, from one person to the next, the human genome differs in only four million to five million places—that's the 0.1% difference mentioned earlier. A variation can be a word(s), a gene(s), or a chromosome(s). Five million seems like a big number, but remember, each person's genome is three billion words long. Are we, therefore, practically identical to each other? Or are we distinct from each other, but not different? Does that 0.1% really matter, and to whom, and for what reason? Perhaps all three are true, or only some are true sometimes, depending on the problem that needs to be solved.

How 'human' is cancer? This question is the basis of the field of cancer genomics: the study of the sequence of the words in the genome to find differences between a person's cancer cells and his normal cells. There is about a 1% difference between the genome of a person's normal cell and any given type of cancer cell that he might have. This is substantially larger than the 0.1% difference between the genomes of normal cells of any two people, but smaller than the difference between us and, say, chimps.

Genes in cancer cells differ from those in normal cells. The differences between the genes of cancer cells and normal cells arise because the instruction guides become corrupted. The reasons for corruption are internal to the person (inherited mutations, hormones, and immune conditions) and external (environmental or acquired, such as tobacco, diet, radiation, and pathogens).

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The differences appear in three categories of genes. Tumor suppressor genes contain the instruction guides to make proteins that help normal cells to govern their behavior: monitoring the speed at which a normal cell divides, repairing misprints (errors or mutations) in the instruction guides, and telling the cell when it must die. DNA repair genes contain the instruction guides to make proteins that help normal cells to correct errors in the instruction guides. In the case of tumor suppressor genes and DNA repair genes, the instruction guides for making the associated proteins are corrupted; the cell either cannot produce the proteins or the proteins do not work. The normal cell then becomes cancerous. The third category, oncogenes, have nothing to do with proteins for cellular self-governance and monitoring. Oncogenes contain the instruction guides for making proteins that deliberately turn a normal cell into a cancer cell by telling it how to grow, spread, communicate, and become immortal.

I would like to turn to the external reasons to bring to you the point of the thought problem of, “How human is the cancer inside you?”

Cancer does not just appear in one day. It takes approximately 20 years for a single cancer cell to develop to the point of being a full-blown metastatic cancer. If someone discovers a cancerous lesion at age 40, it means that a normal cell became cancerous when the patient was 20 years old. It can take up to a decade for that one cancer cell to give rise to millions of cells in a 1 cm spheroid, and another decade for the spheroid to grow into a cancerous mass. But only one in thousands of cancer cells becomes viable at all. The same could be said about humans, given the odds against fertilization, normal gestation, safe birth, and then surviving to maturation to successfully procreate.

For the cancer to grow beyond a 1 mm spheroid in equilibrium (see “Thought problem: a new organism is originating entirely from you”), the cancer cells need the right environment: a “cancerous environment.” Different environments can corrupt the instruction guides differently. This means that a cancer cell might proliferate into a full-blown metastatic cancer or into nothing at all. Different environments also give rise to different cancers that have different observable characteristics (phenotypes). Even though all the normal cells in an individual have the same genome, the genome(s) of his cancer cells will always be different from the genome of the normal cells (and from each other). There are, however, certain “common denominator” characteristics of all cancer cells in all people. Immortality, rapid proliferation, and motility are three such properties.

In experiments with rats that have a type of stomach cancer, it has been found that different environments at the cellular level produce different behaviors of cancer. The instruction guides can be revised, which means that the disease can be controlled. And the unraveling of this mechanism is contributing to the prevention and treatment of cancer. This is important to know. What this means is that an abnormal gene—an error in an instruction book or a malicious set of instructions—is not necessarily equivalent to the start of the disease. I wonder whether Japan will ever realize that genetic diseases are just another proof of individuality. Or that any given Japanese person is practically identical to any other person from anywhere in the world, and from anytime in the world, from modern Nigeria to ancient Greece.

