Eidos volume 5 no. 4 (2021)

A JOURNAL FOR
PHILOSOPHY
OF CULTURE

DOI: 10.14394/eidos.jpc.2021.0041

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The Horizontal-Ontological Nature of The Physical Culture of Cancers

Abstract:
Whereas classical Darwinian evolution is based on the model of vertical development, per species, and related sexual selection and natural mutations, along with environmental selective pressures, epi-genetics presents a supplemental view of horizontal development as DNA is both selectively transcribed and translated by mRNA and influenced by a process of horizontal gene transfer, including genetic melding of microbes, organelles, plants, animals and other types of hominoids. Thus, a philosophy of physical culture is offered in which cancers are conceived of as an extension of a horizontal physical culture in which organisms thrive via a cooperative and synergistic sense of community. However, they are also conceived of as an extreme which manifest a unique type of ontological multiplicity whereby they not only propagate para-sexually leading to vast genetic variations, but also manipulate and appropriate cells and systems of the host, constructing horizontally connected and lethal tumor sites. Is there any hope against such a formidable ontological structure? Cultivation of human metabolism via broad and healthy dietary patterns can support the horizontal microbiome, thus maintaining synchronized and unified horizontal relations between DNA, mRNA and long non-coded RNA functions.

Keywords:
vertical and horizontal evolution; metabolic microbiome, ontological metastatic multiplicity, synchronistic unity of actions

Introduction

Cancers are defined by the speed and number of cell divisions that occur, and how the process is no longer controlled and increases exponentially, leading to mutations that eventually become cancerous. This is turn

leads to an expansive, and in some cases, invasive modality. In fact, recent findings indicate that tumor cells contribute to the horizontal parasexual recombination and diversity of genetic materials with each other, increasing their resistance against the immune system and chemo drugs, and the chances for deadly metastasis in the host. In this respect, cancers are similar to horizontal physical cultures which have been an integral part of natural evolution, and are distinctly known for their genetically and behaviorally cooperative and synergistic sense of community.

Consequently, contrary to the emphasis placed on vertical and species-oriented development in classical evolutionary biology, a close examination of the ontological physical culture of cancers indicates that horizontal developments play a key role in lethal cancerous growth and expansion in the microtumor environment. Moreover, the epigenetic interplay of human culture and the individual, as well as the cultivation of corrosive dietary patterns and related metabolism, infringes on the synergy of the microbiome and the immune system.

Accordingly, ninety-five percent of deaths related to cancers stem from tumors that have metastasized, and initial relapse rates vary depending on cancer stage at diagnosis, but in about seventy percent of patients, tumors recur. Such a rate of recurrence indicates how biological homeostasis involves more than maintaining a functional state, as it entails a unity of action on a multi-dimensional and dynamic set of variables.

With this in mind, the ontological physical culture of tumor development and its range of causal factors will be examined, including genetic mutations, its manipulation of the immune system and macrophages, its appropriation of the wound healing process, as well as disturbances of the unified horizontal interplay of the metabolic microbiome and DNA, mRNA, and long non-coded RNA. Finally, the paper will elucidate these different types of horizontal bio-chemical dynamics, and how they need to be nurtured and regulated, for optimal health and well-being.

PART ONE
The Emergence of Cancers

One out six deaths, worldwide, are related to cancer. While there are probabilistic factors, such as age, gender, geographic location – around the world, and risks of exposure to radiation and other toxins and unhealthy lifestyle behaviors, there are no absolutes in terms who develops a cancer and who does not. In fact, there are no necessary or sufficient conditions that can be determined in mechanistic terms. In other words, a person who is a high-risk category can remain cancer free, and someone in a low risk category can succumb to a cancer. The explanatory relevancy of cellular components also changes over time depending on different states of progression.

In simple physical terms, cancers are defined by the speed and number of cell divisions that occur, and how the process is no longer controlled and increases exponentially, leading to mutations, that eventually become cancerous. In this regard, some cancers can be attributed to the inherent instability of the genetic process, complete with volatile phosphate DNA bonds and protein pathways, and transposons or horizontally jumping genes, which all naturally mix up the genetic arrangements in order to induce change and innovation. Also, chromatin, the DNA–protein complex where genes reside, and a long non-coding RNA can affect genes by controlling chemical modifications on the chromatin. By doing so, they can affect the accessibility of the chromatin to the gene-transcribing machinery, and therefore affect gene activity.

