Narrative Review Article

The Role of p53 in Cell Cycle Arrest, Cellular Senescence and Apoptosis in Cells with DNA Damage

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ABSTRACT

p53, also known as the Guardian of the Genome, has a plethora of functions in cells. This review focuses on the current understanding of p53's roles in three mechanisms (cell cycle arrest, apoptosis, and senescence) and how p53 determines the fate of the cell among them. Cell cycle arrest occurs when cells temporarily halt the cell cycle in response to DNA damage, allowing time for repair. The main way in which p53 induces cell cycle arrest is by activating the target gene p21. Apoptosis is a form of programmed cell death that occurs if a cell is damaged beyond repair. p53 induces apoptosis through its interaction with the BCL-2 family of proteins, such as Bax and Bak. Cellular senescence is distinct from cell cycle arrest or apoptosis because it is an irreversible form of cell cycle arrest mediated by p53. The current understanding is that p53 makes cell fate decisions between cell cycle arrest, apoptosis, or senescence based on the level of DNA damage as well as the pathways it engages. This understanding of cell fate decisions is extremely hypothetical and advancing this understanding is key to being able to induce the various mechanisms of p53 for clinical benefit. This paper aims to investigate the cellular pathways induced by p53 in cells that have undergone DNA damage.

Keywords: p53; Cellular senescence; Cell cycle Arrest; Apoptosis; Cancer biology

INTRODUCTION

It is estimated that healthy somatic cells accumulate about 1.14 mutations per cell division (1). Human cells are prone to errors during division or when exposed to mutagens and toxins. These mutations could have extremely harmful effects because many of them alter genes involved in the growth and division of cells as well as processes that play a crucial role in tumorigenesis, tumor growth, and metastasis (2). However, not all of these mutations lead to cancer because DNA repair mechanisms exist to correct damage and prevent mutations from truly taking effect and consequently protecting human genomes. Protein p53 plays a critical role in regulating these mechanisms (3). Often referred to as the "Guardian of the Genome," p53 is a tumor suppressor protein encoded by a gene located on chromosome 17 (4). Tumor suppressors are a group of proteins that regulate normal cell growth (5). Mutations in tumor suppressor genes can result in tumorigenesis. Though p53's function in cell cycle regulation and apoptosis are most well known, p53 has a plethora of functions, likely due to its structural flexibility, which are required to prevent both tumor initiation and tumor growth, depending on the cell state (3). p53 interacts with hundreds of genes, therefore contributing to a

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variety of biological processes, including metabolism, cell cycle, and DNA damage response (5). As mentioned earlier, the most widely studied functions of p53 are its ability to induce cell cycle arrest, a halt in the cell cycle, and apoptosis, a form of programmed cell death. Both of these functions are widely explored in the context of preventing tumor growth because of their ability to stop the uncontrolled growth and proliferation of cells (3). This review outlines the current understanding of p53's roles in cell cycle arrest, apoptosis, and senescence and how p53 makes decisions on which pathways to drive cell fate.

CELL CYCLE ARREST AND P53

When cells divide, they undergo four distinct phases: G_1, S, G_2, and M phases. The G_1 phase is when a cell grows and produces the various materials needed to undergo DNA replication. The S phase is when a cell's DNA is replicated. The G_2 phase follows DNA replication and is when the cell continues to grow, preparing for mitosis. The M phase is when the cell divides its nucleus and cytoplasm, officially undergoing mitosis (6).

Cell cycle arrest is when cells temporarily halt the cell cycle at G_1, G_2, or M phases (3). Cell cycle arrest typically occurs in response to repairable DNA damage, such as that caused by ultraviolet light, ionizing radiation, oxidative stress (7). Cell cycle arrest provides time to repair DNA damage, allowing cells to stay healthy, and proceed with the rest of the cell cycle (3). Upon DNA damage, ATM/ATR kinases phosphorylate p53. The phosphorylation prevents p53 degradation by MDM2, an E3 ubiquitin ligase, and lessens ARF tumor suppressor activity. ARF functions as a surveillance mechanism to induce and stabilize p53 activity thereby inhibiting tumorigenesis. MDM2 is a key negative regulator of p53 that marks the protein for degradation in normal cells, inhibiting its tumor suppressor functions. Excess MDM2 expression is a common feature in human cancers (8).

