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Cancer, Transformation and Human Behavior

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Perspective

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Abstract

Cancer as a challenging disease may need more than a new drug or a new combination of drugs for its cure; a new level of consciousness seems essential in order to achieve its safe eradication. An in-depth look into the behavior and metabolic activities of cancer cells shows how these cells grow at all costs once new standards are set and repair mechanisms weakened. Moreover introduction of numerous genetic changes seems to take an overly tolerant character in cancer cells. Similarly humans have travelled far long on the trajectory of transformation in mimicking cancer cells behavior. Many of our industries today tend to work for profit, at all costs in order to ensure continued growth and ever-increasing gains. Over-production led to over-exploitation of many natural resources leading as a consequence to the destruction of fragile ecosystems while pollutants are continuing to accumulate at an alarming scale in our air, land, seas and oceans. Human cancerous activities have led to an upheaval of weather conditions, obvious today everywhere on our planet. The limits for tolerance seem to have been lost in both cancer cells and our societies while the gauge for change remains ill-defined. If such human behavior continues; the chief concern then is what will they do when cancer becomes a curable disease?

Keywords: Cancer; Human Behavior; p53; Tolerance; Gauge for Changes

Introduction

There are striking similarities between cellular activities and human activities whether in physiological or pathological settings. Moreover, human activities have largely been inspired by observations made in the natural world, at both the micro-and-macroscopic levels. This work reflects on the protein-model [1] described for cancer genesis and tries to mirror human questionable behavior through cancer cells' activities. At a cellular level and when Nature's Laws are observed, cells live in homeostatic conditions resulting in healthy activity of organs and systems they form. On the opposite, when a cell breaches Nature's Laws such as those governing cell division, diseases like cancer strike. And while normal cells follow regulatory rules for cell division and growth, cancerous cells defy them resulting in metabolically transformed cells which grow indefinitely.

The need to breakout from the rules governing cell growth and cell division becomes therefore obvious for a cell that is to become malignant. And to breakout of Nature's Laws, the cell may need to break up one of its proteins (according to the protein-model for cancer genesis) [1] and use the newly-generated fractions with their newly offered functions, to evade death processes and survive as an "outlaw" cell. This behavior translates into higher adaptation capacities that characterize and shape the immortal trait of cancer.

A new transduction signal proper to cancer cells seems capital in order to sustain unrestrained growth.

Therefore setting new standards becomes cardinal and could be played by the newly earned protein functions resulting from the breakup of a non-mutated protein. Numerous changes are then created and accumulate in cancer cells because DNA mutations – unlike protein entities – are capable of ensuring perpetuity of the malignant character. The new standards have two related objectives: defy death processes and ensure sustained growth; another way of viewing the two-hit hypothesis for cancer development.

While the objective in cancer is to sustain indefinite growth, cellular behavior that shapes transformation seems to follow this scheme: (*i*) a cell that breaks away from regulated growth needs new standards to not only stay alive as a separate cell but also to grow continuously; (*ii*) reinstatement of homeostasis must be prevented to keep transformation on; (*iii*) full malignancy calls for local invasion and paves the way for; (*iv*) the globalization of cancer though metastases formation.

Similar activities have been observed in human societies where a call for a continuous economic growth is the new standard characterized by an over-exploitation of natural resources and transformation of landscape to fit those never ending commercial needs. As a result, the flora and the fauna are both affected with the effect on the weather already visible worldwide. Moreover invasion and colonization of new territories in search for new resources have created dangerous ecological and social imbalances. Destruction, death and famine are remnants of long-fought wars between human populations.

When a Normal Cell becomes Malignant

Setting New Standards

For a normal cell - imbedded in a uniform and harmoniously functioning tissue- to become cancerous, it must breakout from its congeners in order to live a different life, that of a malignant cell. How such a cell could survive and continue to grow? This may be achieved if the cell gains new functions which will help it adapt while forging its way to an independent life style, the cancer style. In this case a transduction signal proper to cancer cells appears to be a prerequisite. Through this newly earned transduction signal, the cancerous cell senses its environment and reacts accordingly to remain alive and continue to defy death processes with all their variegations.