A growing body of evidence indicates that cancers slowly develop for many years, before manifesting themselves as a distinct disease.[1] Over time, from both water and oxygen decay, and by chance, the genomes of cells randomly acquire so-called somatic mutations – nonheritable, spontaneous changes that are largely

1) Hormoz et al., "Reconstructing the Lineage Histories," 514–23.

harmless. As those mutations, spawn new mutations, over time, the chances that one of the mutations will become cancerous, increases. And then, there is only one cell that has the mutation, but perhaps, over the next ten years, there are something like a hundred cancer cells. Finally, it grows exponentially.[2]

Conversely, cases can and do quickly follow physical injuries, especially where inflammation is involved, as well as emotional-moral injuries/periods of intense stress, and exposures to high levels of radiation and other extreme toxins. In these cases, there are often multiple mutations, from the start, and often occur in faster-growing types of stem cells. For example, "It seems certain pathways in breast cells that are usually switched on by hormones during pregnancy are triggered by BRCA1 mutations and cause the cells to grow out of control."[3]

As per a relative midpoint between these two ranges, Tomasetti, professor of oncology at Johns Hopkins, began to wonder whether an underappreciated cause of cancer happens even without the influence of carcinogens or cancer-causing genes: the infinitesimal and inevitable random mutations that occur during normal cell division. Also, a major driver of variation in cancer risk among different tissues could be explained by the number of cell divisions within that tissue over an individual's lifetime. Studying dozens of cancers, there was a correlation across five orders of magnitude of cancer prevalence showing that the higher the lifetime number of cell divisions in a tissue the higher its cancer rate. At one end of the plot were rare cancers of slow-growing bone tissue; at the other were common cancers of the colon, which replaces the cells of its entire lining roughly every four days.

Mutational Proofreading

Notwithstanding the high rate of replication in some organ-tissue cells, and the trauma that injuries bring to the body, technically, there should not be mutations leading to cancerous developments. Replication errors and DNA damage are actually happening in the cells of our bodies all the time. In most cases, however, they do not cause cancer, or even mutations for they are usually detected and fixed by DNA proofreading and repair mechanisms.[4] Or, if the damage cannot be fixed, the cell will undergo programmed cell death to avoid passing on the faulty DNA. Mutations happen, and get passed on to daughter cells, only when these mechanisms fail. Cancer, in turn, develops only when multiple mutations in division-related genes accumulate in the same cell.

Such cancer research extends back to Weinberg's work in the 1970s when much of cancer research was bound to the conviction that the key to understanding cancer was the reverse transcriptase enzyme. These enzymatic reactions are found in many pathways and are implicated in genetic diseases, cancer, and metabolic diseases. Simply put, DNA methyltransferases cause the repression of tumor suppressor genes, which become silent and inactive in some blood cancers.

Nonetheless, during DNA replication most DNA polymerases, which are a large group of enzymes that build DNA in cells and are involved in the regulation of gene expression, can "check their work" with each base that they add by a type of proofreading. If the polymerase detects that an incorrectly paired nucleotide has been added, it will remove and replace the nucleotide right away, before continuing with DNA synthesis. While many errors are corrected by proofreading, a few slip through and mismatch repair is designed to occur right after new DNA has been copied, and to remove and replace mis-paired bases. Mismatch repair can also detect and correct small insertions and deletions that happen when the polymerases enzyme goes a bit astray.

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2) Jiang, "Original Error: When Does a Cancer First Arise?," 21.

3) Bach et al., "Time-Resolved Single-Cell Analysis."

4) An average of just three small mutations occur each time one of your cells divide: an impressively low error rate of about one billion DNA letters copied, but once mutations have occurred they can create different forms of genes that produce altered proteins, which can alter the biology of the cells that inherit them. Nurse, *What Is Life?*

With all this monitoring of mutations in mind, one is left wondering how and why cancers emerge, if the body and its immune systems are not only on the look out for such mutations, but also have a number of mechanisms to resolve whatever they detect. Hence, the paper will now proceed in examining a series of horizonal physical cultures, that either guard against cancerous growth, or, actually encourage the development of the lethal micro tumor environment.

PART TWO
Horizontal Evolutionary Patterns

It is important to bear in mind that a key component to gene selections and immunological development and support is maintained by our metabolic dietary behavior, connected to the microbiome. In fact, more than our genetic inheritance, our epigenetic interaction with our environment influences which genes are selected for expression and in turn activate essential proteins – so that our immunological responses are related to our dietary metabolism.

