再生医療製品として開発された自家培養表皮の有効性と安全性の評価

井家 益和

Efficacy and Safety of First Tissue-Engineered Cellular Product,
Autologous Cultured Epidermis

Masukazu INOIE

Abstract

Regenerative medicine, which achieves a recovery of dysfunction of tissues and organs, might be the main stream of the medical care in this century. We had developed the first tissue-engineered cellular product, JACE®, which received Japanese government approval in October 2007. This product is the autologous cultured epidermis using 3T3-J2 feeder layer system, known as Green’s technique, and is grafted for serious burns. By isolating keratinocytes from a few cm² biopsy and culturing them, the keratinocyte sheets measuring about 10% of the body surface area can be produced in two weeks, or they cover the entire surface of body in 3-4 weeks. On the development of the autologous cultured epidermis product, the characteristics were investigated and lots of data relating to the safety and efficacy were collected. All type and amount of cells except keratinocyte were determined in the cultivation process. And the residual volume of bovine-serum albumin and feeder cells in keratinocyte sheet were analyzed for the selection of shipping inspections. Karyotype analysis, colony formation test in soft agar gels and transplanta-
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Key words: autologous cultured epidermis, JACE, feeder layer, cellular product, regenerative medicine.

1. 緒 言

再生医療は、機能障害や機能不全に陥った組織や臓器を再生させることを目的とした医療テクノロジーであり、今世紀の医療において革新的な役割を担うことが期待されている。再生医療による治療には、必ずしも明確な定義はない。組織工学的手法を用いることなく、ヒト細胞に関連する増殖因子や生分解性材料を広範の再生医療に含めることができる。しかし、再生医療、ヒト細胞を培養して組織工学的に作製した培養細胞を移植する治療と理解される。その意味において、再生医療による世界で最初の臨床成果は、1981年に米国で報告された重症熱傷に対する Green 型自家培養皮膚の移植である2)。

Green は、自身のテラトーマの研究をベースに、マウス 3T3 細胞をフィーダー細胞として用いてヒト表皮細胞を選択的に増殖させる培養法を開発した3)。その手法を用いて患者自身の皮膚から分離した細胞を培養し、作製した培養細胞シートが Green 型自家培養皮膚である。Green 型自家培養皮膚の利点は、小さな皮膚組織から多数の面積の移植用の細胞シートを作製することができることがある、1984 年には、体表面積の 97%を受傷した小児 2 例の熱傷患者の脱皮に残った 2 cm² 程度の皮膚を、4,521 cm² と 6,831 cm² の面積の表皮細胞シートを培養して移植し、救命に成功した症例が報告されたことによって、広範囲熱傷に対する Green 型自家培養皮膚の有用性が広く認知された4)。

Green 型自家培養皮膚は、米国では 1998 年から Epitel® が製品化されており、20 年以上の歴史がある5)。また、いくつかの国における最初の再生医療製品として開発されているほか6)−7)，先進的な医療機関で独自に培