A new standard will allow rewiring metabolic functions through mutational accumulation where tolerance of inner changes and adaptation to outer conditions, take excessively new dimensions in cancer cells. These abusively used concepts of tolerance and adaptation lead to accepting those many changes aiming at the end to replace regulated metabolism of normal cells with an up-regulated metabolism of transformed cells; hence the name of transformation.

During the process of this transformation, oncogenes are over-expressed as such excessive production of key proteins is needed to accelerate growth. Over production leads to over consumption, over consumption translates into rapid activities and creates in turn a chronic state of stress that shapes a cancerous environment. Moreover, this overproduction often loses quality in favor of quantity as seen during the formation of tumor blood vessels [2]. Such overproduction creates overtime an imbalance which manifests as a disease.

Similarly modern human societies are overly stressed because they must compete all the time and adapt to ever-changing markets' needs. According to the modern economic scheme, this is the only way ensuring growth and profit. And while dissection of economics rules and activities is not the scope of this work; it is worth noting that our economic systems today praise overproduction and overconsumption. Table 1 shows a gross comparison of cancer cells' traits and human economic trends as compared to normal cells functions. While mimicking cancer behavior, overproduction of human-made products also praises quantity over quality. Today we are consuming genetically transformed food and foodstuff produced by different industrial processes. While human cancer-like behavior has resulted in great social imbalances and ecological disasters, the invisible and long-term effects of consumption of genetically transformed food have yet to be assessed.

Trait	Normal Cells	Cancer Cells	Economic Growth
Speed of growth	+	+++	+++
Limit of growth	+	–	–
Energy consumption	+	+++	+++
Short-term benefits	+	++	++
Long-term benefits	+	–	+/-
Global effect	+	––	––

Table 1: Common traits in cancer and economic growth as compared to normal cell growth.

Weakening Interventional Repair Mechanisms

In cancer cells, and parallel to the overproduction of oncogenic proteins, tumor suppressor proteins have to be silenced in order to prevent any interventional repair attempt that would restore balance and return the tissue to its homeostatic state. When this condition of shutting off tumor suppressor genes is met; rewiring metabolic functions becomes all possible as seen in cancer cells which accumulate numerous genetic changes.

In normal cells the tumor suppressor p53 protein has been named the guardian of the genome since it is in charge of several cell activities [3]. In cancer, this protein is targeted with mutations and/or deletions to prevent it from accomplishing its role of a tumor suppressor and prevent cancer formation. In some cases, mutated p53 proteins cooperate with cancer to help it grow and advance in malignancy.

Similarly, in healthy societies a p53-like role could be played by government and law authorities in charge of keeping order and restoring justice every time a breach occurs. However when a society shows signs of inequalities and unrest and thus becomes ill, those authorities - entrusted to restore justice and social equality through their tumor suppressor-like functions- are shut off or imprisoned, allowing the cancerous behavior to thrive and gain stage. In worst societies and when corrupt authorities take themselves an active role against their own communities and people, such a behavior mimics that of a p53 mutant working for cancer growth.

Starting Local Invasion

Once key metabolic pathways and key proteins are brought under cancer control, and manipulated according to the newly earned cancer transduction signal, cancerous cells become ready to move and expand locally in order to pave the way for distant growth and colony metastatic formation. However invasion would not succeed without first establishing some sort of partnership with different cells in the immediate microenvironment or hijacking their properties. In cancer a mutual relationship is developed with tumor associated macrophages (TAMs) contributing to tumor growth and metastasis [4]. The tumor microenvironment has also been shown to have a role in regulating cancer cells' behavior with a critical role of cancer associated fibroblasts (CAFs) contributing to the invasive behavior of cancer cells (Reviewed in [5]).

Similarly, at a societal level and when key personalities and leaders of a given community have become corrupt; the entire society becomes corrupt with natural resources being wasted and riches of the land ill-managed, creating as a consequence poverty that leads to crime and insecurity. Poverty, crime and insecurity are signs of ill societies in which corrupt businesses and companies work together with corrupted authorities to increment and install a cancerous model in the everyday life of that society.

Furthermore, when cancer development reaches a stage of a tumor that is detectable with our imaging techniques, it means that the immune system – likened to the army protecting the sovereignty of a nation – has failed to take protective measures and eliminate those cancerous cells. This failure could be due to immune system showing an erroneous tolerance to cancer cells' presence. While the immune system in its integrity remains functional in cancer patients; tolerance shown towards cancer cells is a misplaced tolerance with obviously negative consequences for the organ-bearing the tumor and the whole body suffering from cancer.

