Diagnostic and therapeutic roles of monoclonal antibodies for the hotspot mutant R175H of protein p53

Parth Tipnis

Abstract

According to data from The Cancer Genome Atlas (TCGA), TP53 is the most frequently mutated tumor suppressor gene (TSG), and around 50% of all human cancers contain mutations to the gene. TP53 gene product, p53 protein, plays a crucial role in regulating cell division, repairing DNA damage, and triggering apoptosis (programmed cell death) when the damage is irreparable - a crucial step in suppressing the development of cancer. One of the most common missense mutations, referred to as the hotspot mutation R175H, is found in about 4-7% of all TP53 mutations. Due to this high prevalence, p53-R175H-associated cancer cells are a key target for cancer diagnosis and therapy.

Monoclonal antibodies are manufactured in the laboratory to specifically bind to proteins expressed by p53-R175H-associated tumor cells and are used as diagnostic and therapeutic tools. Unlike regular chemotherapy drugs, which attack both normal and cancer cells, monoclonal antibodies can specifically target tumor cells, minimizing damage to healthy tissues and improving treatment outcomes.

This paper reviews the promising roles of monoclonal antibodies as diagnostic tools and as part of cancer therapy targeting p53R175H-associated cancer cells, and discusses their potential use as bispecific antibodies that simultaneously bind tumor cells and T cells to promote immune-mediated killing of tumor cells.

Introduction

Genetic mutation is one of the prominent causes for the development of cancer. A mutation disrupts the normal cell cycle, resulting in uncontrolled cell growth and tumor formation. Cancer is a genetic disease caused by mutations that disrupt normal cell cycle control. The TP53 gene is one of the most significant genes in cancer treatment; it is mutated in approximately 50% of all human cancers. This makes it the most commonly mutated tumor suppressor gene(Hainaut & Pfeifer, 2016). The TP53 gene, often referred to as the "guardian of the genome," encodes the p53 protein. This is because the p53 protein plays a crucial role in regulating cell division, repairing DNA damage, and triggering apoptosis (programmed cell death) when the damage is irreparable (Rivlin et al., 2011). Most commonly found mutations in the TP53 gene are missense mutations, occurring within the DNA-binding domain of the protein. These mutations are referred to as ‘hotspot mutations’ due to their frequent occurrence and disruptive outcome compared to other mutations. Out of 6 hotspot mutation sites (R175, G245, R248, R249, R273, R282), the mutation at R175 is reviewed here. In this mutation, the amino acid arginine(R) is replaced by histidine (H) at position 175 in the p53 protein, affecting protein conformation and the function of

p53. This results in a loss of tumour suppressor activity, subsequently contributing to uncontrolled cell proliferation (Hainaut & Pfeifer, 2016).

Due to the high prevalence of the R175H mutation, several strategies have been developed, both general and specific to monoclonal antibodies, to target the p53 mutation. Several studies relating to monoclonal antibodies (mAb) have been conducted. For example, foundational work on mAb by Hwang et al. confirmed that monoclonal antibodies are able to recognize their specific mutant (Hwang et al., 2021). Next, the therapeutic application aimed to prepare and test a monoclonal antibody that targets the p53 R175H mutant epitope with a DNA-based delivery system in mouse tumour models (Chai et al., 2024). Finally, diagnostic work by Spiegelberg investigates two newly created monoclonal antibodies, called 4H5 and 7B9, concluding that both the antibodies can detect the R175H mutation of p53 (Spiegelberg et al., 2025). Personalized medicine and immunotherapy are tailored strategies used in modern cancer treatment. Monoclonal antibodies play a crucial role as diagnostic or therapeutic tools in the development of these strategies. This paper has focused on the R175H missense mutation in TP53 and reviewed the possible roles of the monoclonal antibody raised against this mutation.

Therapeutic strategies for TP53 mutation-related cancer

Due to the high prevalence of the R175H mutation, several strategies have been developed, both general and specific to monoclonal antibodies, to target the p53 mutation. In terms of general treatments, Xin Y. et al, explored the effect of small molecule restoration of the wild-type structure of mutant p53 by using zinc-metallochaperone (ZMC1). ZMC1 restores proper zinc binding to the p53-R175H mutant by acting as a zinc metallochaperone, delivering zinc specifically to the native binding pocket to refold the protein into a wild-type–like structure. Next, Xinzhe. et al conducted a study on peptide-based PROTAC molecules designed to specifically bind and degrade the mutant p53-R175H protein via the ubiquitin–proteasome system (Zhuang et al., 2024).