P53 plays a role in cell cycle arrest by activating the transcription of *p21* mRNA, resulting in increased production of the p21 protein. This protein induces cell cycle arrest in the G_1 phase by binding to cyclin E and cyclin D (Cdk2 and Cdk4). This causes Rb to bind to E2F1 which promotes the silencing of the E2F1 target genes. Many E2F1 target genes encode proteins that are necessary for DNA replication. Thus, the silencing of E2F1 target genes causes G_1 phase cell cycle arrest. The 2.4 kb, 1.4 kb and 5' binding sites of the *p21* promoter are some known p53 binding sites when activating *p21* transcription.

While p21 is a major part of inducing cell cycle arrest, it is not necessary. One study found that p21-null cells were still able to achieve cell cycle arrest with the help of other p53 target genes such as 14-3-3σ suggesting a redundancy in their functions (3). 14-3-3σ is a target gene of p53 that is involved with blocking the cell cycle transition between the G_2 and M phase (9). Cell cycle arrest can also occur when cyclin B and cdc25C are repressed by p53. Together 14-3-3σ expression and cdc25C repression allow for G_2 and M phase arrest (10). In more severe cases of DNA damage, p53 may activate a different cellular pathway known as apoptosis.

CELLULAR APOPTOSIS AND P53

Apoptosis is a form of cell death that is carried out if a cell is damaged beyond repair (11). This mechanism removes cells with DNA damage or other irregularities that could potentially become cancerous. There are two main types of apoptosis: the intrinsic and extrinsic pathway, and p53 is involved in both.

The intrinsic, or mitochondrial, pathway is regulated by the BCL-2 family of proteins (3). Because intrinsic apoptosis depends on p53, p53 mutations are common in cancer cells, resulting in uncontrollable growth of cancer cells (12). p53 can induce apoptosis through both transcription-dependent and transcription-independent activities (13). Multiple target genes work together to induce apoptosis by promoting death receptor dimerization, causing mitochondrial outer membrane permeabilization (MOMP), among others. p53 can induce apoptosis by directly promoting MOMP at the mitochondria (3). p53's interaction with the BCL-2 family of proteins, such as Bax and Bak, is the one of the primary forms of apoptosis induction by p53. PUMA (a member of the BCL-2 family of proteins) is a protein that is pro-apoptotic, a factor that is known to promote or induce apoptosis (12). The ASPP family of proteins also plays a large role in activating apoptosis target genes of p53. The ASPP family of proteins (including ASPP1, ASPP2 and iASPP) is a set of p53 binding proteins that bind to the promoters of apoptotic genes on p53 at both the core domain and the proline-rich region. This multisite binding combination allows for a conformational change that prompts p53 DNA binding (3).

The extrinsic, or death receptor, pathway is initiated by death ligands binding to their corresponding receptors, such as FasL/FasR. p53 upregulates the expression of these death receptors. Once engaged, the receptors

activate intracellular signaling intermediates that trigger initiator caspase-8. Caspase-8 then activates caspase-3, or stimulated MOMP, eventually leading to apoptosis. Caspase-3 commonly mediates nuclear apoptosis through cell shrinkage and DNA fragmentation (14).

CELLULAR SENESCENCE AND P53

Another cellular pathway activated by p53 is cellular senescence. Cellular senescence is an irreversible form of cell cycle arrest mediated by p53 (15). This mechanism puts cells in a state where they are not dead, but they no longer go through the stages of the cell cycle: they cannot grow or replicate. Although they are in a permanent state of arrest, they are still considered metabolically active and can secrete molecules in order to communicate with neighboring cells. Two major etiologies of senescence are replication and stress (16). Replicative senescence is linked to telomere shortening, DNA damage, and chromatin alterations, which activate the DNA damage response. This response activates the ATM kinase that phosphorylates p53 and MDM2 (15). Stress-induced senescence is caused by external stressors such as oxidative damage and UV light resulting DNA damage. Similar to apoptosis, severe DNA damage often results in senescence (16). Senescent cells in tissues can also inhibit tissue homeostasis and lead to age-related diseases (17).

