

## INTISARI

**Latar belakang:** Pada pasien kanker payudara yang menerima terapi tamoxifen, ekspresi *GPER-1* dikaitkan dengan resistensi obat dan penurunan kelangsungan hidup bebas kekambuhan (*relapse-free survival/RFS*). Aktivasi *GPER-1* oleh tamoxifen memicu jalur pensinyalan non-genomik melalui PI3K/AKT dan MAPK, yang diduga berperan dalam induksi *epithelial-mesenchymal transition* (EMT). EMT ditandai dengan peningkatan ekspresi *SNAI1* (Snail) dan penurunan *CDH1* (E-cadherin), serta berkontribusi terhadap fenotip sel yang lebih migratorik dan invasif. Deteksi resistensi umumnya terjadi pada tahap lanjut ketika perubahan molekuler bersifat *irreversibel*, sehingga penting untuk dilakukan identifikasi mekanisme awal seperti aktivasi EMT. Penelitian ini mengevaluasi respons seluler pada fase awal paparan tamoxifen untuk mengungkap dinamika awal proses EMT yang terlibat dalam resistensi terapi.

**Tujuan:** Penelitian ini bertujuan untuk mengetahui efek pemberian tamoxifen *citrate* terhadap ekspresi mRNA *GPER-1*, *SNAI1*, dan *CDH1* sebagai penanda EMT pada sel kanker payudara MCF-7.

**Metode:** Sel MCF-7 ditumbuhkan dalam media (DMEM +10% FBS) kemudian diberi perlakuan tamoxifen dengan konsentrasi 17,26  $\mu\text{M}$  selama 48 jam. Setelah perlakuan, RNA total diekstraksi, disintesis menjadi cDNA, dan selanjutnya dianalisis ekspresi gen *GPER-1*, *SNAI1*, dan *CDH1* menggunakan metode qRT-PCR, dengan  $\beta$ -*actin* sebagai gen kontrol internal. Analisis ekspresi gen dilakukan menggunakan metode  $2^{-\Delta\Delta\text{Ct}}$ , dan perbedaan antar kelompok dianalisis menggunakan uji *Independent T-test* dengan nilai  $p < 0,05$  dianggap signifikan.

**Hasil:** Ekspresi mRNA *GPER-1* signifikan ( $p < 0,05$ ) lebih tinggi pada kelompok tamoxifen ( $1,58 \pm 0,05$ ) dibandingkan kelompok kontrol ( $1,01 \pm 0,20$ ). Ekspresi mRNA *SNAI1* pada kelompok tamoxifen ( $3,96 \pm 0,15$ ) lebih tinggi secara signifikan ( $p < 0,05$ ) dibandingkan dengan kelompok kontrol ( $1,00 \pm 0,04$ ). Demikian pula, ekspresi mRNA *CDH1* signifikan ( $p < 0,05$ ) lebih tinggi pada kelompok tamoxifen ( $2,26 \pm 0,39$ ) dibandingkan dengan kelompok kontrol ( $1,00 \pm 0,04$ ).

**Kesimpulan:** Ekspresi mRNA *GPER-1*, *SNAI1* dan *CDH1* signifikan lebih tinggi setelah paparan tamoxifen *citrate* pada lini sel kanker payudara MCF-7 yang mengarah pada dugaan bahwa EMT masih dalam tahap inisiasi.

**Kata Kunci:** Kanker payudara, *GPER-1*, *SNAI1*, *CDH1*, Tamoxifen, EMT

## ABSTRACT

**Background :** *In breast cancer patients receiving tamoxifen therapy, GPER-1 expression has been associated with drug resistance and reduced relapse-free survival (RFS). Activation of GPER-1 by tamoxifen initiates non-genomic signaling pathways, particularly through PI3K/AKT and MAPK, which are thought to contribute to the induction of epithelial–mesenchymal transition (EMT). EMT is characterized by increased expression of SNAI1 (Snail) and decreased expression of CDH1 (E-cadherin), and contributes to a more migratory and invasive cellular phenotype. Resistance is typically detected at a later stage when molecular alterations become irreversible, highlighting the importance of identifying early mechanisms such as EMT activation. This study evaluates cellular responses during the early phase of tamoxifen exposure to reveal the initial dynamics of therapy resistance.*

**Objective:** *This study aimed to investigate the effect of 48-hour tamoxifen exposure on the mRNA expression levels of GPER-1, SNAI1, and CDH1 as markers of EMT in MCF-7 breast cancer cells.*

**Methods:** *MCF-7 cells were cultured in DMEM supplemented with 10% FBS, then treated with 17.26  $\mu$ M tamoxifen for 48 hours. Total RNA was extracted, converted into cDNA, and the expression of GPER-1, SNAI1, and CDH1 was analyzed using quantitative real-time PCR (qRT-PCR), with  $\beta$ -actin as the internal control gene. Gene expression was calculated using the  $2^{-\Delta\Delta C_t}$  method, and differences between groups were analyzed using the Independent T-test with a significance level of  $p < 0.05$ .*

**Results:** *The mRNA expression of GPER-1 was significantly higher ( $p < 0.05$ ) in the tamoxifen-treated group ( $1.58 \pm 0.05$ ) compared to the control group ( $1.01 \pm 0.20$ ). Similarly, the mRNA expression of SNAI1 was significantly elevated ( $p < 0.05$ ) in the tamoxifen group ( $3.96 \pm 0.15$ ) relative to the control group ( $1.00 \pm 0.04$ ). In addition, the mRNA expression of CDH1 was also significantly higher ( $p < 0.05$ ) in the tamoxifen-treated group ( $2.26 \pm 0.39$ ) compared to the control group ( $1.00 \pm 0.04$ ).*

**Conclusion:** *The mRNA expression levels of GPER-1, SNAI1, and CDH1 were significantly higher following 48 hours of tamoxifen citrate exposure in MCF-7 breast cancer cells suggesting that EMT may still be in its initiation stage.*

**Keywords:** *Breast cancer, GPER-1, SNAI1, CDH1, Tamoxifen, EMT*