In this respect, the physical culture of foreign microbes in the human gut is an extension of a long horizontal evolutionary process. For example, just as fungi emerged some 2.4 billion years ago, thirty percent of earthly soil is/has been degraded from rock by fungi activities; many animals, including humans, acquired essential "foreign" genes from microorganisms co-habiting their environment in ancient times through the process of horizontal gene transfer;[5] DNA analyses finds that early Homo Sapiens mated with other human species and hints that such interbreeding played a key role in the triumph of our kind;[6] every human cell embodies the organelles of the mitochondria, which play the essential role of energy production, along with a specialized compartment, called the lysosome, which is also an organelle, containing enzymes that digest proteins, carbohydrates, and lipids; and the human body, like that of other mammals, is colonized by trillions of microbes – bacteria, viruses, and fungi – collectively referred to as the commensal microbiotas.

Interestingly, advanced metabolic modeling-based on thousands of microbial communities across the globe – from soil to the human gut, showed that the co-occurring groups of bacteria are either highly competitive or highly cooperative in the context of microbial ecosystems. But while both competitive and cooperative communities are prevalent, the cooperators seem to be more successful: they are more abundant and occupy a more diverse range of habitats.

Moreover, researchers at the University of Cambridge's MRC Toxicology Unit have learned that horizontal cooperation among microorganisms is key to their communal success. Using a variety of state-of-the-art methods including studying metabolite chemical processes, the genome-produced RNA transcriptions, and mathematical modeling, they were able to observe at the level of amino acids that cooperation is key to their structure and function.[7]

Human Horizontal Metabolic Immune Systems

There is new and compelling evidence concerning the human microbiome or the physical culture of commensal, symbiotic, and pathogenic microorganisms that literally share our body space. In fact, the human body contains over ten times more microbial cells than human cells, although the entire microbiome only weighs about two

5) Crisp et al., "Expression of Multiple Horizontally Acquired Genes."

6) Hammer, "Human Hybrids," 66–71.

7) Machado et al., "Polarization of Microbial Communities," 195–203.

hundred grams, with some weight estimates ranging as high as three pounds. With millions of interactions, and billions of microbes and 100 trillion bacteria, analysis have revealed that there might be a hundred times more bacterial genes in the collective human microbiome than not only genes in the human genome, but stars in the observable universe. However, while modern techniques for sequencing DNA have enabled researchers to find the majority of these microbes, the majority of them cannot be cultured in a lab using current techniques.[8]

We do know that the microbiome is present in all humans shortly after birth, but where and how this signaling occurs has remained unclear, till now. New research demonstrates that this protective response arises from immune cells that reside in the walls of the colon. These cells release protective interferons when stimulated by a surface molecule residing on the membrane of a specific gut bacterium. One of those microbes, *Bacteroides fragilis*, present in the majority of human guts, initiates a signaling cascade that induces immune cells in the colon to release a protein called interferon-beta, an important immune chemical that confers anti-viral protection in two ways: It induces virus-infected cells to self-destruct and also stimulates other classes of immune cells in the innate immune system to attack the viral cells.

By the same token, a healthy human metabolism supported by enough nutrients as part of a varied diet is required for the health and function of all cells, including immune cells. In other words, while certain dietary patterns better prepare the body for microbial attacks and excess inflammation, it is unlikely that individual foods offer special protection. Each stage of the body's immune response relies on the horizontal presence of many micronutrients. Examples of nutrients that have been identified as critical for the growth and function of immune cells include vitamin C, vitamin D, zinc, selenium, iron, and protein (including the amino acid glutamine). All are found in a variety of plant and animal foods.[9]

In contrast, diets that are limited in variety and lower in nutrients, such as consisting primarily of ultra-processed foods and lacking in minimally processed foods, can negatively affect a healthy immune system. It is also believed that a Western diet high in refined sugar and red meat and low in fruits and vegetables can promote disturbances in healthy intestinal microorganisms, resulting in chronic inflammation of the gut, and associated suppressed immunity.

Moreover, cultural dietary patterns that instigate both the digestive and immunological systems, assisting in the suppression of mutated cells which could become cancerous, actually aid in their emergence and further development. In fact, as per obesity, alone, it has been linked to increased risk for over a dozen different types of cancer, as well as worse prognosis and survival. More specifically, new evidence cites that obesity allows cancer cells to outcompete tumor-killing immune cells in a battle for fuel. This occurs because cancer cells reprogram their metabolism in response to increased fat availability to consume energy-rich fat molecules, depriving T cells of the immune system fuel.

