Rereading of the genetic origins of cancer: the puzzle of all eras

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Abstract

This is a scientific introduction to review the concept of cancer from a purely genetic perspective in which we try to link the development of tumors by the driving force of the evolution of living beings: the mutations. And to prove the assumption that cancer diversity has a parallel route instead of the whole development process of the cell. Calling for expanding the rolling concept of cancer and tumors definition in general. Which may contribute to altering the angle of our vision to this dangerous biological phenomenon. This call is based on the hypothesis that cancer is a genetic phenomenon that has arisen on the margins of the evolution process.That has continued since the beginning of creation. The pieces of evidence and indications that support this view were presented successively.

Keywords: evolution, cancer, mutations, natural selection

When Charles Darwin (1809–1882) and Alfred Wallace (1823–1913) announced their researches about natural selection, opponents asked for justifying the pushing force for adaptation in response to natural selection. The supporters replied that mutations can be changing the traits, there are positive mutations. In contrast, “bad” mutations should be existing. In fact, the random manner of environmental factors that affect organisms doesn’t know the good or bad things, just working the mechanisms of complex responses which produce mutations on the gene level. These mutations might block the gene activity and may improve productions of the gene.

Regardless reasons of mutations genesis, new mutations always appears as evolution continues, and the number of mutations increased continuously. Hypothetically, early Homo sapiens have an unknown number of mutations, and by the time the number of mutations distributed vertically by increasing the number of mutations in every generation. And horizontally by increasing the number of individuals carrying it among populations. Every new mutation will not be found in the former ancestor but it will

appear in the next generations/ populations. Logically, if a disease or disorder has a genetic risk distributed widely among human populations, the mutation/mutations caused disease should have an ancient origin. And vise-versa if a genetic defect excluded to a particular population, that means mutation or mutations caused this defect has a modern origin.

An unknown number of "bad" mutations will cause diseases such as tumors. As a result of the previous preface and by the big picture of evolution; cancer seems to be one of the side effects of the evolution process on the genetic level. As a conclusion, many diseases and genetic disorders including cancer are very old, and as a secondary conclusion, new types of cancer will continue appearing. This explains that certain diseases are endemic in certain populations and explains why cancers infect all human being populations on the earth.

The story of cancer, in fact, is deeper in the biological ages; some studies confirm cancer in mammalians (1, 2). All right! Could we conclude that we have inherited risky alleles from Mammalians? If the answer is yes, then we should declare that the mutations causing lethal tumors may have one origin or more of: (A) some of exclusive in certain populations (have modern origin) and (B) common in all humans (have an old origin), and (C) some of common in all primates (have a very old origin) and (D) some of common in all mammalians including primates (have an ancient origin), or (E) tumors started since the beginning of life.

Are tumors mutations exhibiting a parallel route with evolution (complexity of cell regulation, increasing of organ functions and increasing numbers of proteins produced, etc...)? Figure (1) translates these words. Unfortunately, as a direct perspective look, the tumor will be more diverse over time.

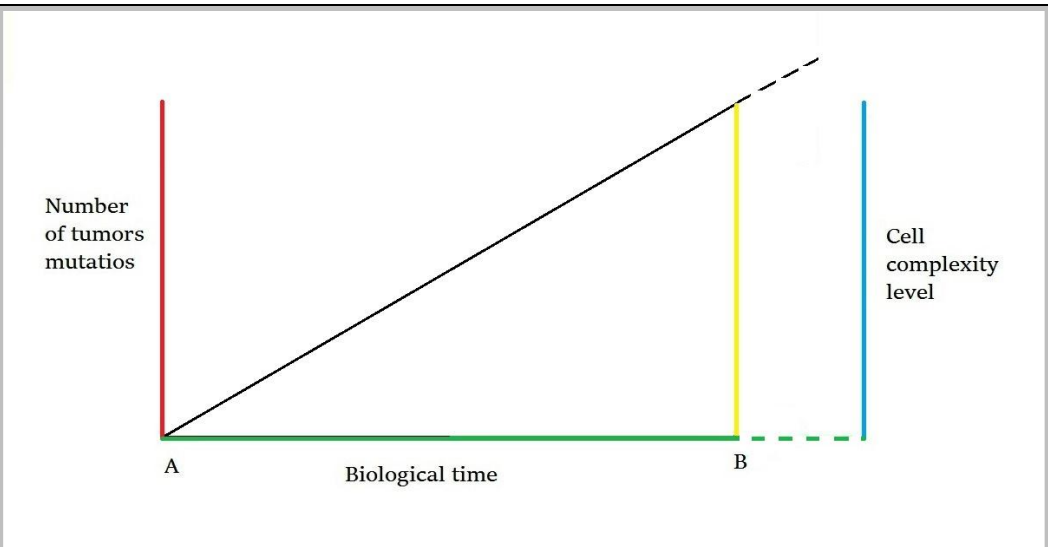

Figure 1: The parallel path between the complexity of cell activities, and the number of mutations causing tumors. The number of inherited mutations that cause different tumors increases as the genome becomes more complex in the organism over biological time. The complexity of the genome includes the mechanisms of cellular regulation, proteins production and other biological processes in living cells. A: beginning of biological time, B: present time.

