ACCSCIENCE PUBLISHING

Cancer Plus

ORIGINAL RESEARCH ARTICLE

Genetic alterations in APC and MYC genes in breast lesions: A pilot study insight into fibroadenoma and invasive ductal adenocarcinoma pathogenesis for personalised gene therapy

Ekundina Victor[1], Kehinde Adedapo[1]*, and Akeredolu Florence[2]

[1]College of Medicine and Health Sciences, Department of Medical Laboratory Science, Afe Babalola University, Ado-Ekiti, Ekiti State, Nigeria

[2]College of Basic Health Sciences, Department of Medical Laboratory Science, Achievers University, Idasen-Owo, Ondo State, Nigeria

Abstract

Breast cancer remains a major public health concern, especially in the female population, and its treatment remains challenging in the world. Targeted gene therapy might prove effective in curbing the prevalence. This Pilot study was to evaluate mutation patterns in Adenomatous Polyposis Coli (*APC*) And Myelocytomatosis (*MYC*) gene in benign and malignant breast lesions. The pilot study consisted the use of 10 formalin-fixed heterogenous paraffin-embedded tissue blocks, 5 fibroadenomas (FA) and 5 invasive ductal adenocarcinomas (IDA) from the pathological archives of Federal Teaching Hospital Ido-Ekiti. Nucleic acid amplification technique by using Dellaporta DNA extraction protocol. Polymerase chain reaction (PCR) technique was used to amplify the DNA fragments, sequenced using a Genetic Analyzer 3130xl sequencer from Applied Biosystems using the manufacturers' manual, Bio-Edit software and Mega 6 were used for all genetic analysis. PCR optimization and Primer specificity, HGVSc, HGVSp, and VAF (%) were analysed. The results were reported that in fibroadenoma in the *APC* gene, single nucleotide polymorphism (SNP) mutation recorded transition in all samples, as well as in the invasive ductal adenocarcinoma it recorded. In functional mutation in the *APC* gene, fibroadenoma showed both silent and missense mutations while invasive ductal adenocarcinoma it recorded only missense mutation. The results reported in the *MYC* gene show that in SNPs mutation for fibroadenoma, showed both transversion and transition. In IDA, transition, InDel and transversion were observed. In functional mutation, fibroadenoma showed silent and missense while in IDA silent and missense were observed. This study carried out demonstrated missense mutation in both *APC* and *MYC* genes in fibroadenoma and invasive ductal adenocarcinoma singly.

Keywords: Targeted therapy; Precision medicine; Adenomatous polyposis coli; Myelocytomatosis; Mutation; Fibroadenoma; Invasive ductal adenocarcinoma

***Corresponding author:**
Kehinde Adedapo
(Kehindeadedapo@achievers.edu.ng)

Citation: Victor E, Adedapo K, Florence A. Genetic alterations in APC and MYC genes in breast lesions: A pilot study insight into fibroadenoma and invasive ductal adenocarcinoma pathogenesis for personalised gene therapy. *Cancer Plus*. 2025;7(4):61-68. doi: 10.36922/CP025200034

Received: May 15, 2025

Revised: September 18, 2025

Accepted: November 11, 2025

Published online: December 31, 2025

1. Introduction

Breast cancer is a major public health concern for the female gender and its treatments remains challenging (Ekundina *et al*., 2023), this cancer cells are usually caused by the loss of genes that are supposedly meant to inhibit tumor development, resistance to apoptosis, and uncontrolled cell proliferation (Aremu *et al*., 2024). Breast cancer remains a major cause of cancer morbidity and mortality, with its epidemic growth, notably in low- and middle-income regions, being underlined in epidemiological data. Environmental factors can interact with genetic mutations to increase cancer risk. Kiljańczyk *et al*. (2024) showed that elevated blood lead levels raise ovarian cancer risk in *BRCA1* carriers, highlighting how environmental toxins can exacerbate genetic susceptibility. Similarly, pollutants and dietary contaminants may promote mutations in genes like *APC* and *MYC*, driving the progression from benign breast lesions to invasive cancers. This underscores the need to integrate environmental risk assessment with genetic profiling for prevention and targeted therapy.

Recent research (Łukasiewicz *et al*., 2021; Xu & Xu, 2023 underscores the significance of early diagnosis via imaging modalities including mammography and MRI, coupled with histopathological examination. The treatment of breast cancer has also undergone significant advancements, with the use of surgery, radiation, and chemotherapy, and more recently, with the use of target-specific drugs. The use of molecular examination has been critical in the determination of personalized treatment modalities, with the use of PARP inhibitors for BRCA-mutated tumors and anti-PI3K drugs for PI3K pathway abnormalities (Cortesi *et al*., 2021; Virga *et al*., 2024).

