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The ecological and evolutionary meaning of cancer

Abstract

Cancer is a serious health problem worldwide. The introduction of an ecological and evolutionary perspective of malignant neoplasms is aimed at a more systemic and objective approach to the nature of this heterogeneous group of diseases. With the aim of an approach to the most generalized ideas existing at present on the ecological-evolutionary perspective of cancer, the present systematic review was carried out. Cancer is a universal phenomenon that affects all forms of multicellular organisms. The risk of developing malignant tumors is closely related to the patterns of life histories traced by the evolutionary process according to the adaptive need of organisms to the different ecological niches they occupy. There is an association between the evolutionary development of protective mechanisms against malignant tumors and the evolutionary cost of these in terms of reproductive success. Reproductive success seems to depend on body size, the distribution of energy towards basic processes and the basal risk of cancer. Natural selection favors effective mechanisms that protect against cancer as long as they allow an optimization of other traits that determine adaptive success. The conclusions derived from these ecological and evolutionary principles should serve to better characterize the factors that depend both on the biological and environmental factors that influence the risk of carcinogenesis. More than 90% of the increase in basal risk of cancer, even in natural species, is due to human activity, and therefore, can be modified.

Keywords: evolutionary carcinogenesis, peto paradox, life history theories, cancer ecology

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Introduction

Cancer is a relevant global health problem. In many countries it already represents the first cause of death.[1–4] The patterns of incidence, prevalence and mortality due to neoplastic diseases vary considerably between developed and underdeveloped countries, registering the most unfavourable records at the level of developing nations.[1–4] In our country, during 2016, malignant tumors accounted for 24 303 deaths (13 956 men and 10 347 women); specifically in Santiago de Cuba, an age-adjusted rate of 108 was recorded, 3 deaths per 100 thousand inhabitants.[5]

In spite of the therapeutic advances obtained in recent decades regarding the management of neoplastic diseases, these continue to behave as potentially fatal entities, since, whenever a malignant tumor becomes clinically manifest, it is very likely that it has culminated with all phases of its natural evolution; therefore there subclones microscopic metastatic spread, or worse, subclones resistant to chemotherapeutics or other cytotoxic drugs peaks[6] cells. The most optimal strategy continues to focus on prevention. From the 50s of last century began to emerge a new perspective on cancer, an ecological-evolutionary perspective.[6,7] To date much has been written on the subject, but there are already ideas that can be generalized; and it would be of great interest to approach such generalizations, which in turn would result in a better understanding of the extent and magnitude of this complex group of diseases encompassed in the term "cancer".[7] The objective of this systematic review focuses precisely on this: To provide the main theoretical and empirical elements that characterize malignant tumors as ecological-evolutionary phenomena.

Development

Evolved by and against cancer

What is adaptive success? It is nothing more than the fact that an organism manages to reproduce itself and transmit its genes to its offspring. Of course, to achieve adaptive success, every organism must first be born, grow, develop and reach reproductive age; and since they are previous stages that can be achieved, or not, we speak of adaptive success in terms of probabilities; so more exactly, adaptive success is the probability that every living organism has of transmitting its genes to offspring.[8]

Why are there protective mechanisms against cancer? At first glance, this seems to be an illogical question that would lead to an obvious answer: there are protective mechanisms against cancer precisely in order not to develop it. However, the answer to the question with which this chapter began has implicit a profound ecological-ecological principle that should not be overlooked from now on if you want to have an approach to the essence of cancer.

There are protective mechanisms against cancer in multicellular organisms, and to maintain the functional harmony and integrity of so many cells, the adaptive success of any of them has to be subordinated to the adaptive success of all the others, or what is the same, of the organism in general.[9] From the perspective of adaptive success, it would be more optimal for a single cell to proliferate independently, even at the expense of forming a dangerous tumor, than to cooperate with the rest of the cells in order to guarantee the reproductive success of the entire multicellular organism. which belongs.[9] In other words, the asexual reproduction of an isolated cell would guarantee the transmission of the totality of its genes to its descendants, and would result in a greater benefit for it than if it suppressed its "egoism" and cooperated in conjunction with as many millions of cells with such that the individual, after growing, maturing, and achieving sexual procreation, transferred part of the genes of said single cell to the descendants of the individual in question. Then, the most appropriate answer to the question of why there are protective mechanisms against cancer would be equally simple, although with another connotation.

