EUROSKINGRAFT: A EUROPEAN PROJECT

After more than 12 years of research, the Tissue Biology Research Unit (TBRU) outlines its new complex skin grafts for clinical application, as Prof Ernst Reichmann explains

Large, full thickness skin defects resulting from burns, congenital giant nevi, disfiguring scars, soft tissue trauma, tumour resection and disease leading to skin necrosis, represent a significant and common clinical problem worldwide, and this problem is far from being solved.

The main challenge encountered is that most autologous skin grafting techniques are based on transplanting split thickness skin (today's gold standard). Split thickness skin contains all of the epidermis, but only remnants of the dermis (see histological section in Fig. 1). This lack of dermal tissue frequently leads to significant scarring, hence to unsatisfying functional and cosmetic results. Our concept to overcome this problem is derived from our long standing and fruitful collaboration between scientists and clinicians.

Insights and innovations

Our work resulted in the insight that improving the quality of the reconstituted dermis is of paramount importance to significantly ameliorate the clinical outcome. In addition, we are stringently aiming at a one-step surgical procedure (instead of the very common two-step procedure that employs acellular templates).

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Based on these insights and concepts, our research has brought about three skin grafts, NovoMaix, denovoDerm and denovoSkin that were successfully tested in preclinical studies (Fig. 1).

The complex, bioengineered skin grafts resemble the properties of normal human skin as closely as possible. They are intended to be applied in clinical disciplines, such as burns and plastic surgery and dermatology, in Europe.

This translational medical project aims at the undertaking of clinical trials, which were started in 2013. Phase I and II trials are (and will be) undertaken in close collaboration with the Pediatric Burn Center in Zurich, the Dutch Burn Centre, Beverwijk and the Unfallkrankenhaus in Berlin, along with the Clinical Trial Center (CTC) and the Swiss Center for Regenerative Medicine (SCRM) in Zurich.

Innovations with impact

At a glance:

- The therapeutic potential of the three novel skin substitution products (denovoSkin, denovoDerm, and NovoMaix) is expected to clearly reach beyond the present clinical possibilities;
- Potential users of the three novel products are burn surgeons, plastic reconstructive and aesthetic surgeons and dermatologists. Clinical application of these novel products is expected to significantly reduce a common and central clinical problem;
- All three skin substitution products are to be applied in only one surgical intervention. This means a significant reduction of the economic burden;
- The above mentioned skin substitutes are expected to grow to the same degree as the body of a child grows. Thus, the problem of skin substitutes that do not grow with the child, in particular at the joints, may not occur. Also this will significantly reduce secondary surgical interventions and therefore costs;
- Patents on the skin substitutes, as well as on the novel devices coming along with disposable elements, are filed;
- Commercial marketing of devices, and skin substitutes is envisaged, and to be supported by the published results of the clinical trial programme; and
- Volume sales will be via a new company (or companies) established to commercially exploit the various products through a conventional manufacturing and sales business model. Alternatively this will be via a commercial licensing agreement with an existing corporation active in this market.

The future of novel skin grafts

The novel skin grafts introduced above are a result of more than 12 years of research. As their approval by the regulatory authorities took quite some time, and at the same time our research activities resulted in new considerable findings and insights, it is clear that we can do more and better than we are presently allowed to do in the foreseen clinical studies.

