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DNA DAMAGE AND REPAIR MECHANISMS: MOLECULAR BASIS OF GENOMIC INSTABILITY AND CANCER DEVELOPMENT

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Abstract: DNA is the fundamental biological molecule responsible for storing, transmitting, and passing genetic information to daughter cells. Throughout the life of a cell, DNA is continuously exposed to various forms of damage caused by both endogenous metabolic processes and external environmental factors. The timely detection and removal of such damage are essential for maintaining genomic stability. The primary function of DNA repair systems is to prevent the accumulation of mutations by restoring damaged genetic material. Impairment of these repair mechanisms can lead to genomic instability, the accumulation of mutations, and alterations in the activity of genes that regulate cell growth. Consequently, the activation of oncogenes, the inactivation of tumor suppressor genes, and the disruption of cell cycle control can contribute to cancer development. This article examines the major types of DNA damage, DNA damage response mechanisms, and principal DNA repair pathways, as well as the role of their dysfunction in genomic instability and cancer pathogenesis. Furthermore, it discusses the mismatch repair system, repair defects associated with BRCA1 and BRCA2, chromothripsis, and the potential use of DNA repair mechanisms as molecular targets in cancer treatment. A comprehensive understanding of the molecular characteristics of DNA repair provides an important scientific basis for improving early cancer detection, molecular classification, and personalized treatment strategies.

Keywords: DNA, DNA damage, DNA repair, genomic instability, mutation, cancer, MMR, BRCA1, BRCA2, chromothripsis, molecular biomarker.

Introduction

DNA is the primary molecule responsible for storing genetic information within cells and ensuring its accurate transmission to daughter cells. However, throughout a cell's life, DNA is continuously subjected to damage caused by various endogenous and exogenous factors. Oxidative processes, ionizing and ultraviolet radiation, chemical agents, errors during DNA replication, and other factors can induce structural alterations in DNA. If such damage is not detected and repaired in a timely manner, it may result in mutations that disrupt normal cellular function.

A complex protective system maintains DNA stability by detecting damage, temporarily arresting the cell cycle, and repairing damaged genetic material. Base excision repair, nucleotide excision repair, mismatch repair, and mechanisms responsible for repairing double-strand breaks play

essential roles in these processes. Deficiencies in DNA repair systems can lead to the accumulation of mutations and chromosomal alterations, ultimately resulting in genomic instability.

Genomic instability is one of the major molecular foundations of cancer development, as it creates conditions that favor pathological alterations in genes responsible for regulating cell growth and division. Therefore, disruption of the balance between DNA damage and its repair is particularly important for understanding cancer pathogenesis. This article analyzes the major types of DNA damage, DNA repair mechanisms, and the molecular role of their dysfunction in genomic instability and cancer development.

Main Body

Major Types of DNA Damage and Their Causes

DNA damage is a natural occurrence during normal cellular activity, and its extent depends on the cell's metabolic activity and exposure to environmental factors. DNA damage may manifest as changes in chemical structure, disruption of bonds between nucleotides, or breaks in DNA strands. The type and severity of the damage determine which repair mechanism is subsequently activated.

Modification of Nitrogenous Bases

The nitrogenous bases in DNA—adenine, guanine, cytosine, and thymine—can undergo alterations as a result of various chemical influences. Deamination, oxidation, and other chemical modifications of these bases can alter their normal base-pairing properties. Consequently, mismatches may occur during replication, increasing the likelihood of mutation formation.

Oxidation

Reactive oxygen species generated during cellular metabolic processes can damage DNA. In particular, modified bases produced by guanine oxidation may cause incorrect base pairing during DNA replication. If oxidative damage is not adequately repaired, mutations may accumulate, compromising genomic stability.

Alkylation

Alkylation is characterized by the addition of alkyl groups to DNA bases. These chemical modifications may alter base-pairing properties and cause errors during DNA replication. Some alkylated bases are directly repaired by specialized enzymes, whereas other forms of damage are addressed through excision repair mechanisms.

Single-Strand Breaks

Breaks occurring in only one strand of DNA are referred to as single-strand breaks. They may arise from oxidative stress, ionizing radiation, and other factors. Such damage is generally repaired

efficiently by the cell; however, if it is not resolved in a timely manner, it may be converted into double-strand breaks during DNA replication.