Because there are multicellular organisms, that in order to maintain ourselves as such, they need the cooperation and ecological harmony of all the cells that make us up.[9] Cancer is one of the ways to break this harmony and multicellular cooperation since, from the activation and start-up of an abnormal somatic evolution, a single cell begins to multiply uncontrollably to form an anomalous tissue that benefits and contributes adaptive success to a set of mutated cells to the detriment of the entire organism.[9–11]

Why are there then multicellular organisms that run the risk of developing an abnormal somatic evolution inside their bodies? To "network wave" the idea, considering that the formation of a multicellular organism requires the subordination of the behavior of a single cell to the demands of the total, it is logical to admit that in every individual composed of many cells there is a real conflict ; the conflict derived from: 1) The advantages that would contribute in the short term for a single cell to begin to multiply in a superior manner to the rest by means of asexual reproduction; 2) The advantages of inhibiting this "selfish temptation" because the cooperation of the whole would favor long-term sexual reproduction of the whole organism.[12]

That is, the conflict of the advantages of a cell against the advantages of an entire individual; cellular organism. The appearance of multicellularity occurred thanks to the grouping of several cells that had the ability to live and reproduce in isolation and independently. Its integration inhibited the self-reproductive potential of each of them, but it has not been able to eliminate it.[12] And this has definitely made evolution in multicellular individuals: sacrifice the advantages of asexual reproduction of a single cell in the short term, in order to ensure the long-term benefits of the whole organism through sexual reproduction.[12] In the second place, and at the root of the first principle, it must be assumed that the appearance of any genetic change in an individual cell that confers reproductive advantage on its neighbours, will reactivate, and start up the somatic evolution; and one of the variants of somatic evolution is cancer.[13,14]

What are these protective mechanisms? Life, in its simplest unicellular and appeared on our planet hará some 4000million years. It is surprising that it existed for two thirds of that time, fulfilling its survival requirements in that microscopic, individual and simple way. But environmental demands, always changing, led to the appearance of multicellularity; and natural selection operated positively on those organisms that had better mechanisms to maintain cooperation and harmony among the millions of cells that constituted them; those that can be summarized in general terms are as follows: 1) decrease in the effective cellular population conducive to the or somatic evolution trend; 2) to "intelligent" tissue architecture that decreases probabilities of activating an inadequate somatic evolution; 3) existence of "tumor suppressor" genes; and 4) the most effective immune and surveillance system.[15–17]

If something needs natural selection to "do its job" it is to act on an effective population; that is, that fraction of the population that is capable of reproducing itself. In this aspect it is so demanding, that it immediately eliminates embryos that carry disadvantageous characters, because undoubtedly they will not contribute to increase the effective population; As for the individuals who are in advanced ages, natural selection becomes "blind" and stops influencing them, because they are not part of the effective population either, since they have surpassed their reproductive age.[18] But, at the level of the body of a multicellular organism, who constitutes its effective population? as stem cells, those that have the property of several cell lines originating from both divisions are now able to self-renew; what makes them "perfect target" for the implementation of a somatic evolution. Multicellular organisms have developed several strategies to reduce their effective cell populations, among which are: 1) l own decrease in the number of stem cells. Pluricellular organisms are constituted by greater proportions of somatic cells completely differentiated or in the process of being compared to the "foci" of the mother cells that serve as a reserve; 2) The stem cells have little tolerance to mutations, so that in the case of minimal events that alter their genetic material, they die; 3) when they divide, they retain their original DNA molecule (DNA matrix); transmitting copies of this to the descendants. With this, the errors that occur during the process are inherited by the daughter cells, who must deal with these errors. If they are course, they will inevitably die; if they are more subtle, it is up to them to solve them or equally to die if they fail to do so.[15] As can be seen, these are mechanisms and strategies that seek, in the main, to reduce the chances that the stem cells, meaning an effective population, can initiate an evolutionary process, suffer mutations that disturb their normal functioning, either by decreasing their number, protecting its genetic information, and even through more drastic measures such as suicide.[15]

