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Review Article

Cancers Are Derived from the Disruption of Cell Differentiation

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Abstract

The mechanisms of cancer are discussed by analyzing the characteristics of the functional state and biological behavior of the abnormal nuclear cells. The abnormal nuclear cells with abnormal nuclear structure and function are a kind of sick cell or functional defect cells having existed in human body for a long time. The abnormal nuclear cells are resulted from the nuclear damage caused by the radiation, viruses and various carcinogenic compounds. Some of genes in human body are expressed, some are not expressed for life. The expressional genes are functional genes, the genes never expressed for life in human body are dormant genes or sealed genes. The nuclear damages destroy cell state of differentiation, affect gene expressional regulation and change gene expressional profiling, resulting in loss of expression of the functional genes and reactivation of the sealed genes; which finally leads to cancer, aging and other chronic refractory diseases. The cancer is not resulted from the genetic mutations or chromosomal aberrations, but rather the reactivation of genes involved in proliferation due to the nuclear damage. The biological characteristics of the cancer cells, such as the shedding and metastasis, immune tolerance, uncontrolled, loss of contact inhibition function and so on, all originate from the nuclear aberrant cells. The nuclear damage can trigger the genes that drive mitosis, leading to cancer. Thus, re-sealing the several genes that trigger the proliferation may completely prevent or cure cancers.

Keywords

Abnormal Nuclear Cell, Abnormal Nuclear, Nuclear Damage, Cancer, Gene, Regulation of Gene Expression, Functional Gene, Sealed Gene

1. Introduction

The cancer is one of the major diseases that threaten human health and safety. In 2020, 4.57 million new cancer patients were diagnosed in China, accounting for 23.7% of the global total; and 3 million cancer deaths, accounting for 30% of the global total. In 2022, 4.82 million new cancer patients and 3.21 million cancer deaths were recorded in China, ranking first in the world in both numbers [1]. In the 2024, there will be 2 million new cancer patients and 610,000 cancer deaths in the United States [2]. Another report, there are an estimated 3,246,625 and 2,510,597 new cancer cases and 1,699,066 and 640,038 cancer deaths in China and the US in 2024, respectively [3]. According to the International Agency for research on cancer, there were about 19.3 million new cases of cancer and 10 million cancer deaths worldwide in 2020. Today, the causes and pathogenesis of cancers are not completely clear, and it is usually thought that it is caused by gene mutation and

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chromosomal aberrations [4-6]. Later studies showed that, nuclear skeletons, ribosomes [7], histones, transcription factors [8, 9], small RNAs [10, 11], related enzymes [12-14], DNA methylation [15-18], and nuclear membrane abnormalities all contribute to the carcinogenesis and progression of cancer. Thus, all the molecular abnormalities in the nucleus, that is, the whole nucleus damage may be carcinogenic. Presumably, cancers are probably caused by the regulatory abnormality of gene expression resulted from the nuclear damage [19, 20]. Today, the mechanisms of cancer are discussed through analyses of the functional status, biological behavior, and gene expression profiling of abnormal nuclear cells; and the relevant studies are also reviewed; some new insights are put forward which may be contribute to cancer prevention and research.

