JOURNAL OF CANCER THERAPEUTICS AND IMMUNOTHERAPY
Jan-Jun 2025, VOL. 2, ISSUE 1, pp. 10-12
https://doi.org/10.61577/jctai.2025.100003

RESEAPRO JOURNALS

MINI REVIEW

OPEN ACCESS

Decoding ovarian cancer: Inheritable mutations, clinical impact, and inventions in treatment

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ABSTRACT

Ovarian cancer is a largely murderous gynecologic malice, with inheritable and molecular mutations playing a vital part in its pathogenesis and progression. This composition explores the crucial inheritable mutations associated with ovarian cancer, including BRCA1, BRCA2, and other less common but significant mutations similar as TP53, PTEN, and KRAS. The focus is on understanding how these mutations contribute to excrescence development, treatment resistance, and prognostic. Advances in inheritable testing and targeted curatives, including PARP impediments, have converted the operation of ovarian cancer, offering individualized treatment options and bettered issues. Ethical considerations, similar as inheritable comforting and threat operation for carriers, are also bandied. This review aims to give a comprehensive overview of the molecular underpinnings of ovarian cancer mutations and their clinical counteraccusations.

KEYWORDS

Prognosis; Genetic counseling; Tumor development; Ovarian cancer; BRCA1

ARTICLE HISTORY

Received 29 March 2025;
Revised 24 April 2025;
Accepted 10 May 2025

Introduction

Ovarian cancer ranks among the most aggressive gynecologic cancers, frequently diagnosed at an advanced stage due to nonspecific symptoms and the lack of effective early webbing styles. Encyclopedically, it accounts for significant morbidity and mortality, with epithelial ovarian cancer being the most common histological subtype [1]. Inheritable mutations, both inherited and physical, have surfaced as critical motorists in the development and progression of ovarian cancer.

The discovery of the BRCA1 and BRCA2 mutations revolutionized our understanding of the heritable ovarian cancer threat. Still, posterior exploration has revealed a more complex geography of inheritable differences that impact excrescence biology, remedial responses, and patient issues [1,2]. This composition examines the major mutations intertwined in ovarian cancer, their mechanisms of action, and the clinical advancements they've prodded.

Genetic Mutations in Ovarian Cancer

BRCA1 and BRCA2 mutations

BRCA1 and BRCA2 are excrescence suppressor genes involved in DNA form via homologous recombination. Germline mutations in these genes are responsible for roughly 10- 15 of all ovarian cancer cases [2]. Women with BRCA1 mutations have a continuance threat of 39- 44 for developing ovarian cancer, while BRCA2 mutations confer a threat of 11- 17.

BRCA- shifted excrescences frequently parade imperfect DNA form, making them largely sensitive to platinum- grounded chemotherapy and poly (ADP- ribose) polymerase (PARP) impediments. The development of PARP impediments, similar as olaparib and niraparib, has marked a significant remedial corner for cases with BRCA- shifted ovarian cancer [3].

TP53 mutations

TP53, an excrescence suppressor gene, is shifted in further than 90 of high- grade serous ovarian lymphomas (HGSOC), the most common and aggressive subtype [3,4]. TP53 mutations disrupt the regulation of cell cycle arrest and apoptosis, leading to unbridled excrescence growth. The high frequency of TP53 mutations underscores their part in the pathogenesis of ovarian cancer and highlights the need for targeted remedial strategies [4,5].

Lynch syndrome and mismatch form genes

Lynch pattern, an inherited condition caused by mutations in mismatch form (MMR) genes similar as MLH1, MSH2, MSH6, and PMS2, is associated with a 10- 12 continuance threat of ovarian cancer [6]. These mutations affect microsatellite insecurity (MSI), a hallmark of imperfect DNA form mechanisms. MSI-high ovarian excrescences are implicit campaigners for immunotherapy using vulnerable checkpoint impediments, similar as pembrolizumab [6,7].

