CHANGER

CHALLENGES AND INNOVATIVE CHANGES IN RESEARCH ETHICS REVIEWS

Gene therapy trials from the perspectives of patients and the public

Phaedra Locquet,
Ph.D. Candidate Centre for Biomedical Ethics and Law (KU Leuven, Belgium)

Funded by
the European Union

Research on public and patients' perspectives on gene therapy

*Aiyegbusi, O.L., Macpherson, K., Elston, L. et al. Patient and public perspectives on cell and gene therapies: a systematic review. Nat Commun **11**, 6265 (2020). https://doi.org/10.1038/s41467-020-20096-1*

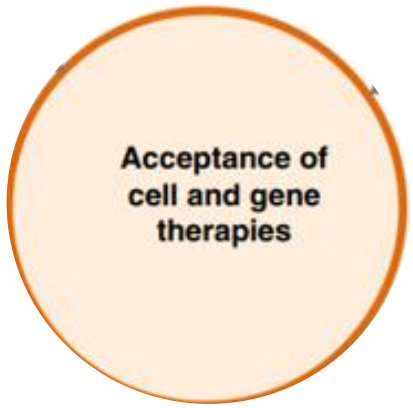
Knowledge and understanding

Varying levels of knowledge and awareness

- Use of viral vectors
- Likelihood of transmitting infection
- Risks of concomitant chemotherapy
- Distinction research vs. approved therapy
- Timeframe scientific discoveries and regulatory approvals
- Misconceptions: clinical trial purpose (Phase 1 = safety)

Desire for information & clarity <> no need to understand, trust healthcare providers

Acceptance



Variable acceptance of cell and gene therapies

- Increased after information provision
- **Drivers of acceptance:** perceived benefits, severe disease, higher mortality risk
- **Influencing factors:** older age, male gender, higher education, greater disease severity (<> public: older age, less supportive)
- **Altruism** as motivation for trial participation (older individuals)

Barrier to acceptance

- Non-therapeutic purposes
- Enhancement
  - → threat for genetic diversity in LT
  - highest levels of support for: increasing life span, improving intelligence, and improving strength and fitness
- Affordability, availability

Trust and regulation: need for strict oversight and clear communication

Understanding risk and benefits

Overestimation of benefits (disease limiting <> disease reversing)

- High: male, older, greater disease severity

Concerns balance uncertainty benefit vs. potential risks

- High: parents of younger children
- Low: older children, greater health deterioration, and limited treatment options

Chemotherapy

Information on these elements required to make an informed assessment of R-B

Information needs and sources

Desire for more information

- Results large, long-term studies
- Report risks & side-effects studies
- Personalised information
- Eligibility **criteria**

Source of information

- Television, magazines, radio, clinicians, friends, colleagues
- Most reliable source: physicians
- Public trust in information from scientist, medical researchers

Patient involvement

From research subject → **CONTINUUM OF INVOLVEMENT** → **to research partner**

Consultation	Collaboration	Co-production
Patients are asked for their views on study design, outcomes, and consent procedures	Patients are co-researchers: involved in planning, recruitment, and data interpretation	Patients and researchers jointly lead the research: equal say in all decisions

Why does this matter in gene therapy? It improves…

- trial design
- consent processes
- relevance of outcomes
- trust in science
- Adaption of new therapeutic approaches

Conclusion

1

Gene therapy trials are ethically distinct

Irreversibility, long-term uncertainty, and small vulnerable populations demand heightened ethical scrutiny beyond standard drug trials.

2

Informed consent is genuinely complex

Therapeutic misconception, vulnerability, and scientific complexity make true informed consent in gene therapy trials particularly challenging.

3

The patient perspective is indispensable

PPI is not a formality. Patients with rare diseases hold unique knowledge about acceptable risk, meaningful outcomes, and unmet needs.