For instance, Breast cancer is one of the most common types of tumors among females in the world. One of the genetic risk factors is BRCA1 gene, where some of the imbalances in this gene are found to be increased in patients with the tumor. The conclusion is that certain inherited mutations in this gene increase the chance of developing the tumor (3, 4). In some men with prostate cancer have been found to have specific SPOP mutations, the mutations in SPOP genes are not limited to specific human origins and are not limited to a geographical area (5,6). These two examples showed that the inherited mutations involve the majority of the human race, which means that the inheritance of these mutations is old. However, there are exceptions here that require reflection. For example, HOXB13 gene, specifically G84E germline mutation, was found to be associated with valuable risk in prostate cancer patients in some European races (7, 8). In contrast, this point mutation does not constitute a valuable risk for Chinese (9) or Jews (10), and there are even other mutations in the same gene Leads to a serious inheritance that causes prostate cancer in the above-mentioned societies.

It seems that cancer is a phenomenon that is older than being of animal origin if we look at it from a purely genetic point of view. Mutations that cause tumors in the first place are only a genetic response to evolution. It is a transient process of genus and species. To understand the mechanisms of tumor development we must analyze the genetic origin of tumors. The complex processes of evolution impose on living cells certain kinds of changes that are unavoidable to keep pace with the complexity of these factors and this imposes a greater complexity in the processes of cellular regulation and production of proteins..., Because individual responses differ from one individual to another within living societies towards these factors, If these events are old and inherited genetic change is appropriate to prevail conditions at the time, these genetic mutations are not suitable for emergency conditions from a distance or are inefficient in the face of new genetic challenges. Besides, genetic errors at the organizational level occur. These genetic errors cause tumors at the highest degree of severity and this depends on where these mutations occur within the DNA or genome. Because different changes at the genetic level are a way to change the genome's structure toward adapting to cell-emergent conditions that ultimately lead to evolution, the next question seems unanswered: are tumors a partial mechanism of evolution or are only side effects of the whole process?

looking well, we find that those who have particular cancer and have a family history of the disease, the rate of emergence of certain mutations, especially the most dangerous ones, is greater than those who do not have a family history in that disease (11,12). These genes range from nonsense or frameshift mutations that lead to the emergence of an inactive partial protein and missense mutations those that replace an amino acid with another unknown effect on the protein's biochemical properties to the synonymous silent mutations with limited impact.

if taking one of the common tumors, prostate cancer, the serious mutation: K1019X (3055A>T) nonsense mutation of EphB2 gene which was present in 15.3% of the African Americans with positive family history than among healthy African American male controls (5.2%) (13). there are also other detailed facts such as that some societies have their own dangerous inherited alleles instead of different types of tumors and the examples are more than we can mention here.

The proportion of tumors inherited is large and cannot be tolerated if we trying to collect evidence on the genetic origins of cancer and redefined in proportion to what this phenomenon, which is almost purely genetic. This definition may mean exploiting the genetic basis and finding new ways to think about cancer and change the angle of view for a noble goal is to reduce the incidence of this deadly disease.

The main dilemma is the suitable definition of cancer regarding its genetic origins; which leads directly to the correct verification of its causes and this opens the doors to deal with it properly. The modern definitions of cancer agree that it is a group of diseases that lead to a defect in cellular growth with the possibility of spreading this imbalance to neighboring cells. If we go back, we find the definition of Galen (129 AD-210 AD) and Avicenna (980-1037) for cancer that happens as a result of increased "black blood juices" that settle in a body organ to form the tumor, and it spreads through the tumors veins from the center of the tumor to neighboring organs. This definition has lasted for centuries. Interestingly, this definition focuses on the blood-immune definition of the tumor in modern terminology. Of course, the old scientists were well aware that something causing the size of the tumor increase, which is the same modern definition that focuses on a defect in cellular growth with the possibility of metastasis in the body. Modern medicine also recognizes the importance of immunotherapy for certain tumors. But the difference between old knowledge and modern knowledge of cancer is the tremendous discoveries in genetics and molecular biology, and the ability to predict gene actions and cellular regulatory levels.

A new revision of definition cancer definition needed to take into account the biological basis of the evolution associated with genetic changes and trace the genetic origins of tumors. It is time to take a bold step in new horizons regarding the concept of cancer and its association with biological evolution. And to study intensively if the tumors are a response to the complex objective conditions imposed by evolution in the form of inherited genetic mutations. And if Cancer is the inevitable tax of the everlasting development of living beings and it is not limited to human, but originated with the emergence of life. The necessary recommendations here are further discussion on how tumors are intertwined with evolution and the emergence of different mutations in the direction of establishing the new concept in the midst of the humanity struggle against cancer: the puzzle of all eras.

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