In spite of how "effective" these mechanisms seem to be, natural selection favoured added strategies that diminished the probabilities of inadequate somatic evolution; and it played an essential papel design tissues.[16]

One of the many facts of evolution that cause admiration is the very architecture of tissues in multicellular organisms. These are formed by subunits called cell compartments. In each cellular compartment are the respective mother cells with their descendants, well delimited by physical barriers of other cellular compartments.[16] In each cell compartment, the number of stem cells is smaller than that of their differentiated progeny; which translates into a lower effective population. Of course, the number and physical size of cellular compartments vary according to the type and function of the tissue or tissues that make up a particular organ of the organism. But the very existence of these compartments is in itself an effective suppressive strategy of somatic evolution, and therefore of cancer risk, since cellular compartments are defined as the proliferative units of multicellular organisms. The phenomenon can be explained through the metaphor distribute the "problem" of maintaining the integrity of organisms in various "sub problems" which come being proliferative units.[16,17]

The above can be illustrated with an example. The cellular compartments, or proliferative units, in the human intestine are structured in the form of crypts, in which the scarce stem cells are located at the bottom of these, while their descendants, many more numerous, are "climbing" by the slopes until reaching the top, where, already aged, they die, they decay, and leave the body. Intestinal crypts are exposed to a huge amount of mutagens (bacteria and toxins in their metabolism, toxins derived from some ingested food, etc.); and it is not cause for surprise that your cells suffer mutations. But the structure of the crypt functions as a true "scrubber" mutations, because the mutated cells they have no other way to reach the top, and eliminated.[17] Things do not end here. It must be remembered that ultimately it is the genes, and their products the proteins, that regulate cellular behaviour. An altered gene creates a disturbed protein that disrupts the behaviour of the cell. And in each of the cells that make up the body there are some genes known as proto-oncogenes, whose essential function is to stimulate cell proliferation and survival. There should be no doubt about its vital importance. However, when said proto-oncogenes undergo alterations, they become oncogenes,

and among other things, they "trigger" cell multiplication in an uncontrolled manner.[19] Fortunately, as there are proto-oncogenes, there are others that control, regulate, and even oppose their activity. They are known as suppressor genes or anti-oncogenes.[17] Like proto-oncogenes, antioncogenes are so numerous, so diverse in structure and function, and are part of genetic programs so complexly interrelated, that characterizing them escapes the purposes of this work. It would be enough to exemplify one of them. The TP53 gene codes for the elaboration of a protein that carries the same name, protein TP53. When the DNA of a given cell suffers some type of injury, the TP53 protein is activated and immediately "orders" the arrest of the life cycle of the cell.[17] It will be unable to divide until TP53 is "informed" that the damage to the DNA has been repaired. Then, and only then, this true molecular police will raise the "cell block" and allow the cell to fulfill its life cycle.[17,19] Another very different thing happens if the damage cannot be corrected. TP53 then launches the process of programmed cell suicide, and the diseased cell is removed immediately.[17,19]

As if that were not enough in terms of antitumor control mechanisms, the existence of the immune system remains; an incredible and sophisticated network of cells specialized in the surveillance and defense of multicellular organisms; both of foreign and invasive agents such as bacteria, viruses and other parasites, as well as of own cells that show anomalous behaviour, such as tumor cells, and even others that enter the physiological process of cell aging.[20] In fact, there are many authors who defend the theory that the immune system emerged and has been "perfected" throughout evolution precisely to maintain cooperation and harmonious balance between the diverse cell populations that make up the multicellular beings.[20,21] The function of the immune system is eminently police; and it is organized hierarchically for detection, warning, and any disturbance suppression which compromises the integrity of every individual.[20] As has been seen, the emergence and evolution of multicellular organisms occurred in response to changes imposed by the environment, and signified an undoubted leap of complexity in the organization of living matter. However, natural selection operated positively only on those organisms that had the most effective mechanisms to maintain cooperation among the numerous cells that make them up. These mechanisms act in a "coercive" or police way in order that the cell vs. organism conflict exists at the "lowest possible" level, and guarantees the reproductive success of the multicellular organism; but the chances of this conflict leading to an inappropriate somatic evolution are by no means non-existent. So there is all the right to ask, cancer for all that is multicellular?