2. Discussion

2.1. The Cancers Are Probably Caused by the Nuclear Damage

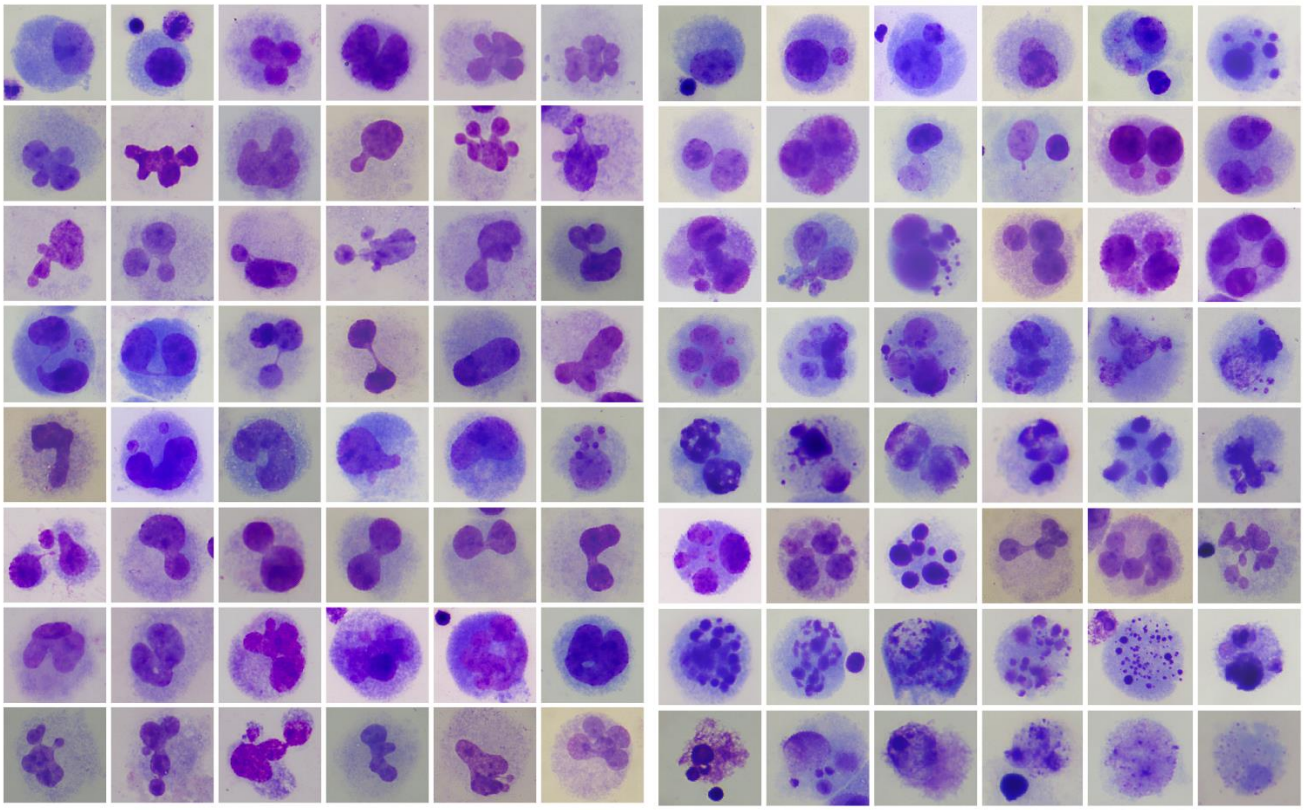

Figure 1. *The abnormal nuclear cells.*

It is customary to use genes to explain the whole body and all diseases, but in many cases there is nothing wrong with the genes themselves (the gene structure), just not opened (gene switch abnormalities) [21, 22]. The gene structural abnormality is mostly caused by the gene mutation and chromosomal aberration, and the abnormal gene expression is mainly caused by the nuclear damage [23]. According to the two-hit theory, a cancer is caused by two gene mutations [24]. However, the probability of having more than two related mutations in the same cell in a row is very low, so the chance of cancer caused by the gene mutation is not much. The chromosomal aberrations are known to cause cancer mainly in retinoblastoma and Philadelphia chromosome leukemia [25, 26]; and most other studies have only described an association of cancer with the chromosomal aberration, but not a cause-and-effect relationship. Recent studies have suggested that cancers are caused by various molecules in the nucleus, such as the nuclear skeletons, ribosomes [7], histones, transcription factors [8, 9], RNA polymerase, DNA methylation abnormalities [15-18] and so on.

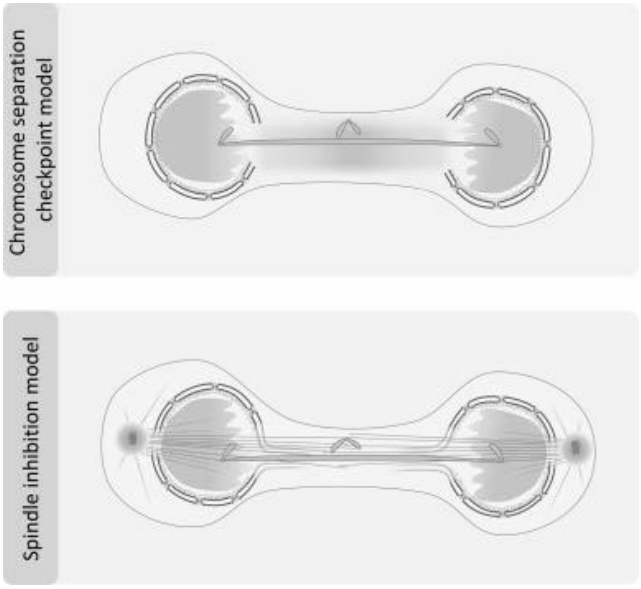

Figure 2. *The model for the nuclear anomalies.*

The radiation generally interacts with water molecules to produce reactive oxygen species (ROS), free radicals (FR), and then with the chromosomal DNA, finally resulting chromosomal aberration. The carcinogenic compounds usually cannot interact with the chromosomal DNA because of difficult entering the cell nucleus. Thus, the gene mutation and chromosomal aberration are indirectly caused by the radiation and carcinogenic compounds, both are resulted from the nuclear damage [27, 28]. In addition, the nucleus has a strong repair system of DNA damage, a system of maintaining structure and active of chromatin, and a strong scavenging system of free radical and reactive oxygen species; therefore, as long as the nuclear function is normal, the gene mutation and chromosomal aberration do not generally occur [14, 28, 29]. Thus, the gene mutation and chromosomal aberration are only a result or manifestation of the nuclear damage, and the high rates of gene mutation and chromosomal aberration in cancer patients are probably only a concomitant phenomenon.

Thus, cancers are probably not resulted from the gene mutation or chromosomal aberration, but rather the gene expression and regulatory disorders caused by the nuclear damage [20, 30]. Any molecular damage in the nucleus may be carcinogenic because the nucleus is an organic whole [8, 12, 17]. The cancer cells are derived from the abnormal nuclear cells (ANC), which refer to a cell with an abnormal nuclear in morphology, structure and function, a kind of morbid cells or functionally defective cells that exist in humans for a long time [24, 31, 32]. The abnormal nuclear cells as a result of nuclear damage are caused by the radiation, viruses and various carcinogenic compounds through molecular adhesions, breaks, and chemical modifications [33-36] (Figure 1). There are currently two model explanations for the nuclear anomalies (Figure 2) [37].

2.2. The Molecular Mechanisms of Cancer Induced by the Nuclear Damage

2.2.1. The Nuclear Damage Affects Gene Expression and Regulation

Some of human genes are expressed and some are not. The expressed genes usually play a role or perform a function in the human body and are therefore called functional genes (FG). There are three types of functional genes, respectively, the genes associated with cell survival (survival genes, SVG), the genes associated with cell role-playing (role genes, RG), and the support genes (helper genes, HG) [38]. Survival genes are mainly the housekeeping genes related to the cell metabolism and energy production, such as glycolysis, tricarboxylic acid cycle, oxidative phosphorylation enzyme genes, transcription factor genes and so on [39, 40]. Role genes play a role in the human body and are also biomarkers of cells. For example, the hemoglobin gene is a role gene of red blood cells, and the insulin gene is a role gene of islet cells, the troponin gene is a role gene of cardiac muscle cells, and so on. Helper genes play supporting or assisting roles in the human body, such as signaling molecule genes, receptor protein genes, adhesion molecule genes, vector channel protein genes, chaperone protein genes, and so on [41] (Figure 3).