Double-Strand Breaks

Simultaneous breaks in both DNA strands represent one of the most dangerous forms of genomic damage. Such lesions can lead to chromosomal fragmentation and rearrangements. Double-strand breaks are repaired through mechanisms including homologous recombination and non-homologous end joining. Improper repair may result in mutations and chromosomal rearrangements.

Replication Errors

During DNA replication, an incorrect nucleotide may be incorporated into the newly synthesized strand, or short DNA sequences may be inserted or deleted. Under normal conditions, such errors are corrected by specialized proofreading and repair mechanisms. When these systems are impaired, replication errors accumulate, increasing the mutational burden.

Interstrand DNA Crosslinks

Certain chemical agents can form stable crosslinks between the two DNA strands. Such lesions prevent the strands from separating properly, thereby disrupting DNA replication and the reading of genetic information. The removal of these complex lesions involves several repair mechanisms, particularly the Fanconi anemia repair pathway.

Chromosomal Rearrangements

Chromosomal rearrangements may occur as a result of extensive DNA damage or the incorrect repair of double-strand breaks. These changes may involve the loss or duplication of chromosomal segments, inversions, or exchanges with segments of other chromosomes. Such alterations can activate oncogenes or inactivate tumor suppressor genes, thereby contributing to the molecular basis of cancer development.

The DNA Damage Response System

When DNA damage occurs, the cell activates a complex set of protective mechanisms responsible for detecting the damage, transmitting signals, and repairing the genetic material. This process is mediated by the DNA damage response (DDR) system. Its primary functions are to temporarily restrict the replication of damaged DNA, activate repair mechanisms, and prevent the proliferation of cells with severe genetic damage.

Damage Recognition

When an alteration occurs in DNA, specialized cellular proteins recognize the damaged region. Once the type and extent of the damage have been identified, an appropriate response mechanism is selected. For example, relatively small base modifications are repaired through specific pathways, whereas double-strand breaks are addressed by distinct repair mechanisms.

Signal Transduction Following DNA Damage

Following damage recognition, intracellular signaling pathways become activated. Specialized protein kinases and checkpoint proteins participate in this process, transmitting information about DNA damage to the mechanisms responsible for regulating the cell cycle. As a result, the cell initiates the molecular responses required to begin DNA repair.

Temporary Cell Cycle Arrest

The cell cycle may be temporarily arrested in response to DNA damage. This provides the cell with time to repair the damaged DNA before the next cell division. The proper functioning of cell cycle checkpoints, particularly those operating during DNA replication and before cell division, is essential for maintaining genomic stability.

If these checkpoint mechanisms are impaired, cells containing damaged DNA may continue to divide. Consequently, existing mutations can be transmitted to daughter cells, further increasing genomic instability.

Activation of DNA Repair

Once DNA damage has been recognized, the corresponding repair mechanism is activated. The cell may replace damaged bases or nucleotides, correct mismatched regions, or restore double-strand breaks.

Thus, DNA repair systems help preserve the original structure of DNA and its genetic information as accurately as possible. Efficient repair limits the accumulation of mutations and enables the cell to maintain its normal functions.

Programmed Cell Death in Response to Irreparable Damage

If DNA damage is too severe or cannot be fully repaired, the cell may undergo programmed cell death, known as apoptosis. This mechanism serves as an important protective process by preventing the proliferation of cells with substantial genetic damage.

Conversely, dysfunction of the DNA damage response system and cell death mechanisms may allow damaged cells to survive. Mutations may continue to accumulate in these cells, creating conditions that can subsequently promote the emergence of tumor cells.

Thus, the DNA damage response system can be represented by the following sequence:

DNA damage → recognition → signal transduction → cell cycle arrest → DNA repair → recovery or programmed cell death.

Dysfunction of this system becomes an important factor contributing to mutation accumulation and the subsequent development of genomic instability.

Major DNA Repair Pathways

Following the recognition of DNA damage, the cell activates a repair mechanism appropriate to the type and extent of the lesion. Although these systems differ in their mechanisms of action, their common objective is to maintain the integrity of genetic information and prevent the accumulation of mutations. The major DNA repair pathways include base excision repair, nucleotide excision repair, mismatch repair, homologous recombination, non-homologous end joining, the Fanconi anemia repair pathway, direct reversal of DNA damage, and mechanisms that allow DNA replication to bypass damaged templates.

