

Grant Number		Duration (years)	Start Date
GGP08095		2	
Project Title			Status
PRE-CLINICAL DEVELOPMENT OF LENTIVIRAL VECTORS FOR GENE THERAPY OF JUNCTIONAL EPIDERMOLYSIS BULLOSA			ON
Project Holder		Institute	
Principal Investigator		RECCHIA ALESSANDRA	DIPARTIMENTO DI SCIENZE BIOMEDICHE, MODENA UNIVERSITA' DI MODENA E REGGIO EMILIA
Granted Funds			
€ 171.700			
Disease			
Epidermolysis bullosa			
Summary			
<p>Junctional epidermolysis bullosa (JEB) is a genetic skin adhesion defect caused by mutations in the genes encoding laminin-5 (LAM5), a key component of the epidermal-dermal junction. The severity of JEB may vary from perinatal lethality (the so-called Herlitz forms) to highly disfiguring clinical pictures characterized by blistering, infections, visual impairment, and an increased risk of skin cancer. There is no cure for JEB, and current therapeutic approaches are essentially aimed at controlling infections and maintaining an acceptable quality of life. In a pilot clinical trial carried out in 2005 on a patient affected by a non lethal form of JEB, our group showed that transplantation of cultured skin derived from the patient's genetically corrected epidermal stem cells is feasible, well tolerated, and leads to long-term functional correction of the skin adhesion defect. The trial was funded by a joint effort of Telethon and the AFM. Unfortunately, the genetic vector used to transfer the therapeutic gene into the stem cells has raised significant safety concerns after five patients undergoing gene therapy for an unrelated disease in France and the UK developed a treatment-related leukemia-like disorder. The first trial was put on hold, and development of a safer gene transfer vector is now necessary to resume clinical investigation. The aim of this project is therefore to develop an alternative gene transfer strategy for epidermal stem cells, based on a new type of vector (a so-called self-inactivating lentiviral vector) and a skin-specific regulatory elements to drive the therapeutic gene. The efficacy and safety characteristics of the new vectors will be tested in parallel with those of the original vector by specifically designed assays. The new vector will hopefully allow to resume clinical investigation on gene therapy of JEB* and to assess its therapeutic potential.</p>			

* Nature Medicine, Vol. 12, No. 12 (19 November 2006), pp. 1397-1402