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## ***Tremendous progress in the development of skin stem cell treatments for butterfly children***

*Scientists at IMBA – Institute of Molecular Biotechnology of the Austrian Academy of Sciences in Vienna have made a major advancement towards a future therapy for butterfly children. A treatment with fibroblasts generated from induced pluripotent stem cells has been highly successful in mice. The next step is to establish this method in humans.*

“Butterfly children” suffer from Epidermolysis Bullosa (EB), a debilitating skin disease. It is caused by a genetic defect that leads to a deficiency or complete lack of various structural proteins. In one particularly severe form, the protein collagen 7 is either missing or present only in insufficient amounts. If that bond is missing, the skin forms blisters or tears at the slightest mechanical pressure, leading to wounds and inflammation that require extensive treatment with creams and bandages. Often these constant lesions also lead to aggressive forms of skin cancer.

Presently there is no cure for this disease. But there are promising approaches that could lead to successful treatments in the future. One of them is a method called “fibroblast injection”. In this procedure, fibroblasts are injected between the layers of the skin, where they can produce the necessary collagen 7.

Researchers at IMBA under the leadership of Arabella Meixner have now been successful in developing this method to treat mice affected by EB. The individual steps of this treatment have been worked out and carefully tested in many years of laboratory work, and the results have now been published in the scientific journal “Science Translational Medicine”.

First the scientists returned skin cells of the diseased mice to the stem cell stage and then repaired the genetic defect, the root cause of the disease. Then the researchers transformed stem cells back into fibroblasts.

Before the repaired fibroblasts could be reintroduced into the organism, measures to prevent inflammation or rejection were necessary. In this study the researchers conducted a type of “toxicity test”, and the results were very promising. After several months of observation, no adverse immune reactions occurred, and the risk of skin cancer did not increase. That is an important consideration because “butterfly children” already have a greatly increased risk of skin cancer.

But the greatest success of the researchers was the significantly increased tear resistance of the skin. Arabella Meixner, research lead, is delighted at the good results: “Our mechanical stress test with a soft eraser brush demonstrated that the skin of the mice treated with the stem cell therapy remained stable, and that no more wounds occurred. That means there was enough collagen 7 between the skin cells to hold them together properly. Our study clearly showed that this method is suitable for a future therapy for “butterfly children.”

The next step is to establish this skin stem cell treatment in humans. To achieve that, the IMBA scientists intend to look for partners with clinical experience. For severe forms of Epidermolysis Bullosa, a systemic application needs to be developed to spread the cells throughout the entire body via the bloodstream to reach epithelial tissues that are more difficult to access, for example the mucous membranes in the



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mouth or bowels. Often in “butterfly children” with milder forms of the disease, only certain areas of the skin are affected. The skin stem cell therapy with local injections successfully tested on mice could lead to a valuable treatment method in the very near future.

The project conducted by IMBA scientists was initiated by the patient organization DEBRA Austria, and has had the financial support of the association and of other generous supporters since 2009. DEBRA’s mission is to ensure that “butterfly children” receive competent specialized medical care and to promote research into options to relieve and cure EB. Further thanks also go to our funding and cooperation partners „Österreichische Lotterien“ and „FK Austria Wien“.

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