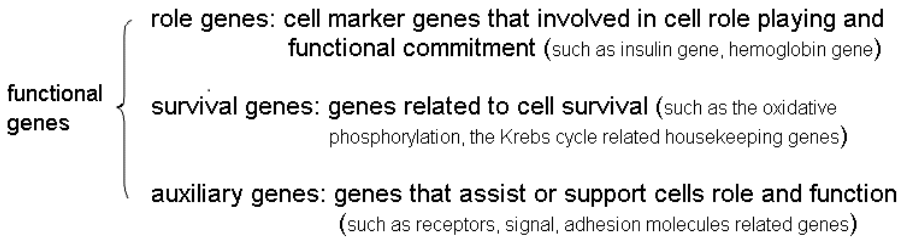

Figure 3. *The functional genes.*

Some of human genes express all the time, some never express for a life, and some express intermittently. The gene being not expressed throughout life is generally referred to as a dormant gene (DG), which seems to be sealed, so is also

called a sealed gene (SG). The intermittently expressing genes can be expressed by the way of phases, periodically, pulsatile, signal-dependent, clock-or time-dependent, or specifically [42, 43]. The gene expressed intermittently is also a functional gene when it opens, a standby gene when it blocked. The standby genes can be switched on and off at any time under the neuroendocrine control. Therefore, the human genes are in three states: open/express, standby/blocked and seal. The sealed gene will be permanently closed and for life no longer expressed. A standby gene in state of close is only temporary and can be opened again when the body needs [44, 45]. The genes in the open state are expressed genes, dominant genes, functional genes, and the genes in the sealed state are sealed genes, dormant genes, and recessive genes. The functional genes are located in the euchromatin region, the continuously expressed genes are located in the active chromatin region; and the never expressed genes (the sealed genes) are located in the constitutive or structural heterochromatin regions, and are probably caused by the developmental gene silencing; the discontinuously expressed genes are mostly located in facultative heterochromatin regions [46]. This kind of gene expression rule and characteristic are formed by the differentiation, the cell nucleus damage can affect the differentiation state, namely affects the gene expression and regulation, and eventually leads to dysfunction of DNA transcription-protein synthesis (Figure 4).

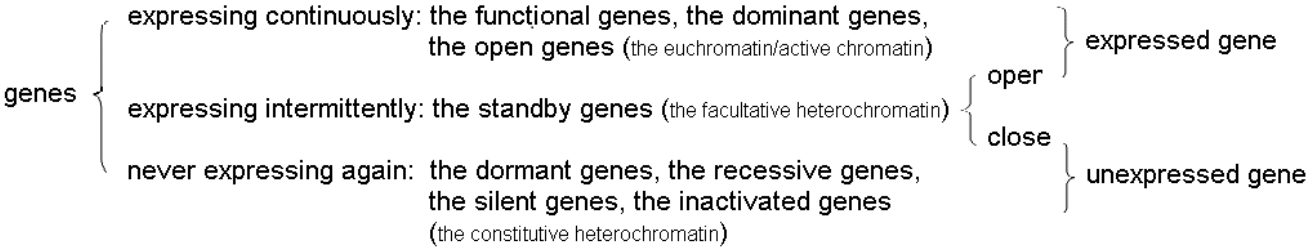

Figure 4. *The gene expressional state.*

2.2.2. The Nuclear Damage Disrupts the Differentiation and Changes the Gene Expression Profiling

The process from a fertilized egg to an adult cell is called differentiation. The essence of differentiation is the process of modifying and establishing to cells, and reorganizing to gene's expressional profiling, which is also the process of blocking or sealing the unrelated genes (blocking standby genes, sealing dormant genes) and open or saving the function genes [47-49]. The goal of differentiation is to make cells into function cells or role cells in order to play a role or perform a function in human body. These cells are unipotent or specialized cells which usually express only a few genes (only functional genes), namely most genes being not expressed. The differentiation not only forms organs and embryos [50], but also remakes cells, alters gene expressional profiling, and especially makes gene expression regulation in a way of patterns, programs, switches, and streamlines.

These three changes are achieved simultaneously, of which the change of gene expressional profiling is the foundation and premise [51-53]. The cell differentiation state must be maintained unchanged because the various functional activities of human body are all carried out and completed on the basis of differentiated cells. Without differentiation, there would be no human and multicellular organisms, and disruption of the differentiation state would also affect various function and states of cells and organisms [54]. The so-called maintenance of differentiation state is also to maintain the gene expression state or the gene expressional profiling unchanged. The so-called disruption of the differentiation state also means that the gene expressional state or gene expressional profiling has changed, that is, the functional genes cannot be expressed, the dormant genes restart, the standby genes express disorderly. In a word, the expressed genes cannot be expressed, the genes that should not be expressed start to express.

The nuclear damages affect or disrupt the state of cell differentiation, change the gene expression or gene expressional profiling. The main mechanisms by which the nuclear damage affects gene expression are the inhibition of RNA polymerase, epigenetic alterations, nuclear skeleton damage, abnormal transcription factors, nuclear envelope defects, changes in the chromatin structure and activity, and so on [8, 15, 55, 56]. Some genes or molecular checkpoints may only activate the proliferation genes, such as the tumor suppressor gene *P53*, *C-Myc*, *bcl-2*, *LAPTM4B*, *NPM1*, *FAM83B* genes, and so on.

2.2.3. The Nuclear Damage Changes the Cell Function and Biological Behavior

When the nucleus is damaged, the cell differentiation state is destroyed and the gene expression profiling is changed, as a result the functional genes cannot be expressed and the dormant genes are reactivated. The functional genes include the survival genes, role genes and helper genes. Failure to express survival genes affects cell survival, and failure to express role genes affects cell role functions [23]. Accessory genes include adhesion molecule genes, signal molecule

genes, and so on. Failure to express the adhesion molecule genes will affect cell adhesion junctions, resulting in cell detachment and wandering. Failure to express the signaling genes can affect cellular information exchange, resulting in poor cell response to environmental signals and neuroendocrine regulation, and even become deaf-mute cells [52, 53]. The abnormal nuclear cells do not express foreign proteins, so they are not cleared by the autoimmune system and show immune tolerance. The human cells as differentiated cells do not divide and proliferate because the genes related to division and proliferation are usually sealed. The carcinogenesis is the process of embryogenesis caused by the nuclear damage. Once the genes related to mitotic proliferation are reactivated, the cells will continuously divide and proliferate and lose contact inhibition, thus transforming into cancer cells. The abnormal nuclear cells have poor functional activity and change in biological behavior [38]. The biological behavior and characteristics of the abnormal nuclear cells are as follows: easy shedding, migration, uncontrolled, immune tolerance, loss of contact inhibition, easy carcinogenesis or metaplasia. The cancer cells are probably originated from the abnormal nuclear cells, the so-called characteristics of cancer cells are derived from the abnormal nuclear cells. Therefore, the abnormal nuclear cells have long been used as biomarkers for cancer diagnosis (Figure 5, Table 1).

