“Towards ex-vivo gene therapy for a permanent treatment of RDEB”

DEBRA International is the patient organisation partner, along with 5 other expert partners, in the GENEGRAFT collaborative project funded by the European Union through the 7th framework programme, and coordinated by Prof. Alain Hovnanian of INSERM (Paris, France). GENEGRAFT started on March 1st 2011 and will last 5 years.

How will the GENEGRAFT gene therapy work?

Skin grafts are being made of the two types of skin cell – keratinocytes and fibroblasts – derived from the patient's own skin and genetically corrected in the laboratory. This is being done using a safer ‘self-inactivating’ vector carrying the collagen 7 gene, which has been created as part of the project. It is expected that the skin cells in the graft will then produce the collagen VII protein that is either missing or faulty in the skin of people with RDEB.

It is important to realize that only the grafted area of skin will have the RDEB fault corrected, but such a therapy type could be very valuable for people who have areas of non-healing chronic wounds. In addition, the technology being developed for this project will be very important in the further development of other gene- and cell-therapies.

The process for making the skin grafts and getting approval for their clinical use is complex, requiring many steps, hence the involvement of many partners in the project, each bringing the necessary specific expertise. Each step in gene correction and the production of the skin grafts is subject to very close scrutiny by ethical and regulatory authorities in Europe to ensure patient safety.

The Stanford ex-vivo (skin grafting) gene therapy trials – similarities with and differences from the GENEGRAFT clinical trial

GENEGRAFT is not the first clinical trial for a grafting (‘ex-vivo’) gene therapy for RDEB. Other researchers in Stanford University (California, USA) have also started an early-stage clinical trial for a grafting gene therapy for people with RDEB, and so far, 4 of the 5 patients enrolled in the trial have been grafted.

However, there are a couple of key differences: first is that the Stanford trial is using an older-style vector, a type which is not currently approved for use in Europe because of possible safety concerns arising from other clinical trials for other disease treatments. GENEGRAFT has developed the new, safer self-inactivating vector, which is allowed by the EU.

In addition, the Stanford trial is grafting gene-corrected keratinocytes only, rather than gene-corrected fibroblasts and keratinocytes. The GENEGRAFT team believe that the fibroblasts play an important role in the RDEB disease process, and that using both cell types in a skin graft may have greater benefits.

www.genegraft.eu

C Robinson, Head of Research DEBRA International

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