The early diagnosis of breast cancer is one of the best approaches to prevent this disease and can be used to inform therapeutic decisions or explored as potential therapeutic targets in our population (Xiao *et al*., 2021, Kehinde *et al*., 2025). Invasive ductal adenocarcinoma (IDC) refers to malignant tumour that has broken through the wall of the duct and invading the tissues of the breast, the lymph nodes and to other areas of the body (Gallas *et al*., 2025). while, Fibroadenomas are benign tumors characterized by stromal and epithelial tissue admixture that develops from the lobules (Olukayode *et al*., 2023), and the glandular tissue and ducts grow over the lobule to form a lump (Jones, 2020).

The *Adenomatous Polyposis Coli (APC)* gene, recognized for its tumor suppressor role (Zheng *et al*., 2013), is crucial in the signaling pathway, a pathway pivotal for regulating cellular proliferation, differentiation, and apoptosis. Mutations in *APC* are linked to colorectal cancer, but recent evidence by Yuan *et al*. (2024) suggests their implication in breast tissue malignancies, underscoring the importance of studying its mutations in various breast pathologies. On the other hand, *Myelocytomatosis (MYC)* is a well-characterized proto-oncogene (Duffy *et al*., 2021) that modulates transcriptional control over key genes influencing cellular growth, metabolism, and survival (Wolf & Eilers, 2020). Deregulation of *MYC*, through gene mutations or amplification, is often a hallmark of aggressive tumor phenotypes (García-Gutiérrez *et al*., 2019).

Recent advances in breast cancer research have underlined the promise of immunotherapy and the need for robust biomarkers to stratify patients. One notable study by Shi *et al*., 2024, characterizing immunogenic cell death (ICD)-dependent subtypes in triple-negative breast cancer (TNBC) demonstrated that tumors with "hot" immune microenvironments, reflected in higher ICD scores, show better prognosis and may respond more favorably to immune checkpoint blockade. Given that early molecular events may influence later therapeutic responses, understanding mutations in APC and MYC in benign versus malignant breast lesions could provide insight into the timeline of tumor evolution and identify early markers for therapy selection. Although data on alternative primary therapies are sparse and some studies suggest worse outcomes when standard treatments are delayed or omitted, some scientific studies such as Wang *et al*., 2024 and Kehinde *et al*., 2024 have reported that alternative therapy give better results compared to convential therapies.

It is important for molecular stratification even in early or benign lesions, to identify early tumorigenic events, and to avoid misclassification of potentially pathogenic mutations or delays in appropriate therapy. Thus, profiling genetic alterations in APC and MYC in fibroadenomas versus invasive ductal adenocarcinomas may offer valuable insights into the timeline of breast tumor progression and potentially inform therapeutic decision-making because the use of alternative and target-specific drugs has been proven effective in altering the prognosis of patients with specific molecular abnormalities, underlining the need for incorporating molecular diagnostics into clinical practice and this pilot study research aims to assess *APC* and *MYC* gene mutation patterns in benign and malignant breast lesions.

2. Materials and methods

2.1. Sample Collection and Histological Confirmation

The pilot study involved the use of Ten (10) processed tissue blocks that were obtained from the pathology archive at the Department of Histopathology, Federal

Teaching Hospital, Ido-Ekiti, Ekiti State, Nigeria. They were confirmed as either cases of fibroadenoma or invasive ductal adenocarcinoma samples. Histological confirmation for all cases was conducted using Hematoxylin and Eosin (H&E) staining, followed by microscopic examination to validate the diagnosis. Fibroadenoma was characterized by stromal and glandular proliferation without cellular atypia, while invasive ductal adenocarcinoma was confirmed by irregular glandular structures invading the stromal tissue. Thin sections were cut using a microtome and dewaxed with xylene. Clinical data were excluded to maintain patient confidentiality, as the study is retrospective. Three main procedures were employed in this study as described below: DNA extraction, polymerase chain reaction (PCR), and DNA sequencing, which were supplemented by integrity testing, purification, and isolation of the gene of interest as described and modified by Olukayode *et al*., (2023).

