Screening: information, not treatment

Genetic testing examines DNA for relevant variants. Screening can identify people who may need further assessment; diagnostic testing investigates a suspected condition. A result must be interpreted in its clinical and family context.

1. THREE EXAMPLES, THREE DIFFERENT INTERPRETATIONS

A. BRCA1 and BRCA2

These genes normally help repair DNA. Certain harmful variants raise breast and ovarian cancer risk; having a BRCA gene is not itself abnormal.

Testing can guide surveillance and risk-reduction discussions. A harmful variant increases risk, but does not mean cancer is inevitable.

B. Huntington's disease

An expanded CAG repeat in HTT can cause an autosomal dominant disorder affecting the nervous system.

Predictive testing can identify an expansion before symptoms and inform life or reproductive planning. Repeat size affects interpretation; exact onset cannot be predicted.

C. Cystic fibrosis

Disease-causing variants in both CFTR copies can disrupt ion transport. A person with one such copy is usually an unaffected carrier.

Carrier testing supports reproductive decisions; testing can also help diagnosis. A limited variant panel may miss other disease-causing variants.

2. EXPLAIN WHAT A RESULT CAN AND CANNOT SAY

Benefits include earlier monitoring, identifying carriers, supporting diagnosis and informed decisions. A negative result does not remove every genetic or non-genetic risk. A variant of uncertain significance is not automatically a disease-causing variant.

BRCA variants and risk interpretation: National Cancer Institute.
Huntington's disease: MedlinePlus Genetics.
Cystic fibrosis and recessive inheritance: MedlinePlus Genetics.

Cambridge Biology 9700: 19.2.1-4, p. 48. Educational summary, not medical advice.

Gene therapy: change cell function

Gene therapy changes genetic material to treat disease. Gene addition supplies a functional copy; it need not remove the original variant. Other approaches edit DNA or alter gene expression. Successful delivery must lead to useful biological function.

1. ADA-SCID: AN EX VIVO EXAMPLE

ADA deficiency can allow metabolites toxic to lymphocytes to accumulate, causing severe combined immunodeficiency (SCID). SCID has several genetic causes; ADA deficiency is one example.

Collect cells

Patient's blood-forming stem cells

→

Add ADA gene

A vector carries a functional copy

→

Return cells

Modified cells repopulate blood lineages

Ex vivo means modification outside the body. Functional ADA production in the resulting cells can restore immune function; long-term follow-up remains important.

2. INHERITED EYE DISEASE: AN IN VIVO EXAMPLE

For eligible RPE65-related retinal disease, a vector delivers a functional RPE65 copy to retinal pigment epithelial cells. The protein supports the visual cycle. Delivery occurs in the body, so this is in vivo therapy. It can improve visual function where viable cells remain; it does not treat every inherited cause of blindness.

3. SOMATIC DOES NOT MEAN HERITABLE

These approaches target body cells, not eggs or sperm, so the therapeutic genetic change is not passed to offspring. The original inherited variant may still be present in other cells and in the germline. Treating a person does not necessarily remove reproductive risk.

ADA-SCID stem-cell gene therapy: NIH Research Matters.
RPE65 gene therapy and visual function: National Eye Institute.
Gene-therapy approaches: MedlinePlus.

Cambridge Biology 9700: 19.2.1-4, p. 48. Educational summary, not medical advice.

Supply the protein, not the gene

A related 19.2 syllabus point: recombinant production uses genetically modified cells to manufacture a protein that is purified for treatment. The patient receives the protein, unlike gene therapy that changes target cells genetically.

1. MATCH THE PROTEIN TO ITS FUNCTION

Human insulin	Helps regulate blood glucose. Recombinant human insulin can replace missing insulin, for example in type 1 diabetes; it does not restore the lost pancreatic beta cells.
Human factor VIII	A blood-clotting protein. Replacement supports clot formation in haemophilia A caused by factor VIII deficiency; it does not correct the inherited DNA variant.
ADA enzyme	Adenosine deaminase breaks down substrates whose accumulation harms lymphocytes. Enzyme replacement can support immune function in ADA deficiency; it is distinct from ADA gene therapy.

2. WHY USE RECOMBINANT HUMAN PROTEINS?

Production can be scaled and quality controlled without relying on extraction from many human donors or animals. A human amino acid sequence avoids some differences associated with animal proteins. Recombinant clotting factors reduce dependence on donor plasma and its pathogen risks. Purification and safety checks are still essential; immune reactions remain possible.

3. PRECISION NOTE: RECOMBINANT IS NOT ALWAYS HUMAN

Cambridge includes ADA in this group of examples. However, the clinical ADA replacement elapegademase is based on a bovine sequence made by recombinant technology. Distinguish the manufacturing method from the species origin of the sequence.

Recombinant human insulin: FDA, 100 Years of Insulin.
Factor VIII replacement and recombinant products: CDC.
ADA enzyme replacement and product distinction: GeneReviews.

Cambridge Biology 9700: 19.2.1-4, p. 48. Educational summary, not medical advice.

Balance benefit, risk and choice

Screening provides information; protein replacement supplies a product; gene therapy changes genetic function in cells. Evaluate each method by its purpose, evidence, limitations and effects on people.

1. SOCIAL AND ETHICAL CONSIDERATIONS

Informed consent	Explain benefits, uncertainty and possible findings. Respect voluntary choice and a person's wish not to learn predictive results.
Privacy and family	A result can reveal information about relatives. Consider confidentiality, who may access records and how findings are shared.
Psychological effects	Risk information can support planning but may cause anxiety, guilt or stigma. Counselling helps people understand the result without directing their choices.
Fair access	Testing, specialist care and gene therapies may be costly or difficult to obtain. Consider whether benefits are available equitably.
Future generations	Germline changes could be inherited, affecting people who cannot consent. Somatic treatment avoids that inheritance issue, but still requires safety evaluation.

2. THERAPY HAS BIOLOGICAL CHALLENGES

Enough appropriate cells must receive and express the therapeutic material. Immune responses, unintended genetic effects or inappropriate expression may cause harm. Effects may not last for life. Risks depend on the vector, target tissue and method; long-term monitoring is needed.

An informed conclusion weighs benefit against uncertainty, asks who benefits and who bears the risk, and separates established evidence from promises. Genetic technology is not a guaranteed cure for every condition.

Informed consent and consequences of testing: MedlinePlus Genetics.
Equity, safety and heritable editing: NHGRI ethical concerns.
Gene-therapy risks and challenges: MedlinePlus.

Cambridge Biology 9700: 19.2.1-4, p. 48. Educational summary, not medical advice.