Therefore one can divide tolerance into positive and negative tolerance. The best example illustrating this point is the appearance of mutations. A controlled low level of mutations that allows diversity is an example of positive tolerance in the sense that these mutations are accepted on the basis that they do not result in harmful consequences. On the other hand when the number of mutations becomes excessive; the limit of positive tolerance is breached and turns into negative tolerance with harmful consequences as seen in cancer. Gross chromosomal abnormalities and aneuploidy are both accepted in cancer cells because tolerated. This is not the case in normal cells where such abnormalities are either corrected or the cell bearing them is sent to apoptosis. This is the role played by the guardian of the genome p53 protein. In cancer cells however that gauge becomes lost and tolerance goes out of control; accepting at the end all sorts of changes in the genome including insertions, deletions and substitutions leading finally to serious changes of the genome landscape [6].

Globalizing Cancer

According to the protein model for cancer genesis [1], cancer behavior links transforming steps from time zero when the protein breaks up till the time of metastases establishment. Invading neighboring cells is not enough for active tumors; the new model of cellular life i.e. the malignant style must be taken to distant organs for a

global change in the entire body inflicted with cancer. Moreover cancer stands for growth; the more the better regardless whether the body where cancer cells live is capable of continuing to sustain that growth or not.

When the new standard-the cancer standard that dictates a continuous cell growth-is set, where the limit could be found? Nowhere; globalizing cancer is globalizing the way a cell should use energy, produce its metabolites, grow and divide. All this is achieved at the peril of healthy cells still working in accord with Nature's Laws regulating cell cycle and division. While the final result is full destruction through impairment of the body's vital activities, such outcome is but the result of a misplaced tolerance accepting all changes without sifting through or calculating their long-term consequences (See figure 1). The gauge that should help in discerning a positive change from a negative one is lost because of cancer cells' selfish character.

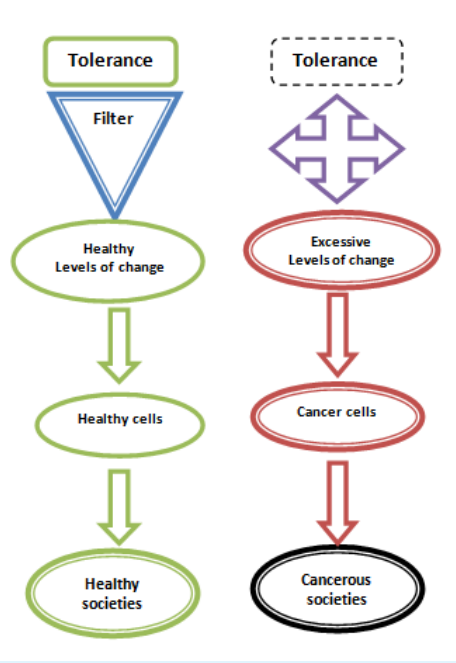

Figure 1: Tolerance in normal and cancer cells and a parallel with society**.**

Filtered tolerance allows positive changes to take place after weighing their long-term consequences, leading to healthy cells and healthy life. Lack of filtering accepts about any change since no weighing of long-term consequences is used and this leads to cancerous cells and cancerous way of life in human societies.

Similar to cancer growth, human cancerous activities have caused many animal species to go extinct as their habitats have been destroyed. Human selfish activities have also caused the disappearance of many plant species before ever discovering their medicinal secrets; creating room for massive production of industrial crops that guarantee huge short-term profits. The standard for human cancerous attitude is growth, expansion and globalization of boundless economic activities. If such behavior continuous; the fate of our planet could well be that of cancer and be destroyed like the human body that is destroyed by cancer. The scientific community must voice this concern as it is crucial for the long-term survival of our species and the wellbeing of our plane.