2.2. DNA Extraction and Spectrophotometric Analysis

DNA was extracted from the tissue sections using a modified Dellaporta protocol. The extraction process involved cell lysis, protein removal, DNA precipitation, and resuspension in Tris-EDTA buffer. DNA quality and concentration were verified using a Nanodrop spectrophotometer (Thermo Scientific, Model 2000). The purity of the DNA was assessed by measuring the absorbance ratios at 260/280 nm and 260/230 nm, with ratios of 1.8–2.0 indicating high-quality DNA. The concentrations ranged from 50 to 200 ng/µL, confirming sufficient yield for downstream applications.

2.3. Polymerase Chain Reaction (PCR)

PCR amplification of target genes was performed using a 25 µL reaction volume containing 1X PCR buffer, 2.0 mM MgCl2, 0.2 mM dNTPs, 0.5 µM of each primer, 1 U Taq DNA polymerase (Inqaba Biotech, South Africa), and 100 ng of template DNA. The primers were designed to target specific exons of the APC and MYC genes. The primer sequences and nucleotide positions are as follows:

APC Forward: 5'-AGCTTGCTGTCATTG-3' (chr5: 112,707,448–112,707,462)
APC Reverse: 5'-TGGTTTCTGCTTGC-3' (chr5: 112,707,580–112,707,594)
MYC Forward: 5'-GGAGCTGGACTGGAA-3' (chr8: 128,748,315–128,748,329)
MYC Reverse: 5'-GTCGTGCTGAGGG-3' (chr8: 128,748,445–128,748,458)

PCR cycling conditions were as follows: initial denaturation at 95°C for 5 minutes, followed by 35 cycles of denaturation at 95°C for 30 seconds, annealing at 58°C for 30 seconds, extension at 72°C for 45 seconds, and a final extension at 72°C for 7 minutes. Amplified products were verified on 1.5% agarose gel stained with ethidium bromide, visualized under UV trans-illumination, and compared against a 100 bp DNA ladder.

2.4. PCR optimization and Primer specificity

Primers were designed using Primer3 and checked for specificity with NCBI BLAST against the human genome. Primer pairs were validated by gradient PCR to determine optimal annealing temperatures and by agarose gel electrophoresis to confirm single, correctly sized amplicons. Where applicable, PCR amplicons were Sanger-sequenced to confirm target identity. Negative (no template) and positive control samples were included in all amplification experiments to monitor contamination and assay performance.

2.5. DNA Purification and Sequencing

Amplified PCR products were purified using ethanol precipitation to remove residual reagents. The DNA pellets were washed, air-dried, and resuspended in sterile distilled water. Purified DNA was verified on a 1.5% agarose gel and quantified using a Nanodrop spectrophotometer. DNA sequencing was conducted using an Applied Biosystems Genetic Analyzer 3130xl with the Big Dye Terminator v3.1 cycle sequencing kit. Sequences were obtained using both forward and reverse primers for accuracy.

2.6. Data Analysis

The obtained sequences were aligned to the human reference genome (hg38) using BioEdit software. Sequence alignment and variant calling were performed using MEGA 6 software. Mutations were classified as pathogenic or benign using the ClinVar databases, which provided information on clinical significance and population frequency. The mutation frequency was compared between fibroadenoma and invasive ductal adenocarcinoma cases. Statistical analysis was conducted using SPSS version 25, with significance set at $p<0.05$.

3. Results

The results of the research study showed that mutations were identified along the APC and MYC genes, which include missense, silent, deletion, and insertion mutations observed at various gene locations using the HGVSc, HGVSp, VAF (%) and Chromosome Positioning classification as shown in table 1, table 2 and table 3. The analysis indicates that mutations within the APC and MYC genes occur at varying frequencies in FA and IDA, suggesting potential roles in tumorigenesis. The observed

mutations include transitions, transversions, InDels, missense, and silent mutations, reflecting the genetic diversity and complexity of these breast lesions.

Figure 1 shows the pie charts of APC single nucleotide polymorphism (SNP) mutations frequency (A), APC functional mutations (B) and APC mutation frequencies in IDA and FA (C) respectively

Table 1. Clinical characteristics and data of patients

Specimen	Diagnosis	Age Range	Gender	Histological type	Confirmed mutation (s)
IDA	Invasive Ductal Adenocarcinoma	45-55	Female	Confirmed via H&E	APC, MYC
FA	Fibroadenoma	25-35	Female	Confirmed via H&E	APC, MYC

Figure 2 shows the pie charts of MYC SNP mutation frequencies (A), MYC functional mutations (B) and MYC mutation frequencies in FA and IDA (C) respectively.

4. Discussion

The mutation spectrum of *APC* and *MYC* in FA and IDA revealed some genetic alterations that contribute to tumor behavior and progession (Yang *et al*., 2022).

