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Review on Effects of Chemotherapy Efficacy in Breast Cancer

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Abstract

A mutation in a known hereditary breast cancer predisposition gene, such as BRCA1 or BRCA2.1, is linked to between 5% and 10% of the 2.3 million breast cancer cases diagnosed annually2. The integration of genomics into the standard diagnostic pathways for breast cancer patients and the availability of targeted treatment approaches for those with hereditary breast cancer predisposition genes are two examples of the effects that chemotherapy has on breast cancer efficacy. These patients now require a different approach to care than they did a decade ago because of mutations. The most recent advances in systemic treatment for hereditary breast cancer are discussed in this review, as well as the challenges that must be overcome in the future to improve clinical outcomes for this particular subgroup.

Keywords: Breast cancer; Chemotherapy; Germline mutations

Introduction

BRCA, BRCA2, PALB2, ATM, CHEK2, and p53.3 are examples of "caretaker" tumor suppressor genes, which are genes whose normal function is to maintain the integrity of the genome but whose dysfunction leads to genome instability. Osteopenia Bone mineral density Anastrozole Risedronate Breast cancer risk, These genes are involved in a lot of the germline mutations that are linked to hereditary breast cancer. For instance, carriers of germline deleterious mutations in BRCA1 or BRCA2 (gBRCA2m), which play important roles in gBRCA1m carriers, typically have the basal-like, triple negative (B-L, TNBC) subtype of breast cancer when they are diagnosed, with a cumulative risk of 46% to 60% over the course of one's lifetime [1-3]. GBRCA1/2m breast cancers in people with a strong family history are typically detected at a younger age than sporadic breast cancers when compared to gBRCA1m carriers. Germline pathogenic variants in PALB2, a partner and localizer of BRCA2 that is also involved in DNA repair by HR, were first linked to an increased risk of cancer in 2007.10 In 2014, Antoniou and colleagues found that patients with gPALB2m had a 35% cumulative risk of developing breast cancer by the time they were 70 years old. Carriers of gBRCA2m have a tendency to develop estrogen receptor-positive (ER1) luminal B subtype breast cancers.6– This study included 51 men, seven of whom also had breast cancer, and 311 women with gPALB2m, 229 of whom also had the disease.

Method

In this context, the term "penetrance" refers to the likelihood that a particular genotype, such as gBRCA1m, will cause a related phenotype (breast cancer). The genes BRCA1, BRCA2, and PALB2 are frequently thought to be high-penetrance susceptibility genes for breast cancer. Additionally, the TP53 tumor suppressor, which is encoded by p53, is a hereditary susceptibility gene for high-particle breast cancer; The caretaker genes ATM (Ataxia telangiectasia mutant) and CHEK2 are two genes that are less likely to spread breast cancer. TP53 also prevents genome instability in people with TP53 germline mutations and prevents uncontrolled cell division and the transmission of mutations to daughter cells. A person's lifetime risk of developing breast cancer is between 25% and 30% if they have germline deleterious mutations in either ATM or CHEK2.

Materials and procedures The proteins BRCA1, BRCA2, and PALB2 encode are all essential to the HR process and play a role in the DNA damage response (DDR). When a sister chromatid that is readily available is used as a DNA repair template, HR, a highly conserved, error-free DDR pathway, is triggered by the detection of double-stranded DNA breaks (DSBs) and stalled DNA replication forks. When DNA damage is detected, the checkpoint kinase ATM is activated, triggering a series of protein phosphorylation events that bring BRCA1 to the damage site. BRCA1 brings the MRN complex, which includes MRE11, RAD50, and NBN, to the site of damage. After that, the MRN complex divides the DNA on either side of the DSB, leaving behind three single-stranded overhangs of DNA that the RPA protein binds to. PALB2 and BRCA1 are required for the loading process of BRCA2. RAD51, a DNA recombinase, has 30 single-stranded overhangs [4], displacing RPA. After that, the DNA/RAD51 nucleoprotein filament invades the double helix of the homologous DNA strand by utilizing RAD51's ATPase activity. Following the use of this double helix as a template for the synthesis of DNA, error-free DNA repair occurs (Fig. 1)15 Loss of function mutations in BRCA1, BRCA2, or PALB2 cause defects in this process, which has led to an increase in the use of nonconservative DNA repair techniques. These nonconservative DNA repair pathways likely promote tumorigenesis by causing mutations in additional cancer driver genes [5].

