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Computational Analysis of *TP53* Mutations in Cataracts and Breast, Prostate, and Oral Cavity Cancers in Senegal

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Abstract

Mutations in the *TP53* gene are among the most common genetic alterations in many cancers, and they are also suspected to play a role in the development of cataracts. *TP53* is a tumor suppressor gene, and its alteration can dysregulate the expression of genes directly or indirectly controlled by the p53 protein. This may lead to impaired DNA damage repair, defective cell-cycle arrest, altered chromatin remodeling, and disrupted apoptosis. Cataracts, the leading cause of blindness, and cancer, the second leading cause of death worldwide, are still often diagnosed at late stages. This study aimed to evaluate the involvement of *TP53* mutations in cataracts and in breast, prostate, and oral cavity cancers in Senegalese patients. A total of 116 patients were included: cataract (n = 29), oral cavity cancer (n = 33), prostate cancer (n = 15), breast cancer (n = 16), and controls (n = 23). Tissue samples were collected during biopsy after informed consent. DNA extraction, PCR amplification, and sequencing were performed. Mutation Surveyor was used to detect mutations; Mutation Taster, SIFT, and PolyPhen-2 were used to predict pathogenicity. DynaMut2 and I-Mutant were used to evaluate the impact of pathogenic variants on protein stability, and Missense3D was used to assess effects on the three-dimensional structure of p53. Cataract and oral cavity cancer tissues harbored more pathogenic variants (19 and 14, respectively) than breast and prostate cancer tissues (7 and 11, respectively). The variants c.506T > G (p. Met169Arg), c.652G > A (p. Val218Met), and c.672 + 1G > T were shared by prostate and breast cancers. The variants c.576G > C (p. Gln192His), c.642T > G (p. His214Gln), c.644G > A (p. Ser215Asn), and c.645T > G (p. Ser215Arg) were common to cataracts and oral cavity cancers. Structural analysis using Missense3D showed that some mutations caused no detectable structural damage, whereas significant conformational alterations were observed at co-

dons 175 and 196 (variants c.524G > C and c.587G > C). These findings suggest that *TP53* mutations may occur early in the development of cataract as well as in oral cavity, breast, and prostate cancers. This study provides baseline molecular data that could contribute to improving early detection and clinical management of these diseases in Senegalese patients.

Keywords

TP53, Somatic Mutations, Cataracts, Breast Cancer, Prostate Cancer, Oral Cavity Cancer, In Silico Analysis, Protein Structure

1. Introduction

Somatic mutations in the *TP53* gene are present in almost all types of cancer, with frequencies ranging from 38% to 50%, making *TP53* a gene of particular interest for epidemiological and molecular studies [1]. This gene encodes a protein that prevents cells carrying DNA damage from proliferating. In the absence of this protein, cells divide uncontrollably and can form tumors [2]. Mutations in this gene have also been implicated in the development of cataracts. Somatic mutations in *TP53* constitute one of the most frequent genetic alterations in human cancers, while germline mutations are responsible for Li-Fraumeni syndrome [3]. Cancer remains the leading cause of death and a major obstacle to increasing life expectancy worldwide in the 21st century [4]. It generally results from an accumulation of mutations within a single cell. In Senegal, cancer constitutes a major public health concern due to frequent late diagnoses and the high cost and complexity of treatment [5]. Alongside cancer, cataract (opacity of the lens) is the leading cause of blindness worldwide.

Among the human diseases potentially associated with *TP53* gene mutations, cataract stands out as a major condition. It is the leading cause of blindness in Senegal, affecting an estimated 35,000 to 50,000 individuals each year [6]. As vision is a predominant sensory function, it plays a crucial role in all aspects of human development and daily life.

According to the World Health Organization (WHO), the most diagnosed cancers in 2022 were breast cancer (2.26 million cases), prostate cancer (1.41 million cases), and oral cancer. In 2020, more than 2.2 million cases of breast cancer were reported worldwide, making it the most prevalent form of cancer [7]. Approximately one in twelve women is at risk of developing breast cancer during her lifetime [8]. Breast cancer is also the leading cause of cancer-related mortality among women, accounting for approximately 670,000 deaths in 2022 [9]. Prostate cancer is among the most common malignant tumors in men worldwide. In 2022, GLOBOCAN [10] reported about 1,467,854 new cases and 397,430 deaths globally, with higher incidence observed in developed countries. On average, around 190,000 new cases and 80,000 deaths occur annually.

Oral cancers are the most common malignancies within the head and neck can-

cer subgroup worldwide. In 2022, they accounted for 389,846 new cases and 188,438 deaths [11], with higher incidence documented in developing countries. Tobacco and alcohol use are the primary risk factors [12]. These cancers are increasingly observed in Senegal, with approximately 1.771 cases of oral cavity cancer, 838 cases of breast cancer, and 800 cases of prostate cancer reported [12] [13].

These diseases are multifactorial, with etiologies that may be environmentally or linked to genetic predisposition [14] [15]. In developing countries, they are often diagnosed at advanced stages, contributing to high morbidity [16]. In Senegal, both cancers and cataracts pose significant public health challenges due to late diagnosis, high morbidity, and the high cost and complexity of treatment [5].

It is therefore imperative to conduct a cross-sectional molecular study to provide a basis for early detection and therapeutic management of these pathologies. Moreover, understanding the genetics of these diseases is a crucial step in guiding the development of medical therapies capable of preventing or delaying their onset, thereby reducing the burden they represent for the population. Consequently, this study aimed to perform an in-silico characterization of *TP53* variants in relation to the development of cataract, as well as breast, prostate, and oral cavity cancers in Senegalese patients.

2. Methodology

2.1. Samples

As part of this study, tissue samples from breast, prostate, and oral cavity cancers, as well as from cataract cases, were collected at Aristide Le Dantec Hospital and Ouakam Military Hospital, following approval from the Cheikh Anta Diop University Research Ethics Committee. These samples were then sent to the Genomics Laboratory for molecular analysis.

A total of 116 patients were included: cataract (n = 29), oral cavity cancer (n = 33), prostate cancer (n = 15), breast cancer (n = 16), and controls (n = 23). All patients were informed about the study and provided written consent prior to recruitment. Cancerous and healthy tissues were collected from each patient during biopsy.

2.2. DNA Extraction, Polymerase Chain Reaction, and Sequencing

DNA from the cancerous tissues was extracted using the Zymo Research DNA extraction kit according to the manufacturer's instructions. For blood samples from cataract patients, DNA was extracted using the QIAamp Mini Kit.

The region spanning exon 5 to exon 6 of the *TP53* gene was amplified using the following primers: Forward: 5'-GTTTCTTTGCTGCCGTCTTC-3' and Reverse: 5'-CTTAACCCCTCCTCCCAGAG-3'. A total PCR reaction volume of 25 µl was prepared, containing 12.5 µl Master Mix, 1 µl of each primer (10 µM), 8.5 µl Milli-Q water, and 2 µl DNA template.