In fact, high-fat diets reduced the presence of CD8 T cells in the tumor environment, but nowhere else in the body.[10] This behavior of the cancer cells illustrates how cellular transcription factors correlating to the epigenetic dynamics, by which genes are selected moment to moment to activate proteins and enzymes, act in accordance to the pressures and needs of our physical cultures. By the same token, although they use the same metabolic pathways that normal cells use, their pathological character involving aberrant differentiation of cells within a tumor and the genetic drift of tumor cells that end up with very different genetic configurations, transcends any underlying genetic or biochemical alteration. In this respect, one is confronted by the endless complexity of the disease.

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8) Miller, "Gut Check."

9) Harvard T.H. Chan School of Public Health, "Nutrition and Immunity."

10) Jiang, "Obesity and Cancer."

Horizontal DNA and RNA Transcription

Of the twenty thousand protein coding genes of the human genome, only about two thousand have been studied in depth, and over five thousand have never been examined. Targeting genes is also tricky and complex, especially as there are often hundreds, if not thousands of genes horizontally involved in a given cellular and organ activity. And even if one is able to correctly isolate and indict a particular gene as being responsible for an illness or disease, once it is turned off or eliminated, it is no longer able to horizontally participate in other bodily functions.

Consequently, as recently reported by Francis Crick Institute, researchers are calling for greater awareness of unintended consequences of CRISPR gene editing, which allows scientists to remove and replace sections of DNA in cells.[11] For example, in a study of the role of OCT4 protein in human embryos during the first few days of development, while the majority of the CRISPR induced mutations were small insertions or deletions, in approximately sixteen percent of samples there were large unintended horizontal mutations.[12]

Genes are also interacting horizontally with environmental heredity, via diet, climate, land masses, and disease.[13] In these respects, DNA tells only a portion of our biological historical nature. More specifically, while it is the case that genetic messages are relayed to proteins via mRNAs which assist in the synthesis of the needed proteins, which in turn direct metabolic processes, the inverse is also true.[14] Based on dietary habits and nutritional intake, metabolic processes can also dictate which genes will be activated, and in turn, which proteins will be synthesized.

By this token, RNA's long primeval history, which actually precedes the existence of DNA, involves its self-replicating molecule combining amino acids into proteins and, via its mutations, creating a double-helix DNA molecule to store its complex intracellular regulation. This also accounts for the fact that when the Human Genome Project was complete in 2001 it was a major surprise that protein-coding genes accounted for as little as 1–2% of the human genome, leading the remainder to be termed as genetic noise or junk DNA.

Accordingly, epigenetics examines how the overall epi-genome interacts within its given environment such that an organism transcribes different genetic regions based on its needs and in response to its environmental pressures. More specifically, a transcription factor is a protein that controls the rate of transcription of genetic information from DNA to messenger RNA, by binding to a specific DNA sequence. For example, animal cells undergo fundamental shifts in gene expression when there are changes in the oxygen levels around them. These changes in gene expression alter cell metabolism, tissue re-modeling, and even organismal responses such as increases in heart rate and ventilation. In a similar way, circadian oscillators within individual cells respond differently to entraining signals and control various physiological outputs, such as sleep patterns, body temperature, hormone release, blood pressure, and metabolism. Changes in daylight, temperature, and metabolism are similar types of transcription factors responding to horizontal changes in environment.

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11) The Novina Dana Farber Lab notes that a major challenge for genome editing is that such "editors" have many unintended off-target effects including promiscuous binding of Cas9 to loci with high sequence similarity to the intended target site and unspecific enzymatic activity of editors leading to unwanted modifications. The lab recently described a novel tool for targeted DNA methylation by tethering a "split-fusion" methyltransferase to an endonuclease-deficient mutant Cas9. Its split-fusion approach minimizes off-target effects by ensuring that enzyme activity is specifically reconstituted at the targeted locus.

12) University of Cambridge, "Researchers Call for Greater Awareness."

13) Zimmer, *She Has Her Mother's Laugh*.

14) Ribonucleic acid (RNA) is a polymeric molecule essential in various biological roles in coding, decoding, regulation and expression of genes. Like DNA, RNA is assembled as a chain of nucleotides, but unlike DNA, RNA is found in nature as a single strand folded onto itself, rather than a paired double strand.

PART THREE
The Horizontal Dimensions of Micro-Tumor Environment

In keeping with prior discussion of how human cultural dietary patterns either support or erode the physical culture of the microbiome and its connections with the immune systems, as well as with its horizontal connections with both DNA and RNA, a closer examination of the ontological microtumor environment will follow.

Weinberg was an important figure due to his discovery of the oncogene, Ras, and the first tumor suppressor gene, Rb. The p53 gene like the Rb gene, is a tumor suppressor gene, that is to say its activity stops the formation of tumors. If a person inherits only one functional copy of the p53 gene from their parents, they are predisposed to cancer and usually develop several independent tumors in a variety of tissues in early adulthood. This condition is rare, and is known as Li-Fraumeni syndrome. However, mutations in p53 are found in about half of all tumor types, and contribute to the complex network of molecular events leading to tumor formation.