Humans, like cancer cells, are an outcome of environments over long periods of time. A small incident that happened in your younger years that goes unresolved can grow into something intractable, later. But there is room for prevention and intervention. Earlier intervention has a higher probability of success, as it is with our cells, be they normal or cancerous, so it is with individuals.

Thought problem: nature versus nurture

A clone is an organism or cell that is produced asexually from one ancestor for which the genome of the clone is identical to the genome of the ancestor.

When a child is naturally conceived, a sperm and an egg, each with its own genome, unite into one fertilized egg having its own genome that is different from the sperm and unfertilized egg. To make a clone, one extracts the nucleus of a cell (where the genome is stored) and inserts it into an unfertilized egg. Electric stimulus is used to expedite cell division and, after several divisions, the blastocyst is implanted in the surrogate mother's uterus. Like so, one can create an individual that has the identical genome as that of the person who provided it.

When a tortoise-shell cat was cloned, however, the clone had a distinctly different color. The genomes of the two cats were identical, so how could this be possible? Whereas the instruction guides in the genomes were identical, the cell's execution of those instructions to make the proteins and/or the proteins' performance of their own jobs were affected by the environment. It is analogous to building a clockwork toy robot (protein) from a kit (using the instructions) to walk from A to B. Whether one puts the toy on a thick carpet, a tabletop, or an inclined surface affects the toy's direction and progress. And even if the instructions had no misprints, one might err in following the instructions and/or the kit might be missing a part, which also affects the outcome. With misprints, the outcome is affected even more. Cats with identical genomes can look totally different.

Differences in appearance, however, are just the tip of the iceberg. Environmental conditions dramatically affect behavior, too.

> Even within the same maternal environment, the cloned kittens can develop differently. Females born nestled between two males within the womb experience a testosterone bath which leads to masculinization of their brains. In dogs, where this effect has been studied, such females turn tomboy. Some lift their legs to urinate and develop a strong desire to sniff everything in their environment.
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> Once the youngsters are born, their environment becomes even more diverse and differences can quickly be amplified. As expected, social contact with the mother during the first four weeks is essential not just to survival, but also to normal emotional development. Those lacking this contact are unusually fearful of other cats and people and they exhibit randomly directed locomotor behavior. They're also slow in the thinking department and show difficulty learning even simple associations such as the location of food sources.[9]

Imagine the permutations at the molecular scale and cellular scale: tens of thousands of types of proteins and types of cells, billions of instructions, trillions of cells, and different environmental factors at all scales, from the molecular to the micro to the macro. There are countless possibilities for variations in physical and behavioral characteristics of two organisms with identical genomes. Now, imagine the permutations among organisms with non-identical genomes… .

So it is with cancer. Genetics is involved in the incidence of cancer only 30% of the time. Again, "genetics" means the instruction guides that the cell needs to make the proteins to do its various jobs. In this case, 30% of cancer arises from corruptions to the instructions that the normal cell needs to make the proteins for suppressing tumors or for repairing corrupted instructions, as well as uncorrupted instructions that show the normal cell how to make proteins that deliberately turn the normal cell into a cancer cell. The remaining 70% is caused by influences from the environment.

This can be used as a therapy directed at cancer. Cancer cells are highly addicted to oncogenes, for example, so changing the environment to deprive the oncogene affects cancer cells more than normal cells.

Environment at the microscopic scale affects cellular behavior and outcomes which affects macroscopic behavior and outcomes, and vice versa. The genome is the other factor that affects behaviors and outcomes. We are able to manipulate genome and environment at both scales, micro and macro.

The old argument of nature versus nurture is moot. The starting point is always nature (i.e., the instruction guides in the cell). The questions are "What are the instructions?" and "How does environment affect the cell's job of reading, writing, and executing those instructions, and the protein's ability of fulfilling its job description?"

Thought problem: sovereignty

The natural state of the existence of man is that he, as with all organisms, has dominion over the use of his energy to direct at some purpose(s) for the duration of the time in his life. This is not a "right," for the universe is ignorant of rights. This is just a practical matter of the severalty of organisms.