CHANGER

CHALLENGES AND INNOVATIVE CHANGES IN RESEARCH ETHICS REVIEWS

Thank you

Project partners

DEMOKRITOS NATIONAL CENTRE FOR SCIENTIFIC RESEARCH

ΠΑΝΕΠΙΣΤΗΜΙΟ ΔΥΤΙΚΗΣ ΑΤΤΙΚΗΣ UNIVERSITY OF WEST ATTICA

SVEUČILIŠTE U SPLITU MEDICINSKI FAKULTET UNIVERSITY OF SPLIT SCHOOL OF MEDICINE

university of groningen

TU WIEN TECHNISCHE UNIVERSITÄT WIEN

NORSUS Norwegian Institute for Sustainability Research

UNIVERSITY OF BUCHAREST

UNIVERSITÄT BONN

K&I Knowledge and Innovation

KU LEUVEN

LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

UNIVERSITY OF MACEDONIA

KIT Karlsruhe Institute of Technology

Funded by the European Union

Views and opinions expressed are however those of the author(s) only, and do not necessarily reflect those of the European Union. Neither the European Union nor the granting authority can be held responsible for them.

CHANGER

CHALLENGES AND INNOVATIVE CHANGES IN RESEARCH ETHICS REVIEWS

Let's get to work!

Case Study

Funded by
the European Union

Case

Over the past 5 years, a team of researchers across the EU have been creating a **gene editing-based gene therapy tool using a CRISPR-based gene editing tool, base editors, to treat Leber congenital amaurosis (LCA10).** The team's approach is to create an ex-vivo gene editing-based gene therapy to treat LCA10 involves the following steps:

- Extraction of retinal cells: cells expressing the disease-causing gene are harvested from the patient's retina
- Laboratory cell modification: Base editors (gene editing intervention) will be used to modify the disease-causing gene to restore healthy function in the lab
- Patient receives transplantation of cells: gene-modified cells are transplanted back into the patient's retina

The study duration will be 24 months, and patients will be checked at regular intervals. **The study aims to recruit 25 patients aged between 18-40 diagnosed with LCA10 (only the CEP290 gene)** and who already have significant visual impairment or blindness. The team conducted extensive pre-clinical studies in rats, which showed that this gene editing therapeutic provided significant improvement in eyesight. The team is hoping to **determine the intervention's safety, patient tolerability for treatment, and clinical efficacy**. Finally, the team has clearly stated that their intentions are only to create this product for therapeutic purposes and will not be creating intentional germline changes.

CHANGER

CHALLENGES AND INNOVATIVE CHANGES IN RESEARCH ETHICS REVIEWS

Up to you, now…

Funded by
the European Union

Reflection

Why the study is ethically acceptable

- Uses **somatic (ex-vivo) gene editing** only; no germline editing or enhancement.
- Targets a **serious inherited disease (LCA10)** with no curative treatment available.
- Potential to address the **genetic root cause** of vision loss.
- Ethical justification depends on **strong pre-clinical evidence** and scientific validity.

Key ethical considerations

- **Informed consent:** participants must understand risks (off-target effects, immune reactions, toxicity, oncogenic risks, unknown long-term effects).
- Prevent **therapeutic misconception** and unrealistic expectations of benefit.
- Respect for autonomy through clear communication, plain-language materials, and the right to withdraw.

Patient protection requirements

- Rigorous safety monitoring and long-term follow-up.
- Data privacy safeguards and psychological support.
- Special attention to vulnerable patient groups and equitable access.

--> The trial is ethically justifiable **if** robust consent procedures, patient protections, safety monitoring, and long-term care measures are implemented.

CHANGER

CHALLENGES AND INNOVATIVE CHANGES IN RESEARCH ETHICS REVIEWS

Thank you

Project partners

DEMOKRITOS NATIONAL CENTRE FOR SCIENTIFIC RESEARCH

ΠΑΝΕΠΙΣΤΗΜΙΟ ΔΥΤΙΚΗΣ ΑΤΤΙΚΗΣ UNIVERSITY OF WEST ATTICA

SVEUČILIŠTE U SPLITU MEDICINSKI FAKULTET UNIVERSITY OF SPLIT SCHOOL OF MEDICINE

university of groningen

TU WIEN TECHNISCHE UNIVERSITÄT WIEN

NORSUS Norwegian Institute for Sustainability Research

UNIVERSITY OF BUCHAREST

UNIVERSITÄT BONN

K&I Knowledge and Innovation

KU LEUVEN

LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

UNIVERSITY OF MACEDONIA

KIT Karlsruhe Institute of Technology

Funded by the European Union

Views and opinions expressed are however those of the author(s) only, and do not necessarily reflect those of the European Union. Neither the European Union nor the granting authority can be held responsible for them.