The amount of information that exists on all aspects of p53 normal function and mutant expression in human cancers is now vast, reflecting its key role in the pathogenesis of human cancers. The p53 gene has been mapped to chromosome 17. In the cell, p53 protein binds DNA, which in turn stimulates another gene to produce a protein called p21 that interacts with a cell division-stimulating protein (cdk.2). When p21 is complexed with cdk2 the cell cannot pass through to the next stage of cell division. Mutant p53 can no longer bind DNA in an effective way, and as a consequence the p21 protein is not made available to act as the "stop signal" for cell division. Thus, cells divide uncontrollably, and form tumors, reflecting its key role in the pathogenesis of human cancers. Most attempts to target p53 involve trying to boost its level, but they have not been too successful. Also, since p53 is involved in many cellular processes, stimulation induces side effects.

Underscoring the ontological complexity in cancers, while quantum mechanics does not tell you what you can and cannot know, it does tell you which questions you can and cannot ask. If you ask what happens to one specific atom, you do not get a good answer, but if you ask what happens to of them, you get an answer that is only inaccurate to one part in. A counterpoint: if you try to explain and predict a cancer cell, you will also fail. But if you try to figure out a cluster of them in a tumor, you are overwhelmed with complexity, due to their parasexual synergies.

In fact, recent findings indicate that tumor cells contribute to the horizontal genetic diversity of the tumor by exchanging a parasexual recombination of genetic materials with each other, increasing their resistance against the immune system and drugs, and the chances for deadly metastasis. Consequently, the average number of mutations in any given cancer can range from 10–20, to the hundreds and thousands, and this numbering can have lethal effects. In this respect, cancerous cells within tumor sites have leveraged a type of ontological multiplicity than has been seen in prior examples of naturalistic horizontal gene transfer, to extreme limits.

Horizontal Manipulations Between Primary and Secondary Tumor Sites

While mutations in p53 are found in about half of all tumor types, and contribute to the complex network of molecular events leading to tumor formation, their statistical rate bears out that they are neither necessary nor sufficient cause for cancerous development, and that a mutated p53 is just one component of a network of events that culminate in tumor formation. Cancer cells can also manipulate the p53, so therapeutic strategies against tumor immunosuppression mainly focus on blocking immune checkpoint receptors, enhancing T-cell recognition and neutralizing inhibitory molecules. Although immunotherapies based on these strategies have improved the clinical outcomes, immunological nonresponse and resistance are two barriers to tumor eradication. But revealing another cellular pathway that is appropriated by cancer cells, a promising development has occurred related to metastasis.

Previous studies from the Massaque lab have shown that a molecule called L1CAM is necessary for numerous types of cancer cells to successfully metastasize to other organs. Normal healthy tissues do not typically make L1CAM, but advanced cancers often do. Using organoids,[15] researchers were able to show that simply separating cells from their neighbors was enough to trigger L1CAM production. Similarly, in metastasis, cells detach from their neighbors and adopt a migratory behavior to reach new locations. Researchers suspected that the wound repair program equips both types of cells to survive this anchorless state. In the first case, it allows cells to move into the breach and make new tissues; in the second, it enables metastatic cells to detach and colonize new secondary sites. In fact, these L1CAM-making cells *were* necessary for tumors to metastasize. Thus, "we now understand metastasis as the regeneration of the wrong tissue – the tumor, in the wrong place – distant vital organs," says Joan Massaque.[16]

In terms of the episodic journeys of cancer cells, they must leave their primary site, break through tissue layers, circulate in the bloodstream or lymph fluid, endure pressure in blood vessels, exit those vessels, prime and acclimate to new cellular surroundings, and proliferate and escape deadly combat with immune cells. Moreover, while only one percent of the cancer cells that separate from a primary tumor, embarking on a journey through either the blood or lymphatic systems – survive the journey, those that do – set-up a secondary tumor, which is the main cause of failure of cancer therapy and the death of the human host in ninety-five percent of cases. But in order to survive the episodic journey, metastatic cells engage in a horizontal connection to the secondary tumor site, via extra-cellular vesicle exchange and resonances of intra-cellular and inter-cellular protein and enzyme cascades. In other words, even before their arrival, cancerous cells enjoy a cooperative and synergistic relationship with the secondary tumor site, awaiting their arrival and invasive colonization.

