

Gene Therapy and Ethics: the Patient View

A tool for **public** dialogue



Colofon

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Introduction

For some years now, gene therapy has been seen as a great promise for the treatment of several serious diseases. In particular, it has been seen as a route for the treatment of genetic disorders. Despite initial optimism and several promising early results, gene therapy has not yet delivered as many clinically available treatments as expected. However, the number of clinical trials for diseases open to gene therapy has increased rapidly. Most of these (potential) gene products are for cancers, with some of the most successful ones in the area of genetic disorders. For example, in the field of primary immunodeficiencies, gene therapy has already been shown to be a life-saving, life-extending treatment leading to dramatic improvements in health and quality of life. This gives substantial hope for future progress of treatment of many other genetic conditions.

Patients and patient organisations are amongst the keenest advocates for research and development in gene therapy. Their benefit is not in getting a scientific degree or title, earning money or even being on the news. Their benefit is in improving health and overcoming a life-threatening disease, in cure rather than care. Gene therapy has the potential to make a gene medicine possible and that potential is the drive for patients to promote gene therapy.

This folder has been created to increase your understanding of the patient perspective on gene therapy and in particular on some of the ethical issues involved.



What is the basis of gene therapy?

When something's wrong with a blue print, or gene, properly functioning proteins cannot be produced: they work less, or not at all. This can have far-reaching effects. Illnesses like haemophilia, some severe primary immunodeficiencies and cystic fibrosis are examples. Sometimes a missing or altered gene can cause cancer.

The idea behind gene therapy is that it aims to replace or repair a faulty gene, and in some cases add an extra gene to cells. This in turn will enable the patient to live a life 'free' of the condition that they are affected by. Some approaches target healthy cells with an extra gene to enhance their ability to fight cancer. Other approaches target cancer cells, to destroy them or prevent their growth.

What are the risks with gene therapy?

It sounds easy, just add, replace or repair a gene, but getting the new gene to the right destination in the cells' DNA is not that simple. For example, in cystic fibrosis one of the faulty genes is in the lungs. In order for the gene to work, the replacement gene needs to get to the lungs. To do so, we need a vehicle: the gene cannot travel there on its own.

Viruses are often used as a transportation vehicle. Viruses naturally deliver their own genes to cells, which can sometimes make you ill. The viruses that are used for gene therapy are made harmless by researchers. They replace the viral genes that cause illness with the genes that need to be delivered to the patient with a particular condition. These modified viruses do not make you ill, but they are able to deliver the gene to the right place in the DNA. In practice, however, this is a bit more complicated than was originally thought. Sometimes the gene is delivered to the wrong spot, resulting in unwanted serious effects. Or the gene is delivered to the right spot, but just does not work at all or works too much.

Scientists continuously look for better-modified viruses that are able to transport and deliver genes more precisely. The safer the transportation methods, the safer gene therapy will be for future patients.

Is it necessary to develop a new concept of therapy with unknown risks when there are alternatives?

Many patients and their families consider gene therapy as a route to tackle the fundamental biological cause of their disorder: the faulty gene being replaced by a healthy gene. It might ultimately eliminate the need for complex services of integrated interventions, care and support, many of which often need to be lifelong.

Most genetic conditions are complex, multi-system disorders: they affect multiple organs in the body. To treat or prevent such a disease, an effective therapy would need to intervene broadly in all affected organs. Even where interventions currently exist, these are often demanding and of limited benefit for the affected person (e.g. the daily treatment regime for children with cystic fibrosis). Or interventions

like bone marrow transplantation that are increasingly successful in some patients, might not be possible in other patients: without a suitable donor they will simply die.

For those patients it is necessary to develop a new concept of therapy, even when it is still in its infancy and even when there are unknown risks: they don't have an acceptable alternative. Gene therapy offers a new perspective on life, on hope and on a future that can be full of plans, instead of living from day to day.

O ptimism or realism?

Patients and many patient organisations strongly encourage research and development in the field of gene therapy. Patients and families know, much as they might wish otherwise, that the reality is a complex biology of their disease and that it will be difficult to unravel what effect a faulty gene has on the whole body functioning. They also know that miracle cures rarely (if ever) happen, and are wary of claimed breakthroughs. Thus the support from patient organisations for gene therapy is not blind or unconditional. Rather it is rational and evidence-based.

P rotections for participants: too rigid or too loose?

To test the safety of any new therapeutic, as is gene therapy, the participation of patients in clinical tests (trials) is crucial. These trials must be done for any potential treatment to advance to the next phase of study and to advance towards a gene medicine. Without this step and without the patient's willingness to participate, gene therapy can never become a cure or true gene medicine.

Regulations on clinical trials are applied by governments to minimise risks for people taking part. Any gene therapy that looks like it is going to work will have to be licensed by the relevant competent authority. The European Commission has introduced the Advanced Therapies and Tissue Engineered Products Regulations. Patient organisations played a key role in persuading the European Parliament and the Council of Ministers of the importance of these legislative proposals.

Participants in a gene therapy trial must sign a form ('informed consent') to confirm they understand the clinical trial, including the risks, and consent to participate. The public's concern about the level of the participant's understanding can be met by including more research participants in the development of clinical trials and informed consent materials. This will increase the transparency and will result in a greater trust that the system is working well for participants.

Issues such as: 'age of consent', 'failure of currently approved standards of care' and 'life versus quality of life' are ethical principles applied in regulation. They are sound principles to protect patients from undue risks. However, sometimes it is necessary to loosen these principles in order for the patient to experience the greatest benefit. For example, to enter clinical trials, existing treatments must fail and patients need to have progressed to advanced stages of the disease. However, probabilities of success are sometimes likely to be higher when patients can enrol earlier.

Too rigid implementation of the ethical principles imposed by law can unnecessarily obstruct the already long road for gene therapy. The patient is the one that accepts unknown effects of new developments in gene therapy more easily. He will set his boundaries lower and is generally speaking more enthusiastic and willing to take more risks; what does he have to lose anyway? Regulations should be based on responsibility towards the patient and on his quality of life.

Patients and researchers partnering in science

Patients and families joining in patient organisations often have a very close relationship with interested/expert clinicians and the research community, as much of the diagnosis and treatment is provided by specifically assigned centres at a national level. This creates a partnership that is mutually beneficial and sustainable, helping to create a framework for realistic decisions on the best way forward. Patient organisations are not blindly committed to gene therapy. If another route were to become more promising their focus of attention would shift. Their interest is the outcome, not the process.



More info

For more information on patient organisations involved in gene therapy:

- * European Genetic Alliances' Network EGAN: www.egan.eu
- * European Organisation for Rare Disorders Eurordis: www.eurordis.org.

This brochure can be downloaded from www.egan.eu and www.biomedinvo4all.com.

Also available: Gene Therapy and Ethics: the Patients View. A tool for Patients Dialogue.

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