

## HSA-MIR-155-5P DAN mRNA HYPOXIA INDUCIBLE FACTOR ALPHA (HIF1A) PADA PLASMA DARAH PASIEN KANKER OVARIUM STADIUM AWAL DAN STADIUM LANJUT

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### Intisari

Kanker ovarium adalah salah satu keganasan ginekologis yang mematikan dan masih menjadi permasalahan kesehatan diseluruh dunia. Proses karsinogenesis pada kanker ovarium melibatkan regulasi tingkat molekular, salah satunya adalah mikroRNA. Beberapa penelitian sebelumnya menyebutkan bahwa disregulasi *Hsa-miR-155-5p* terjadi pada berbagai kanker. Penelitian melaporkan adanya penurunan ekspresi *Hsa-miR-155-5p* pada kanker ovarium. Penelitian sebelumnya menyebutkan bahwa kanker sering berada dalam kondisi hipoksia. Pada penelitian *insilico* yang telah dilakukan, diketahui bahwa *Hsa-miR-155-5p* menarget mRNA HIF1A yang merupakan regulator gen pada kondisi hipoksia. HIF1A terlibat dalam berbagai *hallmark* kanker. Berdasarkan hal tersebut, penelitian ini dilakukan untuk mengetahui apakah terdapat perbedaan ekspresi *Hsa-miR-155-5p* dan mRNA HIF1A pada plasma penderita kanker ovarium stadium awal dengan stadium lanjut.

Sampel plasma diambil dari pasien kanker ovarium di RSUP Dr. Sardjito, stadium awal sebanyak 32 sampel dan stadium lanjut sebanyak 20 sampel. Total RNA diisolasi dari sampel plasma darah pasien kanker ovarium dengan menggunakan *miRCURY RNA isolation Kit-Biofluid*. Sintesis cDNA *Hsa-miR-155-5p* dilakukan dengan menggunakan kit *Universal cDNA synthesis kit II*, 8-64 rxns dan mesin *thermal cycler PCR (Biorad c 1000)* dan qRT-PCR dengan mesin *Real-time qPCR (Biorad CFX 96)*. Sedangkan untuk mRNA HIF1A dilakukan One-step qRT-PCR dengan kit KAPA<sup>TM</sup> SYBR<sup>®</sup>. Hasil qRT-PCR dianalisis dengan menggunakan *Biorad CFX Manager<sup>TM</sup> Software*. Hasil analisis menunjukkan bahwa ekspresi *Hsa-miR-155-5p* lebih rendah 2,18 kali ( $p$  value =0,018\*) pada plasma pasien kanker ovarium stadium lanjut dibandingkan dengan stadium awal ( $p$  value  $\leq 0,05^*$ ). Ekspresi mRNA HIF1A lebih tinggi 2,46 kali ( $p$  value =0,039\*) pada plasma pasien kanker ovarium stadium lanjut dibandingkan dengan stadium awal ( $p$  value  $\leq 0,05^*$ ). Penelitian ini telah berhasil membuktikan bahwa *Hsa-miR-155-5p* mengalami downregulasi dan diikuti dengan upregulasi ekspresi mRNA HIF1A pada stadium lanjut kanker ovarium dibandingkan pada stadium awal. Tidak terdapat hubungan antara ekspresi relatif *Hsa-miR-155-5p* dan mRNA HIF1A.

**Kata kunci:** Plasma, stadium kanker ovarium, *Hsa-miR-155-5p*, mRNA HIF1A

## The Expression of MicroRNA-155 and mRNA Hypoxia Inducible Factor Alpha (HIF1A) in the Early and Advanced Stages of Ovarian Cancer Patients Blood Plasma

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### Abstract

**Background:** Ovarian cancer has the problem turned out to be the greatest and almost half the death rate of mortality throughout gynecological malignancy. Ovarian cancer is found in the female reproductive organs and the second most common cancer after cervical cancer. The process of carcinogenesis of ovarian cancer occurs at the molecular level, regulated by microRNA. At in silico research that has been done, it is known that microRNA-155 (miR-155) targeted mRNA HIF1A which is the regulator genes in hypoxia conditions. HIF1A involved in various cancer hallmarks, where some of them have roles in Warburg effect and also as genetical transcription factors in angiogenesis. Regulation of miR-155 and mRNA HIF1A believed to be involved in the process of ovarian cancer progression and thus potentially as minimally invasive biomarker for prognosis.

**Objective:** The aim of this study is to determine whether there are differences in the expression of miR-155 and mRNA HIF1A in plasma ovarian cancer patients at the early stage compared with the advanced stage.

**Methods:** The samples using blood plasma from ovarian cancer patients RSUP Dr. Sardjito with 32 ovarian cancer patients early stages and 20 ovarian cancer patients advanced stages. Total RNA was isolated from blood plasma samples of ovarian cancer patients. cDNA synthesis from total RNA was performed to obtain cDNA. The expression of miR-155 and HIF1A were calculated using qPCR. qPCR results were analyzed using Biorad CFX Manager Software.

**Result:** The analysis showed that the expression of miR-155 were 2,18 times lower (p-value = 0,018\*) in the plasma of advanced stage ovarian cancer compared with early stage, the differences were statistically significant (p value ≤ 0,05). Whereas the mRNA expression HIF1A were 2,46 times higher (p-value = 0,039\*) in the plasma of advanced stage ovarian cancer compared with early stage, the differences were statistically significant (p value ≤ 0,05).

**Conclusion:** This study has proved that miR-155 expression is downregulated and followed by upregulation of mRNA expression HIF1A at an advanced stage ovarian cancer compared with early stage.

**Keywords:** Plasma, stage ovarian cancer, microRNA-155, mRNA HIF1A