THE NOVEL IPS CELLS GENERATED UNDER HYPOXIC CONDITIONS IN THE ABSENCE OF VIRAL INFECTION AND ONCOGENIC FACTORS AND USED FOR THE ISCHEMIC STROKE THERAPY

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Induced pluripotent stem (iPS) cells have the potential to cell therapy. However, at least two hurdles remain: integrating viral transgenes and introducing oncogenes: c-Myc and Klf4. We tested our hypothesis that iPS cells can be generated by introducing only Oct4 and Sox2 under hypoxic conditions and could use for cell therapy. We observed that the repeated transfection of two expression plasmids (Oct4 and Sox2) into mouse embryonic fibroblasts (MEF) and combined hypoxic condition resulted in novel iPS cells generation. Six hours post-transfection, MEF were subjected to hypoxic conditions for 24 h (3% O2); this procedure was repeated four times. The MEF were seeding on feeder cells on day 9; iPS cell clones were observed 12 days post-seeding and designated as iPS-OSH. The morphology, stem cell markers staining, gene expression profiles, embryonic body, teratoma and chimeric mice formation indicated that the iPS-OSH had pluripotent capability. We differentiated the iPS-OSH into neural precursor cells and used to the ischemic stroke mouse therapy. The behavior analysis showed the therapeutic group was better than the control group. We also observed that iPS-OSH-derived neural precursor cells differentiated into neuron and astrocyte in stroke brain. In conclusion, we generated a novel iPS-OSH in the absence of viral infection and oncogenic factors and could used for the stroke therapy.