Pengaruh *Mimic-Hsa-miR-203a-3p* Terenkapsulasi Eksosom terhadap Viabilitas dan Migrasi Sel Hs578T: Validasi Eksperimental dan Prediksi Gen Target secara *In Silico*

INTISARI

Triple-negative breast cancer (TNBC) merupakan jenis kanker yang sangat berbahaya karena sifatnya yang heterogen, invasif, dan resisten terhadap terapi. Salah satu strategi potensial adalah penggunaan miRNA, khususnya Hsa-miR-203a-3p, yang diketahui mengalami penurunan regulasi pada TNBC. Dalam penelitian ini, digunakan *mimic-hsa-miR-203a-3p* sebagai tiruan hsa-miR-203a-3p endogen. Namun, karena sifat miRNA yang tidak stabil, diperlukan agen pengantar seperti eksosom yang stabil, tidak toksik, dan non-imunogenik sebagai agen enkapsulasi untuk miRNA, membentuk eksomiR. Tujuan penelitian ini adalah untuk mengevaluasi karakteristik eksosom yang digunakan, yang berasal dari sekretom *Umbilical Cord Mesenchymal Stem Cell* (UCMSC), serta pengaruh eksomiR terhadap viabilitas dan migrasi sel TNBC Hs578T. Selain itu, penelitian ini juga bertujuan untuk mengamati ekspresi hsa-miR-203a-3p setelah penambahan eksomiR dan mengidentifikasi gen target hsa-miR-203a-3p melalui analisis *in silico*. Viabilitas sel diuji menggunakan metode MTT *assay*, sementara migrasi sel dianalisis menggunakan *wound healing* assay. Ekspresi gen dievaluasi dengan qRT-PCR. Analisis *in silico* dilakukan menggunakan dataset dari TargetScan, TarBase, dan GSEA, serta analisis metabolisme dilakukan dengan David. Analisis prognosis menggunakan PrognoScan dan visualisasi data dilakukan dengan Cytoscape. Hasil penelitian menunjukkan bahwa pada volume 2 (15%), viabilitas sel tehambat hingga 53% dengan signifikansi P<0,0001. IC50 perlakuan eksomiR sebesar 13,54 %. Hasil *wound healing assay* menunjukkan penghambatan migrasi sel pada volume 2 (15%) hingga 67,7% dengan signifikansi P<0,001. Melalui uji qRT-PCR, ekspresi Hsa-miR-203a-3p meningkat hingga 88,24 kali lipat dengan signifikansi P<0,01. Hasil analisis *in silico* mengidentifikasi 18 onkogen yang menjadi gen target Hsa-miR-203a-3p pada TNBC.

Kata Kunci: *Triple Negative Breast Cancer,* EksomiR, Viabilitas, Migrasi, Ekspresi miRNA.

The Effect of Exosome-Encapsulated Mimic-Hsa-miR-203a-3p on Hs578T Cell Viability and Migration: Experimental Confirmation and In Silico Target Gene Prediction

ABSTRACT

Triple-negative breast cancer (TNBC) is a highly dangerous type of cancer due to its heterogeneous, invasive, and therapy-resistant nature. One potential strategy is the use of miRNAs, specifically Hsa-miR-203a-3p, which is known to be downregulated in TNBC. In this study, mimic-hsa-miR-203a-3p was used to replicate the endogenous hsa-miR-203a-3p. However, due to the unstable nature of miRNA, a delivery agent such as exosomes is required. Exosomes are stable, non-toxic, and non-immunogenic, making them suitable encapsulation agents for miRNA, forming exomiR. The aim of this study is to evaluate the characteristics of the exosomes used, which are derived from the secretome of human Umbilical Cord Mesenchymal Stem Cells (UCMSC), and to assess the effect of exomiR on the viability and migration of TNBC Hs578T cells. Additionally, the study aims to observe the expression of hsa-miR-203a-3p after the addition of exomiR and to identify the target genes of hsa-miR-203a-3p through in silico analysis. Cell viability was tested using the MTT assay, while cell migration was analyzed using the wound healing assay. Gene expression was evaluated by qRT-PCR. In silico analysis was conducted using datasets from TargetScan, TarBase, and GSEA, and metabolism analysis was performed using DAVID. Prognosis analysis was conducted using PrognoScan, and data visualization was done with Cytoscape. The results showed that at 2 volume (15%), cell viability was inhibited by up to 53% with a significance of P<0,0001. The IC50 of exomiR treatment was 13,54 %. The wound healing assay results showed that cell migration was inhibited by 67,7% at 2 volume (15%) with a significance of P<0,001. Through qRT-PCR testing, the expression of Hsa-miR-203a-3p increased by up to 88,24-fold with a significance of P<0,01. In silico analysis identified 18 oncogenes as target genes of Hsa-miR-203a-3p in TNBC.

Keyword: *Triple Negative Breast Cancer, ExomiR, Viability, Migration, miRNA Expression*