Though organisms are several, many of them act jointly; that is, they make communities. Man is one such organism. On this basis, agreements between the members of a community sustain the individual and the members in the community.

One such agreement is that man has sovereignty over his natural state of existence to the extent that he does not encroach on another man's sovereignty over *his* natural state of existence. The agreement is known as a right, and it can be demonstrated that all rights and morality derive from this one. "Labor" is defined as the energy that he directs for some purpose(s) for a duration of time from his life. The agreement, therefore, can alternatively be expressed as "Only an individual has the right to alienate his labor" or "Nobody has a right to another's labor." From that statement comes the concept of private property, insofar as any good or service is a physical representation of the labor from an individual's life, which that individual can trade with other people for labor from their lives.

As for money, it is the physical medium for one person to trade his labor for another's, backed by their respective promises.

A system, actually more of a protocol, arises as a consequence of the natural state of existence for organisms that form communities. In the case of humans, you—*and only you*—decide with whom you trade your labor (i.e., goods or services) and the quantities of your respective labors (i.e., the price) that you exchange with each other. And you enjoy or suffer the consequences of your decision about how you trade your labor; that is, a portion of energy and time from your life—the essence of your very existence. The protocol is driven by the following universal impetus: the individual always seeks to maximize his own economic interest. Popular misapplication of ethics and morality elevates

"Some people lack the self-discipline and behave, as repugnant as it will sound to many, exactly as cancer cells do; they violate another's sovereignty by force and for their own agenda."

man above all organisms while obscuring (or denying) the stark truth of his existence: he is an organism always seeking to reduce his entropy, no different from a paramecium.

Is this not capitalism? The application of the word is inane because its users render abstract the supreme importance of what is being traded (a portion of one's existence) and who decides the conditions of the trade (the man whose portion of existence is being traded).

A truism of human behavior is that nobody spends another's money as carefully as his own, while thinking that everyone except himself is greedy. The result is that some people incessantly try to take that which is being traded between two individuals (i.e., the individuals' labor—a portion of their very existence—which rightly and solely belongs to the individuals) in their private capacities. Such people justify their action in two ways: the belief (or pretense) that they are helping the two individuals or, more commonly, the belief (or pretense) that they are serving the greater good of society. Thugs, such as the modern-day equivalents of the intellectual elites of the Soviet politburo, justify nothing; they take because they can. Regardless of the justification or lack thereof, the taking can be accomplished in only one way: by the intention of physical force exerted by "those who are taking" on "those who are trading."

Therefore, there are no "different" systems, such as capitalism, collectivism, and so on. There simply is one system arising from the natural state of existence, as described above, and all other "systems" are simply degrees of negation of that one system. The negation ranges from the social democratic to the despotic.

For a human to survive, his right must be protected from encroachment by another human. Because man is a social organism, the members of his community also must be protected from the encroachment by members of another community. These are two necessary, but not sufficient conditions for survival.

The cell's natural state of existence

Let's turn our attention to the cells.

As with humans, the human cell has a natural state of existence. As the cell reads and writes the instruction guides in the genes, makes proteins, and does all the jobs of a cell, it expends energy over a period of time taken from its lifetime to do so. This is labor, albeit at the cellular level, but labor nevertheless. The cell is also a social organism. It forms communities of fellow cells to maximize its survivability by exchanging its labor with them. The relationships among these cells are competitive and cooperative, but not adversarial or predatory. To do its job, the cell requires the labor from other cells in the form of certain products. Just as we use currency as a physical means to store and trade our labor, cells have a universal currency for the same purpose: adenosine triphosphate (ATP). ATP is the unique currency that is traded in a competitive manner among all the cells so they can do their jobs. It is an energy-delivery system. Each molecule of ATP carries a tiny packet of energy.