4.1. *APC* Gene and *MYC* Gene Mutation Patterns in IDA and FA

The results reveal an intricate profile of *APC* gene mutations in IDA specimens, characterized predominantly by transition mutations. This is similar to study by Ghatak *et al*., (2017) but at variance with Sousan *et al*., (2020). Notably, A transitions at codon 162 leading to the

Table 2. Summary table showing the effect of mutation along *APC* Gene

Gene	Specimen	Mutation type	HGVSc	HGVSp	VAF (%)	Chromosome position
APC	IDA	Transition	c. 162A>G	p.Asn54Ser	70	Chr5:112175
APC	IDA	Transition	c. 573G>A	p.Ala191Thr	80	Chr5:112586
APC	FA	Transition	c. 625T>C	p.Tyr208Tyr	20	Chr5:112638
APC	IDA	Transition	c. 765A>G	p.Glu255Gly	90	Chr5:112778
APC	FA	Transition	c. 902C>T	p.Pro301Ser	60	Chr5:112915

Table 3. Summary table showing the effects of mutation along *MYC* gene

Gene	Specimen	Mutation type	HGVSc	HGVSp	VAF (%)	Chromosome position
MYC	IDA	Indel	c. 171insC	p.Asp57Asn	90	Chr8:128751
MYC	IDA	Indel	c. 609insG	p.Ala203Thr	90	Chr8:129189
MYC	IDA	Transversion	c. 229T>A	p.Cys77Ser	90	Chr8:128809
MYC	FA	Silent	c. 463C>G	p.Leu155Leu	40	Chr8:129043
MYC	IDA	Transition	c. 589G>A	p.Ala197Thr	90	Chr8:129169
MYC	IDA	Transition	c. 733G>A	p.Ala245Thr	90	Chr8:129313

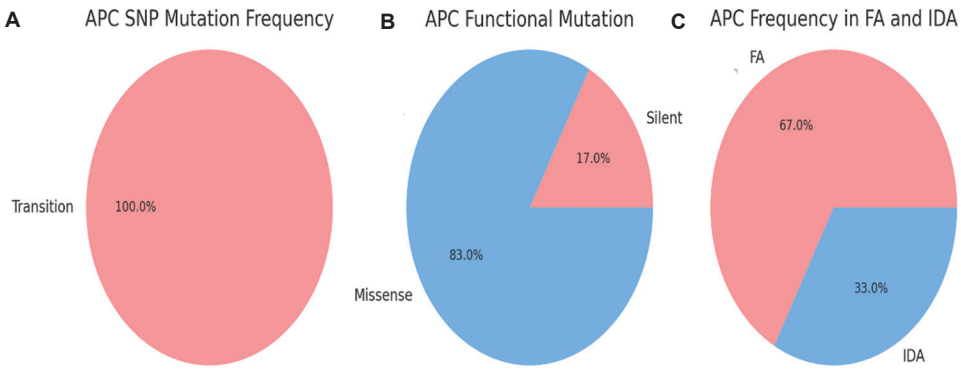

Figure 1. (A-C) Pie charts of APC single nucleotide polymorphism (SNP) mutations in fibroadenoma (FA) and invasive ductal adenocarcinoma (IDA) showed 100% transition, APC functional mutations in FA and IDA were 17% silent and 83% missense and APC mutation frequencies revealed 33% in IDA and 67% in FA respectively