KRAS and BRAF mutations

KRAS and BRAF mutations are more constantly observed in low- grade serous ovarian lymphomas (LGSOC). These mutations spark the MAPK signaling pathway, promoting cell proliferation and survival [8,9]. While these mutations are less common in high- grade serous ovarian cancer, their presence in LGSOC has counteraccusations for targeted curatives, including MEK impediments [4,9].

PTEN and PI3K/ AKT pathway mutations

PTEN mutations and differences in the PI3K/ AKT pathway are associated with endometrioid and clear cell ovarian lymphomas [3]. These mutations contribute to tumorigenesis by dysregulating cell growth, survival, and metabolism. PI3K/ AKT/ mTOR impediments are under disquisition as implicit treatments for these subtypes (table 1) [10].

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Table 1. The genetic mutations and their significance in ovarian cancer research and treatment

Gene	Mutation Type	Associated Ovarian Cancer Type	Function	Clinical Implications
BRCA1	Germline/ Somatic Mutation	High-grade Serous	DNA repair via homologous recombination	Increased sensitivitytoPARP inhibitors, increased risk for hereditarycancer syndromes
BRCA2	Germline/ Somatic Mutation	High-grade Serous	DNA repair via homologous recombination	Like BRCA1: PARP inhibitors, prognosis implications
TP53	Somatic Mutation	High-grade Serous	Tumor suppressor, apoptosis regulation	Universal in high-grade serous, associated with poor prognosis
KRAS	Somatic Mutation	Mucinous	RAS/MAPK signaling pathway activation	Targetable with emerging inhibitors in certain cases
ARID1A	Somatic Mutation	Clear Celland Endometrioid	Chromatin remodeling	Potential target for epigenetic therapies
PIK3CA	Somatic Mutation	Clear Cell and Endometrioid	PI3K/AKT/mTOR pathway activation	Targetable with PI3K or mTOR inhibitors
BRAF	Somatic Mutation	Low-grade Serous	MAPK signaling pathway	Rare inhigh-grade, targetable with BRAF inhibitors
NRAS	Somatic Mutation	Low-grade Serous	RAS/MAPK signaling pathway	Limited therapeutic options currently

Advancements in genetic testing and targeted therapies

The identification of genetic mutations has led to significant advancements in ovarian cancer management:

Genetic testing

Comprehensive panels now enable the detection of BRCA1/2 and other actionable mutations. Testing is recommended for all women with ovarian cancer, as well as individuals with a family history of the disease [11,12].

Targeted therapies

The advent of PARP inhibitors has transformed the treatment landscape for BRCA-mutated ovarian cancer. Additionally, therapies targeting the PI3K/AKT/mTOR pathway, immune checkpoint inhibitors, and MEK inhibitors are expanding options for patients with non-BRCA mutations [13].

Clinical and ethical considerations

Risk assessment and genetic counseling

For individuals with a family history of ovarian cancer, genetic counseling is crucial for risk assessment and decision-making regarding preventive measures, such as prophylactic salpingo-oophorectomy [14]. Counseling also addresses the psychological impact of genetic testing.

Ethical and privacy issues

The integration of genetic data into clinical practice raises concerns about privacy, discrimination, and informed consent [15-17]. Healthcare providers must navigate these challenges while ensuring equitable access to testing and treatment.

Conclusion

Ovarian cancer is a genetically diverse disease, with mutations in BRCA1, BRCA2, TP53, and other genes shaping its clinical behavior and therapeutic responses. Advances in genetic testing and targeted therapies have improved outcomes for many patients, particularly those with BRCA mutations. However, challenges remain in addressing non-BRCA mutations, treatment resistance, and equitable access to care. Ongoing research into the molecular underpinnings of ovarian cancer promises to expand the scope of precision medicine, offering hope for improved detection, treatment, and survival.

Disclosure Statement

No potential conflict of interest was reported by the authors.

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