Cancer for everyone? When cancer is referred to as a phenomenon that disrupts cooperation in multicellularity, it is necessary to talk about "cancer-like" events, which are conceptualized as alterations in cellular cooperation that result in uncontrolled proliferation and altered differentiation. Disharmonizes multicellular architecture.[19] The phenomenon has been recorded from sponges, fungi, bacteria that form colonies or biofilm, green, blue, red and brown algae.[22,23] Neoplasms have been reported in echinoderms, hemicordates, planarians and earthworms (with evidence of tissue invasion, angiogenesis and mass formation with undifferentiated cells), in mollusks (with lethal tumors such as germinomas); in oysters and mussels the prevalence ranges from 3.3% to 50%.[22] They have been described in crustaceans and arachnids. In insects, such as Drosophila, tumors have been recorded that mimic lymphomas, leukemias, neuroepithelial tumors, and gastrointestinal tumors that metastasize and kill the host.[22] It has been documented in anemones, hydras and corals. One type of tumor, the calicoblastic epithelioma, possesses cancerous attributes such as uncontrolled proliferation, tissue invasion, angiogenesis, and decreased reproductive fitness in large coral masses in the Philippines. Its prevalence has been estimated at 39%.[22,24]

Cancer has been witnessed in all chordates. According to the documentation provided by some 9,000 necropsies, it was shown that birds and reptiles have lower rates of tumors than mammals (1.9% in birds, 2.2% in reptiles, and 2.8% in mammals), but all have the risk to suffer it.[25–29] Contrary to what was believed, plants also develop forms of cancer, and it is not surprising given: their larger size, greater longevity, and peripheral location of their stem cells (more vulnerable to the effect of mutagenic agents). The phenomena similar to cancer in plants seem to be less lethal, because in these the genetic instability typical of neoplasms, however, favors a greater morphological and functional diversity that would be useful in adverse environments and constantly changing.[22] It seems that cancer, or its "analogous phenomena", are inherent elements of multicellularity itself, and its distribution is simply universal. There is, however, a very remarkable fact because of the interest that it will surely arouse in the reader. With all of the above, an idea becomes patent: the more complex the multicellularity, the greater the risk there is of developing a tumor. A concept as close as possible to what is referred to as complex multi-cellularity, is obtained from d the following axiom: a multicellular organism has greater complexity while more number of cells has, and more time lasts.[30] And of course, the greater the number of cells, the harder it will be for the organism to maintain cooperation between them. Similarly, the longer the longevity, the longer the exposure to environmental mutagens (external and internal), or the greater accumulation of mutations during the normal DNA replication processes essential for cell renewal. Therefore, the greater the body size and longevity, the greater the complexity, the greater the cell vs. organism conflict and consequently the higher risk of developing cancer.[30] The logic of this axiom is impeccable, but is it really like that?

Peto's paradox: An average human being, about 70 kg in weight, owns approximately 60 trillion cells (60 000 million) of which about 500 trillion are exchanged daily; and has an average risk of suffering cancer throughout his life of 30%. The blue whale, meanwhile, weighs more than 30,000 kg, has 1,000 times more cells than the human being, lasts an average of 200 years when predators and humans are allowed, but has not been shown to have a higher rate of neoplasms, when, according to the logic stated above, it should have 1000 more opportunities to develop them.[30] Contradictory the fact. This phenomenon has been called "Paradoja de Peto", in honor of the author who proposed it in 1975, and it is extended to elephants, horses; to animals that surpass man in body size and surpass him or equal him in longevity; but in the same way to much smaller animals, like mice, in which we would expect lower rates of cancers thanks to their small size and short life, when nevertheless in these the frequency of malignant tumors is quite close to that of the humans.[30] The number of works that Peto's paradox aims to solve is enormous and the debate is still open today.[31–33] There is no doubt that evolution has endowed large organisms (and therefore carriers of a huge number of cells) and long-lived, efficient mechanisms to suppress cancer. Peto's paradox in this aspect seems to have convincing explanations that solve it; that is, the large long-lived multicellular organisms equal their cancer risk to that of small, short-lived organisms by improving their mechanisms of tumor suppression.[31] However, the case is "discordant" with such solutions that, for example, naked mole rats, weighing approximately 35grams, have an exceptional life expectancy of about 30years; and have shown a unique resistance to cancer, both to those that arise spontaneously and to those who have been treated to induce them