The main therapeutic approaches that have been studied for cancers with the TP53 mutation are summarised in Table 1 below. These strategies involve reactivation or correction of the structure of the mutant protein, degradation of the mutated protein to remove any gain-of-function effects, and mutation-specific immunotherapies based on the generation of neoantigens from the R175H mutation. Compounds like APR-246 and ZMC1 try to reactivate the wild-type p53 activity while statins induce the degradation of mutant p53. Newer therapies are aimed at precision immunotherapies, such as those with T-cell receptor (TCR) targeting R175H and at those based on monoclonal or bispecific antibodies specifically targeting mutation-associated neoantigens (MANAs) of tumour cells.

Table 1. Strategies used to treat TP53 gene hotspot mutation-related cancer

Strategy	Treatment	Reference
APR-246 (Eprenetapopt)	It is a mutant p53 reactivator that is converted to the methylene quinuclidinone (MQ) which binds to mutant p53 and induces the restoration of the wild-type structure and tumour-suppressor function. Promising responses have been observed in clinical studies in TP53-mutant cancers.	(Sallman et al., 2021)
ZMC1 (NSC319726)	ZMC1 (NSC319726) is a zinc metallochaperone that can specifically restore the wild-type conformation and zinc binding properties of the structural mutation in p53 (R175H), allowing the mutant protein to regain its normal structure and ability to activate transcription.	(Yu et al., 2014)
Statin-Mediated Mutant p53 Degradation	Statins disrupt the interaction between mutant p53 and molecular chaperones, destabilizing mutant p53 proteins and thus lowering the ability of mutant p53 to exert a gain-of-function effect in oncogenesis.	(Parrales et al., 2016)
R175H-Specific TCR Therapy	The TCR targets neoantigens generated from the p53 mutation R175H, presented on HLA molecules, to permit highly selective immune-mediated killing of tumour cells with the mutation.	(Malekzadeh et al., 2019)
Monoclonal/Bispecific Antibodies Targeting p53-R175H	Novel antibodies that bind to mutation-associated neoantigens (MANAs) created by R175H can be used as a precision immunotherapy strategy to specifically target cancer cells without harming normal tissues.	(Chai et al., 2024)

P53 protein

The P53 protein, commonly referred to as the “guardian of the genome”, is a crucial tumour suppressor that protects cells from becoming cancerous. It monitors DNA integrity, activating when the DNA damage is detected or due to other factors like radiation, chemicals, and replication errors. Upon activation, p53 acts as a transcription factor that halts the cell cycle (typically at the G1/S checkpoint), which gives time for DNA to repair. If the damage to the DNA is too severe and irreparable, p53 triggers apoptosis (programmed cell death). This prevents the damaged cell from dividing, subsequently preventing the formation of tumours. Mutations in the TP53 gene, often missense mutations, change a single nucleotide, resulting in an altered amino acid in the p53 protein. This disrupts the protein's DNA-binding ability. The mutation often occurs

at mutation hotspots, leading to a loss of p53 function. This allows damaged cells to divide uncontrollably, increasing the risk of tumour formation (Xu et al., 2025).