When Humans Behave like Cancer

p53-Like Functions in Human Societies

p53 is a key protein in the life of normal cells with diverse and important roles to help protect cells and guarantee a healthy life. In normal settings, p53 protein is kept at low levels by regulators such as MDM2 which facilitates its degradation. However in the presence of various stresses including DNA damage and deregulated oncogenes; the protein is stabilized in order to carry out the needed functions, depending on the nature of the stress and the cellular context [7]. p53 protein can therefore induce repair, cell-cycle arrest, senescence or apoptosis. Other non-canonical processes in which p53 plays a role include ROS control, autophagy, tissue-remodeling and metabolism.

In front of a cellular stress and if we were to interview a p53 protein on how it would proceed, the answer might be this: first try to repair the damage and provide the means and the time needed. If that is unsuccessful; try next to arrest the cell cycle preventing it from further advancing in order to eliminate ahead of time any risk of making a cancerous cell. If that is unsuccessful and depending on the nature of stress; send the cell into senescence or sentence it eventually to death through apoptosis.

To accomplish these different roles, p53 has under its authority several cooperating gene products such as: p21, 14-3 3 alpha, Gadd45, Bax, Apaf1 and Maspin. This is how homeostasis is maintained at a cellular level; watching over cells activities to detect any misbehavior, signal for correction while providing the means for that end, confinement (senescence) when a cell maintains its non-corrective attitude or finally give orders for death penalty i.e. apoptosis. It's for the benefit of the whole to kill that

individual cell which is rejecting corrective adjustments while maintaining a destructive behavior. At the end p53 ensures the optimal organ-and-body's functions to continue.

Much of human behavior in our society today is based on self-interest at different levels. Self-interest seeks short-term gains regardless of the damage caused to all that is other; individuals, nations, animals, environment or the entire planet. A growing cancerous cell does very much the same; multiplying selfishly, forming tumors and metastases until the entire body is destroyed. Colonialism among nations could also be regarded as a manifestation of a cancerous behavior at a larger scale which insures continued economic growth for the invading nation (cancerous cell) while impoverishing and sickening the invaded nation subdued by force (the organ colonized by tumor growth).

It is therefore tempting to ask here this philosophical question: Since cancer is subsequent to human appearance, could cancer be regarded as a cellular incarnation of human cancerous behavior? Viewing the problem from this angle, could lead to consider cancer appearance as a wakeup call for humans to change their behavior and their attitude towards themselves and towards their human fellows and to Life as a whole. Cancer hurts the body on which it grows and hurts families when their loved ones succumb prematurely due to cancer. Similarly, human cancer-like behavior hurts individuals, societies, nations and the entire planet. Like cancer invasion, human invasion of nations creates suffering and leaves behind death and desolation. If we ignore the pain caused to others and tend to justify our invading action, the human body colonized by cancer tumors can hardly ignore its pain.

Tolerance: Are there Limits?

When a cancerous cell shows tolerance to mutations, it obviously won't correct them moreover this cell accumulating such mutations is not sent to senesce nor is it led to apoptosis for the recycling its components. This trend of tolerance calls for more mutations to accumulate and more metabolic changes to take place and show new phenotypes. This self-centered behavior of cancer cells over-sees the needs of neighboring cells in the organ where they are growing. The excessive tolerance of increasing numbers of cellular changes may also help buildup resistance to drugs and environmental changes in order to foster survival [8]. Mutation-formation becomes therefore a way of living and the only approach that ensures survival and continued cancer growth in a changing environment. Continuity demands adaptation and adaptation is seen as the ultimate cancer hallmark according to the protein-model for cancer genesis. On the other hand adaptation is known to be a feature of all living organisms, but adaptation that is in harmony with Natural Selection favors reproduction and not survival *per se* as is the case in cancer cells. Reproduction ensures homogenous genomic traits to be transmitted to daughter cells, but cancer cells multiplication shows rather heterogeneity [9] more than homogeneity.

The Gauge for Changes

Contemplating on cancer cells adaptation and growth leads to see these cells as favoring changes expressed as cancer heterogeneity. Generally speaking a change brings about innovation and diversity and what could be wrong with such a choice? In cells however, excessive changes may have a detrimental outcome because the natural part that is Nature-Made ends up being gradually lost, reaching at the end of the line something that works completely differently. The crucial question then is how to control the resulting product emerging from those excesses of changes? As cancer cells accumulate mutations, their growth goes out of control because Nature's Laws for coordinated cell division have been gradually broken. Moreover, the elevated mutation number and gross chromosomal aberrations have been suggested to be tolerated in cancer cells only [10].