in laboratories employing the most powerful agents.[22] In fact, no malignant tumor has ever been demonstrated in this peculiar species. That is, although it is small, it has an exceptional longevity, but also an unusual resistance to cancer.

In addition, for the sake of making the reader more didactic, the fact that greater mass and body size, proportionally more and better mechanisms to suppress cancer has been regularized. In all honesty, investigations into the genome of many mammals have not shown a strong correlation between body size and number of copies per cell suppressor gene, as has been evidenced such redundancy in both large organizations and small.[31] There was a reason why it was noted at the beginning of this section that Peto's paradox still provokes a bitter debate. In fact, there are even those who question it through arguments as logical as those that seek to explain it.[34] The problem is that each theory seeks, separately, to satisfy from its perspectives the immense amount of variables involved in the dynamics of multicellular organisms and their mechanisms to reduce the risk of mismatching multicellular cooperation. It is almost certain that all have their part of reason. And evolutionary theory comes to help to integrate them all. The ideal for any multicellular organism would be to use all its energy to maintain itself; or, to be more exact, in maintaining its multicellularity. Each day is a challenging confrontation to the environment, and it is necessary to restore the resources spent, regenerate aged tissues, repair wounds, eliminate parasitic agents, check the state of the cells; that is, to stay.[35] There should be no doubt that if all the energy were invested in body maintenance, every multicellular organism would be eternal, eternally young, and in all probability free of cancer. But this is not the case in real life, because simply every multicellular individual has to grow, develop or mature, has to reproduce once maturity is reached; and each of these biological functions demands energy. As the energy possessed by every individual is finite, it must have to subtract part of the intended on staying, to invest in the basic functions above.[11,36]

Then, the other ideal for any multicellular organism would be to proportionally distribute its energy in growing, developing, and reproducing; administering it with such rigor of equity, that it would always have the indispensable amount to maintain itself, in addition. Unfortunately, it does not happen that way in real life. It is the environmental demands that impose the priority, rhythm, duration, and intensity of the energy investment in all the living beings of the planet.[35] In short, every individual will have to distribute their energy in: grow, develop, maintain their healthy and efficient structures, and reproduce. With regard to cancer, will Peto's paradox find a satisfactory explanation according to the ecological-evolutionary circumstances that determine the development of an individual? Be bigger, last longer, or be smaller and last less, obey evolutionary obligations even if it affects the chances of developing cancer? Almost categorically the answer is: yes.

Before justifying such a strong statement, it is necessary to reiterate one of the premises stated above: Since the energy available to a given organism is unique, by distributing a portion of it to guarantee a certain function, it will necessarily have to subtract it from the total, and with it, subtract it from other functions. In other words, use it at a cost.[35] It cannot grow quickly and mature at the same time with the same intensity. The first requires a high rate of cell multiplication, maturing requires a differentiation rhythm. The use of energy and the cost of doing so to the detriment of other functions is inevitable.[35] This framework of environmental demands and the strategies that derive from them to distribute the energy between growing, maturing, and maintaining, in order to reproduce, is what is known as: Life stories.[37] Generalizing, evolution has not done more than "trace" life stories. Now, does cancer participate in life stories?