Significance of the Zn binding domain of p53 and the R175H mutation

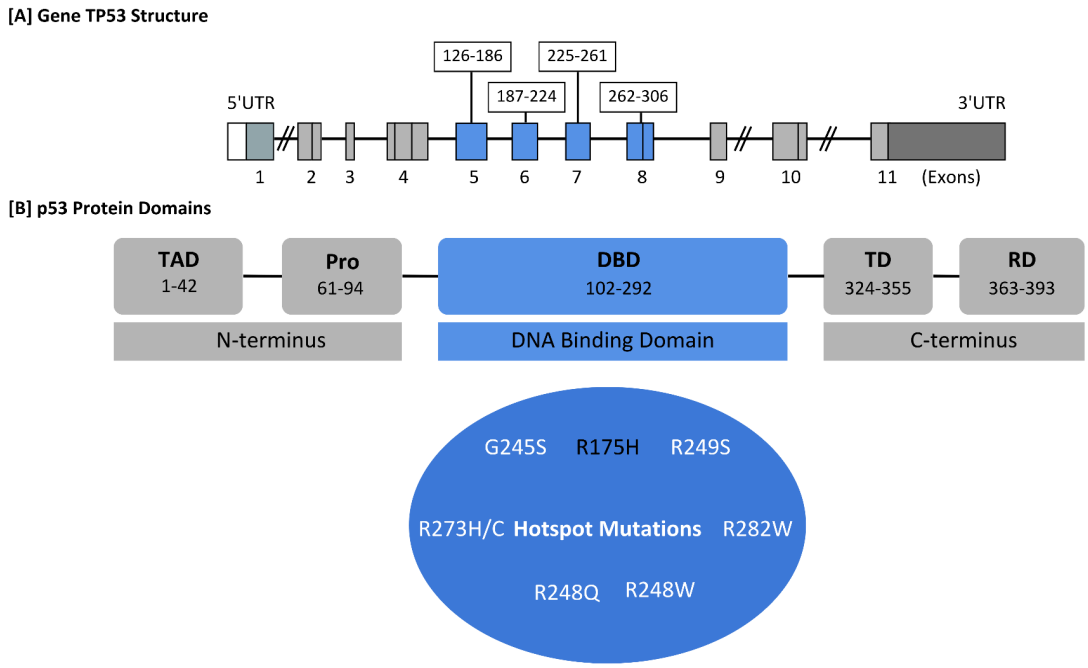

Figure 1. TP53 gene components and p53 protein domains

[A] Schematic representation of TP53 gene structure. It has 11 exons and it codes for p53 protein containing 393 amino acids. Codons for exons 5, 6, 7,and 8 are indicated in the DBD region of TP53 gene.
[B]The p53 protein consists of five domains: the Transactivation Domain (TAD), Proline-Rich Domain (PRD), DNA-Binding Domain (DBD), Tetramerization Domain (TD), and Regulatory Domain (RD). DNA-Binding Domain shows high occurrence of missense mutations called hotspot mutations.

The p53 protein has a DNA-binding domain (DBD in Figure 1.B). This domain of p53 confers regulatory activity when it binds to DNA, controlling the expression of genes that maintain homeostasis and prevent the development of cancer. This region is responsible for attaching to DNA and controlling the genes that prevent cancer. This domain is commonly mutated, creating a mutated p53 protein that impairs its tumor-suppressing activity, leading to the development of cancer. Within this domain, there are certain hotspot mutations which commonly occur in cancer. These mutations, owing to their frequent occurrence, are called hotspot mutations. Hotspot mutations can be classified into two groups, contact mutants (like R248 and R273),

which directly touch the DNA, and structural mutants (like R175, G245, R249, and R282), which help maintain the p53 conformation. The R175 residue belongs to the structural domain, which means it plays a vital role in stabilizing the p53 protein.
A critical feature of this region is the presence of zinc ion (Zn^{2+}), which is held in place by specific amino acids such as cysteine and histidine. The zinc ions act like a support beam, ensuring the protein folds correctly. Zinc also interacts with the negatively charged DNA backbone, helping p53 bind to DNA more firmly. Because this zinc-binding site is so important, any mutation near it can weaken the entire protein's structure.

The R175 residue (arginine at position 175) is located right next to the zinc binding site. When it mutates into histidine, it leads to the formation of the R175H mutation. This results in a complete chemical change of the region. The new histidine can not support the zinc ion like the arginine once did. As a result, the zinc-binding ability is disrupted. Hence, the protein is no longer folded correctly, and thus, it loses its proper shape. As a result of this, p53 can no longer bind to the DNA correctly, so the p53 can no longer regulate tumour-suppressor genes. As a result, damaged DNA is not repaired, and cells with mutations continue to divide instead of undergoing apoptosis. This loss of structural stability is why the R175H mutation is one of the most common and harmful TP53 mutations found in cancer (Kim et al., 2011).

The DNA-binding domain of the p53 protein was viewed using the interactive tool iCn3D, provided by the NIH (Figure 2).