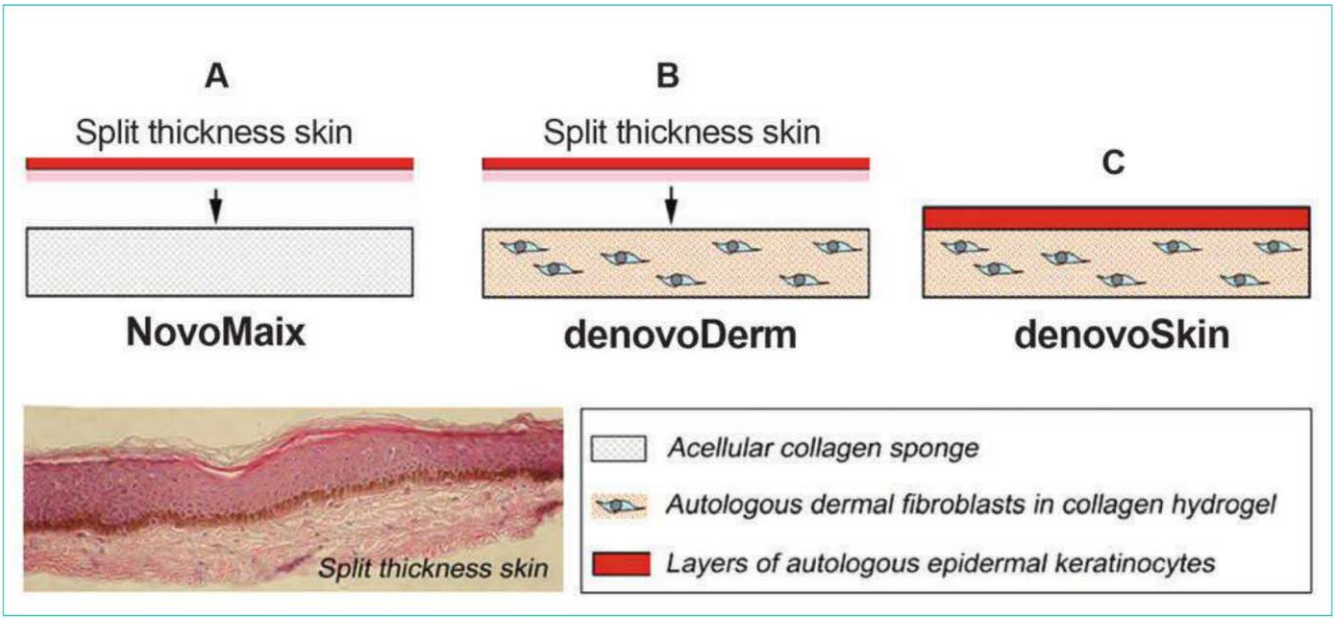

Fig.1 The three skin substitution products NovoMaix, denovoDerm and denovoSkin to be applied in the envisaged clinical trials. A) NovoMaix is an acellular collagen-sponge (scaffold) to be used in combination with autologous split-thickness skin. B) denovoDerm is a neodermis-like regeneration graft consisting of a plastically compressed collagen hydrogel into which autologous dermal fibroblasts are seeded. DenovoDerm is to be used in combination with split thickness skin. C) denovoSkin is a dermo-epidermal skin substitute based on plastically compressed collagen, seeded with autologous dermal fibroblasts and covered by autologous epidermal keratinocytes

Most importantly, we can now introduce both a blood and a lymphatic capillary plexus into dermo-epidermal skin grafts. These exert positive effects on skin structure and graft regeneration.

An additional achievement is that we can insert a functional melanocyte compartment into dermo-epidermal grafts, resulting in an appropriate skin colour.

An uncommon undertaking

The Tissue Biology Research Unit has developed, and is now producing, denovoSkin and denovoDerm, which are two Advanced Therapeutic Medicinal Products (ATMP). In terms of approval, regulatory authorities, such as the FDA, EMA or Swissmedic treat ATMPs like drugs.

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This implies that a research institution like the TBRU has to divert into two branches, namely a basic research unit and a department working on the (GMP) production and approval of the ATMP. This is demanding and extremely expensive, which explains why such an undertaking is usually performed by powerful industrial enterprises ('big pharma').

It is largely due to the financial support of FP6 and FP7 EU programmes that the TBRU, hence an academic institution, was able to achieve that (at least so far). As a 'side effect' of these prestigious EU supports, the TBRU and their European partners were profiting from a greater recognition by their local universities, who also profited from the grant-associated overheads. As a consequence, at least some of the partners, were selected by their universities to participate in additional programmes and financial support, which however was (and still is) urgently needed.

This said, it should be mentioned, that the continuation of the aforementioned clinical testing, and larger scale clinical application, will not be possible without additional funding and networking. However, as the TBRU will always be a 'no risk partner' in a European consortium, we are confident that the envisioned clinical project and perhaps the successful launching of novel skin substitution products on the market, will come into being.

Prof Dr Ernst Reichmann directs the Tissue Biology Research Unit in Zurich and co-ordinates the European Union FP7 project EuroSkinGraft and the Clinical Research Priority Program UZH-SkinGraft of the University of Zurich.

tissue biology research unit

EuroSkinGraft

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