Result

Tumor cells with HR defects, such as those with BRCA1 or BRCA2 mutations, exhibit sensitivity to drugs that cause DNA damage that eventually stalls or collapses replication forks in vitro (and occasionally in vivo); Examples of these include platinum-based chemotherapeutic agents, mitomycin C,17 bifunctional alkylating agents like melphalan or the cyclophosphamide metabolite phosphoramide mustard,18 topoisomerase II inhibitors, the DNA mi- and groove binding compounds lurbinectedin and trabectedin, and topoisomerases I inhibitors. Nedaplatin, lobaplatin, cisplatin, carboplatin, oxaliplatin, and others have been approved as five platinum chemotherapy analogs. The cytotoxic effects of carboplatin and cisplatin, the two most commonly used treatments for breast cancer, are largely attributable to the formation of platinum-containing molecular bonds between

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bases on the same DNA strand (interstrand cross-links) [6]. HR and nucleotide excision repair correct the distorted double helix caused by these cross-links. PARylation is the process by which PARP (Poly-(ADP Ribose) Polymerase) enzymes use NAD 1 to synthesize poly-(ADP- ribose) (PAR) chains on substrate proteins. PARP1, a protein that identifies damaged DNA, such as single double-strand breaks in the double helix and alkylated bases, is responsible for the majority of the PARylation events that take place in cells. given that platinum chemotherapy damages DNA [7].

Discussion

PARP1 binds to DNA using its zinc-finger (ZnF) domains at its N-terminus. The structure of PARP1 is altered, and its catalytic activity is triggered by this event. In general, PARP1's PARylation activity initiates DNA repair in two ways: PARP1 activity PARylates DNA repair proteins (including XRCC1) and histones, both of which enable DNA repair to be enabled.27 PARP1 auto- PARylates after DNA has been successfully repaired, concentrating DNA repair effectors at the site of the damage. The discovery of small molecule inhibitors of PARP1 and PARP2 (PARPi), which were initially intended to be utilized as chemo- or radiosensitizers, was based on the role that PARP1 (and its paralog PARP2) play in DNA repair.

Conclusion

In BRCA1/2-deficient tumor cells, this PARP1 trapping capacity appears to contribute more to tumor cell cytotoxicity than the ability to inhibit PARP1's catalytic activity. Clinically approved PARPi include olaparib, talazoparib, niraparib, and rucaparib. For instance, veliparib, an experimental PARPi, is a potent catalytic inhibitor, but it is less effective than other PARPi at capturing PARP1; In 2005, two independent research groups found that BRCA1 and BRCA2 deficient cells were profoundly sensitive to drug-like PARPi, both in vitro and in vivo.33,34 Later research found that other HR gene defects also caused profound PARPi sensitivity.35 These findings served as the preclinical basis for starting clinical trials to see if PARPi could be used as a single agent, synthetic, lethal treatment for HR-deficient cancers.

References

1. Lorraine E D, Norrie B (2009) An exploration of student nurses' experiences of formative assessment. Nurse Educ Today 29: 654-659.
2. Lambert W T S, Vleuten C P M (2011) Programmatic assessment: From assessment of learning to assessment for learning. Med Teach 33: 478-485.
3. David B, Elizabeth J F, Melinda A, Sara R C (2020) Covid-19 - implications for the health care system. N Engl J Med 383: 1483-1488,
4. Stroup D F, Berlin J A, Morton S C, Olkin I, Williamson G D, et al. (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Jama 283: 2008-2012.
5. Frank S H, Vanna C S, Gonzalez R, Jacques G, Piotr R et al. (2018) Nivolumab plus ipilimumab or nivolumab alone versus ipilimumab alone in advanced melanoma (CheckMate 067): 4-year outcomes of a multicentre, randomised, phase 3 trial. Lancet Oncol 19: 1480-1492.
6. Sarah B G, Scott N G, Amit M, Anne C C, Roy S H et al. (2016) Pembrolizumab for patients with melanoma or non-small-cell lung cancer and untreated brain metastases: early analysis of a non-randomised, open-label, phase 2 trial. Lancet Oncol 17: 976-983.
7. Janine M S, Julien G J, Joost P R, Maarten A B, Leandra J M B et al. (2021) Disease-free and overall survival after neoadjuvant chemotherapy in breast cancer: breast-conserving surgery compared to mastectomy in a large single-centre cohort study. Breast Canc Res Treat.185: 441-451.