EXPRESSION CASSETTES, VECTORS AND USES THEREOF FOR REGULATED LNCRNA EXPRESSION AND TELOMERE MAINTENANCE

A research team from CIEMAT, Fundación Jiménez Díaz and CIBER has developed a novel ex vivo gene therapy approach for telomeropathies caused by TERC haploinsufficiency and other telomere biology disorders.

The Need

Dyskeratosis congenita (DC) is a rare inherited telomere biology disorder characterized by critically short telomeres, progressive bone marrow failure, pulmonary and hepatic fibrosis, and increased cancer susceptibility.

TERC haploinsufficiency causes autosomal dominant DC (AD-DC), with a disease spectrum extending to aplastic anaemia, idiopathic pulmonary fibrosis and related telomeropathies. Current treatments, including androgen therapy and haematopoietic stem cell transplantation (HSCT), have limitations and carry significant morbidity.

Despite advances in gene and cell therapy, few approaches target TERC expression. There remains an unmet need for strategies restoring functional TERC lncRNA expression and correcting telomeric defects, with potential applications in haematopoietic stem and progenitor cells (HSPCs) and other cellular contexts with high replicative demand.

The Solution

The technology is based on expression cassettes and delivery systems for human TERC lncRNA expression. The technology includes vectors, cellular products comprising the cassette of vectors and potential use in telomere binding disorders and high-replicative demand cellular therapies.

Innovative Aspects

Core innovation: a TERC-specific expression cassette combining the endogenous TERC promoter region, the TERC lncRNA sequence and the downstream TERC 3' processing regulatory region. This design retains TERC-specific regulatory elements to support functional TERC availability.

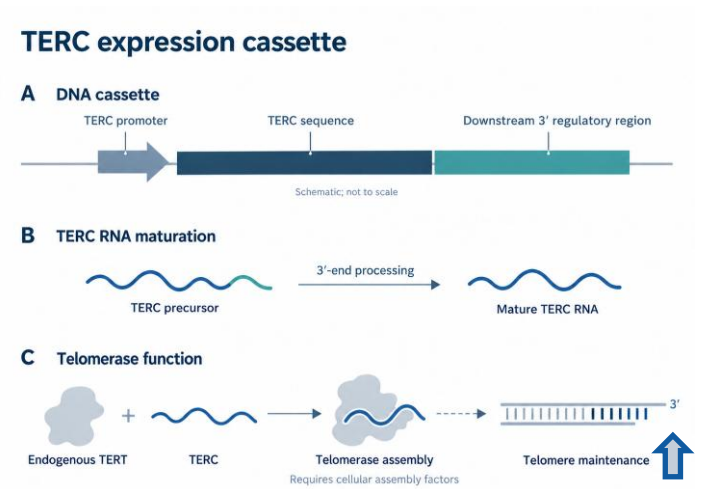
Main advantages:

- Processing-compatible TERC lncRNA output.
- Support of telomere maintenance in TERC-limited cellular contexts.
- Applicability to ex vivo modified HSPCs and immune-cell products.
- Potential improvement of proliferative durability and persistence in high-replicative-demand cells.
- Compatibility with lentiviral, AAV and donor-template configurations.

Therapeutic and cell-engineering applications: the technology is particularly relevant to DC caused by TERC insufficiency. Its potential applications extend beyond inherited telomere biology disorders to cells in which telomerase-mediated telomere maintenance may become insufficient to meet high replicative demand during manufacturing or therapeutic use. Increasing functional TERC availability may support telomere maintenance and preserve replicative capacity where TERC becomes a limiting component of telomerase function, subject to cell-type- and application-specific validation.

Stage of Development: preclinical proof of concept supported by in vitro studies and in vivo evaluation in mouse models of AD-DC and other telomeropathies.

Preclinical results support telomere length restoration and haematopoietic rescue in the models evaluated. Further development includes assessing telomere maintenance and replicative capacity in cell-based medicinal products subjected to extensive ex vivo expansion or sustained proliferative demand, alongside application-specific efficacy and long-term safety evaluation.



Intellectual Property:

European patent application in 2026
Suitable for PCT extension

Aims

Seeking partners interested in licensing and/or co-development agreements to advance this technology toward clinical translation and commercialization.

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