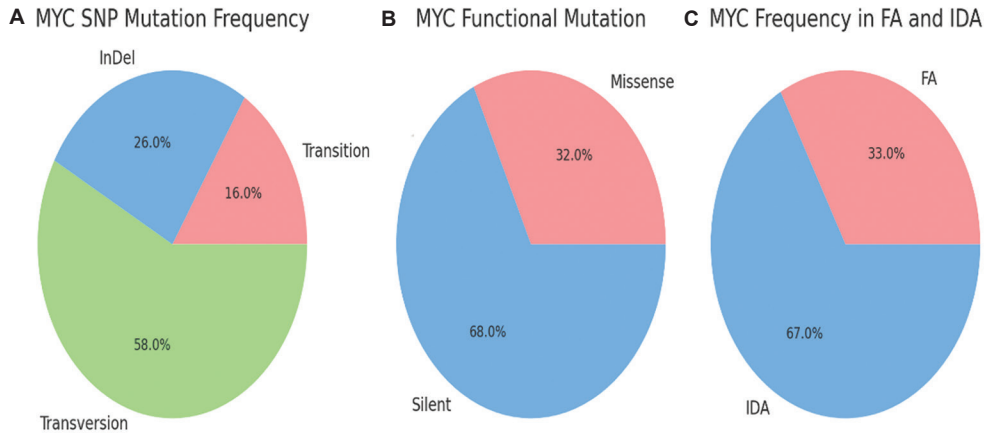

Figure 2. (A-C) Pie charts of MYC SNP mutation frequencies in FA AND IDA showing 16% transition, 26% InDel and 58% transversion, MYC functional mutations in FA and IDA which shows 32% missense mutation and 68% silent mutation and MYC mutation frequencies showing 33% in FA and 67% in IDAs respectively

substitution of asparagine with serine, and G transitions at codon 573 causing alanine to threonine changes, were recurrent findings. These missense mutations are critical as they result in non-synonymous substitutions that can alter the conformation and functionality of the *APC* protein. Such alterations may compromise its tumor-suppressive capabilities, promoting β-catenin accumulation and subsequent transcriptional activation of oncogenic pathways, as suggested by studies on aberrant Wnt signaling in cancer (Erazo-Oliveras *et al*., 2023). The mutation at codon 765, leading to glutamate-to-glycine substitution, further supports the potential disruption in *APC*'s interaction with other cellular proteins such as axin and GSK-3β, crucial for β-catenin degradation. This molecular impairment can lead to unchecked cellular proliferation, facilitating malignant transformation in IDA, aligning with research showing that missense mutations in tumor suppressor genes are strongly associated with invasive cancer phenotypes (Zhang *et al*., 2022).

In FA lesions, the mutation profile in *APC* was predominantly silent, exemplified by the T transition at codon 625. This is in agreement with Faranak *et al*., (2021) in a clinical laboratory analysis which demonstrated the nature and effect of *APC* gene mutation in familial adenomatous polyposis (FAP) tumorigenesis. The silent nature of these mutations indicates a lower pathogenic potential, consistent with FA's benign histological classification. However, the presence of these silent mutations suggests potential genomic instability, which could predispose the tissue to further mutations under stress or during cellular aging (Rahbari *et al*., 2015). The sporadic missense mutations observed, such as the C transition at codon 902 leading to proline-to-serine substitution, suggest that although these may not drive tumorigenesis, they might be an early indicator of genomic alteration preceding malignancy.

The *MYC* gene analysis in IDA samples showcased various mutation types, including indels and transversions. Indels, such as insertions at codon 609 (resulting in alanine insertion) and deletions at codon 231 (cysteine deletion), highlight the dynamic genomic instability seen in invasive carcinomas. Insertions or deletions (indels), such as those observed in inflammatory breast cancer, can disrupt the reading frame or introduce aberrant amino acids, producing truncated or nonfunctional MYC proteins, thereby perturbing its downstream transcriptional programs and promoting oncogenesis (Rypens *et al*., 2021). Moreover, mutations that affect the MYC-MAX interaction interface—such as those targeted by recently developed inhibitors—demonstrate that structural disruption of MYC-MAX dimerization reduces binding affinity and impairs oncogenic transcriptional activation, underscoring the functional significance of such mutations in contributing to malignancy (Yıldırım *et al*., 2024). These findings align with literature that describes the role of *MYC* mutations in enhancing transcriptional activity, promoting oncogenic transformation, and contributing to poor prognosis in invasive breast cancer (Schaub *et al*., 2018). The FA sample displayed a mutation profile in *MYC* skewed towards silent mutations (68%), indicative of mutations that do not alter the protein's coding potential. The predominant silent transversions, such as the G change at codon 463, reflect a lower likelihood of contributing to oncogenesis, which agrees with Xu-Monette *et al*., (2016). How ever, the presence of missense mutations, such as the G transition at codon 733, demonstrates that benign tumors can possess mutations that may serve as molecular

precursors for more aggressive alterations under oncogenic stimuli (Siegel *et al*., 2019).