The role of p53 in senescence is an active field of research. Senescence in cell culture *in vitro* is modeled by triggering telomere shortening, oncogene activation, or artificial DNA damage with drug treatments. For example, one study was conducted to understand the role of splicing factor SRSF3 on cellular senescence. It found that the knockdown of SRSF3 altered the alternative splicing of p53 mRNA, inducing cellular senescence. This was demonstrated by comparing multiple fibroblast cell lines, each with a varying amount of SRSF3 expression. The cell lines with the lowest amount of SRSF3 expression had the largest increase in senescence occurring (18). Another study using chemotherapy to induce senescence in cell culture showed that chemotherapy-induced senescence is temporary and often relapses (15). The choice between inducing these various cellular pathways by p53 is known as cell fate decision.

CELL FATE DECISION

Cell fate decision, while widely studied, still has a lot of unknowns. Many believe that it depends on the pathways with which p53 interacts as well as regulatory proteins like pRb, NF-kb, and mTOR (3). Wang *et al*., explored the idea of cell fate decision based on the level of DNA damage. They showed that different enzymes posttranslationally modify p53 at low or high DNA damage and thereby regulate the cell fate. This study focused on Tip60, an enzyme that acetylates p53 at K120 and induces both p21 and PUMA, proteins that play a role in inducing cell cycle arrest and apoptosis. At low levels of DNA damage, it was found that p21 levels increased while PUMA levels stayed the same, therefore inducing cell cycle arrest (11). p21 silences E2F1 target genes by binding to Cdk2 and Cdk4, causing G_1 phase cell cycle arrest (3). However, at high levels of DNA damage, the levels of both p21 and PUMA expression increased, pushing the cell into apoptosis (11). PUMA, as a member of the BCL-2 family of proteins, is able to promote MOMP and push the cell into intrinsic apoptosis (12). Inhibition of the IGF-1R/AKT pathway increases K120 acetylation, therefore increasing p53 mediated apoptosis, but reduces p53 protein levels and p53- mediated cell cycle arrest as well as cellular senescence (11).

Cell fate decisions may depend on the type of cell responding to p53 activation because of the various cofactors that are expressed in different cell types. For example, hematologic cancer cells have a higher expression of apoptosis-inducing cofactors, making them more susceptible to apoptosis compared to fibroblasts or carcinoma cancers. It is also speculated that cell fate decision relies on metabolic differences, post-translational modifications and the level of stress in a cell (19). One study found that the phosphorylation of p53 at Ser46 induces p53 to commit to apoptotic cell death. Exposure to genotoxic stress activates DYRK2, a protein kinase that translocates into the nucleus, causing Ser46 phosphorylation. This mainly occurs when DNA damage is severe. Upon repairable DNA damage, p53 is phosphorylated at Ser15 and Ser20 activating p21 and causing G_1 cell cycle arrest (20).

One way in which cellular senescence is induced via p53 is through the encoding of plasminogen activator inhibitor-1 (PAI-1). PAI-1 is linked to both replicative and stress-induced senescence. p21 is known to be relevant in inducing senescence and one study proved that the expression of both p21 and PAI-1 together proved to have resulted in inducing the most efficient senescence in human fibroblasts (21). This comprehensive understanding of the role of p53 in healthy cells is crucial in realizing p53's significance in cancer biology.

P53 IN THE CONTEXT OF CANCER BIOLOGY

According to the Cancer Genome Atlas (TCGA) database, around 30.51% of all cancers have p53 mutations. The prevalence of p53 mutation varies across different cancer types. Ovarian serous cystadenocarcinoma has the highest percent of cases affected by a p53 mutation at 87.59% followed by uterine carcinosarcoma at 85.96% and esophageal carcinoma at 84.24%. Sarcomas have the lowest p53 mutation prevalence at 37.45%. Understanding the impact of p53 mutation in cancers is critical because it affects the prognosis of the cancer patients. At a duration of 10 years, p53 wild type cancers such as Lymphoid Leukemias have a survival rate of 48% meanwhile p53 mutant cancers such as Testicular Germ Cell Neoplasms have a significantly smaller survival rate of 32% (1).

There are different types of p53 mutations observed in cancer. The most common type of p53 mutation is a missense mutation (22). 25% of p53 mutations are either nonsense or frameshift mutations, which encode truncated proteins. The rest are considered splicing and in-frame mutations, which don't have a clear biological significance. Loss of function is a common characteristic of these mutations. Cells are prone to becoming cancerous when a mutation occurs in the p53 gene because of its important role in regulating cell growth, cell division and DNA repair. When a mutation occurs, p53 loses its ability to perform these functions, resulting in damaged cells being able to proliferate and allowing for tumorigenesis to occur. p53 mutated cells lose their ability to undergo apoptosis which is a characteristic exploited in many anticancer treatments. This results in many p53 mutated cancers being highly treatment resistant and having a much worse prognosis (5).

