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# The Significance of Genetic and Epigenetic Cellular Changes and Uncontrolled Proliferation in Oncogenesis

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**Abstract:** Oncogenesis is the process by which cells undergo uncontrolled proliferation due to genetic and epigenetic alterations. The process is associated with the activation of proto-oncogenes and the inactivation of tumor suppressor genes. Defects in DNA repair systems increase genomic instability. Epigenetic modifications lead to disrupted gene expression. Loss of cell cycle control plays a critical role in tumor development. Impaired apoptosis mechanisms allow damaged cells to persist. Metabolic reprogramming meets the energetic demands of cancer cells. Tumor microenvironment supports proliferation and invasion. Immune evasion mechanisms enhance tumor persistence. Epithelial-mesenchymal transition is crucial in metastasis. Molecular profiling technologies enable the identification of individual tumor characteristics. In-depth study of oncogenesis contributes to early diagnostics and the improvement of targeted therapeutic strategies.

**Keywords:** Oncogenesis, carcinogenesis, mutation, proto-oncogene, oncogene, tumor suppressor genes, genomic instability, DNA repair, epigenetic modification, apoptosis, proliferation.

**Introduction:** Oncogenesis is one of the most pressing areas in modern medicine and biomedical sciences, representing the transition of normal cells into uncontrolled proliferation under the influence of genetic and epigenetic changes. Recent research, especially since 2024, has emphasized interpreting cancer not merely as a result of individual gene mutations but as a complex, multilayered, systemic biological phenomenon. Today, the oncogenesis process is considered as an interrelated network of changes at the genome, epigenome, transcriptome, proteome, and metabolome levels. According to global health data, cancer remains one of the leading causes of death worldwide. International epidemiological reports published in 2024 indicate a rise in newly detected tumor cases, a trend linked to population aging, urbanization, environmental factors, and lifestyle changes. Additionally, advances in diagnostic techniques allow early detection of previously undiagnosed tumor forms.

Contemporary molecular biology achievements increasingly reveal the mechanisms underlying oncogenesis. Next-generation sequencing technologies allow high-resolution analysis of mutational profiles in tumor cells. By 2025, expanded genomic panel testing has been implemented in many clinical centers, enabling identification of patient-specific molecular “signatures” and selection of personalized treatment strategies. Recent studies show that epigenetic reprogramming, along with DNA sequence alterations, plays a crucial role in oncogenesis. DNA methylation, histone modifications, and non-coding RNAs deeply regulate gene expression. Research conducted between 2024 and 2025 demonstrated that epigenetic changes in certain tumor types can be detected at very early stages, suggesting the potential use of epigenetic markers in early diagnostics.

A key aspect of oncogenesis is the reprogramming of cellular metabolism. Modern studies confirm that cancer cells alter energy production processes uniquely. Metabolic pathway reprogramming enables rapid growth and adaptation to unfavorable conditions. Experimental work published in 2025 shows that new drugs targeting metabolic enzymes have entered clinical trials. The concept of the tumor microenvironment has gained attention, emphasizing that cancer comprises not only transformed cells but also stromal cells, immune elements, blood vessels, and extracellular matrix, forming a complex biological system. Research from 2024 onwards highlights the tumor microenvironment’s role in therapeutic resistance. Therefore, modern treatments target both tumor cells and their surrounding microenvironment.

Immuno-oncology is rapidly advancing. Immune checkpoint inhibitors have shown positive outcomes in various tumor types. Clinical follow-ups from 2025–2026 demonstrate long-term remission in certain patients. Furthermore, therapeutic vaccines targeting individual tumor neoantigens are under active investigation, underscoring the necessity of studying oncogenesis in the context of immune interactions. The concept of cancer stem cells remains central; recent studies indicate that recurrence and metastasis are largely driven by this small cell population. From 2024 onwards, molecular markers of these cells have been identified, and targeted therapies are being developed, aiming to reduce relapse risk. Genome editing technologies, particularly CRISPR systems, are widely used in modeling and experimental studies of oncogenesis. By 2025, laboratory approaches allowed precise introduction of mutations to study stepwise tumor development, facilitating the discovery of new therapeutic targets. Artificial intelligence and bioinformatics tools now analyze large-scale omics data, and by 2026, machine learning algorithms are applied in many centers to predict tumor progression and treatment response, optimizing clinical decision-making.