Cancer and life histories: Peto's own paradox forces to think about the relationship of cancer with life stories; Why the incidence of this disease remains approximately constant between the different species despite the differences in size and longevity, when it should be expected otherwise? It is essential to keep in mind that of all the energy investment needs of a multicellular organism, that destined to body maintenance is the one that has the greatest relationship with the conservation or deterioration of health.[35,36] The somatic maintenance is the one that guarantees in the last instance the optimal functioning of the multicellularity; subtracting energy from this process results in phenomena such as aging, degenerative, infectious, autoimmune diseases, arteriosclerosis, and cancer.[35] With regard to the latter, being larger and lasting longer would entail a greater risk of suffering since both traits simply imply a higher rate of cell multiplication, consequently a greater number of cells "vulnerable" to malignant transformation, and a longer exposure time to environmental mutagenic agents by so many cells, with the consequent increase in the chances of accumulating mutations and epigenetic changes that lead to carcinogenesis, and the chances that the carcinogenesis itself will successfully meet its multiple stages of development. Being smaller and lasting less, of course, would mean the opposite.[37,38]

But there are both extreme sizes in the long *continuum* of life forms. It should not be for pleasure because it obeys to evolutionary pressures. It is pertinent to follow the reasoning of Hanna Kokko[37] and her collaborators.[36]

Obviously, having a larger size also brings many advantages: greater protection against predators; lower energy expenditure during long distance travel; better access to resources and food sources; and, with regard to the ultimate goal of reproducing, a greater success in reproductive competition (in species where males are much larger than females can ensure that there is strong competition among the first to find sexual partners, in which larger individuals have an assured advantage, not so much to fight as to "dissuade" opponents or "captivate" females with their signs of vigor and strength).[36] However, it cannot be denied that growing so much requires a large investment of energy. Hence the maintenance of such a huge multicellularity is extremely costly, and one of the evolutionary strategies to achieve it has been "slowing down" the pace of life of large organisms to "give more time" to maintenance and "not overload" it.[36] The final consequence of this adaptation: an elongated longevity. It seems unquestionable that greater longevity or a slower pace of life as a result of being "large" also requires evolutionary strategies aimed at reducing the risk of cancer. Obtaining this slow pace of life in individuals of large body size, to stay whole and free of cancer, can be achieved through two mechanisms: Slowing down more effectively than small animals the rate of cell multiplication; to part from all the modalities already enumerated (decreasing effective population of stem cells, "smart" tissue architecture, etc.); or: increasing anti-cancer defences (copies of redundant tumor suppressor genes, more effective immune system...).[36]

Problem solved. However, ensuring this slow pace of life behaves, as expressed by Hanna, as a "double-edged sword", since, in effect, it would reduce the risk of cancer, but at the cost of delaying also the time necessary for the organism to reach its reproductive fitness, and be at the mercy of other causes of death extrinsic just before reproducing. And they start from the hypothetical example that if some type of

cancer had an incidence of 100% at two years, for a field mouse, with an average life of precisely this time, or reproduced earlier, or very likely dies by external causes before reproducing; while an elephant on the other hand, will be almost hopelessly condemned to suffer from cancer many before it has managed to leave offspring, and this discounting the fact that, achieving the "miracle" of overcoming such absolute incidence of the tumor, he still had the challenge of escaping the causes of extrinsic deaths.[36] In addition, for animals of large size and prolonged life, or slow life histories, investing energy both to decrease the chances of developing cancer and to increase defences or "barriers" against it, would be exorbitantly expensive, and even evolutionarily inefficient; more when individuals of small size and less longevity, or fast life histories, even when they lacked both mechanisms, they would obtain a similar result with a simple strategy: to stay small.[36] In addition, according to the model proposed by these authors, each magnitude of body growth proportionally increases the extrinsic mortality rate, and in what refers to cancer, for each 10% increase in size, the maximum risk of cancer it is 3.3%. It seems that being big and lasting a lot is not profitable in evolutionary terms.[36] Why then are there large animals oscillating between the expensive investment of pretending to "dodge" cancer and at the same time running the risk of suffering it? It seems an evolutionarily ineffective strategy unless: it provides an adaptive advantage in terms of reproductive success.[36]

