# Peran TMEPAI (Transmembrane Prostate Andorgen-Induced) yang diinduksi TGF-pada resistensi sel kanker payudara triple-negative terhadap doksorubisin = The role of  TGF-Î²-induced TMEPAI (transmembrane prostate androgen-induced) in the resistance of triple negative breast cancer cell to doxorubicin

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Abstrak

Latar belakang: Terapi farmakologi kanker payudara triple negative (KPTN) terbatas pada obat sitostatika seperti doksorubisin. Namun, resistensi doksorubisin sulit dihindari. Salah satu jalur pensinyalan yang penting pada resistensi KPTN terhadap doksorubisn adalah TGF-β. TMEPAI (transmembran prostat androgen-induced protein), regulator negatif sekaligus gen target pada jalur TGF-β diduga merupakan salah satu kunci dalam resistensi KPTN terhadap doksorubisin.
Metode: Teknik CRISPR-Cas9 digunakan untuk menghilangkan TMEPAI pada galur sel KPTN, BT549. Sel diberi perlakuan TGF-β 2 ng / mL dan doksorubisin selama 24 jam. Pengukuran konsentrasi sitotoksik doksorubisin pada 50% populasi sel (CC50) dilakukan terhadap sel KPTN wildtype (WT) dan knock out (KO). Setelah itu, sel dipanen dan dihitung. Rantai Polimerase Waktu Nyata Reaction (RT-PCR) dan western blot (WB) digunakan untuk mengukur tingkat ekspresi penande proliferasi, apoptosis, EMT, dan transporter. Selain itu, SMAD yang terfosforilasi dan aktivitas PI3K / Akt juga belajar.
Hasil: Galur sel yang tidak memiliki TMEPAI (KO) berhasil diperoleh dari sel KPTN, BT549. Sel WT terbukti lebih resistan terhadap doksorubisin dibandingkan sel KO yang ditunjukkan dengan peningkatan CC50 dan Ki-67. TMEPAI menurunkan efek apoptosis doksorubisin dengan memodulasi ekspresi bcl-2 dan kaspase-3, namun tidak kaspase-9 dan bax. Efek TMEPAI mengurangi doksorubisin dengan menekan fosforilasi SMAD. Namun TMEPAI meningkatkan penghambatan PI3K / Akt oleh doksorubisin. TMEPAI juga meningkatkan EMT dan transporter efluks yang diinduksi oleh doksorubisin.
Kesimpulan: TMEPAI terhadap pertarungan dalam resistensi sel KPTN doksorubisin melalui aktivasi jalur sinyal TGF-β non-canonical beserta protein dan gen targetnya.
Background: Triple negative breast cancer (KPTN) pharmacological therapy limited to cytostatic drugs such as doxorubicin. However, doxorubicin resistance hard to avoid. One of the important signaling pathways of resistance KPTN against doxorubisn is TGF-β. TMEPAI (transmembrane prostate androgen-induced protein), a negative regulator as well as a target gene in the TGF-β is thought to be one of the keys in the resistance of KPTN to

doxorubicin.
Method: The CRISPR-Cas9 technique was used to remove TMEPAI on
KPTN cell lines, BT549. Cells were treated with TGF-β 2 ng / mL and doxorubicin
for 24 hours. Measurement of the cytotoxic concentration of doxorubicin at 50%
cell population (CC50) was carried out against wildtype KPTN (WT) cells and knockout
(KO). After that, cells are harvested and counted. Real Time Polymerase Chain
Reaction (RT-PCR) and western blot (WB) were used to measure levels
expression markers of proliferation, apoptosis, EMT, and transporters. Apart from that, SMAD
the phosphorylated and PI3K / Akt activities also learn.
Results: Cell lines that did not have TMEPAI (KO) were obtained from the cells
KPTN, BT549. WT cells have been shown to be more resistant to doxorubicin
compared to cell knockout shown with increased CC50 and Ki-67.
TMEPAI decreases the apoptotic effect of doxorubicin by modulating expression
bcl-2 and caspase-3, but not caspase-9 and bax. TMEPAI reducing effects
doxorubicin by suppressing SMAD phosphorylation. However TMEPAI is improving
PI3K / Akt inhibition by doxorubicin. TMEPAI also increases EMT
and doxorubicin-induced efflux transporters.
Conclusion: TMEPAI against the fight against KPTN cell resistance
doxorubicin via activation of the non-canonical TGF-β signaling pathway along with proteins
and its target genes.