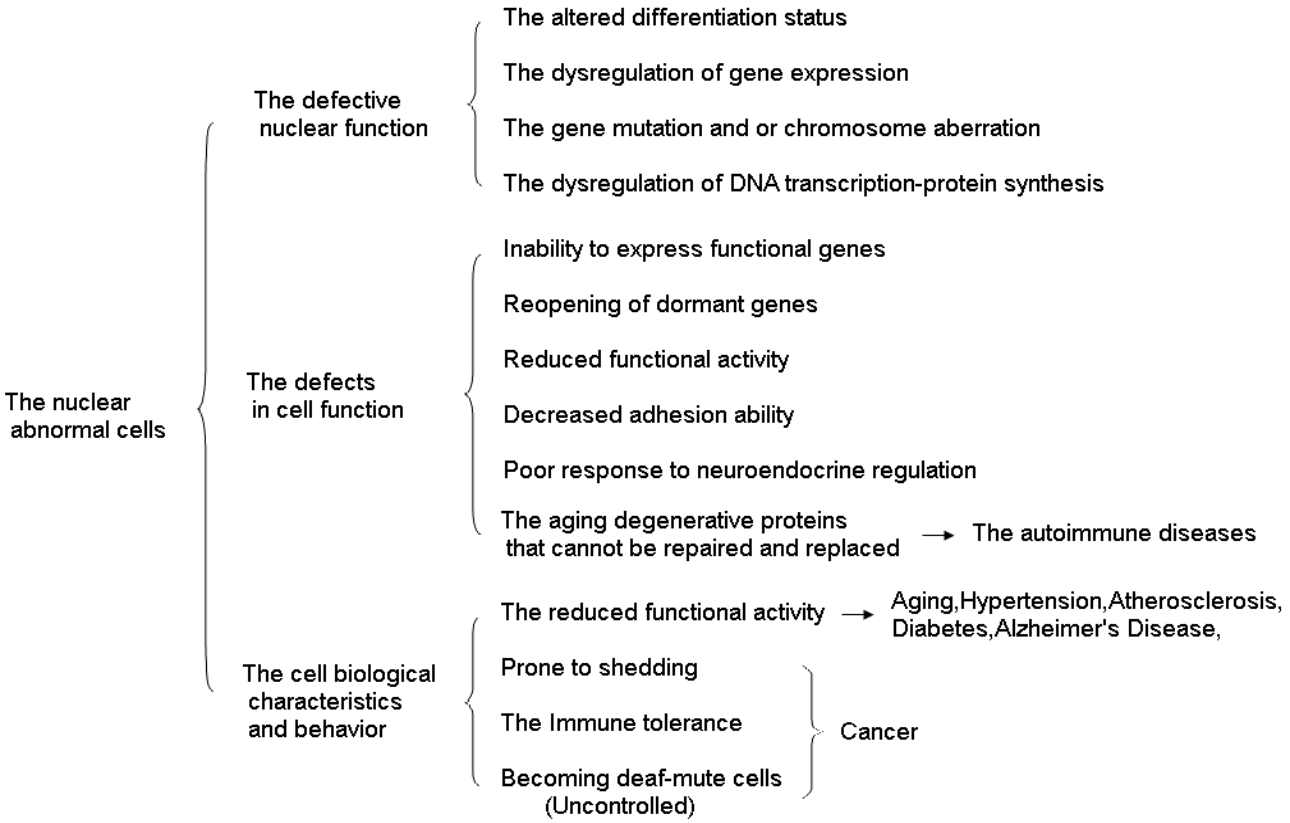

Figure 5. *The cell biological characteristics and behavior of the abnormal nuclear cells.*

Table 1. *Comparison between the normal cells and the abnormal nuclear cells.*

Items	Normal cells	Abnormal nuclear cells
Morphology and structure of nucleus	normal	abnormal
Nuclear function (replication, transcription, ribosome synthesis)	normal	abnormal
Gene mutation	no or yes	yes
Chromosome aberration	no	yes
Gene expression regulation	normal	abnormal
Cell differentiation state	normal	unstable or disrupted

Items	Normal cells	Abnormal nuclear cells
Functional genes	normal expression	abnormal expression
Seal genes (dormant gene)	not expressed (in a sealed state)	start to express
DNA transcription-protein synthesis function	normal	abnormal

In fact, it is not the cancer cells that gain the ability to proliferate, invade, and escape the immune system. Instead, due to the nuclear damage the human cells lose the ability to adhere (easily shed and migrate), lose the ability to respond to signals and neuroendocrine regulation (out of control), lose the ability to seal the genes involved in proliferation, eventually become cancer cells [23]. The abnormal nuclear cells are probably the carcinoma in situ or precancerous lesions. The diagnosis of cancer relies on a histiocytographic diagnosis, mainly to observe whether the morphological structure of the nucleus is abnormal, that is, whether it is an abnormal nuclear cell [31, 32, 57, 58].

Most of the abnormal nuclear cells undergo apoptosis or are cleared by the phagocytosis, only a few of them become cancerous. It is very important to differentiate the cancer cells from the abnormal nuclear cells. It will bring great pain and economic loss for the patients to misdiagnose nuclear abnormality as canceration, and it will delay the treatment if the canceration is misdiagnosed as simple nuclear abnormality. The nucleus abnormality can influence the regulation of gene expression through DNA methylation and epigenetics [59, 60], so the nuclear damage and abnormal gene expression are probably the link between heredity and environment.

Thus, the cancers are essentially caused by the nuclear damage, differentiation collapse, which is a nuclear dysfunction disease. These diseases are not caused by the mutations in a particular gene, but by the gene expression profiling changes, namely the functional genes cannot be expressed and the sealed genes restart [23]. The disorders of expression of only functional genes do not normally cause cancer, but lead to chronic and refractory diseases such as ageing, Alzheimer's disease, degenerative disease, and autoimmune diseases. If the sealed gene is opened on this basis, it can lead to cancer or metaplasia. The mitotic proliferation genes as one of the sealed genes once restarted will cause cancer (Figure 6).

