Pengaruh Anti IGF-1R dan IGFBP-3 Terhadap Ekspresi Gen OCT4, SOX2, dan NANOG pada Sel Punca Pulpa Gigi Permanen Subjek Celah Bibir dan Palatum = The Effect of Anti-IGF-1R and IGFBP-3 on OCT4, SOX2, and NANOG Gene Expression in Dental Pulp Stem Cells of Cleft Lip and Palate Subjects

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Abstrak

Latar Belakang: Rekayasa jaringan tulang memerlukan tiga komponen utama, yaitu sel punca, scaffold, dan faktor pertumbuhan. IGF-1 merupakan salah satu faktor pertumbuhan yang berperan dalam proliferasi dan diferensiasi sel osteoblast. IGF-1 akan berikatan dengan reseptornya, yaitu IGF-1R untuk mengaktivasi jalur hilir. Dalam sirkulasi tubuh manusia, IGF berikatan dengan IGFBP-3 yang dapat memperpanjang waktu paruh serta menghambat IGF-1 berikatan dengan IGF-1R. Pada penelitian sebelumnya, tercatat bahwa tidak ada perbedaan kemampuan proliferasi dan diferensiasi antara DPSC subjek normal dan subjek CLP, namun ada perbedaan signifikan dalam jumlah ekspresi IGF-1. OCT-4, SOX-2 dan NANOG merupakan faktor transkripsi utama pluripotensi yang telah diteliti dapat mengatur pluripotensi, pembaruan diri, proliferasi, serta diferensiasi DPSC. Penelitian terbaru mencatat peningkatan ekspresi ketiga gen tersebut pasca dilakukan penghambatan jalur GSK-3 dan m-TOR yang merupakan jalur hilir dari aksi IGF-1 pada sel DPSC. Namun, belum diketahui secara pasti ekspresi ketiga gen tersebut pada DPSC subjek normal dan CLP setelah dilakukannya penghambatan IGF-1 menggunakan anti IGF-1R dan IGFBP-3. Tujuan: Menganalisis pengaruh anti IGF-1 dan IGFBP-3 terhadap ekspresi gen OCT4, SOX2, dan NANOG pada DPSC subjek normal dan CLP. Metode: Sampel RNA DPSC subjek normal (n=4) dan DPSC subjek CLP (n=3), sebelum dan setelah diberikan perlakuan anti IGF-1R atau IGFBP-3, diperoleh dari bahan biologis tersimpan di Laboratorium Oral Biologi Fakultas Kedokteran Gigi Universitas Indonesia. Selanjutnya, ekspresi gen OCT4, SOX2, NANOG, dan housekeeping gene GAPDH diuji dengan two step Real-Time PCR (RT-PCR). Hasil: Tidak terdapat perbedaan ekspresi gen OCT4, SOX2, dan NANOG, baik antara DPSC subjek normal dan CLP sebelum dan setelah diberikan perlakuan anti IGF-1R dan IGFBP-3 ($p^{3}0,05$). Kesimpulan: Perlakuan anti IGF-1R dan IGFBP-3 tidak memengaruhi tingkat ekspresi gen OCT4, SOX2, dan NANOG sel punca pulpa gigi permanen subjek normal dan subjek celah bibir dan palatum .....Background: Bone tissue engineering requires three main components, namely stem cells, scaffold, and growth factors. IGF-1 is a growth factor that plays role in osteoblast proliferation and differentiation. IGF-1 will bind to its receptor, namely IGF-1R, to activate the downstream pathway. In the human body circulation, IGF binds to IGFBP-3 which can inhibit IGF-1 from binding to IGF-1R. Previous studies noted that there were no differences in the ability to proliferate and differentiate between DPSC from normal subjects and CLP subjects, yet there were significant differences in the level of IGF-1 expression. OCT-4, SOX-2 and NANOG are core pluripotency factors which regulate pluripotency, self-renewal, proliferation and differentiation of DPSC. Recent study has noted an increase in the expression of these three genes after inhibition of GSK-3 and m-TOR pathways, which are the downstream pathways of IGF-1 on DPSC cells. However, the expression of these three genes in DPSC from normal and CLP subjects after inhibition of IGF-1 using anti IGF-1R and IGFBP-3 is still unknown. Objective: To analyze the effect of anti IGF-1 and

IGFBP-3 on OCT4, SOX2, and NANOG gene expression in DPSC of normal and CLP subjects. Methods: RNA samples of DPSC from normal and CLP subjects, before and after being treated with anti-IGF-1R or IGFBP-3, were obtained from Laboratory of Oral Biology, Faculty of Dentistry, Universitas Indonesia. Furthermore, the expression of OCT4, SOX2, NANOG, and housekeeping gene GAPDH were tested using two step Real-Time PCR (RT-PCR). Results: There was no difference between the expression of the OCT4, SOX2, and NANOG in DPSC from normal and CLP subjects before and after anti IGF-1R and IGFBP-3 treatment (p0.05). Conclusion: Anti-IGF-1R and IGFBP-3 did not affect the expression level of OCT4, SOX2, and NANOG in dental pulp stem cells of normal subjects and cleft lip and palate subjects.