Base Excision Repair

The base excision repair system eliminates minor types of DNA damage that do not substantially alter the overall structure of the DNA helix. Such damage includes nitrogenous bases that have been modified as a result of oxidation, deamination, or certain chemical modifications.

The process initially begins with specialized enzymes that recognize the damaged base. Subsequently, the damaged base is removed from the DNA, the resulting gap is filled, and the integrity of the DNA strand is restored. This mechanism is essential for eliminating numerous minor forms of DNA damage that arise during the cell's routine metabolic processes.

Nucleotide Excision Repair

Nucleotide excision repair eliminates bulky DNA lesions that significantly distort the structure of the DNA helix. Pyrimidine crosslinks formed under the influence of ultraviolet radiation are an example of such damage.

During this process, the damaged region of DNA is identified, and the affected segment is excised together with several nucleotides. The resulting gap is then filled using the undamaged strand as a template. Dysfunction of this system may increase DNA susceptibility to external harmful factors and heighten the predisposition to certain types of cancer.

Mismatch Repair

The mismatch repair system corrects errors that occur during DNA replication. During replication, certain nucleotides may pair incorrectly, or nucleotides may be inserted or deleted within short DNA sequences.

Under normal conditions, these errors are recognized by specialized proteins, the mismatched segment in the newly synthesized DNA strand is removed, and the correct sequence is restored in its place. Dysfunction of this system may increase the number of mutations and lead to the development of microsatellite instability.

Homologous Recombination Repair

Homologous recombination repair plays an important role in accurately repairing DNA double-strand breaks. In this process, the cell uses an undamaged, similar DNA sequence as a template.

This mechanism enables the genetic information within the broken DNA region to be restored with a high degree of accuracy. The BRCA1 and BRCA2 proteins are important components of this process. When their function is impaired, the ability to accurately repair DNA double-strand breaks decreases. Consequently, genomic instability increases, potentially creating conditions that favor cancer development.

Non-Homologous End Joining

Non-homologous end joining is a mechanism that enables the rapid repair of DNA double-strand breaks. During this process, the damaged DNA ends are directly joined together, without requiring an intact homologous DNA sequence as a template.

Although the speed of this mechanism is important for protecting the cell against severe DNA damage, nucleotides may sometimes be lost or inserted during the joining process. Therefore, inaccurate non-homologous end joining can cause mutations and chromosomal rearrangements.

Fanconi Anemia Repair Pathway

The Fanconi anemia repair pathway participates in the removal of interstrand crosslinks formed between the two DNA strands. Such lesions interfere with the separation of DNA strands and impede the replication process.

Many proteins of the Fanconi anemia pathway participate in damage recognition, DNA processing, and the recruitment of other repair mechanisms. Inherited defects in this pathway are associated with chromosomal instability and an increased predisposition to certain types of cancer.

Direct Reversal of DNA Damage

In some types of DNA damage, it is not necessary to excise the damaged base from the DNA. Instead, its chemical structure is restored directly with the help of specialized enzymes.

For example, certain guanine residues altered by alkylation can be repaired by specific enzymes. This mechanism helps prevent the damaged base from becoming a mutation during subsequent DNA replication.

Replication Bypass of Damaged DNA

In some cases, DNA damage prevents the replication process from continuing. Under such circumstances, the cell uses mechanisms that temporarily bypass the damaged region, allowing replication to proceed.

This mechanism helps the cell survive under conditions of DNA damage; however, the accuracy of DNA copying may decrease in certain cases. As a result, the likelihood of additional mutations increases.

Overall, these DNA repair pathways form an integrated protective system in which the individual mechanisms complement one another. Efficient repair preserves genomic stability, whereas disruption of these mechanisms leads to the accumulation of mutations and the development of genomic instability. Therefore, defects in DNA repair mechanisms occupy a central position in explaining the pathogenesis of cancer.

DNA Repair Deficiency and Genomic Instability

The primary function of DNA repair systems is to preserve the integrity of genetic material and eliminate damage before cell division. Defects in one or more components of these systems lead to the accumulation of DNA lesions, an increased mutation frequency, and disruption of genomic stability. Consequently, DNA repair deficiency is considered one of the important molecular factors contributing to cancer development.

Repair Deficiency and Mutation Accumulation

In normal cells, most errors arising during DNA replication and damage caused by internal or external factors are eliminated by DNA repair systems. If these systems are insufficiently active, damaged DNA may proceed into subsequent rounds of replication and, over time, become fixed as permanent mutations.

