Evaluasi Aktivitas Eksosom dan Sekretom Berbasis Sel Punca Mesenkimal Human Whartonâ€™s Jelly pada
Sel Kanker Payudara MDA-MB-231 terhadap Regulasi Ekspresi PD-L1
Salsabilla Kristinawati, drh. Retno Murwanti, M.P., Ph.D.; Prof. Dr.rer.nat. apt. Adam Hermawan, M.Sc.
Universitas Gadjah Mada, 2026 | Diunduh dari http://etd.repository.ugm.ac.id/

INTISARI

Triple-negative breast cancer (TNBC) merupakan subtipe kanker payudara yang sangat agresif dan memiliki kemampuan menghindari sistem imun melalui peningkatan ekspresi *programmed death-ligand* 1 (PD-L1). Pendekatan terapi berbasis sel punca, khususnya eksosom dan sekretom dari *human Wharton's Jelly* (HWJ), menawarkan potensi sebagai terapi bebas sel karena mengandung molekul bioaktif seperti miRNA let-7 yang berperan dalam regulasi jalur persinyalan kanker. Penelitian ini bertujuan untuk mengevaluasi efek eksosom dan sekretom HWJ terhadap proliferasi, migrasi, distribusi siklus sel, serta regulasi ekspresi PD-L1 pada sel kanker payudara MDA-MB-231. Penelitian dilakukan melalui pendekatan in silico dan in vitro. Analisis bioinformatik digunakan untuk memprediksi keterlibatan miRNA let-7 dalam regulasi jalur PD-L1, khususnya melalui jalur PI3K dan p53. Uji in vitro meliputi uji sitotoksisitas menggunakan uji MTT, uji migrasi dengan *scratch wound healing assay*, analisis siklus sel menggunakan *flow cytometry*, serta analisis ekspresi gen PIK3CA, AKT1, NF-κB, CD274 (PD-L1), TP53, p21, dan CDH1 menggunakan qRT-PCR. Analisis statistik dilakukan dengan ANOVA ($P < 0,05$).

Hasil menunjukkan bahwa sekretom HWJ pada konsentrasi tinggi secara signifikan menurunkan viabilitas sel dan menghambat proliferasi, terutama setelah inkubasi 72 jam ($P < 0,05$). Sekretom dosis tinggi juga menghambat migrasi sel dan meningkatkan fraksi sub-G1 ($P < 0,05$). Analisis gen menunjukkan peningkatan ekspresi PIK3CA, AKT1, NF-κB, CD274, dan TP53 yang diduga sebagai respons stres seluler, serta peningkatan p21 dan CDH1 yang mengindikasikan penghambatan EMT dan migrasi. Sebaliknya, eksosom HWJ tidak menunjukkan perubahan signifikan ($P > 0,05$). Secara keseluruhan, sekretom HWJ menunjukkan peran ganda dalam modulasi proliferasi, migrasi, siklus sel, dan regulasi PD-L1 pada sel TNBC secara in vitro.

Kata kunci: *triple-negative breast cancer, Wharton's Jelly mesenchymal stem cells,* eksosom, sekretom, PD-L1

UNIVERSITAS
GADJAH MADA
**Evaluasi Aktivitas Eksosom dan Sekretom Berbasis Sel Punca Mesenkimal Human Whartonâ€™s Jelly pada
Sel Kanker Payudara MDA-MB-231 terhadap Regulasi Ekspresi PD-L1**
Salsabilla Kristinawati, drh. Retno Murwanti, M.P., Ph.D.; Prof. Dr.rer.nat. apt. Adam Hermawan, M.Sc.
Universitas Gadjah Mada, 2026 | Diunduh dari http://etd.repository.ugm.ac.id/

ABSTRACT

Triple-negative breast cancer (TNBC) is a highly aggressive subtype of breast cancer with the ability to evade the immune system through the expression of programmed death-ligand 1 (PD-L1). Human Wharton's Jelly (HWJ)–based exosomes and secretome, which contain biological components such as miRNA let-7, have potential as cell-free therapies with immunomodulatory activity against cancer. This study aimed to evaluate the effects of HWJ exosomes and secretome on proliferation, migration, and regulation of PD-L1 expression in MDA-MB-231 breast cancer cells. The study was conducted using in silico and in vitro approaches. Bioinformatic analysis was employed to predict the involvement of miRNA let-7 in regulating the PD-L1 signaling pathway. In vitro assays included cytotoxicity assessment using the MTT assay, cell migration analysis using a scratch wound healing assay, cell cycle distribution analysis using flow cytometry, and gene expression analysis of *PIK3CA, AKT1,* and *CD274* (PD-L1) using qRT-PCR. Statistical analysis was performed using ANOVA with GraphPad 10.0 software ($P < 0.05$).

In silico analysis indicated the involvement of the PI3K and p53 pathways in miRNA let-7–mediated regulation of PD-L1 in breast cancer. In vitro results showed that high concentrations of HWJ secretome significantly reduced cell viability, indicating inhibition of proliferation ($P < 0.05$). Prolonged incubation up to 72 hours significantly inhibited proliferation at moderate to high concentrations ($P < 0.05$). Migration assays demonstrated that high-dose HWJ secretome effectively inhibited cancer cell migration ($P < 0.05$). An increase in the sub-G1 population was observed following treatment with high concentrations of HWJ secretome ($P < 0.05$). qRT-PCR results showed that high concentrations of HWJ secretome increased the expression of *PIK3CA, AKT1, NF-κB, CD274*, and *TP53* ($P < 0.05$), which is suspected to represent a cancer stress response, as well as increased expression of *p21* and *CDH1* ($P < 0.05$), suggesting reduced epithelial–mesenchymal transition (EMT) and inhibited migration. In contrast, HWJ exosome treatment did not produce significant effects in any assay ($P > 0.05$), which is presumed to reflect the inert nature of HWJ exosomes toward MDA-MB-231 cells. This study demonstrates that HWJ secretome exerts a dual role in cancer by inhibiting proliferation and migration, regulating the cell cycle, and altering PD-L1 gene expression in vitro in MDA-MB-231 breast cancer cells.

Keywords: triple-negative breast cancer, Wharton's Jelly mesenchymal stem cells, exosomes, secretome, PD-L1