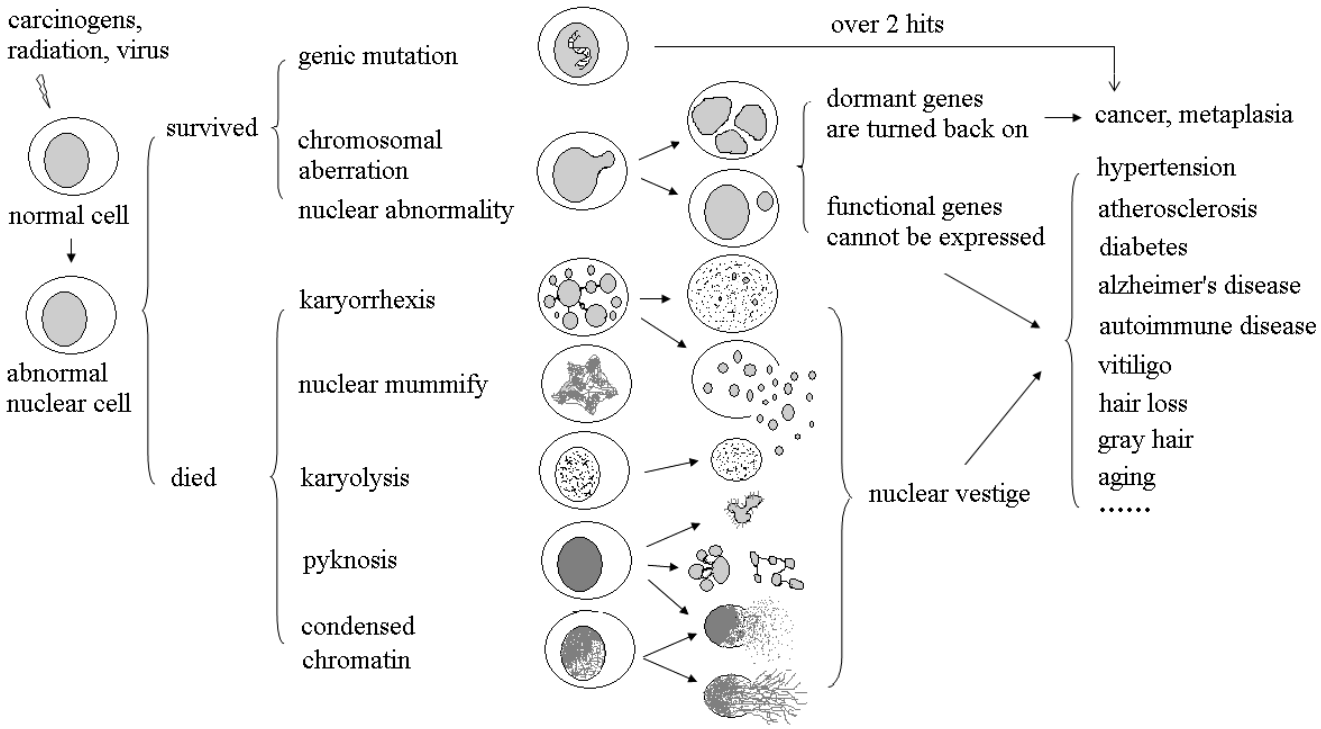

Figure 6. *The chronic intractable diseases probably derived from the nuclear damage.*

2.3. To Reseal the Several Genes Triggering Proliferation May Cure Cancers

Cancer treatment mainly includes chemotherapy, radiotherapy and surgery. The side effects of chemotherapy and radiotherapy are serious, and the operation is often missed the chance because of diagnosis late [61-63]. The biotherapies and immunotherapies are still being explored, and although there are individual clinical applications, they are either less than the ideal or have to be abandoned due to the toxic side effects [64-67]. Although the biotherapies (monoclonal antibody drugs) and immunotherapy are mostly targeted therapies, the targets of the therapies are mainly oncogenes, tumor suppressor genes and some enzymes [68, 69]. The oncogenes and tumor suppressor genes are mainly regulatory protein genes related to cell survival, such as cyclin, apoptosis-related proteins, receptor proteins, signaling molecules, and so on [21, 70]. In fact, these genes or proteins are the result of cancer, not the cause of carcinogenesis. Therefore, the monoclonal antibody and immunotherapy mentioned above are probably not effective in clinical treatment or have too many toxic and side effects.

The cancer cells are derived from the abnormal nuclear cells, and the biological characteristics of cancer cells are derived from the abnormal nuclear cells. The abnormal nuclear cells cannot express the functional genes because of the destruction of differentiation state and the change of gene expression profiling caused by the nuclear damage. Once the genes involved in proliferation as one of the sealed genes are opened, the cell will be transformed into cancer cells. Thus, the cancer is resulted from the nuclear damage leading to the reactivation of genes related to proliferation.

3. Conclusion

The cancer cells are derived from the abnormal nuclear cells, and the biological characteristics of cancer cells, such as the shedding and metastasis, immune tolerance, uncontrolled, loss of contact inhibition function and so on, all originate from the abnormal nuclear cells. Re-sealing the several genes that trigger the proliferation may completely prevent or cure cancers. It is still unclear how the sealed genes are restarted during the occurrence of cancer. The specific molecular mechanisms of expressional disorders of the functional genes also need further research and exploration.

Abbreviations

RNA	Ribonucleic Acid
DNA	Deoxyribonucleic Acid
ROS	Reactive Oxygen Species
ANC	Abnormal Nuclear Cells
SVG	Survival Genes
FG	Functional Genes
DG	Dormant Genes
HG	Helper Genes
SG	Sealed Genes
FR	Free Radicals
RG	Role Genes

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Author Contributions

Maojin Li is the sole author. The author read and approved the final manuscript.

Data Availability Statement

The data that support the opinions of this review are openly available.

