Synopsis of Original Research Paper

The next-generation screening cells for cosmetic components: ES/iPS cells with multiple gene-manipulations

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Primary cultured normal human epidermal keratinocytes (NHEK) have been widely used for evaluation of activities of cosmetic components, however, these cells have considerable lot-to-lot variations and readily to lose differentiation potential upon serial passages. This study aimed to prepare a novel iPS-derived cell system for effective screening of cosmetic compounds. We generated iPS cells that were stably transfected with tet/dox-inducible expression cassette for BMP4 (Tet-BMP4-iPS), so that these cells can be maintained as iPS cells in conventional medium, but undergo differentiation into ectodermal lineages after treatment with retinoic acid (RA) and subsequently into *krt14*-positive keratinocyte progenitors upon treatment with dox. We found that thus generated keratinocyte progenitors were unstable and spontaneously differentiate into several epidermal lineages. To detect the appearance of the specific epidermal lineage, e.g., hair cortex, Tet-BMP4-iPS cells were further introduced with differentiated cell-specific promoter, e.g., KRT31 promoter for hair cortex, which had been connected with luciferase reporter. When treated simultaneously with RA, dox and soluble factors from dermal papilla cells, Tet-BMP4-iPS cells quantitatively increase the expression of luciferase up to three days, suggesting that activity of any soluble components for hair cortex differentiation could be evaluated by this cell system. To find the optimal condition of RA and dox treatment for sensitive detection of hair differentiation, we then developed a model of differentiation process of pluripotent iPS cells into terminally differentiated hair cortex cells.