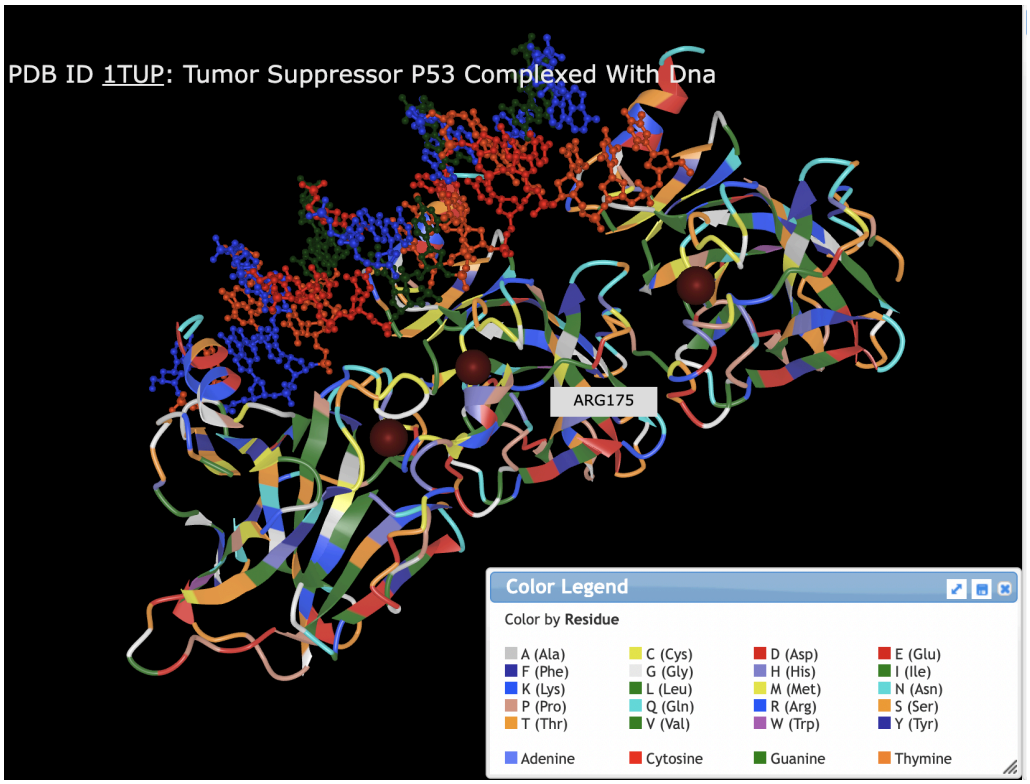

Figure 2. Interaction between the DNA molecule and the p53 protein. All the amino acid residues of the p53 protein are color-coded as indicated in the color legend. Maroon colored balls are Zn molecules. The position of Arginine at 175 is indicated as a blue residue in the proximity of the Zn ion. Mutation (R175H) replaces Arginine with Histidine at position 175, affecting protein folding and the positioning of the Zn ion. Image created using the iCn3D interactive tool.

Methodology

The Cancer Genome Atlas (TCGA) was used to identify the most commonly occurring mutations in the TP53 gene. To access publications related to hotspot mutations in the TP53 gene, the NCBI PubMed database was used. To review the latest developments related to monoclonal antibodies raised against R175H hotspot mutation publications in the last 12 years were considered. iCn3D protein structure analysis tool was used to understand the interaction between DNA binding domain of p53 protein and the DNA molecule. To understand the current development publications from the last three years were reviewed.

Results

Monoclonal antibodies (mAb) - a crucial tool in cancer treatment

In recent years, due to the rapid acceleration of precision medicine, genomic technologies have transformed how cancers are studied and treated. Modern sequencing can detect mutations in DNA and RNA; however, they do not always reflect what happens at the protein level, and therefore, they may not be the best indicator of the functions of the mutated gene. Tumours are highly varied, often containing a different mixture of cells, as such, being able to detect the mutant protein itself directly in the tissue would be invaluable. Unfortunately, current tools can not reliably distinguish between a wild-type protein (normal protein) and the same protein carrying a single amino acid mutation, also known as a point mutation. Although there are existing antibodies that have the potential to detect these single amino acid mutations, it is extremely difficult to produce antibodies that detect exactly one point mutation.