Institution and Ethics Approval

There were no human subjects in the study, the data were from the literature, and were publicly available.

Transparency Statement

I confirm that the manuscript is honest, accurate, and transparent, no aspects of the study have plagiarized.

Consent to Publish Declaration

I agree to publish this manuscript in the journal of Discover Oncology.

Consent to Participate Declaration

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Conflicts of Interest

The author declare no conflicts of interest.

References

[1] Xia C, Dong X, Li H, et al. Cancer statistics in China and United States, 2022: profiles, trends, and determinants [J]. Chin Med J (Engl). 2022, 135(5): 584-590. https://doi.org/10.1097/CM9.0000000000002108

[2] Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024 [J]. CA Cancer J Clin. 2024, 74(1): 12-49. https://doi.org/10.3322/caac.21820

[3] Wu Y, He S, Cao M, et al. Comparative analysis of cancer statistics in China and the United States in 2024. Chin Med J (Engl). 2024, 137(24): 3093-3100. https://doi.org/10.1097/CM9.0000000000003442

[4] Basu AK. DNA Damage, Mutagenesis and Cancer [J]. Int J Mol Sci, 2018, 19(4): 970. https://doi.org/10.3390/ijms19040970

[5] Graham TA, Sottoriva A. Measuring cancer evolution from the genome [J]. J Pathol, 2017, 241(2): 183-191. https://doi.org/10.1002/path.4821

[6] Xueqian Yan, Li Liu, Yueru Ji, et al. Relationship between serum miR-155-5p and miR-146b-5p and chromosome aberration and prognosis of secondary acute myeloid leukemia [J]. Medical Journal of the Chinese People's Armed Police Force. 2024, 35(01): 14-20+24. https://doi.org/10.14010/j.cnki.wjyx.2024.01.010

[7] Qiongyu Li. The study of ribosome biosynthesis involved in ribosomal proteins in cancer [J]. Chinese Journal of Modern Drug Application, 2024, 18(04): 174-180. https://doi.org/10.14164/j.cnki.cn11-5581/r.2024.04.048

[8] Jiramongkol Y, Lam EW. FOXO transcription factor family in cancer and metastasis [J]. Cancer Metastasis Rev. 2020, 39(3): 681-709. https://doi.org/10.1007/s10555-020-09883-w

[9] Geden MJ, Romero SE, Deshmukh M. p53 is required for nuclear but not mitochondrial DNA damage-induced degeneration [J]. CellDeath Dis, 2021, 12(1): 104. https://doi.org/10.1038/s41419-020-03373-1

[10] Abdel Rhman M, Pmo O. Potential therapeutic applications of microRNAs in cancer diagnosis and treatment: Sharpening adouble-edged sword? [J]. Eur J Pharmacol, 2022, 932: 175210. https://doi.org/10.1016/j.ejphar.2022.175210

[11] Jie Jiang, Zai Luo, Haoliang Zhang, et al. Circular RNA-Encoded Proteins in Gastrointestinal Cancer [J]. Acta Academiae Medicinae Sinicae, 2024, 46(01): 72-81. https://doi.org/10.3881/j.issn.1000-503X.15498

[12] Judasz E, Lisiak N, Kopczyński P, et al. The role of telomerase in breast cancer's response to therapy [J]. Int J Mol Sci, 2022, 23(21): 12844. https://doi.org/10.3390/ijms232112844

[13] Engin AB, Engin A. The connection between cell fate and telomere [J]. Adv Exp Med Biol, 2021, 1275: 71-100. https://doi.org/10.1007/978-3-030-49844-3_3

[14] Taylor AMR, Rothblum-Qviatt C, Ellis NA, et al. Coromosome instability syndromes [J]. Nat Rev Dis Primers, 2019, 5(1): 64. https://doi.org/10.1038/S41572-019-0113-0

[15] Yunxiao Xie, Na Ding. Analysis of the Effect of Methylation Alterations on Enhancer Activity in Cancer [J]. International Journal of Geriatrics, 2024, 45(02): 193-198. https://kns.cnki.net/ kcms2/article/

[16] Saghafinia S, Mina M, Riggi N, et al. Pan-cancer landscape of aberrant DNA methylation across human tumors [J]. Cell Rep, 2018, 25(4): 1066-1080.e8. https://doi.org/10.1016/j.celrep.2018.09.082

[17] Zappe K, Cichna-Markl M. Aberrant DNA methylation of ABC transporters in cancer [J]. Cells, 2020, 9(10): 2281. https://doi.org/10.3390/cells9102281

[18] Zafon C, Gil J, Pérez-González B, et al. DNA methylation inthyroid cancer [J]. Endocr Relat Cancer, 2019, 26(7): R415-R439. https://doi.org/10.1530/ERC-19-0093

[19] Capuozzo M, Santorsola M, Bocchetti M, et al. p53: From Fundamental Biology to Clinical Applications in Cancer [J]. Biology (Basel). 2022, 11(9): 1325. https://doi.org/10.3390/biology11091325

[20] Martinez-Fundichely A, Dixon A, Khurana E. Modeling tissue-specific breakpoint proximity of structural variations from whole-genomes to identify cancer drivers [J]. Nat Commun. 2022, 13(1): 5640. https://doi.org/10.1038/s41467-022-32945-2

[21] Tiwari B, Jones AE, Caillet CJ, et al. p53 directly represses human LINE1 transposons [J]. Genes Dev. 2020, 34(21-22): 1439-1451. https://doi.org/10.1101/gad.343186.120

[22] Jingjing Guo, Di Mou, Wenwen Yu, et al. Study on the Biological Function of Abemecilib in Inhibiting the Proliferation, Invasion and Migration of Small Cell Lung Cancer with High c-Myc Expression [J]. Chinese Journal of Lung Cancer, 2023, 26(02): 105-112. https://kns.cnki.net/kcms2/article/

[23] Maojin Li, Anyi Hu. The research progress and biological significance of abnormality of cell nucleus [J]. China Occupational Medicine, 2021, 48(6): 708-711. https://doi.org/10.20001/j.issn.2095-2619.20211995

[24] Ashley DJ. The two "hit" and multiple "hit" theories ofcarcinogenesis [J]. Br J Cancer, 1969, 23(2): 313-328. https://doi.org/10.1038/bjc.1969.41

[25] Jabbour E, Short NJ, Jain N, et al. The evolution of acute lymphoblastic leukemia research and therapy at MD Anderson over four decades [J]. J Hematol Oncol. 2023, 16(1): 22. https://doi.org/10.1186/s13045-023-01409-5

[26] Saleh K, Fernandez A, Pasquier F. Treatment of Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia in Adults [J]. Cancers (Basel). 2022, 14(7): 1805. https://doi.org/10.3390/cancers14071805

[27] Qiang Lu, Qiuling Zhang, Xiujuan Hong. Relationships between chromosome aberration, blood routine, and cumulative dose in 718 radiation workers [J]. Industrial Health and Occupational Diseases, 2023, 49(06): 497-500.