According to the model of Hanna Kokko et al.[37] for large animals and slow life histories, no matter how costly it is to invest energy to decrease, for example, the probabilities of develop a tumor, it will always benefit your reproductive aptitude; since even modest reductions, say 10%, would yield an increase of equal percentage in life expectancy with guaranteed reproductive success. Because, despite the fact that for every 10% increase in body size, the maximum risk of cancer is 3.3%, assuming that reproductive success is accumulated through a life free of cancer, then an individual who lives 3.3% less should enjoy a reproductive success of 1035 times per unit of time greater than a comparatively smaller individual and shorter duration. If this magnitude of reproductive benefit existed, then an increased risk of cancer would not prevent natural selection from favoring large organisms.[36] It is necessary to clarify another question: Intraspecific sexual competition; the one that is established between individuals of the same species. Because here, the Peto paradox is not fulfilled, or in other words, the postulate by Peto is fulfilled: Large individuals within the same species have a higher prevalence of cancer due to their larger size.

Great to reproduce, and to get cancer? Amy M Boddy[39] and collaborators have proposed the following statement: The average probability that an individual survives is given by:

$$P(t) = \left(1 - A(t)\right)\left(1 - B(t)\right).$$[39]

Where, A (t) is the probability of dying at a certain time (t) for causes other than cancer: predation, illness, famine, etc. While B (t) is the probability of dying from cancer, at a certain time (t); assuming that, at least, a single cellular lineage of your organism has experienced all the steps of successful carcinogenesis.[39]

Ultimately, these authors propose that: An individual can complete his reproductive life for two reasons: 1) Dying from causes other than cancer; or 2) Dying from cancer, considering that one of the cell lineages in your body has successfully passed through all stages of carcinogenesis; that is, he had the time required to develop it.[39] And they start from the following principles:

The organisms compete to reproduce, and in the "balance" between succeeding and risking cancer, natural selection will favour the distribution of energy in order to reproduce at the expense of a detriment in the maintenance of the body; either by favouring mechanisms that increase rapid cell proliferation, either by decreasing the efficiency of DNA repair mechanisms or by monitoring the immune system. It should be noted that the authors refer to sexual competition, and focus their focus on that greater cell multiplication would favour body growth, especially of male individuals. But in addition, other features that positively favour sexual competition in males such as: the presence of ornaments and weapons (antlers, horns, exotic plumage, intense colors, etc.), and aggressive behaviour also require a high rate of cell multiplication (although it seems that aggressive behaviour does not require a high level of cellular replication, is closely related to the production of testosterone, a male hormone that has proliferative effects, so that its effect on cell multiplication would be "collateral").[39]

It seems that individuals develop traits that increase their reproductive success even when this increases the risk of cancer, but the extent of these traits depends on the intensity of sexual competition within the same species.[40]

And it seems that the sexual traits that are selected positively increase the risk of cancer in highly competitive males.[39] In this way, tumors have been registered in the horns of male deer; whose most plausible explanation lies in that the bigger, stronger, and better "elaborated" the horns of these, the more successful they will be in the competition between them for the females, and of course, this attribute of virility depends on the intensity with which the antlers grow and are remodelled, a process that depends on an intense proliferation and cell turnover. One could also cite the example of a variety of freshwater fish, the *xiphophorus maculatus*, or vulgarly known as platy, whose male representatives show a black spot on the sides for the purpose of sexually attracting females; The larger and more intense the dark coloration of the stain, the greater "fascination" they provoke in the "little fish". The genes that are in charge of developing this masculine sexual distinction are protoncogenes that when mutating induce the formation of melanomas, a variety of malignant tumor that also appears in the skin of humans.[39] The relationship between the intensity of intraspecific sexual competition and cancer is not limited to males. Ovarian tumors have been described in chickens with high reproductive potential and therefore more effective in competition with other females; moreover possessing the curious fact that it is the only animal representative has one of the most common cancers in human females.[39]