PCR amplification was performed under the following conditions: initial denaturation at 95˚C for 7 minutes; 35 cycles of denaturation at 94˚C for 1 minute,

annealing at 60˚C - 64˚C for 1 minute, and extension at 72˚C for 1 minute; followed by a final extension at 72˚C for 10 minutes.

After agarose gel electrophoresis and visualization under blue light, the amplified products were purified and sequenced using the ABI BigDye Terminator v3.1 Cycle Sequencing Kit and analyzed on an ABI PRISM 3730xl Genetic Analyzer (Applied Biosystems, Foster City, CA, USA).

2.3. Genetic Analyses

2.3.1. Search for Mutations

Raw *TP53* sequences from cancers, cataracts, and controls were BLASTed against the *TP53* reference sequence (GenBank accession NG_017013.2). Mutation Surveyor software v5.0.1 (http://www.sofgenetics.com/) was used to determine the presence and positions of mutations. Mutation Surveyor provides high accuracy and sensitivity with low false-positive and false-negative rates for SNPs, homozygous indels, heterozygous indels, and somatic mutations in direct sequencing.

2.3.2. Pathogenicity of Mutations

Nucleotide sequences were translated into protein sequences using MEGA X v7.0.14. The resulting protein sequences were analyzed with MutationTaster, PolyPhen-2, and SIFT to predict the functional consequences of amino acid substitutions. MutationTaster scores consider the Grantham amino acid substitution matrix (0 - 215) and predict effects of substitutions, intronic and synonymous changes, short indels, and variants at intron–exon boundaries. PolyPhen-2 classifies mutations as probably damaging (>0.95), potentially damaging (0.5 - 0.95), or benign (<0.5). SIFT scores < 0.05 indicate deleterious substitutions; ≥0.05 are considered tolerated.

2.3.3. Prediction of Stability and 3D Conformation on Protein Functionality

The effects of pathogenic mutations on p53 stability were assessed using DynaMut2 and I-Mutant. Mutations predicted to destabilize p53 were further analyzed with Missense3D to evaluate their impact on 3D structure and function. Protein stabilization or destabilization was determined by ΔΔG: negative ΔΔG indicates stabilization; positive ΔΔG indicates destabilization.

DynaMut2 analyzes protein dynamics using normal mode approaches and graph-based signatures to predict mutation effects on stability and flexibility ($p < 0.001$, correlation up to 0.70). I-Mutant predicts the impact of nsSNPs on folding stability and functionality, with ~80% accuracy and correlation coefficient 0.70 relative to experimental ΔΔG.

Missense3D integrates Missense3D-STD and Missense3D-PPI to predict structural changes in proteins and protein–protein interfaces, supporting experimental structures, AlphaFold predictions, GWYRE complexes, and user-uploaded models.

3. Results

3.1. Nature and Position of the Mutations

A total of 116 sequences were obtained: 29 from cataract cases, 33 from oral cavity

cancers, 15 from prostate cancers, 16 from breast cancers, and 23 from control individuals. Comparison with the reference sequence identified 128 unique variants, including 25 previously reported in the dbSNP database, and 103 novel variants.

Comparative analysis across the four pathologies revealed that prostate cancer harbored the highest number of mutations, followed by oral cavity cancer, then cataract, while breast cancer had the fewest mutations, with 38, 34, 30, and 26 mutations, respectively.

3.2. Pathogenicity of Non-Synonymous Mutations

A total of 56 non-synonymous *TP53* mutations were consistently predicted as pathogenic by the computational tools used in this study. Among these, cataract tissues harbored (19) deleterious mutations, oral cavity cancers (14), prostate cancers (10), and breast cancers (5).

Frequency of Deleterious Mutations

Cataract and oral cavity cancer tissues were found to harbor a higher number of pathogenic mutations compared to breast and prostate cancer tissues. Nevertheless, some pathogenic mutations were shared across these pathologies. The mutations c.506T > G (p. 169Met > Arg), c.652G > A (p. 218Val > Met), and c.672 + 1G > T are common in both prostate and breast cancer, with similar frequencies of 6.66% and 6.25%, respectively. Similarly, the mutations c.576G > C (p. 192Gln > His), c.642T > G (p. 214His > Gln), c.644G > A (p. 215Ser > Asn), and c.645T > G (p. 215Ser > Arg) were observed in both oral cavity cancer and cataract cases.

Certain mutations, however, appear to be specific to a particular pathology:

- Oral cavity cancer (CCB) only: c.524G > C (p. 175Arg > Pro), c.526T > C (p. 176Cys > Arg), c.527G > C (p. 176Cys > Ser), c.578A > C (p. 193His > Pro), c.584T > A (p. 195Iso > Asn), c.587G > C (p. 196Arg > Pro), c.638G > A (p. 213Arg > Gln), c.647T > G (p. 216Val > Gly), and c.650T > A (p. 217Val > Glu).
- Prostate cancer (CP) only: c.424C > G (p. 142Pro > Ala), c.631A > G (p. 211Thr > Ala), c.655C > T (p. 219Pro > Ser), c.660T > G (p. Y220*), c.661G > T (p. E221*), and c.665C > G (p. 222Pro > Arg).
- Breast cancer (CS) only: c.412G > C (p. 138Ala > Pro), c.524G > A (p. 175Arg > His), and c.560G > A (p. 187Gly > Asp).
- Cataract (K) only: c.415A > T (p. K139*), c.415A > G (p. 139Lys > Glu), c.442G > A (p. 148Asp > Asn), c.513G > C (p. 171Glu > Asp), c.548C > A (p. S183*), c.586C > G (p. 196Arg > Gly), c.587G > A (p. 196Arg > Gln), c.587G > T (p. 196Arg > Lys), c.589G > A (p. 197Val > Met), c.626G > A (p. 209Arg > Lys), c.628A > T (p. 210Asn > Tyr), c.640C > A (p. 214His > Asn), c.641A > G (p. 214His > Arg), and c.647T > A (p. 216Val > Glu).

These results suggest that while some *TP53* mutations are shared across pathologies, many are disease-specific, reflecting potential roles in the pathogenesis of each condition.

3.3. Protein Stability and Structure

3.3.1. Protein Stability

A total of 47 deleterious mutations were found to destabilize the *TP53* protein. Notably, oral cavity cancer and cataract samples harbored a higher number of these destabilizing mutations compared to prostate and breast cancer samples.