[28] Rageul J, Kim H. Fanconi anemia and the underlying causes of genomic instability [J]. Environ Mol Mutagen. 2020, 61(7): 693-708. https://doi.org/10.1002/em.22358

[29] Garc á-de-Teresa B, Rodr guez A, Frias S. Chromosome Instability in Fanconi Anemia: From Breaks to Phenotypic Consequences [J]. Genes (Basel). 2020, 11(12): 1528. https://doi.org/10.3390/genes11121528

[30] Hongling Ou, Wenchao Ai, Yan Wang, et al. Advances in research and application of ionizing radiation biomarkers [J]. Chinese Journal of Pharmacology and Toxicology, 2024, 38(01): 70-78. https://kns.cnki.net/kcms2/article/

[31] Devadoss S, Raveendranath MC, Kathiresan TS, et al. Genotoxic effect of various forms of tobacco on oral buccal mucosa and nuclear changes as a biomarker [J]. J Pharm Bio allied Sci, 2021, 13(Suppl 2): S1141-S1148. https://doi.org/10.4103/jpbs.jpbs_185_21

[32] Druzhinin V, Bakanova M, Fucic A, et al. Lymphocytes with multiple chromosomal damages in a large cohort of West Siberia residents: results of long-term monitoring [J]. Mutat Res, 2016, 784-785: 1-7. https://doi.org/10.1016/j.mrfmmm.2015.12.003

[33] Lei Wang, Xiaomin Xu, Yanhui Zhang, et al. Effects of Astragalus Polysaccharide on X-ray Radiation-induced Nucleus, Chromosome and DNA Damage in Bone Mesenchymal Stem Cells [J]. China Cancer, 2018, 27(9): 708-714. https://doi.org/10.11735/j.issn.1004-0242.2018.09.A013

[34] Nembhard WN, McElfish PA, Ayers B, et al. Nuclear radiation and prevalence of structural birth defects among infants born to women from the Marshall Islands [J]. Birth Defects Res, 2019, 111(16): 1192-1204. https://doi.org/10.1002/bdr2.1551

[35] Bouza E, Mart n Jim énez M, Alemany L, et al. Overview of virus and cancer relationships [J]. Position paper. Rev Esp Quimioter. 2021, 34(6): 525-555. https://doi.org/10.37201/req/058.2021

[36] Zhang L, Richards A, Barrasa MI, et al. Reverse-transcribedSARS-CoV-2 RNA can integrate into the genome of culturedhuman cells and can be expressed in patient-derived tissues [J]. Proc Natl Acad Sci U S A, 2021, 118(21): e2105968118. https://doi.org/10.1073/pnas.2105968118

[37] Rodriguez-Mu ñoz M, Anglada T, Genesc à A. A matter of wrapper: Defects in the nuclear envelope of lagging and bridging chromatin threatens genome integrity. Semin Cell Dev Biol. 2022, 123: 124-130. https://doi.org/10.1016/j.semcdb.2021.03.004

[38] Maojin Li, Rugang Wang, Anyi Hu. The analysis of lymphocytes with nuclei abnormalities in peripheral blood of patients with cancers [J]. Journal of Public Health and Preventive Medicine, 2019, 30(1): 27-31. https://doi.org/10.3969/j.issn.1006-2483.2019.01.007

[39] Caracausi M, Piovesan A, Antonaros F, et al. Systematic identification of human housekeeping genes possibly useful as references ingene expression studies [J]. Mol Med Rep, 2017, 16(3): 2397-2410. https://doi.org/10.3892/mmr.2017.6944

[40] Joshi CJ, Ke W, Drangowska-Way A, et al. What are housekeeping genes? [J]. PLoS Comput Biol, 2022, 18(7): e1010295. https://doi.org/10.1371/journal.pcbi.1010295

[41] Saini J, Sharma PK. Clinical, prognostic and therapeutic significance of heat shock proteins in cancer [J]. Curr Drug Targets, 2018, 19(13): 1478-1490. https://doi.org/10.2174/1389450118666 170823121248

[42] De Jong TV, Moshkin YM, Guryev V. Gene expression variability: the other dimension in transcriptome analysis [J]. Physiol Genomics, 2019, 51(5): 145-158. https://doi.org/10.1152/physiolgenomics.00128.2018

[43] Signor SA, Nuzhdin SV. The evolution of gene expression in cisand trans [J]. Trends Genet, 2018, 34(7): 532-544. https://doi.org/10.1016/j.tig.2018.03.007

[44] Manda NK, Golla U, Sesham K, et al. Tuning between nuclearorganization and functionality in health and disease [J]. Cells, 2023, 12(5): 706. https://doi.org/10.3390/cells12050706

[45] Funk L, Su KC, Ly J, et al. The phenotypic landscape of essential human genes [J]. Cell, 2022, 185(24): 4634-4653.e22. https://doi.org/10.1016/j.cell.2022.10.017

[46] Bonora G, Ramani V, Singh R, et al. Single-cell landscape of nuclear configuration and gene expression during stem cell differentiation and X inactivation [J]. Genome Biol. 2021, 22(1): 279. https://doi.org/10.1186/s13059-021-02432-w

[47] Ng HL, Quail E, Cruickshank MN, et al. To be, or notch to be: mediating cell fate from embryogenesis to lymphopoiesis [J]. Biomolecules, 2021, 11(6): 849. https://doi.org/10.3390/biom11060849