The successive accumulation of mutations alters the biological characteristics of the cell. Changes in genes that regulate cell proliferation, differentiation, responses to DNA damage, and programmed cell death are particularly important for tumor development.

Mutator Phenotype

Disruption of DNA repair mechanisms increases the rate at which mutations arise in a cell. This condition is described as a mutator phenotype. As a result, even if the initial damage affects a single gene or a small DNA region, changes may gradually develop in additional genes over time.

Thus, DNA repair deficiency not only allows an individual mutation to persist but also increases the cell's capacity to accumulate new genetic alterations. This, in turn, increases the genetic diversity of cancer cells.

Genetic and Genomic Instability

Genetic instability is associated with an increased frequency of mutations at the level of individual genes or nucleotides, whereas genomic instability also encompasses changes in chromosome number and structure, large genomic regions, and gene function.

Disruption of DNA repair systems may result in chromosomal breaks, incorrect rejoining, and the loss or duplication of particular chromosomal segments. These alterations progressively change the genetic composition of cancer cells.

Driver and Passenger Mutations

Not all mutations have the same biological significance during cancer development. Mutations that directly confer an advantage in cellular growth and survival are considered driver mutations. They may be associated with the activation of oncogenes or the inactivation of tumor suppressor genes.

In contrast, alterations that do not directly contribute to cellular growth but accumulate as a result of genomic instability are considered passenger mutations. Nevertheless, their abundance may reflect the complexity of the cancer genome and help establish the evolutionary history of tumor cells.

Chromosomal Instability

DNA double-strand breaks and their inaccurate repair are among the major causes of chromosomal instability. Consequently, chromosomal segments may be lost, duplicated, inverted, or rearranged through joining with other chromosomes.

Chromosomal instability creates conditions for the emergence of new genetic combinations in tumor cells. In some cases, such alterations lead to the activation of oncogenes or the loss of tumor suppressor genes.

Evolution of the Cancer Genome

It is insufficient to regard cancer solely as a disease caused by a single mutation. During tumor development, various mutations and genomic alterations accumulate progressively in cells. Cells with a genetic advantage proliferate more extensively and form dominant clones within the tumor.

From this perspective, disruption of DNA repair is considered one of the factors that accelerate the evolution of the cancer genome. In cells with reduced repair capacity, the accumulation of mutations and chromosomal alterations increases genetic diversity within the tumor. This may subsequently contribute to tumor progression, changes in its biological characteristics, and, in some cases, the emergence of cell populations resistant to treatment.

The Role of DNA Repair Dysfunction in Cancer Pathogenesis

Disruption of DNA repair systems is one of the important molecular mechanisms involved in cancer development. Under normal conditions, DNA damage is detected and repaired; if the damage is irreparable, it may be eliminated through the death of the affected cell. When these control mechanisms fail, cells carrying genetic alterations may survive and continue to proliferate. Consequently, the molecular changes required for tumor development accumulate progressively.

Activation of Oncogenes

As DNA damage accumulates, mutations may arise in genes that regulate cellular proliferation and survival. Activation of oncogenes may increase the cell's responsiveness to division signals or create conditions for uncontrolled proliferation.

Such genetic alterations may persist more readily in the presence of impaired DNA repair systems. This is because, when normal repair mechanisms are absent or dysfunctional, mutations arising within the cell may remain unrepaired and be transmitted to subsequent generations of cells.

Inactivation of Tumor Suppressor Genes

The loss or impairment of tumor suppressor gene function is also important in cancer development. These genes normally participate in restricting cell division, responding to DNA damage, and ensuring the elimination of damaged cells.

If the function of such genes is lost, cells with damaged DNA may continue to divide. Consequently, genetic alterations are transmitted to subsequent cells, further intensifying genomic instability.

Disruption of Cell Cycle Control

The DNA damage response system ensures temporary arrest at specific stages of the cell cycle. This provides the cell with the time required to repair damaged DNA. When the relationship between DNA repair systems and cell cycle control is disrupted, damaged DNA may not be fully repaired before cell division.

As a result, cells carrying mutations proliferate, and a population of genetically altered cells emerges. This process contributes to the progressive selection and development of cancer cells.