Lastly, macrophages, best known for gobbling up bacteria and infected cells, are one type of immune cell that tumors can turn into pro-cancer collaborators. Inflammatory macrophages can also help alert other immune cells, such as killer T cells, to the presence of infected or diseased cells. But macrophages can also help tamp down inflammation and stimulate wound healing, and based on the aforementioned appropriation of the would healing process by cancerous cells, when immature macrophages enter the tumor, the tumor secretes suppressive factors that reprogram these helpful immune cells into suppressor cells, so instead of helping eradicate the tumor these immune cells help maintain the tumor.

Long Non-Coded RNA and Horizontal Immunological Connections

The above discussion on how cancer cells manipulate the immune system and co-opt the use of the wound healing process strongly indicates how biological homeostasis involves more than maintaining a functional state, as it entails a unity of action, and with onset of a cancer some type of cooperation and synchronization is lost.

Beyond the fairly well-known bio engineered mRNA, which has been used in recent pandemic vaccinations as a messenger to activate an antibody reserve, researchers have been uncovering the existence of some hundred thousand long non-coded RNAs. Technically, long non-coding RNAs are loosely described as non-coding protein-coding transcripts of more than 200 nucleotides which promote and inhibit gene expression via a variety of mechanisms. The non-coded status indicates that they do not translate genetic information into the synthesis of proteins. Rather, the potential roles of the thousands of long non-coded RNAs seem

15) An organoid is an artificially grown mass of cells or tissue that resembles an organ. It consists of a chunk of tissue taken out of a tumor site, and then cultured with stem cells which have been programmed to synthesize with the tumor cells.

16) Ganesh et al., "L1CAM Defines the Regenerative Origin." The Novina Dana Farber Lab also discovered an intronic mircoRNA that performs the tumor suppressor function of its host loci on the DNA molecule.

to be more regulatory, especially in relation to transcription of genes, with them either activating or repressing transcription.

They are also more difficult to detect, as their horizontal presence is detected at low levels between protein coding genes, inside genes, and with overlapping genes. In this respect, epigenetics reveals that all cells of the immune system rely on an integrated and dynamic gene expression program that is controlled by both transcriptional and post-transcriptional mechanisms, which in turn, are regulated horizontally by long non-coded RNAs.[17]

In fact, the field of epigenetics is witnessing a burgeoning paradigm of long non-coded RNA-mediated control of gene expression and the differentiation and function of innate and adaptive immune cell types. For example, while traditional biochemical methods to define RNA-protein interactions are limited by low throughput and is biased towards identifying the most abundant RNA-protein interactions, the Novina Lab has developed technologies integrated into a platform that can efficiently define long non-coded RNA function by systematically identifying their associated proteins.[18] [19] As a result, long non-coded RNAs are also reported to be involved in various processes of the immune response in the tumor microenvironment to promote tumor immunosuppression.[20]

For example, developments in characterizing the expression profiles and functions of long non-coded RNAs in brain tumors have generated excitement in the field of brain tumor research and therapy over the past few years. Long non-coded RNAs have been noted to have either tumor suppressive or oncogenic functions in different brain cancers, making them attractive therapeutic targets and biomarkers for personalized therapy and precision diagnostics. By the same token, mitochondrially located long non-coded RNA growth-arrest-specific 5 (GAS5) has been identified as a tumor suppressor in maintaining cellular energy homeostasis, as it negatively correlates with levels of its associated mitochondrial metabolic enzymes in tumors and benefits overall survival in individuals with breast cancer.[21]

Hence, in keeping with the notion that horizontal imbalance between different types of causal dimensions, long non-coded RNA might be at the root of the origin of cancer, and these various dimensions will be clinically explored in greater depth and detail in terms of their horizontal unity of action, especially in terms of their capacity for tumor suppression.

Conclusion

The prior discussion has located the physical culture of cancer cells in a larger and longer evolutionary process, whereby in addition to the classical vertical species oriented development, cancer cells have emerged with their own distinctive ontological status of a physical culture, complete with a cooperative and synergistic horizontal relationship between its member cells.

To start, cancer cell's cunning and clever behavior induced by natural selection and self-organization

17) Long non-coded RNA plays a vital role in cells, tissues, and organs, including: physiologic cellular processes, genomic imprinting, inactivation of chromosome X, maintenance of pluripotency, formation of different organs via changes in chromatin, transcription, and translation, and gene regulatory mechanisms.

18) Long non-coding RNA binding to transcription factors or histone modifying enzymes implicates those RNAs in transcription or locus control, respectively. Moreover, by screening fragments of a disease-relevant long non-coding RNAs against the human proteome, their platform can define the RNA sequence and structural determinant that specify protein interaction.