3.3.2. 3D Structure of the Protein

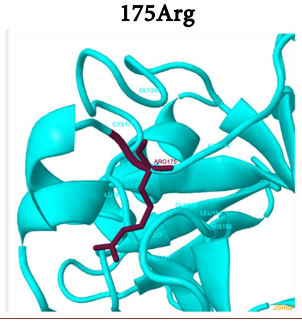
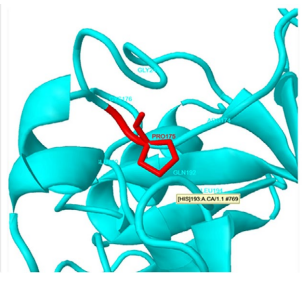
According to Missense3D analysis, several substitutions do not induce any detectable structural damage to the *TP53* protein. These mutations do not replace buried hydrophobic residues with hydrophilic ones, do not trigger alerts related to buried uncharged residues, do not alter the protein secondary structure, and do not replace buried charged residues with uncharged ones. Additionally, they do not disrupt sidechain/sidechain or sidechain/main-chain hydrogen bonds, and the wild-type residue remains buried.

However, 16 mutations are considered deleterious and structurally significant. These include: c.524G > C (175Arg > Pro), c.565G > C (189Ala > Pro), c.578A > C (193His > Pro), c.587G > C (196Arg > Pro), c.638G > A (213Arg > Gln), c.645T > G (215Ser > Arg), c.647T > G (216Val > Gly), c.650T > A (217Val > Glu), c.428T > G (143Val > Gly), c.560G > A (187Gly > Asp), c.412G > C (138Ala > Pro), c.524G > A (175Arg > His), c.586C > G (196Arg > Gly), c.647T > A (216Val > Glu), c.645T > G (215Ser > Arg), and c.587G > A (196Arg > Gln).

Notably, significant structural alterations were observed at codons 175 and 196, corresponding to mutations c.524G > C and c.587G > C, which substitute Arginine with Proline at positions 175 and 196 of p53, as shown in Table 1. These substitutions introduce a buried proline, replace a buried charged residue (Arg) with an uncharged residue (Pro), disrupt all side-chain/side-chain and/or side-chain/main-chain hydrogen bonds formed by the buried Arginine, and break a salt bridge between the NH1 atom of Arginine 175 and the OD2 atom of Aspartic Acid 184 (distance: 2.726 Å).

These two substitutions at codons 175 and 196 were observed exclusively in oral cavity cancer samples, highlighting their potential role in disease-specific structural disruption of the *TP53* protein.

Table 1. Structure 3D of the protein: wild type vs mutant.

Wild type	Mutant
Oral cavity cancer	
175Arg	175Pro
	

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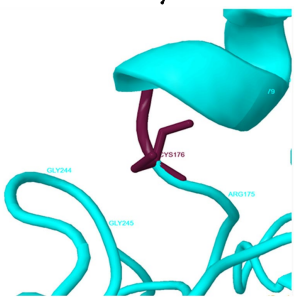
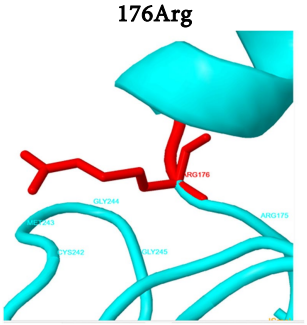
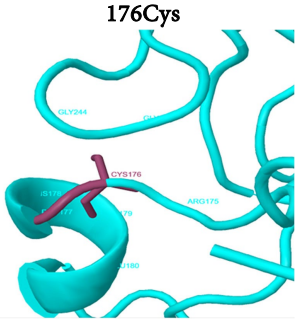
176Cys



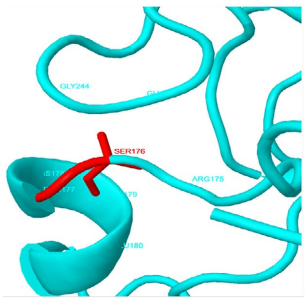
176Arg



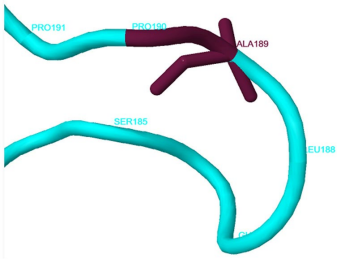
176Cys



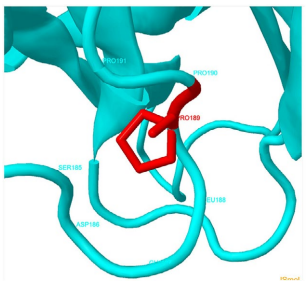
176Ser



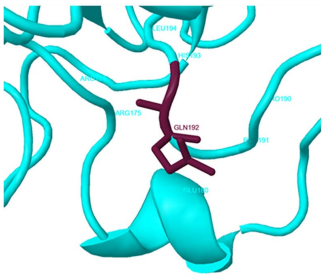
189Ala



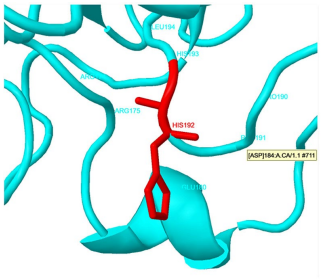
189Pro



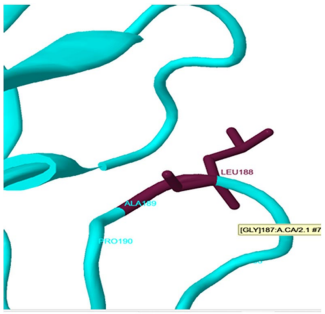
192Gln



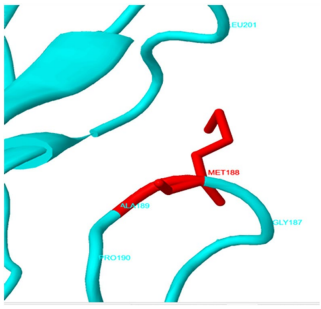
192His



188Leu



188Met



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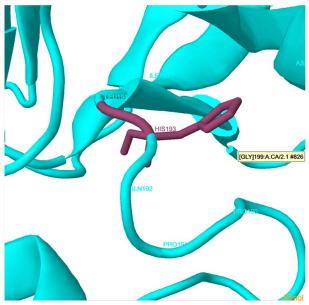
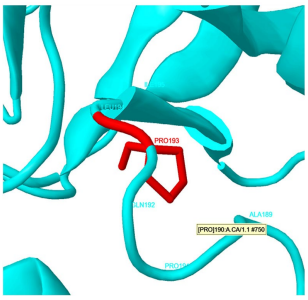
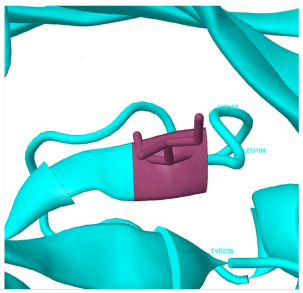
193His



