

TRANSKRIPOTOM TERKAIT *AVOIDING IMMUNE DESTRUCTION* PADA KANKER NASOFARING PASIEN INDONESIA MENGGUNAKAN *NEXT GENERATION SEQUENCING*

INTISARI

Latar belakang: Kanker nasofaring (NPC) adalah kanker dengan penderita keempat terbanyak pada pria di Indonesia. Karena etiologinya yang kompleks, kurangnya pengetahuan dalam mekanisme molekuler, tidak ada penanda yang efektif untuk deteksi dini, dan respon yang buruk terhadap terapi yang tersedia saat ini. Salah satu aspek kunci dalam penelitian kanker adalah untuk memahami mekanisme perubahan ekspresi gen. *Next generation sequencing* (NGS) telah digunakan untuk mengeksplorasi ekspresi gen dari data transkriptom pada berbagai jenis kanker. *Avoiding immune destruction* (AID) adalah karakteristik transkriptomik utama pada kanker yang mengalami metastasis dan invasif. Penelitian ini bertujuan untuk mengetahui transkriptom terkait *avoiding immune destruction* pada kanker nasofaring pasien Indonesia menggunakan *next generation sequencing*. **Metode:** Sampel kontrol berjumlah dua sampel dan sampel kanker nasofaring berjumlah tujuh sampel dari hasil isolasi total RNA. Total RNA dipreparasi untuk dijadikan *library* dan disekuensing dengan *next generation sequencing*. Hasil sekuensing dianalisis dengan *tools* bioinformatik menggunakan FastaQC, Genious, Hisat2, Htseq, edgeR, Lionproject, Pantherdb dan DAVID. **Hasil:** diperoleh 2046 gen yang mengalami perubahan ekspresi. 90 gen mengalami *down-regulated* dan 1956 gen mengalami *up-regulated* dari analisis edgeR. Dari 2046 gen dianalisis dengan Pantherdb diperoleh 20 gen terkait dengan proses biologis sistem imun, 18 gen mengalami *up-regulated* dan 2 gen mengalami *down-regulated*. Gen yang mengalami *up-regulated* yaitu gen HEPACAM, BTNL3, REG3A, REG1B, DPP6, REG1A, CXCL11, CLEC6A, GGT1, CXCL9, CRYAB, HSPB6, FAM43B, PGLYRP3, PGLYRP2, COLEC12, PLA2G2F, dan CXCL10 sedangkan gen yang mengalami *down-regulated* yaitu ALOX15 dan HMGB4. Berdasarkan analisis lionproject didapatkan gen yang terkait langsung *hallmark avoding immune destruction* ada 6 gen yaitu gen CXCL9,-10,-11, CRYAB, PGLYRP2 dan PGLYRP3. Analisis menggunakan DAVID untuk analisis *signaling pathway* diperoleh 3 gen yang terkait dengan kemokin *pathway* yaitu gen CXCL9,-10,-11 mengatur ekspresi PD-L1 terkait *immune evasion*. **Kesimpulan:** gen CXCL9,-10,-11 merupakan gen yang terkait dengan kemokin *pathway* yang mengatur ekspresi PD-L1 terkait *immune evasion*. Gen CXCL9,-10,-11 dapat dijadikan kandidat *biomarker* tambahan terkait *immune evasion* pada kanker nasofaring pasien Indonesia.

Kata kunci: kanker nasofaring, transkriptom, *next generation sequencing*, *avoiding immune destruction*

TRANSCRIPTOME RELATED TO AVOIDING IMMUNE DESTRUCTION OF NASOPHARYNGEAL CANCER PATIENTS IN INDONESIA USING NEXT-GENERATION SEQUENCING

ABSTRACT

Background: Nasopharyngeal cancer (NPC) is cancer with the fourth most sufferers in men in Indonesia. Because of its complex etiology; lack of knowledge in molecular mechanisms, there are no effective markers for early detection and poor response to currently available therapies. One key aspect of cancer research is to understand the mechanism of changing gene expression. Next-generation sequencing (NGS) used to explore gene expression of transcriptome data on various types of cancer. Avoiding immune destruction (AID) is the main transcriptomic characteristic of metastatic and invasive cancers. This study aims to determine the transcriptome associated with avoiding immune destruction of nasopharyngeal cancer in Indonesian patients using next generation sequencing. **Method:** The results of total RNA consisted of two samples of control sample and the nasopharyngeal cancer sample consisted of seven samples. Total RNA is prepared to be used as a library and sequenced with next-generation sequencing instrument. Sequencing results were analyzed by bioinformatic tools using FastaQC, Genious, Hisat2, Htseq, edgeR, Lionproject, Pantherdb and DAVID. **Results:** 2046 genes were obtained, which had changes in expression. Ninety genes were down-regulated and 1956 genes were up-regulated from edgeR analysis. Of the 2046 genes analyzed by Pantherdb, 20 genes related to the biological processes of the immune system were obtained, 18 genes were up-regulated and 2 genes were down-regulated. The up-regulated genes are HEPACAM, BTNL3, REG3A, REG1B, DPP6, REG1A, CXCL11, CLEC6A, GGT1, CXCL9, CRYAB, HSPB6, FAM43B, PGLYRP3, PGLYRP2, COLEC12, PLA2G2F, and CXCL10 and genes with down regulated namely ALOX15 and HMGB4. Based on lionproject analysis, there are 6 genes that are directly related to hallmark avoiding immune destruction, that genes are CXCL9, -10, -11, CRYAB, PGLYRP2 and PGLYRP3. Analysis using DAVID for signaling pathway analysis obtained 3 genes associated with chemokine pathway, that genes are CXCL9, -10, -11 genes that allegedly regulate expression of PD-L1 related to immune evasion. **Conclusion:** CXCL9,-10,-11 genes are genes associated with the chemokine pathway that regulates PD-L1 expression related to immune evasion. The CXCL9,-10,-11 genes can be an additional biomarker candidate related to immune evasion in nasopharyngeal cancer in Indonesian patients.

Keywords: nasopharyngeal cancer, transcriptome, next-generation sequencing, avoiding immune destruction