ABSTRAK

Induced Pluripotent Stem Cell (iPSC) merupakan terobosan penting dalam kedokteran regeneratif karena mampu menghasilkan sel pluripoten tanpa menggunakan embrio serta berpotensi digunakan dalam terapi autologus dan pemodelan penyakit dalam konteks *Personalized Medicine*. Namun, efisiensi *reprogramming* fibroblas kulit manusia masih rendah (0,01–0,1%) yang kemungkinan salah satunya dipengaruhi oleh karakteristik biologis sel sebelum reprogramming. Penelitian ini bertujuan untuk mengkaji dan membandingkan karakteristik awal sel fibroblas kulit abdomen wanita dewasa dan fibroblas kulit prepusium anak lelaki sebagai dasar prediksi potensi efisiensi *reprogramming*, terutama terkait morfologi, proliferasi, metabolisme mitokondria, dan ekspresi basal gen pluripotensi, serta didesain secara deskriptif, kuantitatif, observasional, dan *in vitro*. Karakterisasi dilakukan melalui penilaian morfologi sel dalam kultur; pemantauan jumlah sel dan perhitungan *doubling time* untuk menilai proliferasi dengan metode CCK-8; analisis aktivitas metabolisme dengan Seahorse *metabolic assay* ATP *rate*; serta kuantifikasi ekspresi basal gen pluripotensi yaitu *OCT4, SOX2, KLF4, MYC, LIN28A, NANOG*, dan *SOCS1* dengan qRT-PCR metode $2^{-\Delta\Delta Ct}$. Parameter morfologi menunjukkan hasil skoring kesehatan fibroblas yang lebih tinggi pada fibroblas prepusium anak dibanding abdomen dewasa (14 vs 11). Ekspresi basal gen *LIN28A* (2,56 kali lipat) dan *SOCS1* (2,17 kali lipat) lebih tinggi pada fibroblas prepusium anak dibandingkan fibroblas abdomen dewasa. Parameter tingkat proliferasi menunjukkan hasil fibroblas abdomen dewasa yang lebih rendah secara bermakna dibanding fibroblas prepusium anak dalam jumlah sel di hari ke 8 (51.504 ± 3.417 vs 93.367 ± 7.275 sel) (p=0,000) dan perhitungan *doubling time* (85,97 ± 17,99 vs 59,62 ± 15,05) (p=0,037). Parameter metabolisme menunjukkan total ATP *rate* pada fibroblas abdomen dewasa sebesar 400,88 ± 40,07 pmol/menit dengan dominansi glikoATP, lebih tinggi secara bermakna (p=0,006) dibanding fibroblas prepusium anak dengan nilai sebesar 306,07 ± 5,13 pmol/menit dengan dominansi mitoATP. Temuan ini menunjukkan bahwa fibroblas prepusium anak memiliki keunggulan pada parameter morfologi dan ekspresi gen pluripotensi, sedangkan fibroblas abdomen dewasa menunjukkan karakteristik proliferasi dan metabolisme yang juga berkaitan dengan proses *reprogramming*. Secara keseluruhan, kedua sumber fibroblas menunjukkan potensi biologis yang relatif sebanding sebagai kandidat sel donor dalam pembentukan iPSC. Penilaian karakterisasi sumber sel pada fase pra-*reprogramming* ini diharapkan menjadi studi awal (preliminary study) yang memiliki kontribusi untuk pengembangan iPSC berbasis *Personalized Medicine* di Indonesia.

Kata Kunci: *Induced Pluripotent Stem Cells* (iPSC); fibroblas kulit; pra-*reprogramming*; proliferasi sel; metabolisme mitokondria; ekspresi gen pluripotensi; *personalized medicine*.

ABSTRACT

Induced Pluripotent Stem Cells (iPSCs) represent a major breakthrough in regenerative medicine, as they enable the generation of pluripotent cells without the use of embryos and hold potential for autologous therapy and disease modeling within the framework of Personalized Medicine. However, the reprogramming efficiency of human skin fibroblasts remains low (0.01–0.1%), which may be influenced by the biological characteristics of the cells prior to reprogramming. This study aimed to investigate and compare the baseline characteristics of adult female abdominal skin fibroblasts and male pediatric preputial skin fibroblasts as a basis for predicting potential reprogramming efficiency, particularly in relation to cell morphology, proliferation, mitochondrial metabolism, and basal expression of pluripotency genes. The study was designed as a descriptive, quantitative, observational, and in vitro investigation. Cell characterization was performed through morphological assessment of cultured cells; monitoring of cell numbers and calculation of doubling time to evaluate proliferation using the CCK-8 method; analysis of metabolic activity using the Seahorse ATP rate metabolic assay; and quantification of basal expression of pluripotency-related genes, including OCT4, SOX2, KLF4, MYC, LIN28A, NANOG, and SOCS1 using qRT-PCR with the 2-ΔΔCt method. Morphological parameters demonstrated a higher fibroblast health score in pediatric preputial fibroblasts compared with adult abdominal fibroblasts (14 vs 11). Basal expression of LIN28A (2.56-fold) and SOCS1 (2.17-fold) was higher in pediatric preputial fibroblasts than in adult abdominal fibroblasts. Proliferation parameters showed significantly lower values in adult abdominal fibroblasts than in pediatric preputial fibroblasts, as reflected by cell number on day 8 (51,504 ± 3,417 vs 93,367 ± 7,275 cells) (p = 0.000) and doubling time (85.97 ± 17.99 vs 59.62 ± 15.05 hours) (p = 0.037). Metabolic analysis showed that the total ATP rate in adult abdominal fibroblasts was 400.88 ± 40.07 pmol/min, predominantly derived from glycolytic ATP (glycoATP), which was significantly higher (p = 0.006) compared with pediatric preputial fibroblasts (306.07 ± 5.13 pmol/min) with mitochondrial ATP (mitoATP) predominance. These findings indicate that pediatric preputial fibroblasts demonstrate advantages in morphological parameters and pluripotency gene expression, whereas adult abdominal fibroblasts exhibit proliferation and metabolic characteristics that are also relevant to the reprogramming process. Overall, both fibroblast sources demonstrate relatively comparable biological potential as donor cell candidates for iPSC generation. Evaluation of cell source characteristics during the pre-reprogramming phase is expected to serve as a preliminary study contributing to the development of iPSC-based personalized medicine in Indonesia.

Keywords: *Induced Pluripotent Stem Cells (iPSC); skin fibroblasts; pre-reprogramming; cell proliferation; mitochondrial metabolism; pluripotency gene expression; personalized medicine.*