193Pro

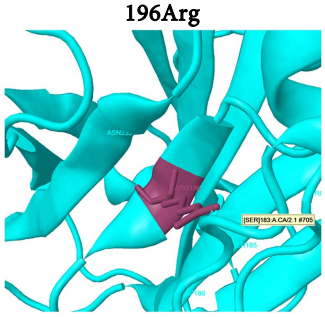


195Iso

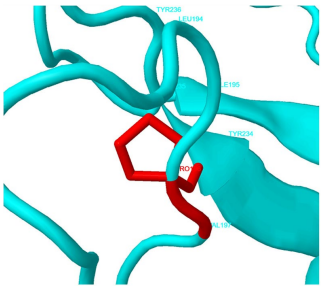


195Asn

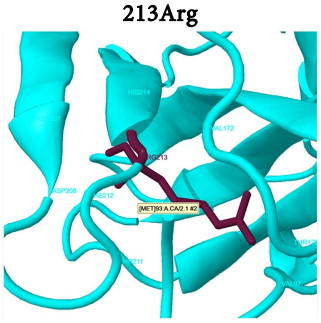
196Arg



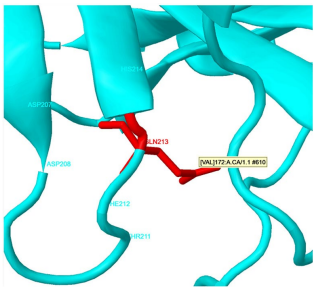
196Pro



213Arg



213Gln



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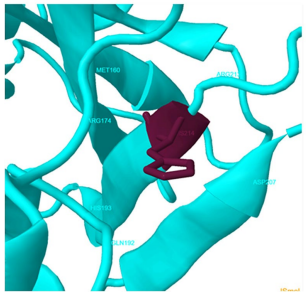
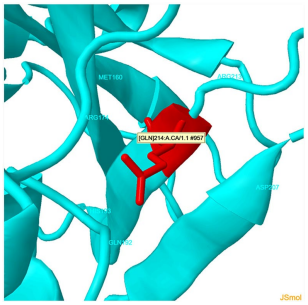


214Gln



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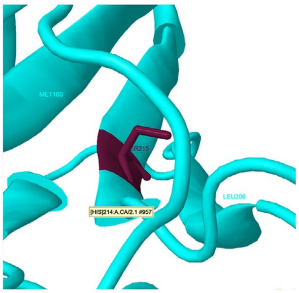	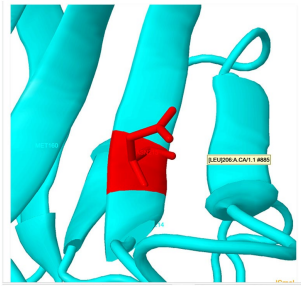
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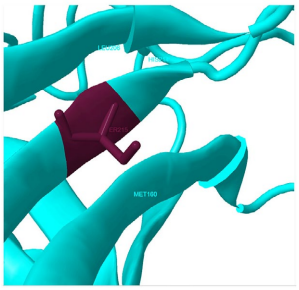	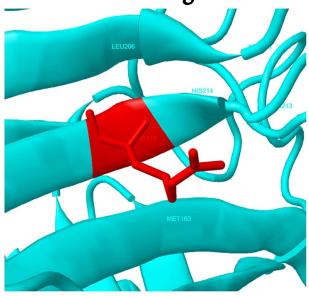
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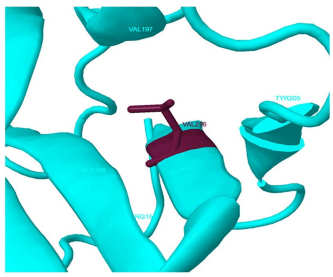	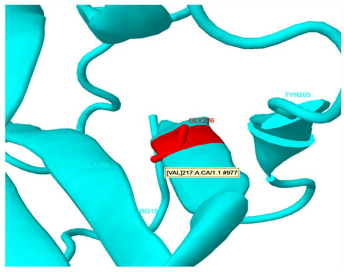
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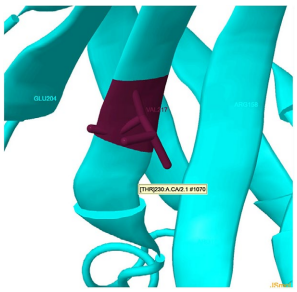
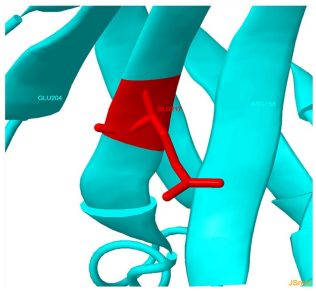
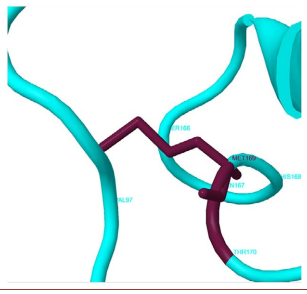
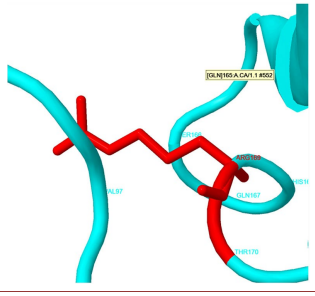
	
Prostate cancer	
169Met	169Arg
	

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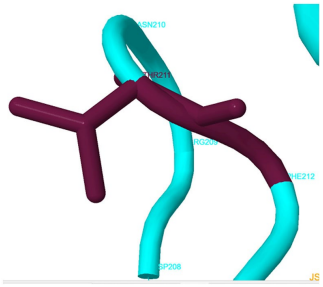
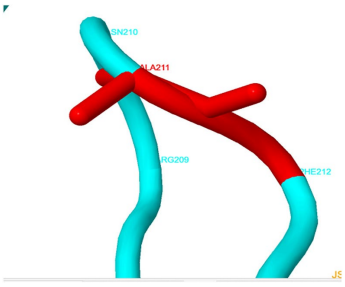
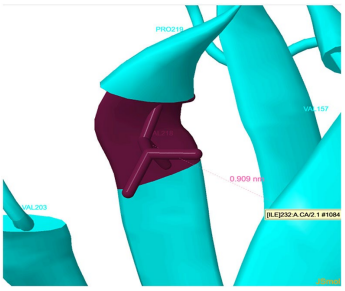
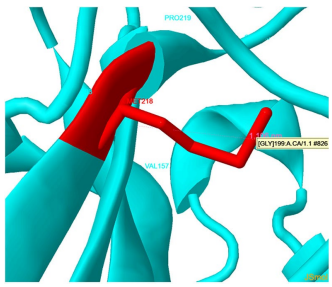
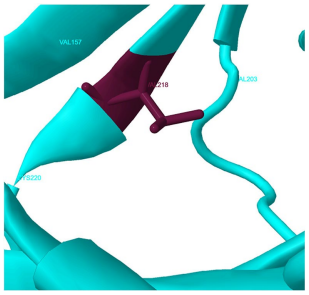
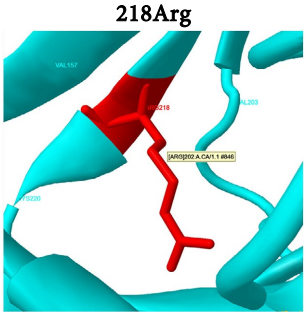
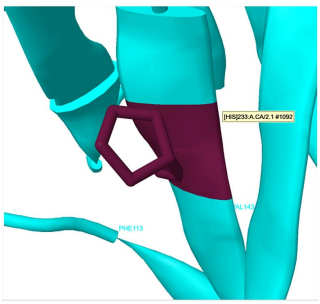
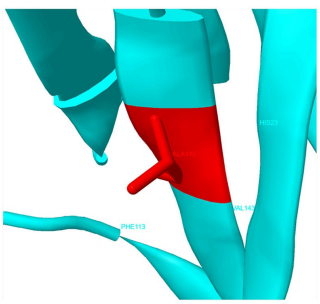
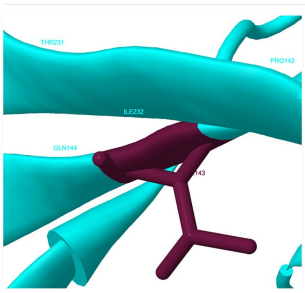
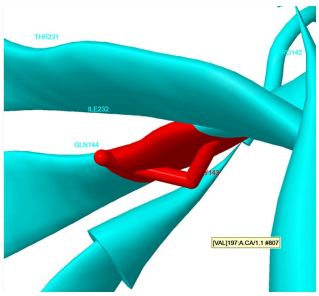
211Thr	211Ala
	