[48] Jaiswal SK, Raj S, DePamphilis ML. Developmental Acquisition of p53 Functions [J]. Genes (Basel). 2021, 12(11): 1675. https://doi.org/10.3390/genes12111675

[49] Gordeeva O. TGFβ Family Signaling Pathways in Pluripotent and Teratocarcinoma Stem Cells' Fate Decisions: Balancing Between Self-Renewal, Differentiation, and Cancer [J]. Cells. 2019, 8(12): 1500. https://doi.org/10.3390/cells8121500

[50] Kim YJ, Tamadon A, Kim YY, et al. Epigenetic Regulation of Cardiomyocyte Differentiation from Embryonic and Induced Pluripotent Stem Cells [J]. Int J Mol Sci. 2021, 22(16): 8599. https://doi.org/10.3390/ijms22168599

[51] Wu Z, Guan KL. Hippo signaling in embryogenesis and development [J]. Trends Biochem Sci, 2021, 46(1): 51-63. https://doi.org/10.1016/j.tibs.2020.08.008

[52] Leu S. The role and regulation of Pnn in proliferative and non-dividing cells: Form embryogenesis to pathogenesis [J]. Biochem Pharmacol, 2021, 192: 114672. https://doi.org/10.1016/j.bcp. 2021.114672

[53] Sigvardsson M. Molecular regulation of differentiation in early B-lymphocyte development [J]. Int J Mol Sci, 2018, 19(7): 1928. https://doi.org/10.3390/ijms19071928

[54] Shparberg RA, Glover HJ, Morris MB. Modeling Mammalian Commitment to the Neural Lineage Using Embryos and Embryonic Stem Cells [J]. Front Physiol. 2019, 10: 705. https://doi.org/10.3389/fphys.2019.00705

[55] Kovacs MT, Vallette M, Wiertsema P, et al. DNA damage induces nuclear envelope rupture through ATR-mediated phosphorylation of lamin A/C. Mol Cell. 2023, 83(20): 3659-3668.e10. https://doi.org/10.1016/j.molcel.2023.09.023

[56] Bonora M, Missiroli S, Perrone M, et al. Mitochondrial Control of Genomic Instability in Cancer. Cancers (Basel). 2021, 13(8): 1914. https://doi.org/10.3390/cancers13081914

[57] Janssen A, Breusegem SY, Larrieu D. Current methods and pipelines for image-based quantitation of nuclear shape and nuclear envelope bbnormalities [J]. Cells, 2022, 11(3): 347. https://doi.org/10.3390/cells11030347

[58] Abdalla F, Boder J, Markus R, et al. Correlation of nuclear morphometry of breast cancer in histological sections with clinic pathological features and prognosis [J]. Anticancer Res, 2009, 29(5): 1771-1776. https://pubmed.ncbi.nlm.nih.gov/19443402/

[59] Bian Z, Wang L, Fan R, et al. Genetic predisposition, modifiable lifestyles, and their joint effects on human lifespan: evidence from multiple cohort studies. BMJ Evid Based Med. 2024, 29(4): 255-263. https://doi.org/10.1136/bmjebm-2023-112583

[60] Johnston RA, Aracena KA, Barreiro LB, et al. DNA methylation-environment interactions in the human genome. Elife. 2024 Feb 26; 12: RP89371. https://doi.org/10.7554/eLife.89371

[61] Minqiang Xie. Research progress in the treatment of nasopharyngeal carcinoma [J]. Chinese Journal of Otorhinolaryngology-skull Base Surgery, 2023, 29(06): 1-10. https://kns.cnki.net/kcms2/article/

[62] Cronin KA, Scott S, Firth AU, et al. Annual report to the nation on the status of cancer, part 1: National cancer statistics [J]. Cancer. 2022, 128(24): 4251-4284. https://doi.org/10.1002/cncr.34479

[63] Yang X, Chen H, Sang S, et al. Burden of All Cancers Along With Attributable Risk Factors in China From 1990 to 2019: Comparison With Japan, European Union, and USA [J]. Front Public Health. 2022, 10: 862165. https://doi.org/10.3389/fpubh.2022.862165

[64] Zafar A, Khan MJ, Abu J, et al. Revolutionizing cancer care strategies: immunotherapy, gene therapy, and molecular targeted therapy [J]. Mol Biol Rep. 2024, 51(1): 219. https://doi.org/10.1007/s11033-023-09096-8

[65] Shoaib S, Islam N, Yusuf N. Phytocompounds from the Medicinal and Dietary Plants: Multi-target Agents for Cervical Cancer Prevention and Therapy [J]. Curr Med Chem. 2022, 29(26): 4481-4506. https://doi.org/10.2174/0929867329666220301114251

[66] Jiasi Yan. Research progress of biotherapy and biotechnology drugs [J]. Modern Chemical Research, 2023,(05): 8-10. https://doi.org/10.20087/j.cnki.1672-8114.2023.05.003

[67] Brown DW, Beatty PH, Lewis JD. Molecular Targeting of the Most Functionally Complex Gene in Precision Oncology: p53 [J]. Cancers (Basel). 2022, 14(21): 5176. https://doi.org/10.3390/cancers14215176

[68] Qiaomei Wu, Jinglin Yang, Ya Peng, et al. Analysis of occurrence and symptom groups of lung cancer patients dur-ing immunotherapy [J]. China Modern Medicine, 2024, 31(04): 144-148. https://kns.cnki.net/kcms2/article/

[69] Fei Duan, Yi Chen, Guanjin Cha, Xunhuang Duan. Effects of miR-340-5p targeting regulation of ARID1A on activity, migration and invasion of thyroid cancer [J]. Chinese Journal of Gerontology, 2024, 44(06): 1480-1485. https://kns.cnki.net/kcms2/article/

[70] Sammons MA, Nguyen TT, McDade SS, et al. Tumor suppressor p53: from engaging DNA to target gene regulation [J]. Nucleic Acids Res. 2020, 48(16): 8848-8869. https://doi.org/10.1093/nar/gkaa666