COMMENTARY

Spatial -Temporal Biphasic Carcinogenesis - A New Theory of the Cancer System

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Abstract

Cancer is now a worldwide problem. Although we have obtained a deeper understanding of the disease with the help of the science and technology, we still cannot reach the essence of cancer. Based on the former theory of carcinogenic and researches, we submit a new theory called "Spatial -Temporal Biphasic Carcinogenesis" to explain its development from the viewpoints of time and space.

Keywords: Spatial - temporal biphasic carcinogenic - time and space - multi-biomarkers

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Introduction

It has been more than 200 years since the concept of the cancer come into the people's vision, especially in the recent 40 years, the human got a deeper understanding of it (Nowell et al., 2002). After entering the 21st century, although we got a rapid development in the technology, it seems that we feel more confused about the cancer. A lot of theories were developed to try to explain it, and they were reasonable, partial. The scientists found thousands genes and proteins which all seem to have a close relationship with tumor. For example, there are more than two hundred genes mutations in a VHL-associated RCC specimen; there are different biomarkers in different regions. Gerlinger et al (2012) proved the intratumor heterogeneity, which depress the clinicians deeply, but it made the human closer to the essence of the cancer. They portrayed the branched evolutionary tumor development; the mutational genes in the cancer were assorted to be the "trunk genes" and the "branch genes".

Everything the proper way, time and space are the two most basic factors. Everything is closely related to them, including the development of the cancer. We submitted a new theory about the cancer called "Spatial -Temporal biphasic carcinogenic" which based on the former theories and researches, we tried to explain the cancer from the time and space.

Which is the First Cancer Cell?

Although it is impossible to detect the first cancer cell, we can't ignore that it do exist. It is the single spark which can start a prairie fire. Now the question is which is the first cancer cell? So far, the most accepted carcinogenic theory is the "gene mutation", in fact, we really found thousands mutation genes in all kinds of cancers. It is confused that every mutation genes seems to be important to the carcinogenic. But we speculate that from the normal cell to the cancer cell, it doesn't need so many mutation genes but two--the "Tap gene" and the "Key gene". The Tap gene mutation is like the switch makes a normal cell to be the cancer susceptible cell. For example, just like the disease in the VHL syndrome, the VHL gene is the Tap gene, making the normal cells in the kidney, adrenal, pancreas and the CNS system to be the cancer susceptible cells. However the VHL patients don't have tumors in all susceptible tissues, we can suspect that another gene we call the "Key gene" takes mutation, and this make a cancer susceptible cell to be the first cancer cell.

The Signal Pathway

The transfer of the information in the human body depends on all kinds of signal molecules. Not only in the normal physiologically, but also in the development of the cancer. The research of the signal pathway in the cancer was the hot years ago. More than one hundred pathways were detected in the last ten years. Every abnormal pathway is like a rope which connects the normal cells with the cancer cells. But there are so many pathways, they now become the coil, no one can disarray the clue. In my opinion, we can assort them as the extracellular signal pathway (ESP) and intracellular signal pathway (ISP) according to the location of the function, and the space dependent signal pathway (SSP) and time dependent signal pathway (TSP) according to the mechanism. When making a comprehensive consideration, we classify them as the space dependent extracellular signal pathway (SDEP), space dependent intracellular signal pathway (SDIP), time dependent extracellular signal pathway (TDEP), time dependent intracellular signal pathway (TDIP).

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Resistance from the normal cells

The cancer cells are stronger than the normal cells. But for the body, the cancer cells are the foreign matters. They are resisted by the adjacent normal cells. In the beginning, there are only few cancer cells, the power of resistance from the normal cells is great. But with the development of the cancer, the cancer cells become more and stronger, the resistance from the normal cells is weaker. So there are two kinds of power in the body, the power of proliferation of the cancer (PP) and the power of resistance from the normal cells (PR). In the beginning, the PP is strong, and it will rouse the PR to inhibit it. The PR will be stronger and stronger to be equal with the PP to stop the cancer growth. However, PR has the positive correlation with the number of normal cells. So with the development of the cancer, the PR is weaker and weaker. That is why the tumor grow faster and faster.

The spatial -temporal biphasic carcinogenic

Gerlinger et al found that the somatic genetic mutations were different within a tumor, and they portrayed the branched evolutionary tumor development. It was a bad news for the treatment but good news for the mechanism. Here we submit a new tumorigenesis theory called the "Spatial -Temporal biphasic carcinogenic". It may be a supplement and theoretical basis for the intratumor heterogeneity and branched evolution. When a cancer cell is formed, it can proliferate by mitosis; and in the same time, in a certain space, it can make the adjacent susceptible cells to be the cancer cells by some signal pathway, which we call the Space dependent signal pathway. In the process of the proliferation, the tumor is resisted by the normal cells, and then the growth is suspended. And then, in a certain time, the original cancer cell will switch on another signal pathway to split to be its copy to keep the growth, which we call the Time dependent signal pathway (Figure 1 and Figure 2). In the process, the space and the time can decide the speed of the tumor growth. At first, the speed is slow because of the resistance power from the round normal cells, but, with the development of the tumor, more and more cancer cells replace the normal cells, the speed is faster and faster. Overall, every signal pathway means the formation of a special bio-makers cancer cells. And the Space dependent signal pathway can decide the proliferation of the cancer, at the same time, time dependent signal pathway can decide the infiltration of the cancer (Figure 3).