218Val	218Met
	
218Val	218Arg
	
142Pro	142Ala
	
143Val	143Gly
	

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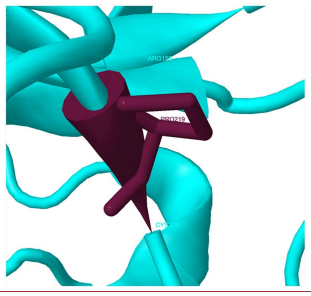
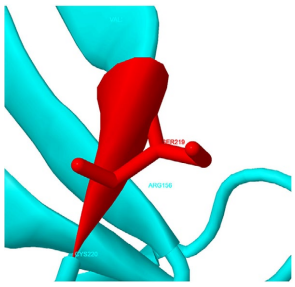
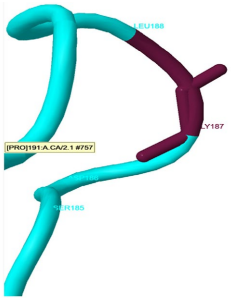
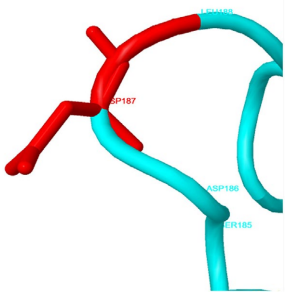
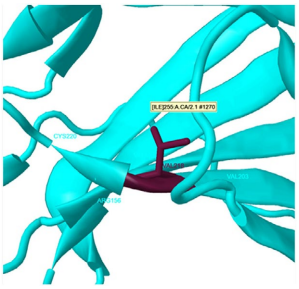
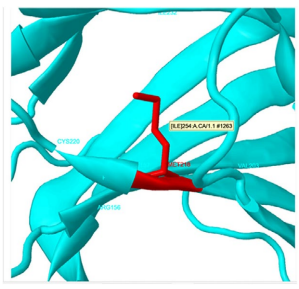
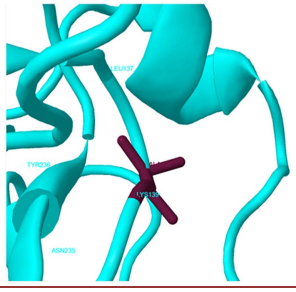
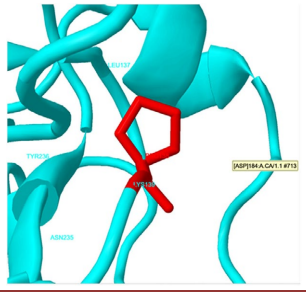
222Pro	222Arg
	
219Pro	219Ser
	
Breast cancer	
187Gly	187Asp
	
218Val	218Met
	
138Ala	138Pro
	

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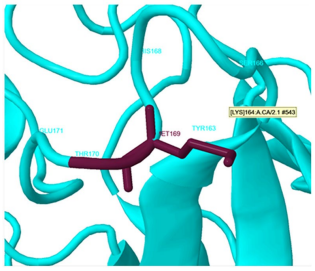
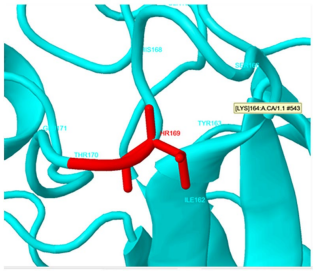
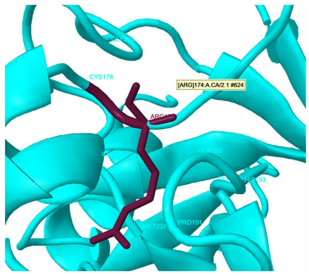
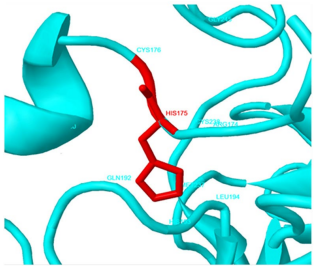
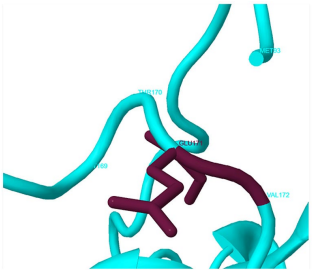
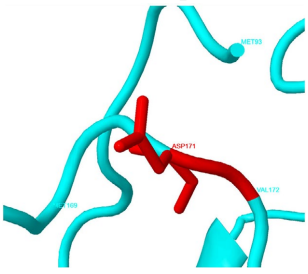
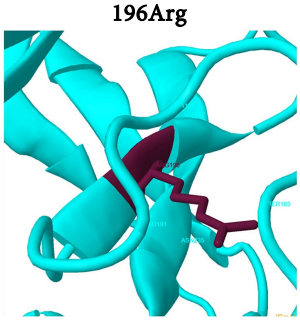
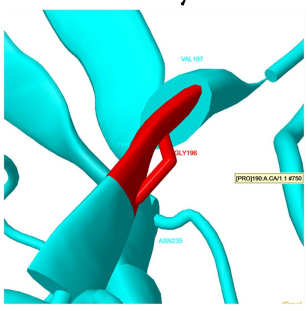
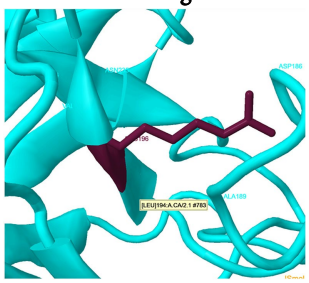
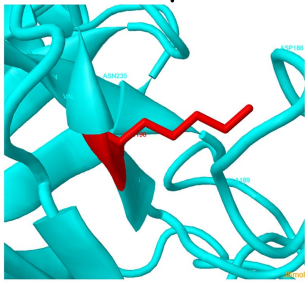
169Met	**169Thr**
	
