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On the Cancer

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ABSTRACT

This article theoretically speculates that after replication of a pair of DNA they must be allocated to two daughter cells in a transverse division or erect division manner. Transverse division represents differentiation, while erect division represents transformation. The molecular structure determines that DNA has greater hydrophobicity than RNA. The hydrophobic modification of chromatin regulates gene activity and centromere similarity between new and old DNA. A difference in division between cancer cells and embryonic stem cells is discussed.

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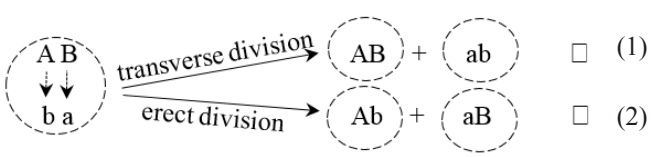
On the Cancer

Cancer is still the number one disease that endangers human life to this day. For a long time, theoretical and experimental research data on molecular genetics and molecular epigenetics of cancer has been very abundant, and clinical cases and research data have also piled up like mountains. However, there is still a lack of basic theoretical logical reasoning for the mechanism of cancer production. The purpose of this article is to fill the gap in this logical reasoning.

Cell Differentiation and Transformation Mechanisms Based on Molecular Genetics

Any cellular organism inherits to daughter cells through the replication of one or more pairs of DNA molecules in the mother cell. We use Capital A and B to represent the original pair of DNA in the mother cell, and small a and b to represent the newly replicated pair of DNA [1,2]. During cell division, they must be allocated to two daughter cells through one of the following two ways



where the (1) - ① mode is called transverse division, which represents the differentiation of cells, and the (1) - ② mode is called erect division, which represents the transformation of cells.

Telomeres are a special nuclear protein complex located at the end of linear chromosomes. The DNA in the telomere region is a repetitive sequence rich in G, consisting of thousands of base pairs that terminate in a short single stranded DNA (ssDNA) overhang [3]. During replication, the telomere regions of complementary mother strands of DNA molecules A and B are entangled or enveloped by telomeres, losing their template function, resulting in a shorter telomere region of the newly replicated daughter strands of DNA molecules a and b. If cells divide according to mode ①, for every division, the telomeres of the DNA a and b in the daughter cells must be shortened by a segment, which represents the division of the somatic cell. If cells divide according to mode ②, the telomere regions of A and b or a and B complementary chains will exhibit a pattern of one long and one short. Under the action of telomerase, using the old A or B as a template can extend the telomeres of a or b to achieve the same length. By dividing in this way, the length of telomere DNA in daughter cells will not be shortened. Embryonic stem cells or cancer cells belong to this situation. What determines the mode cells divide? What is the difference between embryonic stem cells and cancer cells during division? We will discuss it below.

The Essence of Deoxidation and Methylation is the Enhancement of Reducibility and Hydrophobicity

Many biochemical reactions that occur within cells are related to the hydrophobicity of molecules or functional groups. As shown in Figure 1, the difference in molecular structure between DNA and RNA determines their different hydrophobicity [4] . They are macromolecules formed by connecting ribose with bases through phosphate ester bonds. Their phosphate ester bonds are all the same, with the only difference being the ribose and base. Ribose is a five carbon sugar that contains one aldehyde group and four hydroxyl groups. Its 1-aldehyde group and 4-hydroxyl group condense and dehydrate to form a cyclic ribose. Its 3-hydroxy and 5-hydroxy

groups condense with phosphate groups to form phosphate ester bonds. Therefore, in the ribose of RNA, the 2-hydroxy group is the only remaining free hydrophilic bond. In the ribose of DNA, deoxygenation of 2-hydroxyl group forms hydrophobic carbon hydrogen bonds. The essence of deoxygenation is that hydrophilic bonds become hydrophobic bonds, and the oxidation state changes to the reduction state.

Both DNA and RNA contain four types of bases, of which three are identical. They are adenosine, guanosine, and cytosine. There is only one different base, thymine is present in DNA and uracil is present in RNA. As shown in Figure 1, the 5-hydrogen of uracil is connected to a double bonded carbon, so 5-hydrogen has acidity and has certain hydrophilicity and oxidizing properties; The 5-carbon connected in thymine is methyl, which has hydrophobicity and reducibility. Therefore, thymine has greater reducibility and hydrophobicity than uracil.

Comparing ribose and base, it can be seen that DNA has greater hydrophobicity than RNA. During the nuclear phase of a cell, DNA replicates and functions within the nucleus, while RNA, although synthesized within the nucleus, mostly functions in the cytoplasm. Therefore, it can be inferred that nucleoplasm has greater hydrophobicity than cytoplasm.

The hydrophobicity of chromatin within the nucleus is also not uniform. Highly hydrophobic chromatin usually aggregates into heterochromatin, distributed near the nuclear membrane. Chromatin with poor hydrophobicity usually aggregates into euchromatin, while chromatin with the worst hydrophobicity, which is the strongest hydrophilicity, typically extends to the nucleolar region to perform active functions. Chromatin includes various nuclear proteins that make up nucleosomes. The modification of DNA and nuclear proteins both affect the hydrophobicity of chromatin.