That energy is used in every aspect of a cell's work. There are approximately 250 g of ATP in the body at any given time, and the body consumes its weight in ATP molecules in a day. The cell needs about 2,000 ATP molecules to power itself to construct a medium-size protein. The cell consumes millions of ATP molecules per second to sustain its activities. And it can accumulate and store electrical energy by using its membranes as batteries. This is wealth and trade on the cellular level. To mint the ATP, cells take in food from their environment in exchange for beneficial products and services that it provides to members of its community (tissues).

The cell is the most basic unit that we know that has sovereignty over its natural state of existence. In physics terms, the cell seeks to lower its entropy, as with humans and all other organisms. In economics terms, the cell seeks to maximize its own economic interest in the cellular economy. And in doing so, tissues, organs, and systems rise to their maximum potential of prosperity (health, productiveness, longevity, etc.).

As with humans, this right of sovereignty must be protected for the cell to survive. The cells must be protected from each other (e.g., from encroaching on each other's natural state of existence to take what does not belong to them), and their communities must be likewise protected. Cancer is the most vivid example of what happens when the protection fails. And cancer cells treat each other by the same principles as the normal cells. The role, therefore, of the entire human body is to protect cells from each other, to protect cellular communities (tissues, organs, and systems) from each other, and ultimately to protect the entire world contained within the body from existential threat (e.g., a bacterium, an attacking animal, or another human).

At the cellular level, the protection is managed by the immune system, safety mechanisms that are written into the instruction guides of the genes, and other means. At the level of the entire body, the consciousness of the individual manages the protection with, for example, the "fight or flight" response…or by using one's intellect to fight cancer. The protectors do *not* take it upon themselves to tell the cell how to do its job nor to attempt to do the cell's job. The protectors trade products (directly or indirectly) with the cell to create ATP so they can execute its duties of protection and *nothing* more. Governance is kept close to the cellular level, where its constituents (i.e., individual cells) are and where almost all the threats against a human are encountered.

Our consciousness cannot dictate to the cells what is best for them to perform their jobs and to interfere in their "transactions" in the ATP economy. It has no way of knowing any of the details of a pathogen attack or oncogenesis on a cellular level on a real-time basis, let alone responding to it. The consciousness serves the cells that are unaware of the consciousness, but the consciousness is aware of the cells. This is the governance configuration that allows the entire body to survive.

What happens when one attempts to favor one part of the body over another? The internal economics are disrupted. There is a trade-off. Somewhere else in the body, some other cell, tissue, or system is compromised. It is easy to see the benefit to the part that is favored, and often difficult, if not impossible, to see the negative trade-off elsewhere in the body. But the trade-off is there. Is there any drug or therapy without a side-effect? Does satiating oneself by overeating not have consequences?

Turning our attention again to the macro scale, the same phenomena can be observed. Government (which itself is just a group of individuals, not an omniscient entity) has three legitimate purposes: to protect one individual from encroaching on the sovereignty of another, to protect the members of one community (e.g., tribe, nation) from encroaching on the sovereignty of other communities, and to enforce the rules of governance impartially as a referee. Any other involvement of the government requires expropriation of more labor from sovereign individuals by the intention of physical force. Taxation is exactly this: a violent breach of an individual's sovereignty over his natural state of existence. And intervention in one part of the community results in a negative trade-off in another part of the community.

The body's defense mechanisms and internal governance mechanisms have the self-discipline not to interfere in the sovereignty of normal cells, which is sacrosanct. The goings-on of individuals at the macroscopic level are no less complicated than those within them at the cellular level. So, why would some people think that they have special knowledge and ability to interfere in the sovereignty of their fellow man by means of intention of physical force? Such people lack the self-discipline and behave, as repugnant as it will sound to many, exactly as cancer cells do; they violate another's sovereignty by force and for their own agenda. The outcomes are, tragically, the same as on the cellular level.

I am hard-pressed to think of a single case of such interference existing among normal cells. Cell A does not commandeer ATP from Cell B in order to give it to Cell C, while keeping some ATP for itself in the process. Yet, this is precisely what legislators and government bureaucrats do—and what intellectual elitists advocate.