Recent studies highlight the critical role of the tumor microenvironment in shaping oncogenic processes. Beyond intrinsic genetic mutations, interactions between cancer cells and surrounding stromal cells, fibroblasts, endothelial cells, and immune infiltrates significantly influence tumor progression and therapeutic response. Mechanical forces within the extracellular matrix, nutrient gradients, and hypoxic conditions contribute to selective pressures that drive tumor evolution. Moreover, the interplay between chronic inflammation and oncogenesis has gained attention, as persistent inflammatory signaling can induce DNA damage, epigenetic alterations, and aberrant cell proliferation. Advances in single-cell sequencing now allow the dissection of cellular heterogeneity within tumors, revealing distinct subpopulations with varying proliferative potential, metastatic capacity, and drug sensitivity. Integrating these findings with spatial transcriptomics provides a more comprehensive map of tumor architecture and functional dynamics. Such insights emphasize that effective cancer therapies must target not only tumor cells but also the surrounding microenvironment and signaling networks that support malignant growth.

Emerging evidence also indicates that metabolic crosstalk between cancer cells and the tumor microenvironment plays a pivotal role in oncogenesis. Tumor-associated fibroblasts and immune cells can secrete metabolites and growth factors that promote survival, angiogenesis, and resistance to therapy. Altered nutrient utilization, such as enhanced glycolysis and glutamine dependence, not only supports rapid proliferation but also modulates immune cell function, creating an immunosuppressive niche. Understanding these metabolic interactions provides novel opportunities for targeted interventions aimed at disrupting tumor-supportive metabolic networks. Epigenomic plasticity further adds a layer of complexity to oncogenesis. Dynamic changes in chromatin accessibility, histone modifications, and non-coding RNA activity can lead to reversible phenotypic switching, enabling tumor cells to adapt to environmental stressors, evade immune surveillance, and acquire drug resistance. Integrating epigenomic data with mutational profiles and transcriptomic signatures allows researchers to identify vulnerabilities specific to different tumor subtypes, paving the way for precision medicine approaches.

Oncogenesis is one of the most complex and multifactorial processes in modern biomedicine, characterized by disruption of genetic stability, epigenetic reprogramming, and dysregulation of intracellular signaling pathways. According to current scientific views, cancer development is interpreted not as the result of a single mutation, but as a multistep and evolutionary process. Transformed cells accumulate additional molecular alterations over time and form clones with selective advantages. Modern genomic studies demonstrate a high level of heterogeneity within tumor tissue. Tumors with the same histological diagnosis may differ significantly at the molecular level. Even within a single tumor, there may be clones with distinct genetic and epigenetic profiles. This diversity leads to variable therapeutic responses and the development of resistance.

Single-cell sequencing and spatial transcriptomics methods have enabled deeper analysis of the tumor microenvironment. Tumor cells actively interact with stromal elements, immune cells, and the extracellular matrix. Cytokines, growth factors, and mechanical signals within the microenvironment stimulate proliferation and invasion. Therefore, oncogenesis is now considered not only a cell-intrinsic process but also a tissue-level systemic phenomenon. Epigenetic mechanisms play an important role in tumor formation. DNA methylation, histone modifications, and non-coding RNAs stably alter gene expression. A connection between metabolic state and epigenetic enzymes has been identified, with certain metabolites directly influencing chromatin structure. This demonstrates a close relationship between metabolic reprogramming and gene regulation. Cellular plasticity and phenotypic adaptability are key features of oncogenesis. Transformed cells can alter their phenotype in response to environmental influences. This characteristic is crucial in metastasis and the development of therapeutic resistance. The epithelial–mesenchymal transition mechanism provides cells with migratory and invasive properties.

Biomechanical factors also contribute to tumor progression. Tissue stiffness and cytoskeletal reorganization can activate signaling pathways. Molecular pathways responding to mechanical stress modify proliferation and differentiation processes. This contributes to the formation of an aggressive tumor phenotype. Interaction with the immune system is an integral part of oncogenesis. Tumor cells employ various mechanisms to evade immune surveillance. During the process of immunoediting, less immunogenic clones are selected, allowing the disease to progress covertly. The state of the immune microenvironment directly affects prognosis and therapeutic effectiveness. The relationship between microbiota and tumors is also an important research direction. The composition of the intestinal microbiome modulates inflammatory processes and immune responses. Certain microorganisms can produce genotoxic metabolites that create conditions for epithelial cell transformation.