THERAPEUTIC APPROACHES TO TARGETING P53

Though p53 is commonly mutated in various types of cancers, not all cancers harbor p53 mutations. Exploiting intact p53 in combination with targeted therapy or chemotherapy can cause synergistic effects in treating cancer. For instance, a combination of MDM2 inhibitors and DNA-damaging drugs are proven to be effective in synergistically inducing apoptosis in cancer cells without p53 mutations. As MDM2 targets p53 for degradation, MDM2 inhibitors block the pathway between MDM2 and p53, thereby activating p53 pathways (23). p53-mediated apoptosis in tumors is extremely helpful in controlling them, however many side effects of drugs are results of apoptosis taking effect in healthy tissue (3).

Developing treatment options for cancers with p53 mutations has been a challenge. Currently, p53 mutant cancers are treated with standard chemotherapy and radiotherapy, but these cancers continue to be highly treatment-resistant. One study performed on patients with p53 mutated acute myeloid leukemia (AML) tested the outcomes of intensive chemotherapy (IC), hypomethylating agents (HMA), and combination (VEN+HMA) treatments. The study looked at the complete response rate (CR rate), which measures detectable evidence of cancer post treatment. CR rates are calculated by taking the average number of patients diagnosed with a certain cancer type that show a complete response to the provided treatment. The study showed that regardless of the type of treatment administered to p53 mutated AML, outcomes remained poor with a low percentage of patients that had no detectable evidence of cancer. The CR rate ranged between 13 and 49%. In contrast, p53 wild-type AML has a CR rate of approximately 85%. The same study highlighted other novel therapy options for p53-mutant AML such as immunotherapy, chimeric receptor antigen T-cell therapy, and monoclonal antibodies, which have shown efficacy in other hematologic malignancies (24). Another potential therapy is the use of non-coding RNAs (ncRNAs). ncRNAs modulate DNA transcription, regulating mRNA degradation and interacting with proteins. Further modulating ncRNAs can affect their regulation of cellular responses and signaling pathways. This shows lots of potential in being a target for drug development. The use of ncRNAs is in early stages of research for p53 mutated cancer treatments but it is promising for future therapeutic options. Other studies highlighted that because p53 often deals with G_1 cell cycle arrest, treatments for p53 mutant cancers should focus on targeting G_2 cell cycle arrest (23).

DISCUSSION

Here, the current understanding of p53 biology and its implications in cancer biology are reviewed. p53 has a wide range of functions, including inducing cell cycle arrest, apoptosis, and senescence, as well as playing a major role in cancer biology and cancer therapeutics (Table 1). Cell cycle arrest occurs in response to repairable DNA damage (11). The p21 protein plays a major role in cell cycle arrest, halting the cell cycle so that DNA repair mechanisms can take place (3).

Table 1. Overview of the major cellular pathways regulated by p53, highlighting representative target genes involved in cell cycle arrest, apoptosis, and senescence, along with the corresponding biological outcomes.

Mechanism	p53 Target Genes	Outcome	References
Cell Cycle Arrest	p21: p53 activates by binding to gene promoter 14-3-3σ: p53 activates by direct transcription CDC25C: p53 inhibits with transcriptional repression and by promoting protein degradation	The Cell Cycle is halted at G_1, G_2, or M phases	(11) (9) (10)
Apoptosis	PUMA: p53 activates by direct transcription Bax and Bak: p53 activates through transcription dependent and independent pathways FasL/FasR: p53 activates with direct binding	Programmed cell death where the complete destruction of a cell takes place upon irreversible DNA damage	(11) (12) (14)
Cellular Senescence	p21 and PAI-1: p53 activates by binding to the gene promoter	Cells enter a state of permanent arrest but remain metabolically active	(21)

Apoptosis is programmed cell death that occurs because of irreparable DNA damage (11). It is often induced by the BCL-2 family of proteins. Cellular senescence is an irreversible form of cell cycle arrest in which cells can no longer grow or replicate but remain metabolically alive (3). Cell fate decision, as currently understood, relies on the various pathways that p53 interacts with, or the various cofactors within the cell that p53 is responding to (19). Because of p53's critical role in preventing tumorigenesis, tumor growth often relies on p53 mutations (3). This also means that p53 mutant cancers have a much lower survival rate and are much more difficult to treat. Current treatment options for p53 mutant cancers include chemotherapy and radiotherapy but there are studies for new therapeutic methods including those targeting G_2 cell cycle arrest and the use of ncRNAs. However, regardless of treatment type, p53-mutant cancers remain largely treatment resistant (24).