175Arg	**175His**
	
Cataract	
171Glu	**171Asp**
	
196Arg	**196Gly**
	
196Arg	**196Lys**
	

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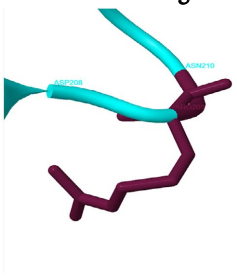
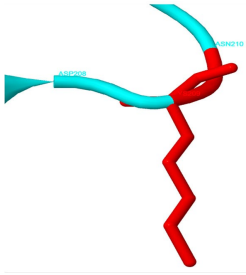
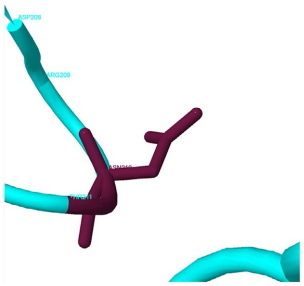
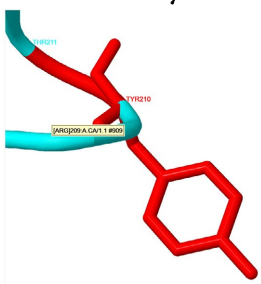
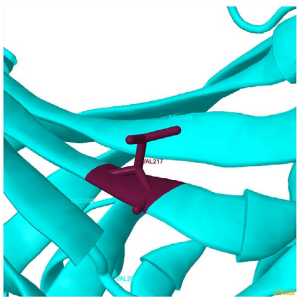
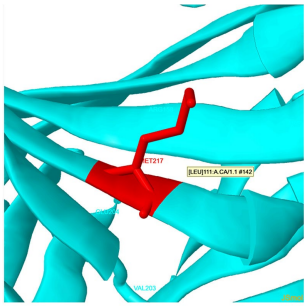
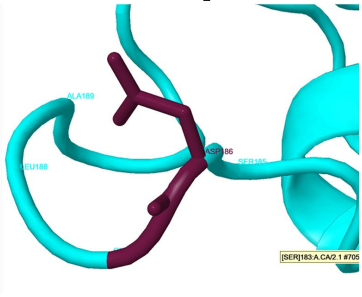
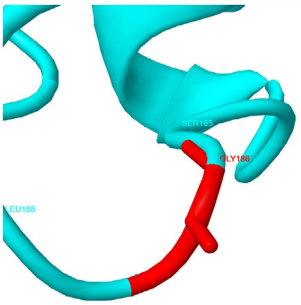
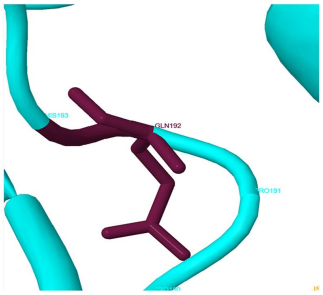
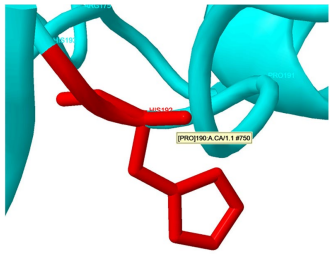
209Arg	209Lys
	
210Asn	210Tyr
	
217Val	217Met
	
186Asp	186Gly
	
192Gln	192His
	

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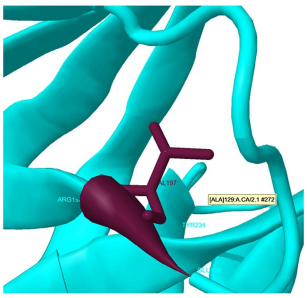
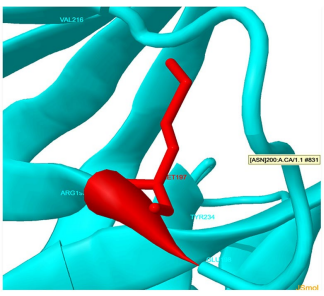
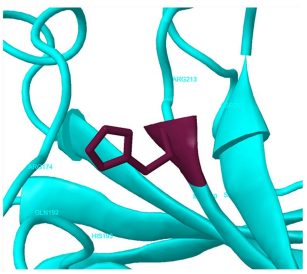
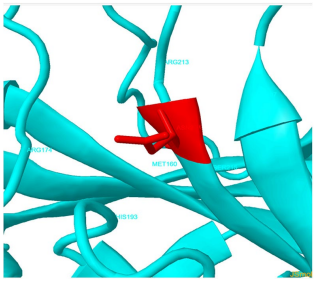
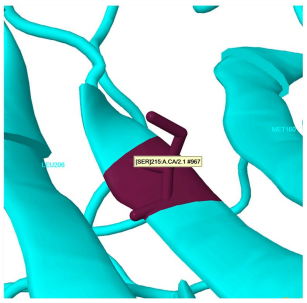
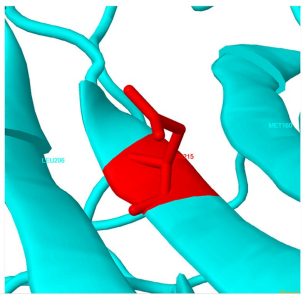
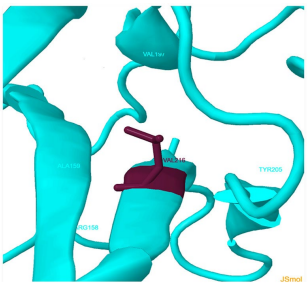
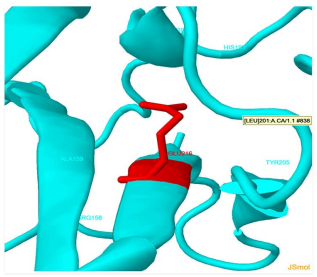
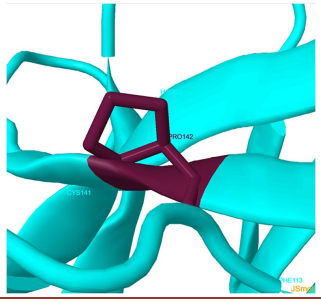
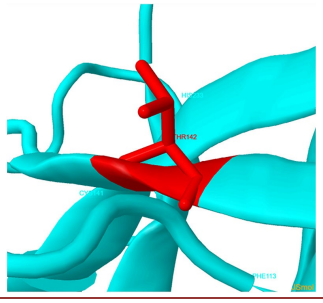
197Val	**197Met**
	