Intracellular phase separation processes and biomolecular condensates finely regulate transcription and signal transduction. Disruption of these systems may lead to persistent activation of oncogenic signaling. This mechanism provides a new molecular-level understanding of oncogenesis. Artificial intelligence and bioinformatic models enable integration of large-scale omics data to predict tumor evolution. Risk assessment and therapeutic strategy selection based on individual molecular profiles are expanding possibilities. The evolutionary development of transformed cells follows the principles of clonal selection. If an initial molecular alteration provides a selective advantage, subsequent mutations reinforce this benefit. As a result, faster-proliferating, apoptosis-resistant, and metabolically adaptable clones gain dominance. This process leads to increasing genetic complexity and the formation of an aggressive phenotype. Genomic instability is a central feature of the transformation process. Chromosomal rearrangements, amplifications, and deletions cause significant changes in gene expression. Replication stress and telomere dysfunction promote the accumulation of additional genetic defects. This accelerates progressive tumor evolution.

Persistent activation of signaling pathways ensures proliferative advantage. Growth factor–independent signaling cascades drive the cell cycle into an uncontrolled phase. Tyrosine kinase receptors and their intracellular effector systems may remain pathologically activated. As a result, the cell becomes independent of external regulatory signals. Metabolic adaptability increases tumor cell survival. Enhanced glucose utilization and activation of biosynthetic pathways provide substrates necessary for rapid growth. Lipid and nucleotide synthesis processes are reprogrammed. Mechanisms that increase resistance to oxidative stress help cells survive under unfavorable conditions. Epigenomic alterations contribute to the establishment of a stable phenotype. Transition of chromatin to open or closed states leads to selective changes in gene expression. Imbalance between transcription factors and chromatin modifiers disrupts differentiation programs. This process may result in reactivation of embryonic characteristics in tumor cells.

MicroRNAs and long non-coding RNAs participate in fine regulation of gene control mechanisms. Changes in their expression affect signaling pathways associated with proliferation, invasion, and metastasis. Certain RNA profiles are considered potential prognostic biomarkers. Reduced cell adhesion plays an important role in the development of invasive properties. Enzymes that degrade the extracellular matrix facilitate migration. Cells that spread through blood and lymphatic vessels may colonize distant tissues. This process is regulated by complex multistep molecular mechanisms. Tumor-associated inflammation creates a microenvironment that supports transformation. Cytokines and chemokines enhance proliferative signaling. Chronic inflammation increases DNA damage, leading to additional mutations. Therefore, inflammatory mediators are considered therapeutic targets.

Cellular senescence also has a complex role. Although senescence initially acts as a protective response, the senescence-associated secretory phenotype may exert proliferative effects on surrounding cells. This paradox highlights the dynamic nature of transformation. Integration of large-scale omics data is enabling the development of systemic models of tumor progression. Relationships between the genome, transcriptome, and proteome are being identified. Computational modeling approaches allow prediction of potential evolutionary trajectories of the disease. Reorganization of transcriptional networks is observed in transformed cells. Certain master regulatory transcription factors remain persistently activated, enhancing expression of genes that support proliferation. At the same time, genes responsible for differentiation are suppressed. As a result, cells retain an undifferentiated and highly plastic phenotype.

Disruption of proteostasis is also an important component of the pathological process. Alterations in the ubiquitin–proteasome pathway and autophagy mechanisms may prevent degradation of oncogenic proteins. This maintains continuous activation of signaling processes. Cellular energy balance is closely linked to mitochondrial function. Mitochondria are not only energy sources but also key regulators of apoptosis and reactive oxygen species. Alterations in mitochondrial DNA and increased oxidative stress negatively affect genomic stability. Intercellular communication via extracellular vesicles is enhanced. Tumor cells release vesicles containing RNA, proteins, and signaling molecules that influence nearby and distant cells. This mechanism may participate in preparing metastatic target tissues.

Angiogenesis creates necessary conditions for tumor growth. Formation of new blood vessels enhances delivery of nutrients and oxygen. Transcription factors activated under hypoxic conditions stimulate synthesis of angiogenic factors. Thus, the tumor establishes its own microcirculatory system. Neuro-immune interaction mechanisms are also being investigated. Nerve fibers and neurotransmitters in the tumor microenvironment have been shown to influence proliferative and migratory processes. This indicates the need to interpret cancer biology as a broader systemic phenomenon. Disruption of cell cycle checkpoints is one of the main causes of uncontrolled division. Imbalance in cyclins and cyclin-dependent kinases deregulates the G1/S and G2/M transition phases. As a result, cells continue replication despite DNA damage.