Despite extensive research on p53 biology, how cells decide between undergoing cell cycle arrest versus apoptosis remains elusive. Gaining a better understanding of the mechanisms governing cell fate decisions in p53-intact cells is important for clinical applications. This especially holds true for cell fate decisions because of the role the various p53 pathways can play in cancer treatment. Apoptosis is one of the most beneficial outcomes in cancer therapies, so understanding how to effectively and safely trigger it in affected cells could significantly improve treatment outcomes. The same principle holds true for cell cycle arrest and senescence. As described earlier, cells undergo cell cycle arrest, senescence, or apoptosis in the presence of DNA damage. Investigating how to stably induce normal cells to enter cell cycle arrest upon DNA damage, instead of cells entering senescence or apoptosis, will allow us to prevent excessive apoptosis in normal cells that often occur due to cytotoxic chemotherapy (24). Stably inducing cell cycle arrest in normal cells gives the body enough time to repair DNA damage and better react to the treatments. Understanding cell fate decisions would allow for medical professionals to design effective treatments that properly exploit p53's functions in cancer cells.

CONCLUSION

As discussed in this paper, p53 is related to a vast set of functions and processes within the cell, including cell cycle arrest, apoptosis, and cellular senescence. The cell fate decision that regulates which of these processes is carried out is speculated to be related to the various other pathways with which p53 interacts, as well as the level of damage a cell has experienced. In the context of cancer biology, p53's role varies depending on if it is damaged or not. In a cancer cell where p53's function remains, p53 is often exploited to rid the cell of damage; however, p53 mutant cancers are often resistant to the standard cancer therapy because cancer cells lacking p53 fail to undergo apoptosis effectively. It is important that cell fate decision continues to be studied because of its importance in exploiting p53's pathways which could be crucial to developing more effective treatments for both p53-intact and mutant cancers. Future studies should focus on the various cofactors and specific levels of DNA damage that influence the cell fate decision between cell cycle arrest, cellular senescence and apoptosis.