P53 is the most mutated gene across all cancers, with over 50% (Rivlin et al., 2011)of tumours carrying a mutation in this gene. Many of these mutations occur in the DNA-binding domain, leading to a loss in p53's tumour-suppressing activity. Because different mutations of p53 behave differently, having tools that could identify each mutation would be useful for diagnosis, research and personalized patient therapy. This study by Hwang et al. (2018) set out to develop monoclonal antibodies (anti-R175H, anti-R248Q and anti-R273H) designed to recognise three of the most common p53 hotspot mutations: R175H, R248Q, and R273H respectively. To generate them, researchers used bacteria to produce a small piece of the mutant p53 protein, attaching it to a carrier protein (Thioredoxin-TrxA) to ensure that it could be easily recognized by the immune system. They injected this into mice, which triggered the mice to create antibodies against the mutated protein. The scientists then extracted the mouse's immune cells and

created hybridoma cells. The hybridoma cells continuously produced monoclonal antibodies that were highly specific and recognized only that specific p53 mutation.
The main goal of the study was to test whether these antibodies could recognize only their specific mutant. This means that the monoclonal antibodies being developed should not bind to wild type p53 or any other p53 mutation. Using several techniques like ELISA, immunoblotting, immunoprecipitation, and immunofluorescence, researchers were able to confirm that each antibody only recognized its specific p53 mutation.
ELISA screening of one to three monoclonal antibody clones per mutation demonstrated the hybridomas were highly specific against all three p53 mutants. Additionally, there was no reaction with the wild type p53 protein as well as other mutants. Immunoblotting with mutant specific monoclonal antibodies show that the mAbs produced were only able to detect the respective mutant p53 proteins in cell lines even though many different p53 mutants and wild type p53 protein was present- indicating high specificity. Immunoprecipitation results also supported this pattern because results showed that the antibodies only pulled from their matching mutant protein from cell extracts. Immunofluorescence studies in cultured cells also showed clear nuclear staining only when the correct mutant was present. A strong example of this specificity was observed with the anti-R248Q antibody, which did not bind the very similar R248W mutant, even though both mutations occur at the same codon. All in all, these results highlight how precisely the antibodies produced can distinguish point mutations in p53. A key limitation was that not all antibody clones performed equally well across all tests. For example, the anti-R175H antibody consistently showed strong results in all tests, while the antibodies targeting the R248Q and R273H showed more variation. While they were highly specific in immunoblotting and immunofluorescence, they showed increased cross-reactivity during immunoprecipitation and immunohistochemistry (Hwang et al., 2018).

To conclude, the study demonstrated that it is possible to create monoclonal antibodies to recognize a point mutation in p53 with high specificity. These monoclonal antibodies have the potential to become powerful tools used to diagnose cancer, by identifying specific mutations in p53 protein and supporting precision medicine as a whole. This can be an important tool in the development of personalized immunotherapy.

Therapeutic tool

The p53 gene is the most altered tumour suppressor gene in human cancers- approximately half of all cancers have mutations in TP53. The most popular one is the R175H missense mutation that is located in the DNA-binding domain and essentially silences the protective activity of p53 and provides the cell with novel oncogenic capabilities. Although it is so widespread, there is actually no approved drug or immunotherapy targeting the mutant p53 as yet. Therefore, this study aimed to prepare and test a monoclonal antibody that targets the p53 R175H mutant epitope with a DNA-based delivery system in mouse tumour models.

