skin showed increased expression of both ST18 and TNF-α, and the study of 100 patients with PV showed the more severe phenotype in the PV group with the risk variant in the ST18 gene. The results of this study clearly indicate that the risk variant of the ST18 gene increases the expression of ST18 and TNF-α in the skin, which in turn exacerbates acantholytic changes in PV, suggesting anti-TNF biologics as a potential candidate for PV therapy.

This is an important study, which unravelled the novel PV pathomechanisms resulting from ST18, leading to the development of a new therapeutic strategy in this still untreatable disease. So far, some clinical trials have shown different effects of treatment with anti-TNF biologics in PV. Thus, the results of the present study may lead to the first precision medicine based on DNA information for the treatment of PV, i.e. anti-TNF therapy used to treat selected patients with PV who have the ST18 pathogenic variant.

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Expanding the use of allogeneic haematopoietic cell transplantation in dermatology

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Epidermolysis bullosa (EB) comprises a group of rare, genetically determined skin fragility disorders characterized by (muco)cutaneous blistering following mild mechanical trauma. The most severe clinical symptoms occur in patients affected by mutations in genes coding for type VII collagen and the subchains of laminin 332. In these patients, mainly mutations leading to protein chain termination result in disease manifestations in the bronchopulmonary, gastrointestinal, urogenital and ophthalmic systems in addition to the skin.[1]

Pathogenetically derived therapy needs to replenish the missing protein in a systemic fashion. However, life-saving and quality-of-life-improving results have also been shown by several ground-breaking studies using transplantations of gene-corrected skin transplants.[2–6] Despite this success, the logistic challenges of producing these transplants and the imminent possibility of gene dysregulation by genomic insertion of vectors or off-target effects of gene editors encourage investigating different approaches.

One straightforward idea would be using skin from related haploidentical people with healthy skin. Not surprisingly, graft rejection is the main threat in this procedure.[7] In this issue of the *BJD*, Ebens *et al.*[8] have now combined allogeneic haematopoietic stem cell transplantation with transplantation of donor skin from the initially related blood donor. In a prospective, open-label clinical trial for postallogeneic haematopoietic cell transplantation (post-alloHCT) in eight patients with RDEB, up to nine chronic wounds per patient were grafted over 1 year. These patients received a total of 35 epidermal allografts at a median of 1157 days post-alloHCT. The median percentage reduction in wound surface area was almost 100% at 52 weeks after grafting. In one patient, biopsy evaluation at 1 year of an epidermal allograft site revealed wildtype type VII collagen, anchoring fibrils, and 42% full-thickness-skin whole DNA donor chimerism. These results suggested that epidermal allografts included nonterminally differentiated cells and might trigger recruitment of bone-marrow-derived cells to mediate wound healing.

Where is this study positioned in the potential armamentarium of the responsible physician? The logistic hurdles of hologene detection and expansion in 'conventional' transplantation studies with gene-corrected cells in an environment of good manufacturing practice change against the logistic setting of

haematopoietic stem cell transplantation associated with considerable morbidity and (depending on the protocol) mortality. If the alloHCT is successful, further transplantation procedures are easily performed in an outpatient setting.

In case further improvement of the HCT procedure is possible, combining this procedure with donor cell grafts of different origins is a thinkable alternative to ameliorate not only the skin symptoms in EB. In any case, it is interesting to see how alloHCT could drastically change therapy options in dermatology.

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