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CONFLICT OF INTEREST

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REFERENCES

1. Cancer Genome Atlas Research Network, Weinstein JN, Collisson EA, *et al*. The Cancer Genome Atlas Pan-Cancer analysis project. *Nat Genet*. 2013; 45 (10): 1113-1120. doi:10.1038/ng.2764
2. Durland J, Ahmadian-Moghadam H. Genetics, Mutagenesis. In: StatPearls. Treasure Island (FL): StatPearls, 2022. Available from https://www.ncbi.nlm.nih.gov/books/NBK560519/ (accessed on 2025-09-19)
3. Chen J. The Cell-Cycle Arrest and Apoptotic Functions of p53 in Tumor Initiation and Progression. *Cold Spring Harb Perspect Med*. 2016; 6 (3): a026104. Published 2016 Mar 1. doi:10.1101/cshperspect.a026104
4. Hernández Borrero LJ, El-Deiry WS. Tumor suppressor p53: Biology, signaling pathways, and thera-peutic targeting. Biochim Biophys Acta Rev Cancer. 2021;1876(1):188556. doi:10.1016/j.bbcan.2021.188556
5. Kastenhuber ER, Lowe SW. Putting p53 in Context. *Cell*. 2017; 170 (6): 1062-1078. doi:10.1016/j.cell.2017.08.028
6. Coffman JA. Cell cycle development. *Dev Cell*. 2004; 6 (3): 321-327. doi:10.1016/s1534-5807(04)00067-x
7. Clay DE, Fox DT. DNA Damage Responses during the Cell Cycle: Insights from Model Organisms and Beyond. *Genes (Basel).* 2021; 12 (12): 1882. doi:10.3390/genes12121882
8. Cheng Q, Chen J. Mechanism of p53 stabilization by ATM after DNA damage. *Cell Cycle*. 2010; 9 (3): 472-478. doi:10.4161/cc.9.3.10556
9. Bersani C, Xu LD, Vilborg A, Lui WO, Wiman KG. Wig-1 regulates cell cycle arrest and cell death through the p53 targets FAS and 14-3-3σ. *Oncogene*. 2014; 33 (35): 4407-4417. doi:10.1038/onc.2013.594
10. Liao WL, Lin JY, Shieh JC, *et al*. Induction of G2/M Phase Arrest by Diosgenin via Activation of Chk1 Kinase and Cdc25C Regulatory Pathways to Promote Apoptosis in Human Breast Cancer Cells. *Int J Mol Sci*. 2019; 21 (1): 172. Published 2019 Dec 25. doi:10.3390/ijms21010172
11. Wang P, Bao H, Zhang XP, Liu F, Wang W. Regulation of Tip60-dependent p53 acetylation in cell fate decision. *FEBS Lett*. 2019; 593 (1): 13-22. doi:10.1002/1873-3468.13287
12. Al-Aamri HM, Irving HR, Bradley C, Meehan-Andrews T. Intrinsic and extrinsic apoptosis responses in leukaemia cells following daunorubicin treatment. *BMC Cancer.* 2021; 21 (1): 438. doi:10.1186/s12885-021-08167-y
13. Chao C, Saito S, Kang J, Anderson CW, Appella E, Xu Y. p53 transcriptional activity is essential for p53-dependent apoptosis following DNA damage. *EMBO J*. 2000; 19 (18): 4967-4975. doi:10.1093/emboj/19.18.4967
14. Nosalova N, Keselakova A, Kello M, Martinkova M, Fabianova D, Pilatova MB. Involvement of Both Extrinsic and Intrinsic Apoptotic Pathways in Tridecylpyrrolidine-Diol Derivative-Induced Apoptosis *In Vitro*. *Int J Mol Sci*. 2023; 24 (14): 11696. doi:10.3390/ijms241411696
15. Tonnessen-Murray CA, Lozano G, Jackson JG. The Regulation of Cellular Functions by the p53 Protein: Cellular Senescence. *Cold Spring Harb Perspect Med*. 2017; 7 (2): a026112. doi:10.1101/cshperspect.a026112
16. Mijit M, Caracciolo V, Melillo A, Amicarelli F, Giordano A. Role of p53 in the Regulation of Cellular Senescence. *Biomolecules.* 2020; 10 (3): 420. doi:10.3390/biom10030420
17. Beck J, Turnquist C, Horikawa I, Harris C. Targeting cellular senescence in cancer and aging: roles of p53 and its isoforms. *Carcinogenesis*. 2020; 41 (8): 1017-1029. doi:10.1093/carcin/bgaa071
18. Tang Y, Horikawa I, Ajiro M, *et al*. Downregulation of splicing factor SRSF3 induces p53β, an alternatively spliced isoform of p53 that promotes cellular senescence. *Oncogene*. 2013; 32 (22): 2792-2798. doi:10.1038/onc.2012.288
19. Duan L, Maki CG. The IGF-1R/AKT pathway determines cell fate in response to p53. *Transl Cancer Res.* 2016; 5 (6): 664-675. doi:10.21037/tcr.2016.09.16
20. Taira N, Nihira K, Yamaguchi T, Miki Y, Yoshida K. DYRK2 is targeted to the nucleus and controls p53 via Ser46 phosphorylation in the apoptotic response to DNA damage. *Mol Cell*. 2007; 25 (5): 725-738. doi:10.1016/j.molcel.2007.02.007
21. Kortlever RM, Higgins PJ, Bernards R. Plasminogen activator inhibitor-1 is a critical downstream target of p53 in the induction of replicative senescence. *Nat Cell Biol*. 2006; 8 (8): 877-884. doi:10.1038/ncb1448
22. Olivier M, Hollstein M, Hainaut P. TP53 mutations in human cancers: origins, consequences, and clinical use. *Cold Spring Harb Perspect Biol*. 2010; 2 (1): a001008. doi:10.1101/cshperspect.a001008
23. Hu J, Cao J, Topatana W, *et al*. Targeting mutant p53

for cancer therapy: direct and indirect strategies. *J Hematol Oncol*. 2021; 14 (1): 157. doi:10.1186/s13045-021-01169-0

24. Daver NG, Iqbal S, Renard C, *et al*. Treatment outcomes for newly diagnosed, treatment-naïve TP53-mutated acute myeloid leukemia: a systematic review and meta-analysis. *J Hematol Oncol*. 2023; 16 (1): 19. doi:10.1186/s13045-023-01417-5