They started with the expression and purification of an anti p53 -R175H monoclonal antibody and verified its specificity (Chai et al., 2024). They demonstrated the antibody strongly bound to the mutant protein using SDS -PAGE, western blots, and biolayer interferometry and were unable to identify wild -type p53. It passed human p53 -R175H in the HEK293T and MC38 cells, even selected the mouse p53 -R172H since the sequence around the mutation is very conserved. In brief, therefore, the antibody was hyper specific to the mutant.
They cultured tumour cells expressing p53 -R175H in cell culture tests and incubated them with the antibody, occasionally with peripheral blood mononuclear cells. The antibody had a rather limited ability to kill cells in large concentrations, and it failed to induce antibody-dependent cellular cytotoxicity. They also produced CAR -T cells with the single-chain variable fragment of the antibody but the CAR -T cells did not kill the p53 -R175H tumour cells as well. Bottom line: the antibody was not able to destroy cancer cells alone in the test tube.
Next, the researchers used electroportation to deliver a DNA plasmid encoding an anti-p53-R175H antibody into the mice. This induced anti-R175H antibodies in the blood, reducing tumour growth in an MC38 mouse model compared to controls. Anti-PD-1 therapy suppressed tumour growth, but, in combination with the antibody plasmid, it provided no benefit. In a second CT26 model with a p53-R172H knock-in mutation, tumor inhibition was seen with the antibody plasmid but not with the anti-PD-1. Researchers also tested a DNA-encoded bispecific antibody which targeted p53-R175H and mouse CD3. On its own, this did not inhibit MC38-R175H tumours. However, when combined with anti-PD-1m it reduced tumour growth more than anti-PD-1 alone. Flow-cytometry confirmed antibody binding to tumour and immune cells, which showed that the antibodies recognised the mutant antigen in vivo.

Overall, this study shows that DNA-encoded monoclonal and bispecific antibodies can specifically target mutant p53, subsequently inhibiting tumour growth in a mouse model. The article indicates that while NA-encoded p53 mutant antibodies represent a feasible platform, a combination with a bispecific antibody and immune checkpoint inhibition can generate more potent anti-tumour responses.

Diagnostic tool

This paper investigates two newly created monoclonal antibodies, called 4H5 and 7B9. The 4H5 and 7B9 monoclonal antibodies were designed to recognise a specific mutant form of the p53 protein.
The main goal of this study was to test if the two antibodies, 4H5 and 7B9, can specifically identify the R172H mutation in mice (which is the equivalent of the R175H mutation in humans), ignoring the normal wild type p53. After testing these antibodies in mice, the researchers found that both antibodies specifically attached to the R172H mutation, ignoring any other form of p53.
To track the antibodies using imaging machines, the researchers also attached radioactive labels (iodine-125) to the antibodies. The antibodies stayed stable and functional after this labelling. Next the researchers tested the antibodies in mice. Each mouse had two tumours,

Mut-T-B6 tumour and B16-KO tumour. The Mut-T-B6 tumour had the R172H mutation of the p53 protein while the B16-KO tumour did not. This allowed a clear comparison. Upon being injected into the mice, the radioactive antibodies travelled through the bloodstream. Imaging scans showed that 4H5 and 7B9 collected more in the tumours with the R175H mutation than in the tumours without p53 mutation. 48 hours after injection, the best imaging quality could be observed where the difference between the mutant and non-mutant was stark. The researchers also checked the organs and found no unwanted accumulation. This means that the antibodies did not stick to the healthy tissue (Spiegelberg et al., 2025).
To confirm these results the researchers removed both the tumours and examined thin slices [sections] of them under a machine which detects radioactivity. These tests showed that both antibodies mainly attached to the tumours carrying the R175H mutation. However, the main limitation was that the antibodies remained in the blood stream for long periods of time. This reduced image clarity.

To conclude, this study showed that both 4H5 and 7B9 antibodies can detect the R175H mutation of p53. If further developed, the technology can be applied for patient stratification and monitoring the response that patients have for targeted p53 treatments.

Discussion of recent research
Recent studies have worked on mutation-specific diagnostic agents of p53 based on earlier studies which found out that the mutation of Tp53 were the main cause of tumor formation but did not have an accurate in-vivo detection method. This research examines two recently engineered monoclonal antibodies 4H5 and 7B9 that are generated so that they recognise the R175H mutant form of p53 (R172H in mice) but not wild-type p53. When labeled with iodine-125, the two antibodies were injected into mice with both normal and mutant tumour cells and it was found that they specifically targeted the cancerous cells with mutant p53 and were present in the maximum in the tumours and minimal in normal tissues within 48 hours. Selectivity was demonstrated in tumour sections by autoradiography, with improved selectivity over the previous methods, to the mutant p53. However, there was a problem as the longer the antibodies stayed in the blood, the fuzzier the images became. The R175H mutation has also been identified as a potential therapeutic target, as well as diagnostic, and is associated with other mutations. Each cell has a unique group of surface proteins that are crucial for cell-to-cell communication, and sometimes cancer cells have extra proteins that are specific to the mutations they contain. These mutation-associated neoantigens (MANAs) can be recognised by the immune system (DiNapoli et al., 2026). Since the R175H is found in numerous cancer types, researchers have found MANAs linked to this mutation, and are creating bispecific antibodies that target both R175H-specific MANAs and receptors on T cells, thus helping to guide these immune cells to selectively kill tumour cells. Overall this paper provides a glimpse of the current research trends related to cancer and the possibility of using mutation-specific immunotherapies