What's lost from view as cancer cells grow is weighing the effect of these changes in the long run. But why cancer cells should be concerned with that? A selfish behavior that is centered on short-term benefits does not care about weighing long-term effects. The immediate gain of survival is what matters most for cancer cells confronted for example with anti-cancer drugs. And cancer goes one step at a time in fulfilling its mission for malignancy: change to adapt, adapt to survive, survive to grow, grow to invade and invade to metastasize. This seems to be the motto for being cancerous. When p53 protein (with other proteins involved) foresees a positive long-term effect; it allows the mutation to be fixed. However when such benefit cannot be calculated or a negative outcome is obvious, that genetic change is not fixed in daughter cells.

On the other hand and if changes are able to bring about innovation and diversity it means that there aren't only negative consequences for making changes but positive ones as well. The question then is how to know a positive from a negative outcome of any given change? One must weigh long-term effects of any change made and the way to do it could be seeing those changes through

the window of Natural Law and Evolution. How any given change will evolve in the long-run? When Nature's Laws are observed; the change can bring about positive outcomes while the opposite holds true. Figure 2 outlines the gauge for positive and negative changes which lead respectively to progress and regress. Change is important when carefully designed however resisting change can also lead to stagnation and survival in this case will not evolve to see the lights of progress and Evolution.

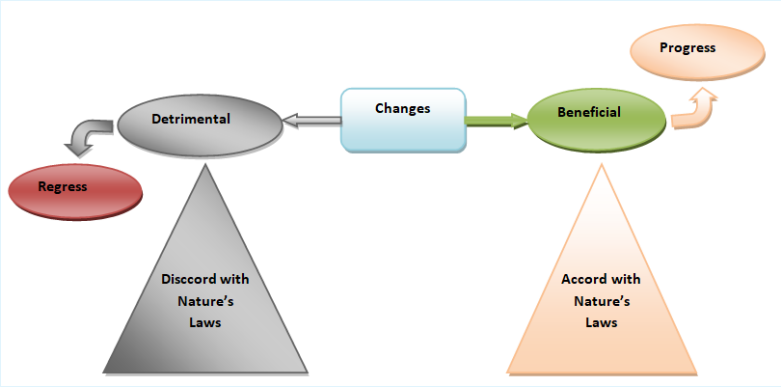

Figure 2: The Gauge for making changes. A change is beneficial when it shows real advantages in the short-and-long-run, thus in accord with Nature's Laws: this leads to Progress. A change is detrimental when it shows apparent advantages in the short-run but no advantage in the long-run, thus in discord with Nature's Laws: this leads to Regress. When a cell or a society resists change; this behavior leads to stagnation and in this case survival may be ensured but the lights of progress will not be seen, also in discord with the Law of Evolution.

It is worth noting that making several changes within a short period of time makes it difficult to weigh the long-term consequences of those modifications. While genetic changes result into a faster growth rate of cancer cells, at a societal level -and mimicking cancer growth- technological changes also result in fast economic growth. Many fast developing economies ensure short-term benefits while creating in the long run serious problems for our planet such as pollution. The idea of recycling material has emerged too late instead of evolving side-by-side with each new technology. Normal cells recycle their by-products without delays otherwise a pathological state would be created and the cell would be polluted with its own-made metabolic toxins.

Discussion

When a normal cell is to become malignant, it sets different standards for its growth and creates along the way, numerous mutational changes to which it shows excessive tolerance. Parallel to this and in order for these new standards to work and achieve the goals of malignancy, repair mechanisms aiming at restoring homeostasis must be shut off, hindering their action through loss-of-function mutations or destroyed through genetic deletions. And once important metabolic pathways are brought under control, cancer cells become ready for invasion and metastases formation in order to globalize the malignant character.

Knowing cancer cells behavior, one can hardly ignore similar behavior when observing human activities. Excessive tolerance to rapid changes without a guiding gauge, are a trait of cancer cells. In our societies today tolerance is misused to legalize what once was illegal without ever weighing the long-term consequences of such shifts. When short-term benefits are shown, why complicate matters and think about possible negative effects in the far future? While innovation seeks changes for the better, the question is how a single change fits in the whole? But selfishness – a cancer trait– does not care for the whole nor does it consider the bigger picture as an important issue.