When any kind of disruption occurs to the body, the body develops an optimum path to cope with the disruption by means of molecular negotiations at the individual-cell level. The negotiations are bounded by the constraints of sovereignty and reduction of entropy that I explained earlier. The aggregated results of those trillions of negotiations have a macroscopic effect. In the case of a wound, a clot will form and the immune system will rally to eradicate pathogens in the wound, trading their goods and services as individual cells. Is the man starving? In the ATP economy, muscle cells trade proteins that contain energy, which eventually makes its way to the cells of organs and other systems. Those organs and systems provide products that go into the cellular economy to provide some derivative product that the muscle cells need, and for which they had traded some proteins away.

These days, public health officials in the United States and Japan are enamored of "collective values of society." They use the notion of "collective values" to justify measures that they claim are for the greater good of society. They always talk in terms of population data and helping populations, never about data of a specific individual with a name and a face and of helping that particular individual. Implementation of these sorts of measures are predicated on violating individual sovereignty.

First, society does not have values, unless there is some kind of societal sentience that is unknown to us in the same way that cells in our bodies are unaware of our sentience. Not to say that such a sentience could not exist, but if it does, it is of no practical use today because we know nothing about it and are not able to ask it "What are your values?" It is analogous to a small group of cells in your appendix asking you, "What are your values?"

Second, it is an unequivocal fact that individuals *do* have values, consciousness, and sentience.

The burden of proof of any measure, therefore, is on the shoulders those who are advocating the measure, not on the shoulders of the individual from whom they want to take labor by intention of physical force to implement the measure. Even if it could be proven that the measure is in the interest of the individual, the final decider is the individual, not the public health official, who must have the self-discipline not to violate the individual's decision.

There is no greater act of violence and depravity than for one man to encroach on another's sovereignty. Cancer cells do it to normal cells all the time. But even a cancer cell does not do it to his brother.

Thought problem: anchoring to advance

The inchworm is the larva of the *geometridae* family. There are approximately 300 types in Japan. The inchworm is widely used in research all over the world, from biology to robotics. Classical Chinese literature says the inchworm's tight contraction is what allows it to take a big step forward.

Of all the cancer buds, only the strongest survive, and they know the ropes for survival. This can be exemplified by the inchworm. According to Kazuo Nakahara, chief of the National Cancer Institute, "The inchworm anchors itself by attaching its sucker. It then pushes its front legs forward to advance, without moving the anchor point. The inchworm never loses its originality." The inchworm's method of maintaining its originality is the idea behind a theory that Dr. Nakahara had presented on the progress of cancer, which secures a leverage point and advances like an inchworm.

In a closed society, as with our lives, it is essential to secure a point of leverage to effect change. One must decide how to live within the constraints and opportunities of one's time and place; this anchor must come before goals are set.

Thought problem: distinguishing outward positions from inward interests

The deconstruction of the mechanism of cancer cells will lead to treatments.

This can be explained by analogy to the mafia. A mobster lives, as one would expect, by intimidation, violence, drug trafficking, and so on. He outwardly looks no different from a law-abiding citizen, but his actions and the outcomes of his actions betray his interests.

Had Robinson Crusoe lived alone on that isolated island, we would not have been able to tell whether he was a man of good or evil. Likewise, it often is difficult to determine the nature of a cancer cell when it is alone. It looks like any other normal cell. We only find out the cell's true interests when it is placed among other cells and we can see the outcome of its actions.

According to Dr. Yoshida, the pathologist whom I introduced at the beginning of this treatise, there is a continuity of states between a normal cell and a cancer cell. It often is difficult to determine "Is this a cancer cell?" by appearance alone. When cells are put together, however, it is easier to determine their nature by the outcomes of their actions.

This method also tends to be useful in ascertaining a person's position (outward stance, appearance, opinion) from his interest (true intentions)—look for the answer in the outcomes of his actions.