A comparison between FA and IDA highlighted that the mutation frequency was higher in FA (67%) compared to IDA (33%). This counterintuitive finding may reflect a broader range of non-functional mutations in FA, whereas IDA harbors fewer but more impactful, pathogenic mutations. This observation aligns with current literature stating that benign lesions often carry a variety of genetic alterations that do not necessarily confer an advantage for cancer progression but signal potential vulnerability (Jones *et al*., 2020), while *MYC* mutations were more frequent in IDA, consistent with its role as a potent oncogene in breast cancer progression. The high incidence of indels and transversions in IDA supports the hypothesis that *MYC* mutations contribute to genetic instability and the tumor's capacity for adaptation and survival in a hostile microenvironment (Koh *et al*., 2016). A functional breakdown of the mutations revealed that 83% of the mutations in IDA were missense, contrasted with 17% silent mutations, reinforcing the concept that missense mutations in *APC* contribute significantly to the malignancy's invasive nature. Missense mutations impact the protein's structural integrity, likely leading to the disruption of the tumor suppressor role of *APC,* this is supported by studies indicating that the loss of *APC* function promotes the stabilization and nuclear translocation of β-catenin, a central player in oncogenic transcriptional programs (Zhang *et al*., 2024). In IDA, missense mutations constituted 32% of *MYC* mutations, indicative of a direct role in modifying protein function. The presence of mutations causing substitutions, such as alanine to threonine at codon 589, can impact the protein's interaction with transcriptional co-factors and DNA binding, enhancing its oncogenic potential (Zhou *et al*., 2022). Silent mutations, although deemed non-pathogenic, could still influence splicing or mRNA stability, contributing to *MYC* overexpression, a common occurrence in breast cancer linked to aggressive behavior.

Also, the counterintuitive result in the FA and IDC can be of technical factors like the small sample size, biological explanations like such as FA harbors a wider range of low-impact or "passenger" mutations that accumulate during benign proliferation but do not confer selective growth advantages, and the absence of matched normal controls sample to help distinguish somatic mutations from rare germline polymorphisms.

4.2. Functional Implications of APC and MYC Mutations

The functional breakdown of mutations revealed that 83% of APC mutations in IDA were missense, compared to only 17% silent mutations. This strongly supports reinforcing the concept that missense mutations in APC contribute significantly to the malignancy's invasive nature. This is supported by more recent work showing that truncating APC mutations disrupt the β-catenin destruction complex (by interfering with Axin-mediated condensate formation), thereby inhibiting β-catenin phosphorylation and degradation, leading to its stabilization and nuclear accumulation. (Zhang *et al*., 2024). Similarly, in IDA, 32% of MYC mutations were missense, suggesting direct disruption of MYC's transcriptional control mechanisms. Notably, amino acid substitutions such as alanine-to-threonine at codon 589 may enhance MYC's interaction with transcriptional co-factors, promoting tumor progression (Zhou *et al*., 2022). While silent mutations were more common in FA, they may still influence mRNA stability or splicing, indirectly contributing to MYC overexpression—a known driver of aggressive breast cancer behavior.

5. Conclusion

The observed mutations in *APC* and *MYC* genes across FA and IDA highlight crucial insights into their roles in breast tissue tumorigenesis. The *APC*'s involvement in IDA underscores the loss of tumor-suppressive functions through missense mutations that likely promote cellular pathways leading to invasion and metastasis. While in *MYC* mutations, particularly in IDA, align with its role in enhancing oncogenic pathways through complex mutations that disrupt normal cellular controls and drive malignancy. The contrasting mutation frequencies between FA and IDA for both genes may indicate that while benign tumors harbor a variety of mutations, invasive tumors possess targeted genetic changes with higher pathogenic potential. The mutational spectrum of *APC* and *MYC* in FA and IDA reveals critical differences in genetic alterations that contribute to tumor behavior. IDA is more diverse and functionally significant mutation profile suggests a stronger association with aggressive tumor characteristics, whereas FA, despite carrying mutations, predominantly harbors non-pathogenic changes. These findings underscore the importance of further genomic and proteomic studies to elucidate the roles of these mutations in breast cancer progression, potentially guiding targeted therapeutic strategies for more precision in the management of breast cancer disease.

6. Limitation and Recommendation

This study is a small, pilot investigation (n = 10) and therefore was underpowered to detect low-frequency variants or to provide robust estimates of mutation prevalence. The small sample size increases the risk of

sampling bias and limits generalizability. Consequently, our findings are hypothesis-generating and require validation in larger cohorts with prospectively collected specimens and matched normal controls. Protein validation was not performed in the pilot study.

Matched normal controls were not available in this pilot and described our population-frequency filtering. No information on hormone receptor status, HER2 expression, or tumor grade.

A larger cohort of sample with information on hormone receptor status, should be considered for translating results to clinical care should be considered in future study. Protein validation is important and its recommended that IHC/proteomics approaches and the potential analyses, PolyPhen-2 and SIFT analysis that would link genotype to phenotype in a larger cohort. There is need for matched normal sampling for future validation.

