

ABSTRAK

**PERBEDAAN EKSPRESI mRNA *PROLYL 4-HYDROXYLASE SUBUNIT ALPHA 2 (P4HA2)* PADA *LOW GRADE* DAN *HIGH GRADE* *ORAL SQUAMOUS CELL CARCINOMA (OSCC)*
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Oral Squamous Cell Carcinoma (OSCC) merupakan keganasan yang paling umum terjadi di rongga mulut dengan *survival rate* ≤ 5 tahun mencapai 40-50%. *Gen Prolyl 4-Hydroxylase Subunit Alpha 2 (P4HA2)* diketahui berkorelasi dengan progresi kanker yang berperan dalam proses invasi dan perubahan EMT. Namun, perbedaan ekspresi mRNA P4HA2 berdasarkan grading histopatologi belum diketahui pada kejadian OSCC di Indonesia. Penelitian ini bertujuan untuk mengetahui perbedaan ekspresi mRNA P4HA2 pada kelompok *low grade* dan *high grade* OSCC. Jenis penelitian ini adalah observasional analitik dengan rancangan penelitian *cross sectional study* menggunakan 18 sampel FFPE OSCC yang dipilih dengan teknik *random sampling*. Pada penelitian dilakukan deparafinasi sampel, isolasi RNA, sintesis cDNA, dan kuantifikasi ekspresi mRNA P4HA2 menggunakan qPCR. Ekspresi mRNA P4HA2 dianalisis dengan metode *livak's* menggunakan software *GenEx MultiD 6* dan nilai perbedaan ekspresi dianalisis menggunakan *independent T-test*. Analisis bioinformatika menggunakan STITCH dan STRING-db dilakukan untuk mengetahui interaksi dan mekanisme kerja P4HA2. Hasil penelitian menunjukkan nilai ekspresi mRNA P4HA2 pada kelompok *low grade* adalah $1,83 \pm 1,49$ sedangkan *high grade* adalah $3,14 \pm 1,50$. mRNA P4HA2 menunjukkan peningkatan ekspresi pada kelompok *high grade* sebesar 2,48 kali jika dibandingkan kelompok *low grade*, namun secara statistik tidak signifikan ($p > 0,05$). Hasil analisis bioinformatik menunjukkan P4HA2 dibentuk oleh HIF-1 α saat sel mengalami hipoksia dan berperan mengubah *prolin* menjadi *4-hydroxyproline* yang membuat kolagen menjadi lebih kaku pada matriks ekstraseluler yang tampak pada kelompok *high grade* dan mempengaruhi progresi kanker. Simpulan penelitian ini adalah tidak terdapat perbedaan ekspresi mRNA P4HA2 pada *low grade* dan *high grade* OSCC.

Kata Kunci: OSCC; P4HA2; qPCR; *low grade* OSCC; *high grade* OSCC.

ABSTRACT

**DIFFERENTIAL EXPRESSION OF mRNA *PROLYL 4-HYDROXYLASE*
SUBUNIT ALPHA 2 (P4HA2) IN LOW GRADE AND HIGH GRADE
ORAL SQUAMOUS CELL CARCINOMA (OSCC)
(Study of Patients in Pathology Anatomy Laboratory
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Oral Squamous Cell Carcinoma (OSCC) is the most common malignancy in the oral cavity with a 5-year survival rate of 40-50%. The Prolyl 4-Hydroxylase Subunit Alpha 2 (P4HA2) gene is known to correlate with cancer development which plays a role in the process of invasion and changes in EMT. However, the difference in P4HA2 mRNA expression based on histopathological grading is not known in the incidence of OSCC in Indonesia. This study aims to determine the differences in P4HA2 mRNA expression in the low-grade and high-grade OSCC groups. This type of research is analytic observational with a cross-sectional study design using 18 samples of FFPE OSCC selected by random sampling technique. This study carried out sample deparaffination, RNA isolation, cDNA synthesis, and quantification of P4HA2 mRNA expression using qPCR. The expression of P4HA2 mRNA was analyzed by the livaks method using GenEx MultiD 6 software and the value of the difference in expression was analyzed using an independent T-test. Bioinformatics analysis using STITCH and STRING-db was conducted to determine the interaction and mechanism of action of P4HA2. The results showed that the P4HA2 mRNA expression value in the low-grade group was 1.83 ± 1.49 , while in the high-grade group was 3.14 ± 1.50 . P4HA2 mRNA showed an increase of expression in the high-grade group by 2.48 times compared to the low-grade group, but not statistically significant ($p > 0.05$). The results of bioinformatics analysis showed that P4HA2 is formed by HIF-1 α when cells are hypoxic and plays a role in converting proline to 4-hydroxyproline which makes collagen more rigid in the extracellular matrix which is seen in the high-grade group and affects cancer development. This study concluded that there was no difference in P4HA2 mRNA expression in low-grade and high-grade OSCC.

Keywords: OSCC; P4HA2; qPCR; low grade OSCC; high grade OSCC.