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学 位 論 文 名	培養ヒト毛包内の異なる部分由来上皮前駆細胞及び創傷治癒に関する研究
論 文 審 査 委 員	(委員長) 教授 山本 直人 (委 員) 教授 野口 忠秀 准教授 前川 武雄

論文内容の要旨

1 研究目的

Human hair follicle is consistent of epithelial stem cells, progenitor cells and various lineages of keratinocytes. Follicular epithelial cells (FECs) belong to epithelial cells, as the same as epidermal epithelial cells (EECs). And it was presented that the different portions of human hair follicle showed different patterns of biomarker expressions. To investigate the potential effects of FECs derived from different portions of hair follicle on wound healing and epithelization, compared with human epidermal epithelial cells (hEECs); and to explore the regeneration of excised part of hair follicle.

2 研究方法

A novel and mature isolation method of FECs from different parts, which include cells from bulb part (BECs), lower part of outer root sheath (LECs), and upper part of outer root sheath (UECs), was established. The proliferative abilities and biomarker expressions of these cells were investigated with comparison to EECs. The effects of different portions' FECs, when compared to EECs and control group, on wound healing and epithelization were investigated with mice wound healing models. Histological examinations were applied to healed mice wound skin. The regeneration of excised part of hair follicle was explored via rat's experiments.

3 研究成果

The BECs showed best proliferous ability *in vitro*, then the LECs, when compared with EECs. Cultured FECs showed positive expression of CK-10 and CK-14, and the BECs showed lowest positive ratio of CK-10 and highest positive ratio of CK-14 when compared with other types of cells. During mice wound healing experiments, the group with BECs applications showed best enhancement on wound healing, then the LECs group and EECs group, then the UECs group, which all have better performance compared to control group of culture medium. Histological analysis of healed skin samples indicated that BECs-treated group had thinner

and smaller scar tissue. The expressions of TGOLN2 and CK14 at scar area showed that the BECs-treated group had more TGOLN2+ cells, higher percentage of human-derived cells in the epidermis, and higher ratio of co-stained TGOLN2+ and CK14+ cells in CK14+ cells. At rat's experiment, all excised bulb part of hair follicle can regenerate after removing, while the regenerated hair shafts were thin, curve and short then original ones.

4 考察

The BECs showed best proliferous ability and it contained more proliferating epithelial cells when compared with other cells. The groups of FECs and EECs applications all have positive effects on wound healing and epithelization *in vivo* compared to control group of culture medium, especially the BECs. And the histological examinations of healed wound skins revealed that the BECs group showed better tissue regeneration after wounding and this group had more human-derived cells survived and localized in epidermis to enhance epithelization. Besides, all bulb part can regenerate from the left hair follicle after surgical excision, which means that it will cause lowest damage to donor sites if the bulb parts need to be harvested for BECs isolation and culture.

5 結論

The FECs, especially the BECs, could be promising tools in tissue regeneration and wound healing with lowest damage to donor sites.

論文審査の結果の要旨

本論文は、毛包由来上皮細胞が皮膚欠損の創傷治癒を促進する効果を有することを示し、さらにその結果に基づく臨床応用の可能性を示唆した。特に、毛球由来の細胞は他の部位に比べて効果が高く、よりきれいな瘢痕で治癒することを示した。そのメカニズムは創傷面に置かれたヒト由来の上皮細胞が長期間生存し活動し続けることであり、またその中でも毛球由来細胞は他の細胞に比べて生着が良好であることも判明した。これらの結果に基づいて、難治性皮膚潰瘍への使用や、広範な皮膚欠損に対する毛球由来細胞の局所スプレー製剤の使用という新しい臨床応用への期待が提示された。毛包由来細胞、特に毛球由来が創傷治癒に効果的であるというのは新しい知見であり、新しい皮膚創傷の治療につながる学問的意義を持っている。

用語の記載方法、過去の研究に関する言及、実験データの解釈についての審査委員からの修正意見に対し、適切な修正がなされた。

最終試験の結果の要旨

学位審査委員会では全員一致して医学博士として十分な知識、プレゼンテーション能力を有すると考え、合格と判定した。