Conflict of interest

The authors declare no conflict.

References

Aremu AO, Ekundina VO, Enye LA, Kehinde AO, Ogunlayi AC. Assessing the Diagnostic Impact of p53, p16, Retinoblastoma and bcl-2 Proteins in Human Papillomavirus-associated Squamous Cell Carcinoma of the Cervix. *Journal of Preventive, Diagnostic and Treatment Strategies in Medicine*. 2024;3(2):115-21.

Cortesi L, Rugo HS, Jackisch C. An overview of PARP inhibitors for the treatment of breast cancer. *Targeted oncology*. 2021 May;16(3):255-82.

Dang CV. *MYC* on the path to cancer. *Cell*. 2012;149(1):22-35.

Duffy MJ, O'Grady S, Tang M, Crown J. *MYC* as a target for cancer treatment. *Cancer treatment reviews*. 2021;94:102154.

Ekundina VO, Kehinde AO, Azuh OV, Okah S. Retinoblastoma (Rb) and Kirsten Rat Sarcoma Viral Oncogene Homolog (Kras) Mutation Signature in Fibroadenoma and Invasive Adenocarcinoma of the Breast. *International Journal of Forensic Medical Investigation*. 2023;9(1).

Erazo-Oliveras A, Muñoz-Vega M, Mlih M, Thiriveedi V, Salinas ML, Rivera-Rodríguez JM, Kim E, Wright RC, Wang X, Landrock KK, Goldsby JS. Mutant APC reshapes Wnt signaling plasma membrane nanodomains by altering cholesterol levels via oncogenic β-catenin. *Nature Communications*. 2023;14(1):4342.

Gallas AE, Morenikeji GO, King RE, Adegbaju MS, Ayoola A, Taiwo G, Morenikeji OB. An Overview of Invasive Ductal Carcinoma (IDC) in Women's Breast Cancer. *Current Molecular Medicine*. 2025; 25(4):31-371.

García-Gutiérrez L, Bretones G, Molina E, Arechaga I, Symonds C, Acosta JC, Blanco R, Fernández A, Alonso L, Sicinski P, Barbacid M. *MYC* stimulates cell cycle progression through the activation of Cdk1 and phosphorylation of p27. *Scientific reports*. 2019;9(1):18693.

Ghatak S, Chakraborty P, Sarkar SR, Chowdhury B, Bhaumik A, Kumar NS. Novel *APC* gene mutations associated with protein alteration in diffuse type gastric cancer. *BMC Medical Genetics*. 2017;18:1-1.

Gupta N. DNA extraction and polymerase chain reaction. *Journal of cytology*. 2019;36(2):116-7.

Jones RH, Casbard A, Carucci M, Cox C, Butler R, Alchami F, Madden TA, Bale C, Bezecny P, Joffe J, Moon S. Fulvestrant plus capivasertib versus placebo after relapse or progression on an aromatase inhibitor in metastatic, oestrogen receptor-positive breast cancer (FAKTION): a multicentre, randomised, controlled, phase 2 trial. *The Lancet Oncology*. 2020;21(3):345-57.

Kehinde AO, Ekundina VO, Iyiola S, Avwioro G, Enye LA. Synergistic Nutraceutical Effects of Aqueous Extracts from Vernonia amygdalina and Moringa oleifera: A Promising Therapeutic Strategy for Gastric Ulcer Management. *Journal of Preventive, Diagnostic and Treatment Strategies in Medicine*. 2024 3(4):296-302.

Kehinde AO, Olukayode EV, Akinpelu M, & Oluwaseun OO. MicroRNAs in personalized medicine: Targeted therapeutic interventions and their emerging role as non-invasive biomarkers in cancer biology. International *Journal of Biological & Medical Research*, 2025, 16(1), 7974–7979.

Kiljańczyk A, Matuszczak M, Marciniak W, Derkacz R, Stempa K, Baszuk P, Bryśkiewicz M, Lubiński K, Cybulski C, Dębniak T, Gronwald J. Blood lead level as marker of increased risk of ovarian Cancer in BRCA1 carriers. *Nutrients*. 2024;16(9):1370.

Lourenco C, Resetca D, Redel C, Lin P, MacDonald AS, Ciaccio R, Kenney TM, Wei Y, Andrews DW, Sunnerhagen M, Arrowsmith CH. *MYC* protein interactors in gene transcription and cancer. *Nature Reviews Cancer*. 2021;21(9):579-91.

Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast cancer—epidemiology, risk factors, classification, prognostic markers, and current treatment strategies—an updated review. *Cancers*. 2021 Aug 25;13(17):4287.