In summary

The modifiable environmental conditions give particular characteristics to the different ecological systems or niches, and in turn require that the organisms that live in them live in need of adaptation. During the process of adaptation, organisms evolve, and it is the evolutionary process that determines the patterns of life histories, with their particular strategies in energy distribution and investment. Energy investment that in principle is intended for body maintenance, can be maintained, increased, or subtracted depending on the special type of life history drawn according to evolution. In fact, there are individuals who are forced to invest their energy in growing rapidly, reproducing, and almost immediately dying. These are organisms with fast life histories.[41,42] At the other extreme, there are species that have to, after growing, go through a long period of maturation before reaching their reproductive stage, then reproduce,

and as their descendants inherit this need for a long maturation, they need from their parents of prolonged care before achieving their biological independence. Parallel to All this, the energy investment in body maintenance is enormous because it is about individuals with prolonged multicellularity or slow life histories, and they need to continuously renew and supervise the state of their multicellularity for long periods of time; investment that is under constant tension, then, there are obligations both to conserve and to use energies: the indispensable to maintain multicellularity as we indicated before, and the one that we must subtract from it to devote to basic functions.[35,36,41,42]

The dynamics of conservation and utilization of energy in organisms of fast life histories is in some way simpler than that of individuals with slow lives. While in the former the law of all or nothing can be fulfilled, and sacrificing the corporal maintenance in pursuit of functions that its ecosystem has established as peremptory, even at the cost of its own existence, beings with slow life histories will be in need of necessarily adjusting their energy requirements for somatic maintenance, given that it is essential for them to stay alive and biologically fit for long periods of time, and at the same time consume part of that energy in their life processes. In these, the sacrifice of the energy required for body maintenance in order to guarantee its life cycle, will also be nuanced by the demands of the environment in which they develop.[35,36,41,42] The essential function that guarantees the conservation of the foundations of the multicellularity and with it the reduction of the risk of developing cancer is the somatic maintenance; which in turn is synonymous with: supervision of the cellular state (both physical and behavioral), balanced regulation between the processes of division and cell death, repair of tissue damage, repair of genomic damage, etc. This function demands an energy expenditure that increases considerably in large organisms and long lives, reaching the point of being in need of being "sacrificed" in order to guarantee other functions such as growth, development, and definitive reproductive success. Reproduce, and thereby ensure the genetic perpetuation of the species in organisms with histories of slow lives, Implicit in the risk of disrupting multicellularity, one of its consequences being cancer, without ignoring other causes of extrinsic mortality to which they are exposed given their greater longevity. Evolution has selected those organisms that have anti-cancer mechanisms effective enough to allow them to reach a healthy reproductive age; and even favors genes that increase the reproductive potential even when they entail the added danger of being oncogenic. Evolution has selected those organisms that have anti-cancer mechanisms effective enough to allow them to reach a healthy reproductive age; and even favors genes that increase the reproductive potential even when they entail the added danger of being oncogenic Evolution has selected those organisms that have anti-cancer mechanisms effective enough to allow them to reach a healthy reproductive age; and even favors genes that increase the reproductive potential even when they entail the added danger of being oncogenic.[35,36]

Conclusion

Undoubtedly, the human being is included among large pluricellular organisms and slow life histories; and cancer is one of the variables that condition our development. However, this logic assertion should not lead to fallacious s logics; that is, our species has, like the rest of the species that inhabit the planet, a basal risk of cancer conditioned by our peculiar evolutionary evolution and ecological development, but without reaching extreme conclusions like those of the scientists Christian Tomassety & Bert Vogelstein[43,44] who claim that two thirds of human tumors they originate by "bad luck", since they depend on the normal number of stem cell divisions throughout life. A more objective view of human carcinogenesis is imposed. Perhaps one of the most relevant approaches to this vision lies in the model proposed by Noble & Hoshberg[45] Both authors suggest that novel factors originating from environmental action act on the basal risk of cancer in the natural environment. Incredible as it may seem, more than 90% of these novel factors are due to human activity itself. The conclusions derived from it, the forced reflections, the actions to take, seem more than obvious.

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Conflicts of interest

We declare we have no competing interests.

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