# Technology Offer

**Ref.-No.0212**

## Use of transglutaminase 1-liposomes for topical enzyme replacement therapy for transglutaminase 1 deficient lamellar ichthyosis

### Introduction

Transglutaminase 1-deficient lamellar ichthyosis is a severe genetic skin disease, which is characterized by collodion baby at birth, dramatically increased transepidermal water loss with the inherent clinical problem of dehydration, which can be life threatening during the first weeks of life, and a lifelong pronounced scaling of the skin. Additional complications include fluid and electrolyte imbalances and failure to thrive. Despite of modern intensive care the mortality rate of newborns is around 5-10%.Currently no causative therapy for transglutaminase 1-deficient lamellar ichthyosis is available. A variety of other treatment methods can provide symptomatic relief and are directed at improving symptoms and severity of the disease.

### Invention

In the present invention recombinant human transglutaminase 1 encapsulated in specialized, sophisticated liposomes (rhTG1-LUVs) should compensate for the defective cross-linking activity of TG1 and thus be a promising strategy to restore epidermal integrity and barrier function in individuals with lamellar ichthyosis due to transglutaminase 1 deficiency.

### Advantages of the invention

We developed sophisticated liposomes with encapsulated recombinant human TG1, which were coupled with a specialized peptide to mediate cellular uptake. In cell culture experiments these topically applied liposomes provided sustained delivery of TG1 into primary keratinocytes. To show the general feasibility of this approach we used a skin-humanized mouse model for TG1-deficiency (Aufenvenne et al. 2012) which allows us to test the TG1-liposomes in a humanized context.

We believe that a pharmacological approach using recombinant human transglutaminase 1 encapsulated in liposomes (rhTG1-LUVs) should compensate for the defective cross-linking activity of TG1 and thus be a promising strategy to restore epidermal integrity and barrier function in individuals with lamellar ichthyosis due to transglutaminase 1 deficiency.

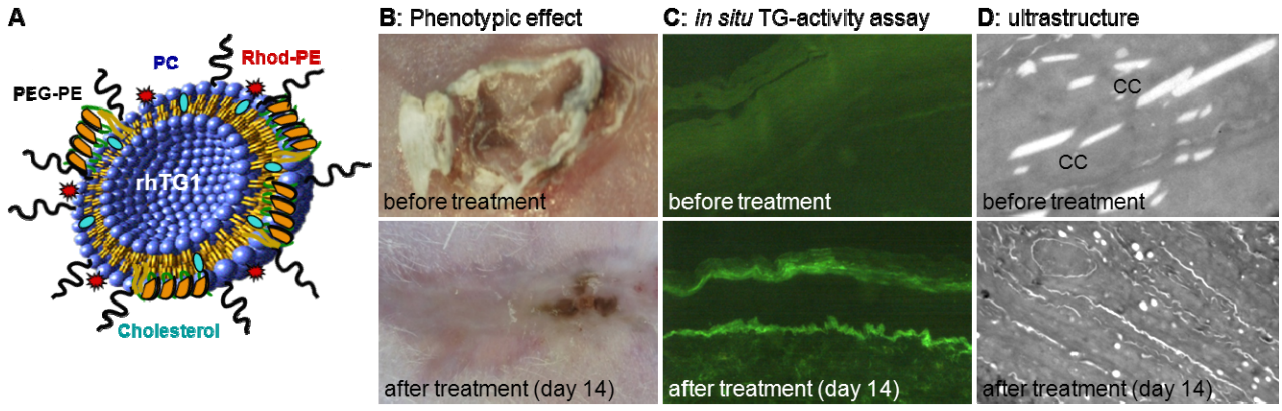


**Fig. 1**: (**A**) Liposomes with encapsulated recombinant human transglutaminase 1 which permit cellular uptake of the enzyme. (**B-D**): A skin humanized mouse model for TG1-deficient LI was used to test rhTG1-liposomes. We show evidence that in human skin derived from patients with TG1-deficiency the clinical LI-phenotype can be reversed (**B**). After treatment we observed a considerable improvement of the ichthyosis phenotype. Treatment with TG1-liposomes, in contrast to empty liposomes, resulted in normalization of the regenerated LI skin: *in situ* monitoring showed a restoration of TG1-activity (**C**) and ultrastructurally *cholesterol clefts* as important diagnostic markers were no longer detectable (**D**).


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