to treat the R175H-positive cancers with a mutation-specific tracer antibody to improve the detection of the tumour, stratify patients and assess the response to targeted p53 therapies.

References

Chai, D., Wang, X., Neeli, P., Zhou, S., Yu, X., Sabapathy, K., & Li, Y. (2024). DNA-delivered monoclonal antibodies targeting the p53 R175H mutant epitope inhibit tumor development in mice. Genes and Diseases, 11(4). https://doi.org/10.1016/j.gendis.2023.04.027

Chasov, V., Zaripov, M., Mirgayazova, R., Khadiullina, R., Zmievskaya, E., Ganeeva, I., Valiullina, A., Rizvanov, A., & Bulatov, E. (2021). Promising New Tools for Targeting p53 Mutant Cancers: Humoral and Cell-Based Immunotherapies. Frontiers in Immunology, 12, 707734. https://doi.org/10.3389/FIMMU.2021.707734/TEXT

Chiang, Y.-T., Chien, Y.-C., Lin, Y.-H., Wu, H.-H., Lee, D.-F., Yu, Y.-L., Lin, Y.-H. ;, Wu, H.-H. ;, Lee, D.-F. ;, Yu, Y.-L., & Baldi, A. (2021). The Function of the Mutant p53-R175H in Cancer. Cancers 2021, Vol. 13, Page 4088, 13(16), 4088. https://doi.org/10.3390/CANCERS13164088

DiNapoli, S. R., Wright, K. M., Mog, B. J., Pearlman, A. H., Nichakawade, T. D., Marcou, N., Hsiue, E. H. C., Hwang, M. S., Douglass, J., Liu, Q., Watson, E., Dal Molin, M., Cohen, J. D., Popoli, M., Paul, S., Konig, M. F., Wyhs, N., Azurmendi, P. A., Glavaris, S., … Vogelstein, B. (2026). Bispecific antibodies and CAR T cells targeting a TP53 mutation–associated neoantigen show discordant affinity requirements. The Journal of Clinical Investigation, 136(2), e192885. https://doi.org/10.1172/JCI192885

Hainaut, P., & Pfeifer, G. P. (2016). Somatic TP53 Mutations in the Era of Genome Sequencing. Cold Spring Harbor Perspectives in Medicine, 6(11). https://doi.org/10.1101/CSHPERSPECT.A026179

Hsiue, E. H. C., Wright, K. M., Douglass, J., Hwang, M. S., Mog, B. J., Pearlman, A. H., Paul, S., Dinapoli, S. R., Konig, M. F., Wang, Q., Schaefer, A., Miller, M. S., Skora, A. D., Azurmendi, P. A., Murphy, M. B., Liu, Q., Watson, E., Li, Y., Pardoll, D. M., … Zhou, S. (2021). Targeting a neoantigen derived from a common TP53 mutation. Science (New York, N.Y.), 371(6533). https://doi.org/10.1126/SCIENCE.ABC8697

Hwang, L. A., Phang, B. H., Liew, O. W., Iqbal, J., Koh, X. H., Koh, X. Y., Othman, R., Xue, Y., Richards, A. M., Lane, D. P., & Sabapathy, K. (2018). Monoclonal Antibodies against Specific p53 Hotspot Mutants as Potential Tools for Precision Medicine. Cell Reports, 22(1), 299–312. https://doi.org/10.1016/J.CELREP.2017.11.112

