Grant agreement n. 874807

Anchored Muscle cELls for IncontinencE

D5.2 Validation of qualitative PCR methodology for detection and phenotypic analysis of transplanted human myoblasts

Work Package: 5

Due date of deliverable: month 7

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Lead beneficiary for this deliverable: UCL

Contributors: UCL

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Dissemination Level		
PU	Public	
CO	Confidential, only for members of the consortium (including the Commission Services)	X
CI	Classified, as referred to in Commission Decision 2001/844/EC	

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Version log

Version	Date	Released by	Nature of Change
1.0	28.06.2021	Silvia Gigli	N.A.

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Definition and acronyms

Acronyms	Definitions
AMELIE	Anchored Muscle cELls for IncontinencE
CRL	Charles River Laboratories
EMA	European Medicines Agency
MHRA	Medicines and Healthcare products Regulatory Agency
SMDC	Skeletal muscle derived cell
SCID	Severe Combined ImmunoDeficiency
TIPS	Thermally Induced Phase Separation
UCL	University College London
WP	Work Package

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Non-clinical evaluation of safety and expected biological behaviour of the finished product

As with all biological products, non-clinical safety programmes for cell-based medicinal products are very much product-specific and designed on a case-by-case basis. Current EMA guidance for the preclinical evaluation of cell-based medicinal products requires demonstration of safety in a non-clinical model. Discussion between AMELIE beneficiary UCL and the regulatory authorities in the UK (MHRA) and Europe (EMA) has indicated non-clinical safety assessment (biodistribution) should be conducted using human cells attached to the product rather than performing autologous transfer in pre-clinical species. Previous non-clinical studies conducted by UCL in athymic rats have demonstrated rejection of human SMDC when attached to TIPS microcarriers due to the cytotoxic response of the innate immune system. For non-clinical safety studies in the AMELIE project, a more immunocompromised model (NOD SCID gamma mice - homozygous for the SCID mutation, impaired T and B cell lymphocyte development and deficient natural killer cell function) has been identified as being suitable for implantation of human cells for biodistribution studies.
The non-clinical safety testing programme in WP5 has been rationally designed with a strong scientific understanding of the finished product, including its method of manufacture, purity, structure, pharmacological and immunological effects and intended clinical use.

At the project planning stage it was deemed necessary (based on preliminary discussions with CROs) to establish and validate qPCR methodology to identify appropriate markers that would confirm the presence of human skeletal muscle cells implanted into immunocompromised mice. This was included in Task 5.1 (Design, optimisation and validation of qualitative PCR methodology for detection and phenotypic analysis of transplanted human myoblasts) of the original project plan and Deliverable 5.2.

The non-clinical safety studies to be subcontracted in Work Package 5 was put out to competitive tender. Based on our discussions with three possible providers we determined Charles River Laboratories (CRL) to be best suited to deliver this work. This was based on our judgement of technical and regulatory understanding of the requirements, responsiveness, availability to deliver within the timelines of the grant and cost.

Furthermore, CRL are able to provide PCR evaluation of the transplanted human cells in mouse tissues using their inhouse off-the-shelf hTERT method. The availability of existing qPCR methodology will reduce the time required for Work Package 5 and has resulted in Deliverable 5.2 (validation of qualitative PCR methodology) no longer being required.

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