# INTISARI

**Latar Belakang :** Sebanyak 7,8 juta wanita di seluruh menderita kanker payudara pada tahun 2020 dimana 15-20% dari total kasus merupakan *triple negative breast cancer* (TNBC) yang memiliki prognosis terburuk. Pasien TNBC berisiko mengalami resistensi yang menyebabkan kegagalan terapi pada 90% kasus. Resistensi PTX melibatkan berbagai jalur persinyalan dan regulasi berbagai onkogen namun belum dikaji secara mendalam. Teknologi modifikasi ekspresi gen kini memungkinkan peneliti untuk mengkaji efek onkogen terhadap karakteristik dan resistensi kanker. Maka dari itu, penelitian ini diharapkan dapat mengkaji studi-studi mengenai peran onkogen terhadap kemoresistensi paclitaxel.

**Metode:** Penelitian ini merupakan penelitian sekunder berupa *systematic review* berdasarkan PRISMA. Literatur dicari dari PubMed, Cochrane, Scopus, ScienceDirect, dan Google Scholar *hand search* dengan kata kunci *"Triple Negative Breast Cancer" AND "Knockout" OR "Knockdown" AND"Sensitivity" AND"Paclitaxel".* Seleksi studi dilakukan berdasarkan kriteria eligibilitas yang telah ditentukan. Studi terinklusi dinilai berdasarkan JBI *Critical Appraisal Tool.*

**Hasil:** Berdasarkan hasil seleksi artikel diperoleh 19 artikel dengan risiko bias rendah (rentang skor 8-9 poin). Berdasarkan studi tersebut, mekanisme utama yang mendasari resistensi PTX antara lain: (1) *transporter-mediated resistance* mencakup gen TMEPAI dan AURKB, (2) *cell cycle arrest dan apoptosis-mediated resistance* mencakup gen BRCA1-IRIS, PGK1, SERPINE1, PLS3, MITR, ADAM10, Pin1, eIF4E, dan HMGA1, (3) *epithelial-mesenchymal transition* (EMT) & cell *stemness-mediated resistance* mencakup gen JAG2, SOX2, LEMD1, GABRP, CYP1B1 (4) *Autophagy-mediated resistance* mencakup gen GBP dan eEF2K, (5) *Inflammation-mediated resistance* oleh gen TLR4. Sebanyak 13 studi menunjukkan modifikasi ekspresi onkogen dapat meningkatkan sensitivitas sel TNBC terhadap PTX, sedangkan 2 studi lainnya menurun. Sebanyak 3 studi menunjukkan perubahan aktivitas proliferasi, invasi, dan apoptosis pada sel TNBC pasca modifikasi ekspresi onkogen.

**Kesimpulan:** Modifikasi ekspresi onkogen memiliki pengaruh signifikan terhadap ekspresi mRNA yang terkait dengan kemoresistensi PTX pada sel TNBC melalui berbagai mekanisme. Modifikasi ekspresi onkogen juga berpengaruh signifikan terhadap sensitivitas sel, aktivitas proliferasi, invasi, dan apoptosis sel.

**Kata kunci :** *Triple Negative Breast Cancer,* Modifikasi Ekspresi Onkogen, Transkriptomik, Kemoresistensi

# ABSTRACT

**Background:** About 7.8 million women worldwide suffer from breast cancer in 2020, which 15-20% of the total cases are triple negative breast cancer (TNBC) with the worst prognosis than other subtypes. TNBC patients are at risk of developing resistance which causes therapy failure in 90% of cases. PTX resistance involves various signaling pathways and regulation of various oncogenes but has not been studied comprehensively. Gene expression modification technology now allows researchers to study the effects of oncogenes on cancer characteristics and resistance. Therefore, this research aims to review studies regarding the role of oncogenes in paclitaxel chemoresistance.

**Method:** This systematic review conducted based on PRISMA. Literature was searched from PubMed, Cochrane, Scopus, ScienceDirect, and Google Scholar hand search with the keywords "Triple Negative Breast Cancer" AND "Knockout" OR "Knockdown" AND "Sensitivity" AND "Paclitaxel". Study selection was carried out based on eligibility criteria. Included studies were assessed based on the JBI Critical Appraisal Tool.

**Results:** Based on the results of article selection, 19 articles were obtained with a low risk of bias (score range 8-9 points). Based on this study, the main mechanisms underlying PTX resistance include: (1) transporter-mediated resistance including the TMEPAI and AURKB genes, (2) cell cycle arrest and apoptosis-mediated resistance including the BRCA1-IRIS, PGK1, SERPINE1, PLS3, MITR genes , ADAM10, Pin1, eIF4E, and HMGA1, (3) epithelial-mesenchymal transition (EMT) & cell stemness-mediated resistance includes the JAG2, SOX2, LEMD1, GABRP, CYP1B1 genes (4) Autophagy-mediated resistance includes the GBP and eEF2K genes, (5) Inflammation-mediated resistance by the TLR4 gene. A total of 13 studies showed that modification of oncogene expression could increase the sensitivity of TNBC cells to PTX, while in 2 other studies shows otherwise. In addition, 3 studies showed changes in proliferation, invasion and apoptosis activities in TNBC cells after modification of oncogene expression.

**Conclusion:** Modification of oncogene expression has a significant influence on the expression of mRNA associated with PTX chemoresistance in TNBC cells through various mechanisms. Modification of oncogene expression also has a significant effect on cell sensitivity, proliferation activity, invasion and cell apoptosis.

**Keywords:** Triple Negative Breast Cancer, Modification of Oncogene Expression, Transcriptomics, Chemoresistance