Olukayode EV, Olajide KA, Preye MG. The study of mutations of CDK4 and TP53 genes in selected breast lesions. Sokoto *Journal of Medical Laboratory Science*. 2023 May 29;8(1).

Rypens C, Bertucci F, Viens P, Martens JW, Smid M, Schröder C, Ueno NT, Cristofanilli M, Dirix P, Vermeulen P, Dirix L. Abstract P3-03-03: Inflammatory breast cancer exhibits amplification and transcriptional activation of MYC in conjunction with NOTCH and TGFβ signaling. *Cancer Research*. 2020;80(4):P3-03.

Schaub FX, Dhankani V, Berger AC, Trivedi M, Richardson AB,

Shaw R, Zhao W, Zhang X, Ventura A, Liu Y, Ayer DE. Pan-cancer alterations of the *MYC* oncogene and its proximal network across the cancer genome atlas. *Cell systems*. 2018;6(3):282-300.

Shi Y, Wu Y, Li F, Jiang K, Fang X, Wang Y, Song X, Wang R, Chen L, Zheng J, Wu C. Investigating the immunogenic cell death-dependent subtypes and prognostic signature of triple-negative breast cancer. Phenomics. 2024;4(1):34-45.

Sun YS, Zhao Z, Yang ZN, Xu F, Lu HJ, Zhu ZY, Shi W, Jiang J, Yao PP, Zhu HP. Risk factors and preventions of breast cancer. *International journal of biological sciences*. 2017;13(11):1387.

Virga A, Gianni C, Palleschi M, Angeli D, Merloni F, Maltoni R, Ulivi P, Martinelli G, De Giorgi U, Bravaccini S. A Novel AKT1, ERBB2, ESR1, KRAS, PIK3CA, and TP53 NGS Assay: A Non-Invasive Tool to Monitor Resistance Mechanisms to Hormonal Therapy and CDK4/6 Inhibitors. *Biomedicines*. 2024 Sep 26;12(10):2183.

Wang XH, Fu YL, Xu YN, Zhang PC, Zheng TX, Ling CQ, Feng YL. Ginsenoside Rh1 regulates the immune microenvironment of hepatocellular carcinoma via the glucocorticoid receptor. *Journal of Integrative Medicine*. 2024;22(6):709-18.

Wolf E, Eilers M. Targeting *MYC* proteins for tumor therapy. *Annual Review of Cancer Biology*. 2020;4(1):61-75.

Xiao W, Zhang G, Chen B, Chen X, Wen L, Lai J, Li X, Li M, Liu H, Liu J, Han-Zhang H. Characterization of frequently mutated cancer genes and tumor mutation burden in Chinese breast cancer. *Frontiers in Oncology*. 2021;11:618767.

Xu H, Xu B. Breast cancer: Epidemiology, risk factors and screening. *Chinese Journal of Cancer Research*. 2023 Dec 30;35(6):565.

Xu-Monette ZY, Deng Q, Manyam GC, Tzankov A, Li L, Xia Y, Wang XX, Zou D, Visco C, Dybkær K, Li J. Clinical and biologic significance of *MYC* genetic mutations in de novo diffuse large B-cell lymphoma. *Clinical Cancer Research*. 2016;22(14):3593-605.

Yang PS, Chao YT, Lung CF, Liu CL, Chang YC, Li KC, Hsu YC. Association of Pathway Mutations with Survival in Taiwanese breast cancers. *Frontiers in Oncology*. 2022; 12:819555.

Yıldırım S, Kocabaş F, Mermer A. Development, synthesis and validation of improved c-Myc/Max inhibitors. *Journal of Cellular and Molecular Medicine*. 2024 Apr;28(8):e18272.

Yuan S, Almagro J, Fuchs E. Beyond genetics: driving cancer with the tumour microenvironment behind the wheel. *Nature Reviews Cancer*. 2024 Apr;24(4):274-86.

Zhang D, Ni QQ, Wang SY, He WF, Hong ZX, Liu HY, Chen XH, Chen LJ, Han FY, Zhang LJ, Li XM. APC mutations disrupt β-catenin destruction complex condensates organized by Axin phase separation. *Cellular and Molecular Life Sciences*. 2024 Dec;81(1):57.

Zhou S, Liu S, Zhao L, Sun HX. A comprehensive survey of genomic mutations in breast cancer reveals recurrent neoantigens as potential therapeutic targets. *Frontiers in Oncology*. 2022;12:786438.