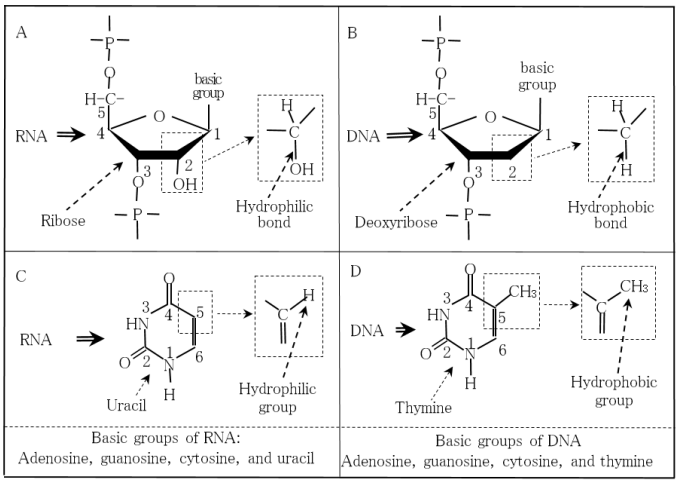


Figure 1: Comparison of hydrophobicity between DNA and RNA. A) The second position of the ribose that constitutes RNA is a hydrophilic bond; B) The second position of the ribose that makes up DNA is a hydrophobic bond; C) The fifth position of uracil, which constitutes RNA, is a hydrophilic hydrogen atom; D) The fifth position of thymine, which constitutes DNA, is a hydrophobic group

The Mechanism of Cancer Occurrence Based on Epigenetics

So far, research on the hydrophobic modification of chromatin has mainly focused on two directions. One is DNA methylation modification, and the other is histone modification. The main site of concern for DNA methylation is CpG islands [5]. CpG island refers to the cytosine dense region present at the gene promoter. The high methylation of CpG islands gives them strong hydrophobicity, making them easy to bind to heterochromatin regions and leading to gene inactivation. The low methylation of CpG islands endows them with strong hydrophilicity, making them easy to bind to the autosomal region and even extend to the nucleolar region, performing the transcription function of templates, manifested as gene activation.

The focus of attention on histone modification is also on the methylation modification of nucleosome histones near the promoter. A recent article by [6]. suggests that the histone H3K27me3, which aggregates around the promoter region of genes that should be correctly expressed, is a hallmark of cancer. H3K27me3 concentrates chromatin structure and suppresses genes crucial for cell identity and appropriate function [6].

In the S phase of cells, DNA replication begins with the hydrophilic nucleolus and euchromatin regions, followed by heterochromatin replication. The hydrophilicity of the replication environment determines the methylation state of the newly formed chains. The new chain replicated by the CpG island of the active gene is still hypomethylated. The CpG islands replicated in the heterochromatin region are still highly methylated. This results in epigenetic inheritance of both active and inactive genes.

Both the two types of chromatin methylation modification that people are concerned about above are located near the promoter, and their degree of methylation mainly determines the activity of the gene, but it is not directly related to the cell transformation or differentiation determined by formula [1]. Methylation is also an important way to maintain gene stability. Methyl is a reducing group, and the maintenance of methylation under oxidative damage will be disrupted.

What factors determine the allocation of four DNA molecules (A, B, a, and b) from each pair of chromosomes to two daughter cells during cell division? This article believes that on the basis of complementary chains, it is determined by the similarity of four DNA molecules in the centromere region, especially the increased hydrophobicity of both DNA and nucleoprotein methylation in the centromere region, and the increased hydrophilicity of nucleoprotein phosphorylation. If the similarity of the centromere regions between A and B is greater than that between A and b, the allocation will be carried out according to formula (1)-①; If the similarity of the centromere regions between A and B is greater than the similarity of the centromere regions between A and B, the allocation will be carried out according to formula (1)-②.

In tissue stem cells, active genes are often located on DNA that has undergone multiple generations of differentiation and division with significantly shortened telomeres. These chromosomes have a limit on the number of divisions, and during division, the similarity between A and B is greater than that between A and b, meaning that AB has a higher degree of methylation than ab. When these cells are damaged by oxidative stress, oxidative free radicals oxidize the centromere region of A or B chains, resulting in differences between A and B. As a template, the similarity between A and b after replication is greater than the similarity between A and B, and cell division transitions from differentiation to transformation. This transformation has epigenetics, which is the molecular mechanism of cancer production. And it can be seen that the worse the differentiation, the greater the malignancy of

cancer derived from tissue stem cells.

The Difference Between Cancer Cell Division and Embryonic Stem Cell Transformation

What is the difference between cancer cells and embryonic stem cells, which both divide in a erect division pattern represented by formula (1)-②? The transformation of embryonic stem cells occurs before the formation of the cardiovascular oxygen supply system. The internal cells of the embryo are in a state of oxygen deficiency, during the peak period of methyltransferase activity. On the one hand, oxygen deficiency keeps the centromere region of newly replicated DNA in a high reduced state (methylation state), and on the other hand, the differences between chromosomes A and B from the paternal and maternal parents still exist to some extent. As a result, the similarity between A and b was greater than the similarity between A and B, and the cells underwent transformation. After the formation of the cardiovascular oxygen supply system, the internal cells of the embryo receive better oxygen supply, and the activity of methyltransferase weakens. The centromere region of newly replicated DNA using the DNA where the active gene is located as a template shows a lower methylation state (oxidized state). The similarity between A and B is greater than the similarity between A and b, and cells begin to differentiate.

Although there is a similarity between A and b in both cancer cells and embryonic stem cells, the transformation of cancer cells is a similarity of low methylation in the centromere region of the DNA where the cancer gene is located, while the transformation of embryonic stem cells is a similarity of high methylation in the centromere region.

Acknowledgments

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