214His	**214Asn**
	
215Ser	**215Asn**
	
216Val	**216Glu**
	
142Pro	**142Thr**
	

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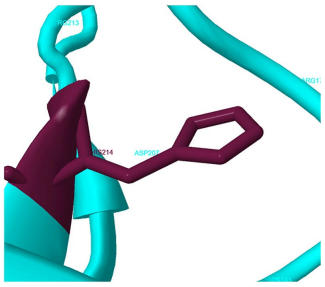
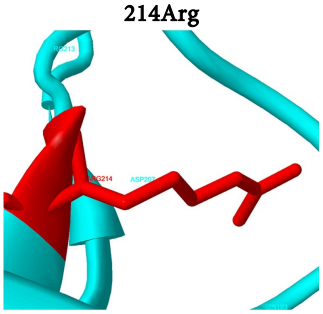
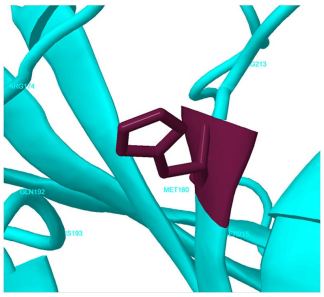
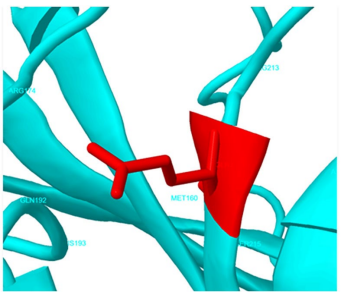
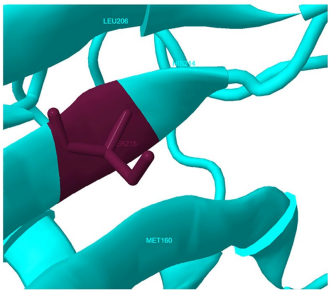
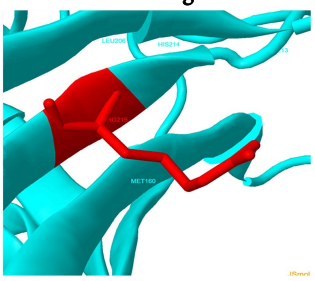
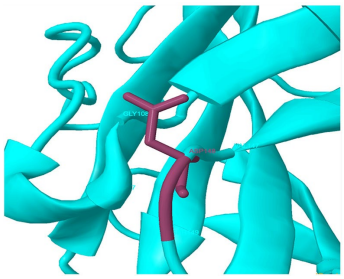
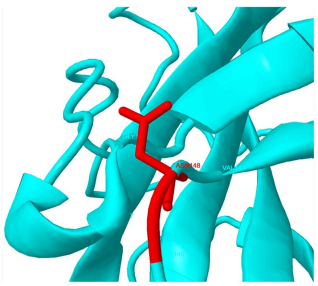
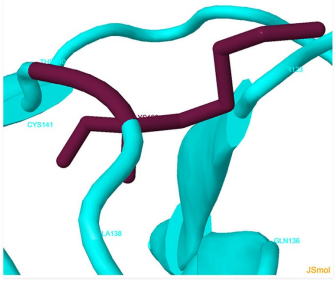
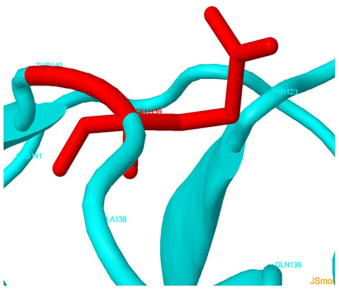
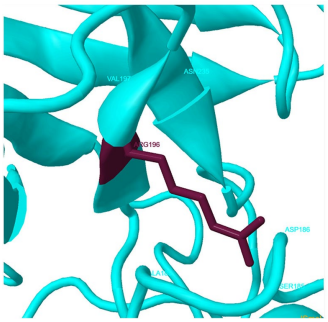
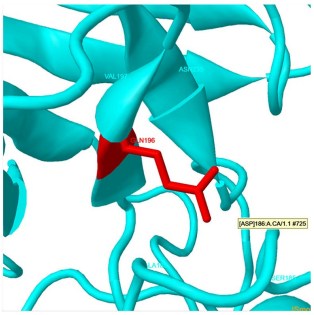
214His	214Arg
	
214His	214Gln
	
215Ser	215Arg
	
148Asp	148Asn
	
139Lys	139Glu
	

Continued

196Arg	196Gln
	

4. Discussion

This study aimed to perform an in silico analysis of the *TP53* gene to investigate its involvement in the development of cataracts, as well as breast, prostate, and oral cavity cancers in Senegalese patients. Specifically, exons 5 and 6 of the gene were targeted for this analysis. A total of 128 mutations were detected, of which 103 were novel and 25 had already been reported in mutation databases. The identification of 103 new *TP53* variants is an important discovery as their submission to public genetic databases could contribute to understanding diseases caused by mutations in *TP53*. In oral cavity cancer, 34 mutations were identified in 33 cases, which is fewer than the 105 mutations reported by Samb, [17] in her study of 92 patients in Senegal. *TP53* mutations were found in 54 of 67 patients (80.6%) with oral cavity cancer, which is higher than our results, according to Hyodo *et al.*, [18] in Tochigi, Japan. In prostate cancer, 38 mutations were detected in 15 cases, which is higher than the 10 mutations found in 24 Tunisian prostate cancer patients but lower than the 137 mutations reported in 48 Moroccan prostate cancer patients [19]. In breast cancer, 26 mutations were identified in 16 cases, fewer than the 172 mutations reported in 650 patients in Seoul, Korea [20], and fewer than the 25 patients with *TP53* mutations among 50 breast cancer patients reported in Beijing, People's Republic of China [21]. In our 29 cataract cases, 30 *TP53* mutations were identified, which is higher than the 11 mutations reported in 21 cases of ocular pathology due to *TP53* mutations in Helsinki, Finland [22]; furthermore, 14 mutations were identified in the *TP53* genes of 9 out of 20 patients affected by various eyelid malignancies in a study conducted by Maurya *et al.*, [23], in India. These differences may be explained by variations in sample sizes and by discrepancies in the specific regions of the *TP53* gene that were sequenced. These differences could also be explained by genetic origins specific to a population (ethnic origins, for example) or distinct environmental exposures (such as exposure to aflatoxins, which are powerful carcinogens) in Senegal. Our study demonstrated that some mutations are common across different pathologies in exons 5 - 6 of the *TP53* gene. *TP53* mutations, which code for the p53 protein, are among the most common genetic alterations associated with cancer and cataracts. The majority of *TP53* mutations are missense mutations, altering a single amino acid in the p53

protein, thereby affecting function without changing overall protein structure [24]. Specific codons such as R175, G245, R248, and R273 are frequently mutated and associated with dominant negative effects, leading to impaired p53 activity. In addition, nonsense mutations, frameshift mutations, and splicing variants also contribute to the loss of function, accounting for a significant proportion of *TP53* alterations [24]. *TP53* polymorphisms significantly influence cancer susceptibility and progression across different types of cancer [25].