19) Robison and Covarrubias, "The How and Why of lncRNA Function."

20) Luo et al., "Long Non-Coding RNAs."

21) Sang et al., "Mitochondrial Long Non-Coding RNA GAS5."

principles is both daunting and impressive: cancer cells appropriate cellular and bodily processes including, vascular systems, stem cells, T cell regulators, and macrophages of the immune system, and the wound healing mechanism in order to establish secondary tumor sites. They also suppress the gene responsible for tumor suppression.

There is also the aggressive and ruthless nature to the micro-tumor physical culture where cancerous cells, tissues, and tumors ferment. What is most striking, ontologically, is that cancer cells engage in polymorphic-horizontal parasexual relations, which inject hundreds or even thousands of genetic variations within a given tumor. In addition, they appropriate and invert the natural healing process for the cancer cluster en route from the primary to secondary tumor site – enabling the metastatic cells to detach and, after a perilous journey, be supported by horizontal bio-chemical connections to the target site – to colonize new and distant secondary sites; and lastly, they facilitate a classic bait and switch whereby the immune system is tricked into thinking the tumor is a wound that never heals: initiating the reprogramming of the role of macrophages from natural eradication to maintenance of the tumor.

As such, cancers represent radically emergent and/or chaotic systems – or those that lie beyond explicable and predictable parameters of naturally complex systems. In fact, there is neither a logic of discovery and/or invention, nor Bayesian priors and self-credences relative to probability charts based on initial conditions, momentum, and boundary conditions. In this respect, prevention and early detection stand as the best ways of containing and repressing the uncontrollable ontology.

In this regard, cultivation of healthy dietary patterns can support the horizontal metabolic microbiome, which is more effective in its own cooperative and synergistic relations when provided with a broad-based program of nutritional elements. This is especially true as the consumption of fats and sugars promotes cancerous growth and the construction of vascular systems and migratory patterns both in and between tumor sites.

Lastly, a broad based microbiome physical culture also helps to maintain horizontal balances between DNA, mRNA, and long non-coded RNA, which play essential regulatory roles, especially the long non-coded RNA: which independently perform activities of proteins and enzymes, and whose circular shape directly communicates with the immune system, and provides specific sequences and other new kinds of instructions for the cell.[22] In this respect, the ontological physical culture of cancers is not just a breakdown of mechanistic causalities and micro circular feedback loops, but rather, is intimately interwoven with the synchronization of dimensional fields and the unity of horizontal actions.

22) It has been explored and inferred how biological and existential influences interplay with each other and affect the regulation of the immune systems in cells, tissues, and organs. DeCarlo, "The Symbolic Link Between Bio Tech and Neuro Tech."

Bibliography:

Bach, Karsten, Sara Pensa, Marija Zarocsinceva, Katarzyna Kania, Julie Stockis, Silvain Pinaud, Kyren A. Lazarus, Mona Shehata, Bruno M Simões, Alice R. Greenhalgh, Sacha J. Howell, Robert B. Clarke, Carlos caldas, Timotheus Y. F. Halim, John C. Marioni, Walid T. Khaled. "Time-Resolved Single-Cell Analysis of Brca1 Associated Mammary Tumourgenesis Reveals Aberrant Differentiation of Luminal Progenitors." *Nature Communications* 12, no. 1 (March 2021): 1502. https://doi.org/10.1038/s41467-021-21783-3.

Crisp, Alastair, Chiara Boschetti, Malcolm Perry, Alan Tunnacliffe, and Gos Micklem. "Expression of Multiple Horizontally Acquired Genes is a Hallmark of Both Vertebrate and Invertebrate Genomes." *Genome Biology* 16, no. 50 (2015). https://doi.org/10.1186/s13059-015-0607-3.

DeCarlo, John F. "The Symbolic Link Between Bio Tech and Neuro Tech: An Imaginative Melding of Biological and Existential Homeostasis." *The Junkyard,* December 9, 2020. https://junkyardofthemind.com/blog/2020/12/4/the-symbolic-link-between-bio-tech-amp-neuro-tech-an-imaginative-melding-of-biological-amp-existential-homeostasis.