Uncontrolled Cell Proliferation

One of the defining characteristics of cancer pathogenesis is the loss of normal control over cellular proliferation. DNA repair dysfunction may directly or indirectly intensify this process. As a result of mutations, signals that stimulate cell proliferation become stronger, while mechanisms that restrict proliferation become weakened.

Over time, these cells may accumulate additional genetic alterations. Consequently, populations of cells with distinct biological characteristics emerge within the tumor.

The Impact of Genomic Instability on Tumor Development

Genomic instability is one of the most important consequences of DNA repair dysfunction in cancer development. In addition to nucleotide-level mutations, it may involve chromosomal alterations, changes in gene copy number, and chromosomal rearrangements.

As genomic instability increases, the probability that cells will acquire genetic alterations conferring an advantage for tumor development also rises. Thus, the following sequence emerges:

DNA damage → impaired DNA repair → mutation accumulation → genomic instability → tumor development.

At the same time, the significance of repair defects in cancer development is not identical across all tumor types. Dysfunction of a particular repair pathway may determine the molecular characteristics of a tumor and influence its biological behavior and sensitivity to certain treatments. Therefore, it is important to examine the associations between individual DNA repair systems and cancer in greater detail.

The MMR System, BRCA1/BRCA2, and Cancer

Disruption of certain DNA repair pathways substantially increases the risk of cancer development. In particular, defects in the mismatch repair (MMR) system and the homologous recombination repair mechanism lead to important molecular alterations in tumor cells. Dysfunction of these systems may result in mutation accumulation, genomic instability, and the acquisition of tumor-associated characteristics by cells.

The MMR System and Its Significance in Cancer Development

The primary function of the MMR system is to recognize and correct mismatches that arise during DNA replication. Although DNA polymerase operates with high fidelity during replication, certain nucleotides may pair incorrectly, or nucleotides may be inserted or deleted within short DNA sequences. The MMR system specifically recognizes such errors and repairs the affected region of the newly synthesized DNA strand.

When MMR system activity decreases, replication errors accumulate. Changes become particularly frequent in short, repetitive DNA sequences, resulting in microsatellite instability. Therefore, MMR deficiency is considered one of the important molecular features of the cancer genome.

MMR Deficiency and Microsatellite Instability

When the function of MMR proteins is impaired, errors arising during DNA replication are not corrected efficiently. As a result, the lengths of short, repetitive DNA sequences known as microsatellites begin to change. This condition is characterized as microsatellite instability.

Microsatellite instability is not merely an individual genetic alteration; it is also an important molecular marker indicating that the MMR system is not functioning adequately in the tumor genome. It has particular diagnostic and clinical significance in colorectal and endometrial tumors.

Inherited defects in the MMR system constitute the molecular basis of certain hereditary cancer syndromes, particularly Lynch syndrome. In such cases, a reduced ability to correct DNA replication errors increases susceptibility to the development of certain types of tumors.

The Role of BRCA1 and BRCA2 in DNA Repair

The BRCA1 and BRCA2 genes are important for the highly accurate repair of DNA double-strand breaks. They participate in ensuring the effective functioning of repair processes that use homologous sequences. This mechanism enables damaged DNA to be repaired using an intact, homologous DNA sequence as a template.

When the function of the BRCA1 or BRCA2 genes is impaired, the ability to accurately repair DNA double-strand breaks decreases. Consequently, the cell may become more dependent on alternative mechanisms that are relatively less accurate. This leads to the accumulation of mutations and chromosomal rearrangements, thereby intensifying genomic instability.

BRCA Mutations and Cancer

Inherited or acquired alterations involving BRCA1 and BRCA2 are associated with the development of certain types of cancer. BRCA-associated repair defects are of particular clinical significance in breast, ovarian, and prostate cancers.

Impairment of BRCA function makes cells more vulnerable to DNA damage and increases genomic instability. At the same time, determining BRCA status is important not only for assessing cancer risk but also for selecting certain treatment approaches.

Chromothripsis and Complex Alterations in the Cancer Genome

Alterations in the cancer genome are not limited to point mutations in individual genes. In some cases, a large portion of a chromosome may fragment into numerous pieces within a short period, after which these fragments may be reassembled in a disorganized manner. This phenomenon is known as chromothripsis and is considered one of the mechanisms that can lead to the extensive reorganization of the cancer genome.

During chromothripsis, a particular region of a chromosome breaks into numerous fragments. Subsequently, only some of these fragments are rejoined, while certain genetic segments may be lost. As a result, multiple rearrangements may arise simultaneously within a single chromosomal region.

