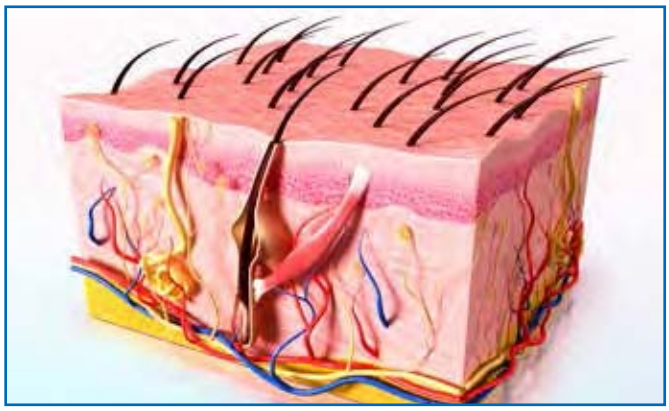
BIOLOGY AND MEDICINE

Optimised artificial grafts for severe skin defects

A European research initiative is continuing development of the skin substitutes Novomaix, denovoDerm and denovoSkin. Clinical studies will test a one-step surgical procedure.



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Large full-thickness skin defects resulting from burns and tumour removal, for example, still present significant clinical problems. Taken from the patient, an autologous graft can result in significant scarring due to possible lack of dermal tissue.

The project EUROSKINGRAFT[1] aims to bring the three novel skin-reconstitution products through clinical trials and then to European and international markets. The dermal substitutes were developed for clinical use with substantial support from the EU's Sixth Framework Programme (FP6) project EUROSTEC[2].

At the halfway stage, EUROSKINGRAFT researchers have successfully worked on optimising the production of denovoSkin and denovoDerm. MagNA Lyser Green Beads have been successfully used for homogenisation of the skin substitutes. For the dermis, two marker candidates give a good indication of fibroblast activity that is necessary to maintain skin integrity. Relevant genes have been selected for the epidermis and quantified using 'quantitative polymerase chain reaction' (qPCR).

Approval has been given to two partners for phase I clinical trials, and personnel have received training in good clinical practice. Novomaix has received *Communauté Européenne* (CE) certification and is already in phase I trials. The required toxicology studies for denovoSkin and denovoDerm have been finalised using 'good laboratory practice' (GLP) standards.

All three substitute skins have the advantage that they require one surgical intervention, unlike most current treatment alternatives. In contrast to acellular options on the market, the three EUROSKINGRAFT products exhibit the structure and function of skin immediately. The artificial skins are expected to grow at the same rate as those of a child, thus also eliminating the need for additional surgery.

The artificial skins are all highly functional and represent the pinnacle of regenerative medicine as applied in the clinic. Towards the project end in 2016, it is anticipated that devices and matrix templates as well as the skin substitutes will all be marketed commercially.

The project was coordinated by the University of Zurich in Switzerland.

1 'A novel generation of skin substitutes to clinically treat a broad spectrum of severe skin defects'.
2 'Soft tissue engineering for congenital birth defects in children: new treatment modalities for spina bifida, urogenital and abdominal wall defects'.

Funded under the FP7 specific programme 'Cooperation' under the research theme 'Health'.
http://cordis.europa.eu/result/brief/rcn/12315_en.html
Project website:
http://www.euroskingraft.eu/

The hippocampus in memory and behaviour

The role of brain structures such as the hippocampus and associated neural circuits in regulating anxiety and memory is still poorly understood. The EU-funded HIPPOPROJECTION project was initiated to elucidate their role in anxiety and memory regulation using mice models.

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HIPPOPROJECTION[1] successfully developed a pharmacogenetic tool to selectively inhibit neural projections associated with the hippocampus. This tool comprises 'adeno-associated viruses' (AAVs) expressing a human 'M4 DREADD receptor' along with certain drugs. Results have been validated in mice models and further optimised, enabling testing in wild-type mice models rather than necessitating the development of genetically modified mice.

The 'dentate gyrus' (DG) in the hippocampus is believed to have a role in memory, learning and plasticity. Researchers selectively and reversibly inhibited neural activity in the DG using mice models to study hippocampus-dependent memory tasks during trace eye-blink conditioning. Scientists were able to identify the structures and neural circuits associated with rapid and persistent memory loss during conditioned responding and learning-associated plasticity.

Recording electrodes were implanted in mice to characterise brain structures associated with the hippocampus. Some important areas investigated include the 'ventral hippocampus' (vHIP), the prelimbic area of the 'medial prefrontal cortex' (mPFC) and the 'rostral lateral septum' (rLS). To test anxiety behaviour, these rats were subjected to open field, elevated plus maze and familiar arena tests, and their local field potentials were analysed.