Ganesh, Karuna, Harihar Basnet, Yasemin Kaygusuz, Ashely M. Laughney, Lan He, Roshan Sharma, Kevin P. O'Rourke, Vincent P. Reuter, Yun-Yan Huang, Mesruh Turkekul, Ekrem Emrah Er, Ignas Masilionis, Katia Manova-Todorova, Martin R Weiser, Leonard B. Saltz, Julio Garcia-Aguilar, Richard Koche, Scott W. Lowe, Dana Peer, Jinru Shia, and Joan Massagué. "L1CAM Defines the Regenerative Origin of Metastasis-Initiating Cells in Colorectal Cancer." *Nature Cancer* 1, (2020): 28–45. https://doi.org/10.1038/s43018-019-0006-x.

Hammer, F. Michael. "Human Hybrids." *Scientific American* 308, (May 2013): 66–71.

Harvard T.H. Chan School of Public Health. "Nutrition and Immunity." Accessed January 2021. https://www.hsph.harvard.edu/nutritionsource/nutrition-and-immunity/.

Hormoz, Sahand, Debra Van Egeren, Javier Escabi, Maximilian Nguyen, Shichen Liu, Christopher R. Reilly, Sachin Patel, Baransel Kamaz, Maria Kalyva, Daniel J. DeAngelo, Ilene Galinsky, Martha Wadleigh, Eric S. Winer, Marlise R Luskin, Richard M. Stone, Jacqueline S. Garcia, Gabriela S. Hobbs, Fernando D. Camargo, Franziska Michor, Ann Mullally, and Isidro Cortes-Ciriano. "Reconstructing the Lineage Histories and Differentiation Trajectories of Individual Cancer Cells In Myeloproliferative Neoplasms." *Cell Stem Cell* 28, no. 3 (March 2021): 514–23. https://doi.org/10.1016/j.stem.2021.02.001.

Jiang, Kevin. "Obesity and Cancer." *Harvard Medical School, News and Research*, December 19, 2019. https://hms.harvard.edu/news/obesity-cancer.

Jiang, Kevin. "Original Error: When Does a Cancer First Arise?" *Harvard Medical School, News and Research*, March 4, 2021. https://hms.harvard.edu/news/original-error.

Luo, Ya, Jiqiao Yang, Jing Yu, Xiaowei Liu, Chune Yu, Jianping Hu, Hubing Shi, and Xuelei Ma. "Long Non-coding RNAs: Emerging Roles in the Immunosuppressive Tumor Microenvironment." *Frontiers in Oncology* 10, no. 48 (January 2020). https://doi.org/10.3389/fonc.2020.00048.

Machado, Daniel, Oleksandr M. Maistrenko, Sergej Andrejev, Yongkyu Kim, Peer Bork, Kaustubh R. Patil, and Kiran R. Patil. "Polarization of microbial communities between competitive and cooperative metabolism." *Nature Ecology & Evolution* 5, (2021): 195–203. https://doi.org/10.1038/s41559-020-01353-4.

Miller, Jen. "Gut Check." *Harvard Medical School, News and Research*, May 18, 2021. https://hms.harvard.edu/news/gut-check.

Nurse, Paul. *What Is Life? Five Great Ideas in Biology*. W.W. Norton Company, New York: 2021.

Robison, E.K., Sergio Covarrubias, and Susan Carpenter. "The How and Why of lncRNA Function: An Innate Immune Perspective."*Biochim Biophys Acta Gene Regul Mech* 1863, no. 4 (April 2020). https://doi.org/10.1016/j.bbagrm.2019.194419.

Sang, Lingjie, Huai-qiang Ju, Zuozhen Yang, Qiwei Ge, Zhen Zhang, Fangzhou Liu, Luojia Yang, Hangdi Gong, Chengyu Shi, Lei Qu, Hui Chen, Minjie Wu, Hao Chen, Ruihua Li, Qianqian Zhuang, Hailong Piao, Qingfeng Yan, Weishi Yu, Liangjing Wang, Jianzhong Shao, ian Liu, Wenqi Wang, Tianhua Zhou, and Aifu Lin. "Mitochondrial Long Non-Coding RNA GAS5 Tunes TCA Metabolism in Response to Nutrient Stress." *Nature Metabolism* 3, (January 2021): 90–106. https://doi.org/10.1038/s42255-020-00325-z.

University of Cambridge. "Researchers Call for Greater Awareness of Unintended Consequences of CRISPR Gene Editing." University of Cambridge Research News, April 12, 2021. https://www.cam.ac.uk/research/news/researchers-call-for-greater-awareness-of-unintended-consequences-of-crispr-gene-editing-0#:~:text=CRISPR%2DCas9%20genome%20editing%20can,human%20DNA%20in%20laboratory%20research.

Zimmer, Carl. *She Has Her Mother's Laugh: The Powers, Perversions, and Potential of Heredity*. Pan Macmillan-Dutton, 2018.