Improvements of the clinical phenotype in collagen XVII knockout mice by bone marrow transplantation

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There are currently no effective treatments to improve the prognosis in epidermolysis bullosa (EB), which is a group of congenital genodermatoses caused by the lack of basement membrane proteins. Recent studies have shown that bone marrow-derived cells (BMDCs) can play a significant role in regenerative medicine by differentiating into various cell types. We previously reported that 0.05% of epidermal keratinocytes at wound sites were derived from donor BMDCs in bone marrow transplantation (BMT) model mice. The purpose of this study was to determine whether a knocked-out protein can be re-expressed after BMT, and to explore the possibility of using this technique to treat severe forms of EB.

Firstly, we investigated whether human cells could differentiate into keratinocytes as demonstrated by our mouse BMT model. Human cord blood cells were transplanted into immunodeficient NOG (NOD/Shi-scid, IL-2Rγ<sup>−/−</sup>) mice. At the wound site we found cord blood-derived keratinocytes as well as expression of human BMZ proteins such as collagen XVII (COL17). Subsequently, BMT was accomplished using cells from green fluorescence protein (GFP) expressing-transgenic mice into our recently established adult COL17 knockout mice, which was used as a model for human junctional EB. The expression of COL17 beneath GFP+ epidermal cells was found at the wound site in BMT-treated COL17 knockout mice. Furthermore, BMT-treated mice showed fewer EB-associated erosions and better survival rates (73.2% versus 20.6%, 150 days after BMT, p<0.05). These findings indicate that conventional BMT techniques show significant potential as systemic therapeutic approaches for treatment of human severe EB.