The frequency of *TP53* polymorphisms can vary among populations, and sample sizes differ considerably across studies. Polymorphism in this gene is a significant genetic alteration, particularly in African populations [26]. A study conducted in Senegal in 2022 reported a high mutation frequency in the population, with 52.27% of patients carrying at least one *TP53* mutation. Eleven genomic variants were identified, seven previously reported in mutation databases and four novel variants [27]. The most recurrent variants were p. Pro72Arg (rs1042522; allele frequency 31.26%) and a 16 bp deletion in intron 3 (rs59758982; allele frequency 26.25%). These results suggest greater overexpression or variability of *TP53* in certain populations [28].

Analysis of mutation types in this study revealed that missense mutations were the most frequent (58), followed by synonymous mutations (19) and nonsense mutations (5). These findings are consistent with those reported by Aboulalaa *et al.*, [19], who identified 22 missense mutations (16%) among 34 cases (71%). Similarly, Samb *et al.*, [29] found that 72.09% of mutations were missense, 25.56% were silent, and 2.32% were nonsense mutations. Van Kempen *et al.*, [30] reported 94 nonsynonymous mutations in 81 patients, primarily located in exons 5 and 6.

Most *TP53* mutations cluster within the DNA-binding domain of the p53 protein, encompassing exons 5 and 6. The tumor suppressor p53 is one of the most frequently mutated genes in human cancers. Among the 29.891 genomic mutations reported in the *TP53* database, 1.297 are unique somatic missense mutations, excluding frameshift, intronic, deletions, nonsense, silent, splicing, and other unknown variants [31]. The presence of stop codon mutations highlights the high mutability of *TP53* and reinforces the idea that missense mutations are preferentially selected in cancer due to their specific pro-oncogenic functions [29].

The frequency of deleterious mutations observed in this study showed that cataract and oral cavity cancer tissues harbored more pathogenic mutations (19 and 14, respectively) than breast and prostate cancer tissues (7 and 11, respectively). This pattern may reflect the dual impact of *TP53* mutations: loss-of-function and gain-of-function effects promote tumor progression [31]. Nevertheless, some pathogenic mutations were shared across different pathologies. For example, the c.376-2A > T mutation was found in both oral cavity and prostate cancer, with frequencies of 2.94% and 6.66%, respectively. This splice-site mutation could produce a truncated or dysfunctional p53 protein, impacting genomic stability and cell cycle regulation [32].

Nonsense mutations were identified in two cases of prostate cancer, two cata-

ract cases, and one control sample. Approximately 50% of all human tumors carry *TP53* mutations, with around 10% being nonsense mutations [33]. Aboulalaa *et al.*, [19] reported a nonsense mutation at codon 126 (tyrosine) in a patient. Such mutations introduce premature stop codons, leading to truncated, inactive p53 proteins, which are associated with poor prognosis in oral cavity cancer [18].

Certain mutations were shared among pathologies: c.506T > G (p. 169Met > Arg), c.652G > A (p. 218Val > Met), and c.672 + 1G > T in prostate and breast cancers, and c.576G > C (p. 192Gln > His), c.642T > G (p. 214His > Gln), c.644G > A (p. 215Ser > Asn), and c.645T > G (p. 215Ser > Arg) in oral cavity cancers and cataracts. These shared mutations suggest common genetic pathways in tumorigenesis or susceptibility among individuals [31] [34].

Mutations in exons 5 - 6 significantly affect p53 protein stability and dynamics, compromising DNA-binding and tumor-suppressing functions. Tanaka *et al.*, [35] demonstrated that mutant *TP53* overexpression enhances invasive cell growth in p53-deficient cells. In this study, 47 mutations were predicted to destabilize p53, while 10 were non-destabilizing. These results are consistent with those of Balasundaram and Doss, [36], showing that missense mutations often reduce protein stability and function.

Structural analyses revealed that specific amino acid substitutions, such as c.524G > C (p. 175Arg > Pro) and c.587G > C (p. 196Arg > Pro), disrupt hydrogen bonding networks, increasing cancer or cataract risk. Substitutions replacing buried charged residues with uncharged residues or altering side-chain interactions can compromise protein function. Among the 16 mutations considered deleterious by Missense3D, the most structurally impactful include 175Arg > Pro, 189Ala > Pro, 193His > Pro, 196Arg > Pro, 213Arg > Gln, 215Ser > Arg, 216Val > Gly, 217Val > Glu, 143Val > Gly, 187Gly > Asp, 138Ala > Pro, 175Arg > His, 196Arg > Gly, 216Val > Glu, 215Ser > Arg, and 196Arg > Gln. Balasundaram and Doss, [36] reported that missense mutations in the DNA-binding domain inhibit protein activity and reduce DNA-binding affinity.

Protein stability and structural integrity are essential for proper p53 function. Mutations that compromise these properties can lead to loss of tumor-suppressing activity and contribute to disease progression. The p53 protein remains a critical tumor suppressor, and alterations in exons 5 - 6 can disrupt its role in apoptosis and cell cycle regulation, underscoring the importance of these mutations as prognostic markers and potential therapeutic targets. Identification of *TP53* mutations holds significant potential for early cancer detection, which is essential for improving patient outcomes. Mutations in *TP53* are prevalent in a variety of diseases, making them a valuable target for diagnostic strategies. The translation of these molecular data into practical screening or diagnostic strategies requires leveraging non-invasive methods and advanced technologies to detect these mutations at an early stage of the disease process.

5. Conclusions

The pathologies studied above remain conditions that are often diagnosed at a late

stage in Senegal. Mutations in the *TP53* gene, which encodes the p53 protein, represent the most common genetic alterations associated with various cancers, particularly breast, oral cavity, and prostate cancers. These mutations frequently result in a loss of p53 tumor-suppressor function and may also confer novel oncogenic properties, contributing to cancer progression and resistance to therapy.

Emerging research in Senegal has also highlighted a potential link between *TP53* mutations and cataracts, suggesting that specific genetic polymorphisms, possibly in combination with environmental factors, may influence cataract development.

This cross-sectional study, despite limitations in sample size, provides a molecular basis for the early detection and management of cataracts and cancers of the oral cavity, breast, and prostate among Senegalese patients. Mutations common to multiple pathologies were identified, as well as several potentially pathogenic alterations in exons 5 and 6 of the *TP53* gene. These findings underscore the relevance of *TP53* mutations as prognostic and predictive markers. Shared mutations across different pathologies offer insights into common genetic mechanisms and potential therapeutic targets.

Mutations in exons 5 and 6 can significantly impact the structure and function of the p53 protein, resulting in impaired tumor suppressor activity. Given that these exons are frequently mutated in multiple cancer types, understanding their genetic variations is crucial for improved diagnosis, prognosis, and treatment strategies. We suggest that studies on larger samples be conducted on the *TP53* gene in order facilitate the functional validation of new variants of high interest of this gene.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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