Thought problem: the physician's character and full disclosure

In a Japanese newspaper's survey that asked "Would you like to be notified if you were diagnosed with cancer?", 76% responded "yes." But when asked whether you would notify a family member who was diagnosed with cancer, only 37% said that they would.

This is the reality of communication in Japan.

Why would one not want to tell a family member about his cancer, when one would want to be told oneself? The psychology behind this needs to be explored more.

In the litigious United States, it is important that the doctor conveys what he knows, completely and unadulterated, to the patient. Japan is more arbitrary. Physicians' explanations tend to be rosier than the evidence.

Metastatic cancer is difficult to treat with just two or three therapeutic sessions. At what the patient thinks is the end of the treatments, the physician informs him that the effect was not as expected. The patient then asks, of course, the reason. The doctor—having given a rosier explanation beforehand—does not say much. The patient is left with the feeling that the doctor is cold and indifferent.

In Japan, even the family is not entirely honest. But the nature of our people is partially to do with this situation. It is difficult for some Japanese people to make candid remarks because the custom to encourage someone is not comfortable or within their culture (as some people think). On the other hand, we now hear of doctors who exaggerate the prognosis to avoid problems should they arise in the future. In this pet-crazy era, one can see the same phenomenon when veterinarians explain diagnoses to pet owners.

This shows how medicine in Japan is about 30 years behind that of the United States. Whether this is for better or worse, I cannot say. But it is the reality of Japan.

What is important is having the kind of love, rooted in honesty and compassion, for the doctor to do what most needs to be done: provide his objective, professional opinion by means of good doctor-patient communication. To do so, the doctor must maintain his objectivity while respecting the patient as a unique individual. This is as old as the Hippocratic Oath. Sadly, this principle is in question now, and doctors are starting to think: "It's about not what is said. It is about who says it."

My Reflection on Lessons from Cancer

The other day I read two books: *Kokka no Hinkaku (The Class of a Nation)* by Masahiko Fujiwara and *Chōbaka no Kabe (The Barriers of the Very Stupid)* by Takeshi Yōrō. The two are bestsellers, perhaps because the authors wrote beyond their scientific backgrounds—Mr. Fujiwara a mathematician and Mr. Yōrō an anatomist—and that was what appealed to the readers. I feel that this describes our time today, but I sense a difference in the way they make their point.

Mr. Fujiwara's method is straightforward, clear, and concise, whereas Mr. Yōrō uses compelling factors to portray a fool and thereby causes the reader to ponder such things. I see this as a comparison between the "paper and pencil" type of mathematician whose thinking is straightforward, and the biological scientist who knows that not all situations can be clear-cut and practical. As one who studies the teachings of Inazō Nitobe and sees the philosophy of cancer as my axis, I understand the two very well.

Before World War II, Kunihiko Hashida, minister of education in the Tōjō cabinet, explained the importance of having a "science spirit." Tadao Yanaihara, however, added that this needs to be a criticizing spirit that cannot be distorted by the government. I think that readers saw this scientific spirit in Mr. Fujiwara and Mr. Yōrō. Still, the critical mind is in essence the conscience of the scientist.

In cancer research, we often hear the term formative stimulation. This is a specific form of stimulation that initiates cancer development. Cancer does not originate from nothing. It is the result of a repeated stimulation.

The same can be said about education. I was told in my childhood days to read a different type of book for 30 minutes before I went to sleep, and so I did for 30 years.

Because of this habit, I cultivated an attitude to embrace non-linear thinkers, such as Shigeru Nanbara, Inazō Nitobe, Kanzō Uchimura and Tadao Yanaihara. Stimulation is greater when it is from an influence that is new to you.

I thought of this as I discussed Inazō Nitobe's *Bushido* in my college class the other day. Students, although they may not listen to my lecture, seem to enjoy it when I digress. I find it important to consciously think outside the box.

Shigeru Nanbara said that what our country is missing is, above all, the vision, passion, and ideals that touch the hearts of young people and students who are our future.

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