Such complex chromosomal alterations may lead to the activation of oncogenes or the loss of tumor suppressor genes. Therefore, chromothripsis is regarded as a mechanism that can contribute to rapid and extensive changes in the cancer genome in certain tumors.

Chromosomal instability, DNA double-strand breaks, and their inaccurate repair play important roles in the development of chromothripsis. Thus, disruption of DNA repair can lead not only to the accumulation of small-scale mutations but also to complex chromosomal alterations affecting large portions of the genome.

DNA Repair Systems as Molecular Targets for Cancer Treatment

The role of DNA repair systems in cancer development has enabled their investigation as molecular targets for treatment. When particular repair pathways are defective in tumor cells, these cells may

become more dependent on other repair mechanisms. Therapeutic strategies designed to target tumor cells by exploiting this characteristic have subsequently been developed.

Synthetic Lethality

Synthetic lethality is a phenomenon in which a cell dies when two distinct molecular defects are present simultaneously, whereas the cell may survive if only one of these defects is present.

This principle is important for targeting cancer cells with impaired DNA repair. For example, cells with defective BRCA1 or BRCA2 function have a reduced capacity for homologous recombination repair. Such cells become more dependent on other DNA repair mechanisms.

BRCA1/2 and Poly(ADP-Ribose) Polymerase Inhibitors

The combined impairment of BRCA1/2-associated repair and poly(ADP-ribose) polymerase activity can substantially reduce the ability of tumor cells to survive. Therefore, poly(ADP-ribose) polymerase inhibitors are used as a therapeutic approach in certain BRCA-associated tumors.

This approach is based on exploiting the specific molecular vulnerabilities of cancer cells. In other words, blocking an additional repair pathway in a tumor cell whose repair capacity is already restricted, relative to that of a normal cell, makes its survival more difficult.

Treatment Based on DNA Repair Status

Determining the DNA repair status of tumor cells may be important when selecting a treatment strategy. Molecular features such as MMR deficiency, microsatellite instability, or BRCA-associated repair defects help characterize the biological properties of a tumor.

This approach broadens the ability to assess cancer not solely according to its anatomical location but also on the basis of its molecular characteristics.

Molecular Mechanisms of Treatment Resistance

Although treatments targeting DNA repair can be effective, resistance to treatment may also develop in certain tumor cells. Reactivation of repair pathways, the emergence of additional genetic alterations, or the use of alternative cellular survival mechanisms may play important roles in this process.

Therefore, studying DNA repair systems is important not only for developing new therapeutic agents but also for understanding the causes of resistance to existing treatments.

Discussion

The balance between DNA damage and its repair is essential for maintaining genomic stability. Disruption of repair systems leads to the accumulation of DNA lesions and mutations, thereby

increasing genomic instability. This, in turn, creates conditions that can disrupt the function of genes regulating cellular proliferation and promote cancer development.

In particular, defects in the MMR and BRCA1/BRCA2 systems are among the important molecular mechanisms underlying cancer development. While MMR deficiency leads to the accumulation of replication errors and microsatellite instability, impaired BRCA1/BRCA2 function reduces the efficiency of DNA double-strand break repair.

The role of DNA repair defects in cancer development is making these defects important molecular targets for diagnosis and treatment. In particular, the principle of synthetic lethality, which exploits BRCA-associated repair defects, enables the selective targeting of tumor cells.

Overall, the sequence of DNA damage → impaired DNA repair → mutation accumulation → genomic instability → cancer development represents one of the important molecular foundations of tumor pathogenesis.

Conclusion

DNA damage is a continuous process that occurs within cells, and its timely detection and repair ensure genomic stability. Disruption of DNA repair systems, however, leads to the accumulation of mutations, genomic instability, and an increase in chromosomal alterations.

As a result of repair defects, the activation of oncogenes, the inactivation of tumor suppressor genes, and the disruption of cell cycle control create conditions that favor cancer development. In particular, repair defects associated with MMR and BRCA1/BRCA2 constitute important molecular mechanisms underlying cancer.

Thus, the sequence of DNA damage → impaired DNA repair → mutation accumulation → genomic instability → cancer development represents one of the important foundations of tumor pathogenesis. In-depth investigation of DNA repair mechanisms is a promising area of research for advancing the molecular diagnosis of cancer and developing individualized treatment approaches.

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