Hwang, L. A., Phang, B. H., Liew, O. W., Iqbal, J., Koh, X. H., Koh, X. Y., Othman, R., Xue, Y., Richards, A. M., Lane, D. P., & Sabapathy, K. (2021). Erratum: Monoclonal Antibodies against Specific p53 Hotspot Mutants as Potential Tools for Precision Medicine (Cell Reports (2018) 22(1) (299–312), (S2211124717317965), (10.1016/j.celrep.2017.11.112)). Cell Reports, 36(6). https://doi.org/10.1016/J.CELREP.2021.109498

Kim, H., Kim, K., Choi, J., Heo, K., Baek, H. J., Roeder, R. G., & An, W. (2011). p53 Requires an Intact C-Terminal Domain for DNA Binding and Transactivation. Journal of Molecular Biology, 415(5), 843. https://doi.org/10.1016/J.JMB.2011.12.001

Malekzadeh, P., Pasetto, A., Robbins, P. F., Parkhurst, M. R., Paria, B. C., Jia, L., Gartner, J. J., Hill, V., Yu, Z., Restifo, N. P., Sachs, A., Tran, E., Lo, W., Somerville, R. P. T., Rosenberg, S. A., & Deniger, D. C. (2019). Neoantigen screening identifies broad TP53 mutant immunogenicity in patients with epithelial cancers. Journal of Clinical Investigation, 129(3), 1109–1114. https://doi.org/10.1172/JCI123791

Parrales, A., Ranjan, A., Iyer, S. v., Padhye, S., Weir, S. J., Roy, A., & Iwakuma, T. (2016). DNAJA1 controls the fate of misfolded mutant p53 through the mevalonate pathway. Nature Cell Biology, 18(11), 1233–1243. https://doi.org/10.1038/NCB3427

Rivlin, N., Brosh, R., Oren, M., & Rotter, V. (2011). Mutations in the p53 Tumor Suppressor Gene: Important Milestones at the Various Steps of Tumorigenesis. Genes & Cancer, 2(4), 466–474. https://doi.org/10.1177/1947601911408889

Sallman, D. A., DeZern, A. E., Garcia-Manero, G., Steensma, D. P., Roboz, G. J., Sekeres, M. A., Cluzeau, T., Sweet, K. L., McLemore, A., McGraw, K. L., Puskas, J., Zhang, L., Yao, J., Mo, Q., Nardelli, L., al Ali, N. H., Padron, E., Korbel, G., Attar, E. C., … Komrokji, R. S. (2021). Eprenetapopt (APR-246) and azacitidine in TP53-mutant myelodysplastic syndromes. Journal of Clinical Oncology, 39(14), 1584–1594. https://doi.org/10.1200/JCO.20.02341;PAGEGROUP:STRING:PUBLICATION

Spiegelberg, D., Hwang, L. A., Pua, K. H., Kumar, S. C., Koh, X. Y., Koh, X. H., Selvaraju, R. K., Sabapathy, K., Nestor, M., & Lane, D. (2025). Targeting mutant p53: Evaluation of novel anti-p53R175H monoclonal antibodies as diagnostic tools. Scientific Reports, 15(1). https://doi.org/10.1038/S41598-024-83871-W

Xu, B., Maimaitijiang, A., Nuerbiyamu, D., Su, Z., & Li, W. (2025). The Multifaceted Role of p53 in Cancer Molecular Biology: Insights for Precision Diagnosis and Therapeutic Breakthroughs. Biomolecules, 15(8), 1088. https://doi.org/10.3390/BIOM15081088

Yu, X., Blanden, A. R., Narayanan, S., Jayakumar, L., Lubin, D., Augeri, D., David Kimball, S., Loh, S. N., & Carpizo, D. R. (2014). Small molecule restoration of wildtype structure and function of mutant p53 using a novel zinc-metallochaperone based mechanism. Oncotarget, 5(19), 8879–8892. https://doi.org/10.18632/ONCOTARGET.2432

Zhuang, X., Guo, Y., Sun, X., Chen, J., Xie, S., Yang, F., & Li, J. (2024). Promising Proteolysis-Targeting Chimera for Mutant p53-R175H. ACS Omega, 9(45), 45138–45146. https://doi.org/10.1021/ACSOMEGA.4C06177