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Repigmentation by Outer-Root-Sheath-Derived Melanocytes: Proof of Concept in Vitiligo and Leucoderma

Wolfgang Vanscheidt[a] Thomas Hunziker[b]

[a]Dermatologische Gemeinschaftspraxis, Freiburg, Germany; [b]Department of Dermatology, University of Bern, Bern, Switzerland

Key Words
Melanocytes · Outer root sheath · Vitiligo · Leucoderma

Abstract
Background: Treatment of depigmented skin is an unmet medical need. ***Objective:*** Melanocytes or stem cells thereof residing in the outer root sheath (ORS) of hair follicles might be used to repigment skin. ***Methods:*** After de-epidermisation, autologous ORS cell solutions were applied to 5 patients with vitiligo and 1 with leucoderma. ***Results:*** Stable repigmentation in a variable percentage was documented in all the patients. ***Conclusion:*** Applying ORS-derived melanocytes is a promising technology to improve autologous melanocyte transplantation.

Permanent skin depigmentation by loss of melanocyte function such as in vitiligo or leucoderma (postlesional hypopigmentation) has a significant negative psychological as well as social impact mainly on people of dark complexion, i.e. in large parts of the 'third world'. Efficient treatment of vitiligo is an unmet medical need. Autologous melanocyte transplantation is an option in case of disfiguring, stable vitiligo, but the optimal modality is still debated. So far, the focus has been on procedures of isolation, application and eventually cultivation using interfollicular epidermal melanocytes harvested by skin biopsy from the patient [for reviews, see 1–6]. As for keratinocytes, a stem cell pool resides in the outer root sheath (ORS) of hair follicles also for melanocytes [7], illustrated clinically by the well-known phenomenon of follicular repigmentation in spontaneously healing vitiligo. Only 4 publications have reported on vitiligo treatment in hairy skin by the laborious procedure of hair follicle grafting [8–11].

With institutional review board approval and after getting written informed consent of the patients, we applied solutions of autologous ORS cells isolated by trypsinisation of plucked anagen scalp hair follicles (1 ml/cm^2 containing approx. 5×10^3 cells) to stable lesions of vitiligo and depigmented scars de-epidermised by erbium:YAG laser. After re-epithelisation, treated areas of vitiligo were irradiated with suberythematogenous doses of 311 nm UVB 2–3 times weekly. The clinical outcome was documented monthly by standardized photographs for up to 6 months. In 3 of 5 patients with vitiligo there was almost complete, in another around 50% repigmentation within 3 months with a diffuse repigmentation pattern (fig. 1a, b), while in 1 patient there was less than 10% repigmentation (table 1). In a patient with large depigmented scars on his back after acne conglobata there was even diffuse hyperpigmentation of the treated areas 4 months after ORS cell application without subsequent UVB irradiation.

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Prof. Thomas Hunziker
Department of Dermatology
Inselspital
CH–3010 Bern (Switzerland)
Tel. +41 31 632 22 88, Fax +41 31 632 22 33, E-Mail thomas.hunziker@insel.ch

In conclusion, melanocytes or stem cells thereof present in the ORS of plucked anagen scalp hair follicles can be used to treat depigmented skin. Harvesting of these autologous cells is non-invasive, which allows easy, immediate and repeated application. Using the patient's own skin as an incubator and thus avoiding cultivation of the cells in vitro is a further practical and also regulatory advantage of this technology, since malignant transformation of melanocytes upon stimulation of proliferation in vitro is still an issue. Optimal application modalities and cell numbers [12] have to be defined, and benefit evaluation [13] should be included in further studies. In depigmented scars, repigmentation may even be achieved without subsequent UVB irradiation.

Table 1. Vitiligo patients

Gender	Age years	Type, localization	Stable years	Repigmentation, %
Female	46	segmental, chest	3	>90
Male	57	focal, periorbital	10	>90
Male	25	focal, perioral	1	>90
Female	60	focal, chin	1	~50
Male	57	focal, back of hand	10	<10

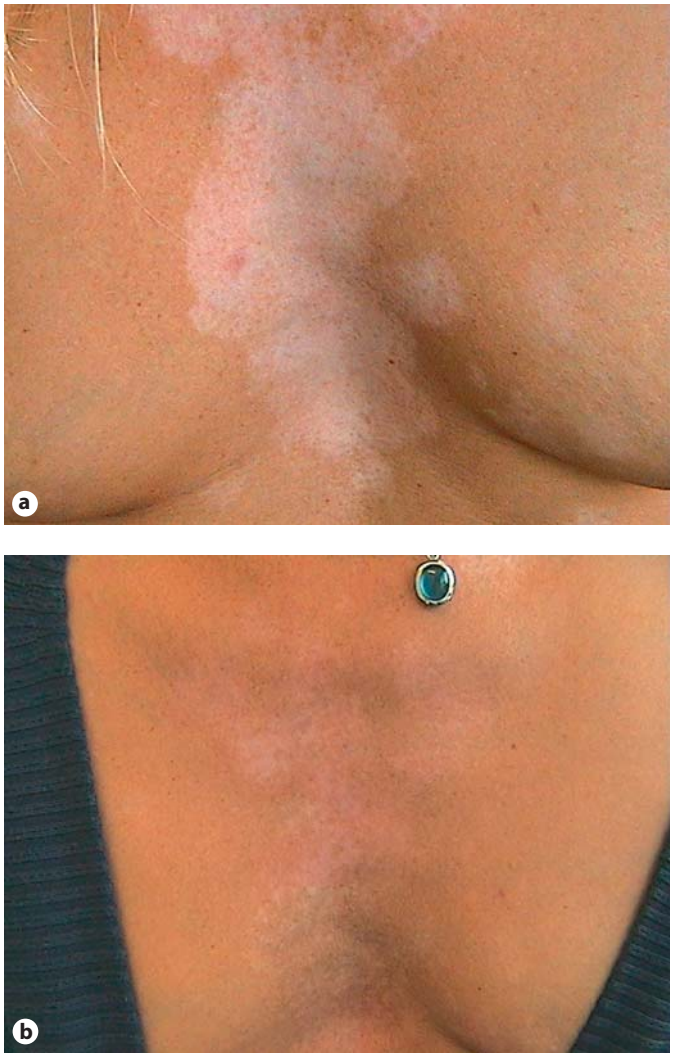

Fig. 1. Forty-six-year-old female with vitiligo on her chest stable for 3 years. **a** Before ORS cell treatment. **b** Diffuse repigmentation 3 months after ORS cell application followed by 20 sessions of UVB irradiation.

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