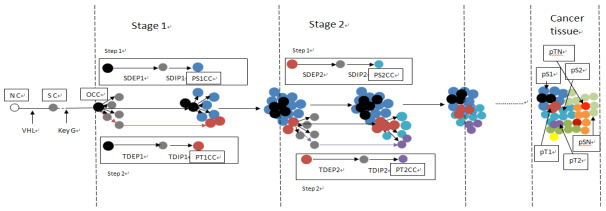

Figure 1. The VHL Mutation Make the Normal Cells (NCs) in Several Tissues Like the Kidney Become the Tumor Susceptible Cells (SCs). But the fact is not every susceptible organ develop the tumor. We speculate a "key gene" plays a key role in the tumor-development. So a "VHL-Key gene" mutation makes a SC to the original cancer cell (OCC). The theory of "Spatial -Temporal biphasic carcinogenic" shows that in the step1, the OCC can proliferate by mitosis; meanwhile, the SCs adjacent to the OCC turn into the PS1CCs (protein S1-specific cancer cell) by the "SDEP1- SDIP1", which have the special tumor-maker PS1. However, with the resistance from the around normal cells, the proliferation of the PS1CCs is limited. In order to keep the evolutionary advantage, after receiving the feedback of limitation , the OCC make a SC to be its copy named PT1CC (protein T1-specific cancer cell) by the "TDEP1-TDIP1", which has the special tumor-maker PT1. In the stage 2, the PT1CC acts like the OCC. And so, the SC can develop a multi-makers tumor finally. In summary, the SDP decides the size of the regional proliferation which has the same tumor-makers. And the TDP can decide the infiltration of the cancer. According to the theory, we can detect a lot of tumor-marker in a tumor tissue; they are pS1, pS2, pS3….pSN and pT1, pT2, pT3….pTN. (SDP-Space dependent signal pathway, SDEP-Space dependent extracellular signal pathway, SDIP-Space dependent intracellular signal pathway, TDP- Time dependent signal pathway, TDEP-Time dependent extracellular signal pathway, TDIP-Time dependent intracellular signal pathway)

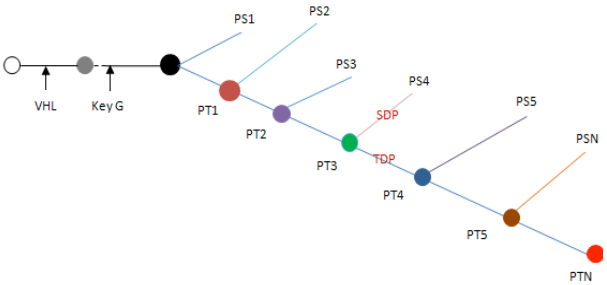

Figure 2. According to the New Theory, the "VHL-Key gene" Mutations Make A Normal Cell to be the Original Cancer Cell. In the process of the cancer proliferation, the original cancer cell will develop to the PTICC, PT2CC, PT3CC and PTNCC via Time dependent signal pathway. They are the copies of the OCC, but their bio-markers are different. They are related with the growth time of the tumor. The OCC and PTNCCs can radioactively make the adjacent SCs to be the CCs via the Space dependent signal pathway; the PTNCCs decide the features of the corresponding PSNs

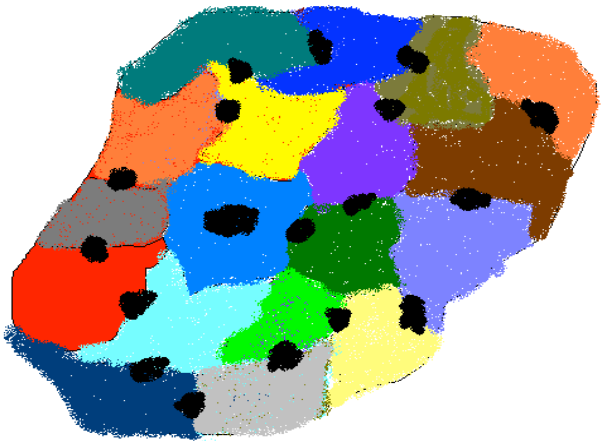

Figure 3. According to the new theory, We Can Find A Lot of Special Markers in the Specimen. They are regional distribution. The black religions represent the special bio-markers PTI, PT2, PT3 and PTN. The cells in the religions are the copies of the OCC

Conclusion

The cancer is a like the Himalayas before us, it is still the most mysterious disease to the scientist. With the development of the science and technology, people get closer and closer to it, but we still can't reveal the essence of the cancer. Here we hypotheses a new theory of carcinogenic based on the time and space character during the proliferation of the cancer, we try to explain it from another point of view.

References

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