Clinical Potential of Hair-Follicle Derived Mesenchymal Cells in Cell Therapy: Multiple Therapeutic Applications

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INTRODUCTION
The hair follicle (HF) is a dynamic organ, which undergoes continuous morphogenesis and regeneration via the hair cycle throughout an animal’s life. To support this unique characteristic of self-renewal, the HF retains reservoirs of multipotent cells. The dermal mesenchyme compartment of the HF comprises the dermal papilla (DP), a small aggregation cells at the base of the HF bulb; and dermal sheath (DS), which surrounds the bulb and envelops the HF. A specialized group of DS cells that localize at the base of the bulb and supports the growth of the DP is termed the dermal sheath cup (DSC) (Figure 1). Tissue engineering studies have demonstrated that DP and DSC cells play essential roles in hair development, growth and regeneration. Previously, we have demonstrated that cultured DSC cells can stimulate hair growth in mice, and our Phase I data show safety and efficacy in humans. Non-bulbar DS cells (NBDS), in comparison, do not possess HF inductive abilities, but do produce collagen. Exploiting the unique properties of HF cells, we have developed tissue-engineered cell-specific products containing autologous DSC cells or NBDS cells to treat various indications including androgenetic alopecia, tendinosis and aging skin.

OBJECTIVES
To assess preclinical safety and efficacy of cultured NBDS cells in treatment of tendinosis and aging skin.

METHODS AND RESULTS
NBDS cells were isolated from HF samples collected from three independent healthy subjects. Collagen production of NBDS cells in response to mechanical stress was analyzed by immunohistochemistry. Using immunodeficient mice and homologous rabbit models, biodistribution, tolerance and tumorigenicity of cultured human NBDS cells were examined in GLP-compliant in vivo studies.

The results show that upon application of mechanical force, NBDS cells responded by producing type I collagen in the plane of the stretch and expressed other ECM-proteins including type III collagen and elastin. Our GLP-compliant in vivo studies showed that subcutaneously, or intratendon, injected NBDS cells were well tolerated, did not migrate to secondary sites and did not form tumours.

CONCLUSIONS
Our preclinical studies showed that cultured human NBDS cells express proteins essential in restoring healthy tendon and skin, and our in vivo studies confirmed safe application of human DS cells. A Phase I/II clinical trial using NBDS cells for the treatment of tendinosis in humans has been initiated.

CONFLICT OF INTEREST
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