Cancer defies regulations set by Nature in order for Life to continue in harmony, hinders the functions of the organs on which it grows to finally cause the collapse and death of the entire body. Similarly the entire planet is affected with the consequences of human cancer-like practices occurring everywhere in the globe. We have

already indulged in a dangerous behavior and continue to pollute our planet in million ways because growth must not halt and profit must continue at all costs. Moreover, globalization of business practices could put in peril markets worldwide as failure of one part may trigger the failure of the whole, similar to liver failure that cause failure of the whole body.

On the other hand, it is thought that Evolution has allowed cancer to manifest but without selecting for it [11]. The question then; is the manifestation of cancer a lesson for us to see the harm of our own actions? If cancer lessons are not learnt and human behavior does not reinter back in harmony with Nature and respect Nature's Laws; destruction could be our fate. Great civilizations have perished before us but we still hold a chance today to reshape our fate and give it a safe direction. Moreover, we do not know better than Nature and human populations need to make collective conscious decisions and respect Nature's Laws. Scientists must make their voice heard with the objective of enlightening the public otherwise unqualified individuals will continue to make harmful choices and walk us from disaster to disaster; creating new problems while thinking of solving the old ones. The matter here is not about stopping economies from growing nor is it to prevent the rich from becoming richer –if that were the unique goal of businesses and industries– but rather to instill in them a new consciousness that which will foster change and innovation while preserving Life and protecting our planet. Once this shift in consciousness is earned; it is enough in itself to inspire those same minds to become positive creators instead of remaining pioneers of negative catalysis worldwide.

While human cancerous behavior is obvious, the chief concern behind this work is what will happen to the human species in the long-run when cancer becomes a curable disease? Would a smoker of one cigarette-package smoke two packages? Would radiation safety rules be neglected? Will we make a backward step and produce over and again those banned substances? Or find for them new utilizations now that cancer is no longer a threatening disease? To which lower level can we go for the sake of economic growth? And will scientists step back and let lay individuals decide the path and the fate of human species?

There isn't cancer as the only disease to worry about; there are other diseases and health complications that can be caused by cigarette smoking, radiation exposure or harmful chemicals. Moreover a harmful substance remains harmful even when cancer is prevented from occurring. What a lay person needs to understand is how human body responds to harmful substances as they exert their stressful effect on different organs. If the human body can no longer respond with cancer (because vaccinated against cancer) it may well respond with a new disease that could be far more dangerous that cancer itself. This point will be illustrated by empirical data in animal experiments when they become available.

Finally choosing to cure cancer is important for the human population's well-being and its survival. The benefits sought behind are: (*i*) Alleviate human suffering in cancer patients; (*ii*) Stop human mutilation provoked by mastectomy, prostatectomy and other surgical practices; (*iii*) Increase life expectancy; (*iv*) Allow cancer-research budgets to be channeled to research on other diseases in order to find cure for them; (*v*) Ensure human prosperity and progress. And while it is worth curing cancer, wise decisions and positive factual actions are of capital importance and first needed to avoid a human disaster in the era when cancer becomes curable.

Conclusion

Cancer is a transforming disease taking a cell from a regulated and healthy growth to an up-regulated and unhealthy growth. In cancer, the cells' metabolism is rewired to serve a selfish growth and unchecked expansion through colonic metastases formation. The landscape of organs on which cancer grows is modified until life can no longer be sustained.

There is a striking similitude between cellular metabolic activities and human societal activities. Today our economy seems to follow a cancerous model seeking continued growth and never-ending profit at the peril of our ecosystems. While growth and profit are a right in themselves, these must not be made at the detriment of Life or Nature.

Continuing to breach Nature's laws as we are doing today can only lead us to perilous consequences. A clear gauge weighing long-term effects must be dressed for every new technological achievement or major change in our societies. Recycling our waste will succeed only when we endorse healthy economical activities, similar to healthy but not cancerous cells' activities. Without a shift in consciousness human species risks regress instead of continuing to evolve. Scientists have a pivotal role to play and must step in to not only educate lay population but also to enlighten our economy leaders and law makers;

help them build healthier industries with unselfish profits which serve life while preserving our planet.

Conflict of Interest

The author has no conflict of interest.

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