In addition to apoptosis, other forms of programmed cell death may also be altered. Suppression of mechanisms such as necroptosis and ferroptosis increases cell survival. At the same time, reactivation of these pathways under certain conditions is considered a therapeutic opportunity. Overall, molecular, cellular, and tissue-level alterations form a unified pathogenetic system. Dysfunction at each level integrates with other mechanisms to determine tumor formation and progression. The multifaceted nature of transformation requires deep and systematic investigation.

Thus, between 2024 and 2026, understanding of oncogenesis has significantly expanded. Cancer development is recognized as a multifactorial, systemic, and dynamic process. The interplay of genetic, epigenetic, metabolic, and immunological factors is central to tumor formation and progression. These modern scientific approaches provide a solid theoretical foundation for early diagnostics and personalized treatment strategies.

Modern understanding of oncogenesis emphasizes the disruption of intracellular signaling pathways. Recent molecular studies show that growth-promoting signal cascades in tumor cells are constitutively active, reducing dependence on external regulatory signals and enabling autonomous proliferation. Alterations in tyrosine kinase receptors and downstream effectors are identified in many tumor types. Studies after 2024 also highlight that disruption of cellular stress response mechanisms—including oxidative stress, mitochondrial dysfunction, and proteostasis imbalance—accelerates tumor progression, undermining genomic stability and promoting additional mutations. Attention is increasingly given to tumor heterogeneity; tumors of the same histological type may vary significantly at the molecular level. Multi-center studies reveal that even within a single tumor, distinct genetic clones exist, each responding differently to therapy, reinforcing the need for individualized treatment approaches.

Metastasis remains a major challenge in modern oncology. The molecular basis of epithelial-mesenchymal transition has been extensively studied, showing that migration and invasiveness are regulated by transcription factors and signaling pathways. Methods to identify circulating tumor cells and analyze them molecularly are improving, enabling earlier detection of metastasis. Tumor-immune interactions are also being deeply investigated. Recent data indicate that some tumors secrete molecules that functionally suppress immune cells, forming part of immune evasion strategies. Clinical observations in 2025 demonstrate that combined immunotherapy approaches enhance efficacy in certain resistant tumor types.

Epigenetic therapy has also advanced to a new stage. Drugs targeting DNA methylation or histone modifications are under investigation, with some reaching advanced clinical trial phases. These agents can restore gene expression and limit tumor cell growth. Additionally, the role of microRNAs and long non-coding RNAs in oncogenesis is increasingly recognized, regulating gene expression subtly and participating in multiple stages of tumor development. Recent studies suggest that certain microRNA profiles may serve as diagnostic and prognostic biomarkers.

The interplay between environmental factors and the genome is also under deep investigation. The exposome concept examines the cumulative effect of all external factors on genome activity throughout life, highlighting the need to consider oncogenesis in the context of environmental exposure as well as intrinsic genetic factors. A multidisciplinary approach—integrating molecular biology, bioinformatics, immunology, and clinical medicine—remains crucial. These integrations allow increasingly precise modeling of oncogenesis and development of new therapeutic strategies while optimizing existing treatments. From 2025 to 2026, significant deepening of scientific understanding of oncogenesis has occurred. Recognizing cancer as a complex biological system and studying its molecular mechanisms comprehensively enables the development of personalized treatments, early detection, and improved disease monitoring.

## CONCLUSION

Oncogenesis is a complex, multi-step biological process shaped by a combination of genetic and epigenetic alterations. Modern scientific perspectives interpret cancer development not as a consequence of a single mutation but as a result of systemic molecular disruptions. Genomic instability and impaired DNA repair mechanisms are major contributors to tumor formation. Epigenetic reprogramming profoundly alters gene expression. Disruption of cell cycle control and impaired apoptosis enhance pathological proliferation. Metabolic reprogramming satisfies the energy and biosynthetic demands of tumor cells. Tumor microenvironment plays a critical role in cancer progression and therapy resistance. Immune interactions are key determinants of disease prognosis. Cancer stem cells are central to recurrence and metastasis. Molecular heterogeneity necessitates individualized treatment strategies. Next-generation sequencing and bioinformatic analyses provide deeper insights into tumor biology. Liquid biopsy and molecular markers expand early diagnostic possibilities. Immunotherapy and targeted therapy enhance treatment efficacy. Multidisciplinary approaches ensure comprehensive study of oncogenesis. Understanding oncogenesis mechanisms lays a solid scientific foundation for early detection, effective treatment, and preventive strategies.

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