

Possibilities of Gene Therapy of Tumors

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Gene therapy is "gene treatment". This is a new approach to treating disease by altering the patient's gene expression. If a patient has a disease that is caused by a defect in a gene, gene therapy is a treatment that corrects that defective gene. It is assumed that this method will not only be able to treat diseases, but also prevent them. This method is currently under development, the possibilities of its use are being investigated in basic research laboratories. Therefore, it cannot be used in clinical practice.

Gene therapy as a treatment method was created on the basis of knowledge about the influence of genes on human diseases. Today, it is clear that every human disease has something to do with human genes that were obtained from parents. Minor differences in each person's genes help shape their personality from height to eye color. Unfortunately, some of these differences lead to the development of diseases, which are then passed on from generation to generation. Some of them are caused by an error in one gene, others are affected by a whole set of genes. The advantage of gene therapy is that it cures human diseases at their "roots" - it repairs damaged genes.

Types of Gene Therapy

Somatic gene therapy

- corrects the patient's genes without heritable transfer of the corrected genes to the next generations

Germline gene therapy

- it would change genes already in the germ cells (sperm, egg) and the gene change would be transmissible to future generations. This type of therapy is not yet allowed.

Gene Therapy Strategies

Direct gene therapy

- error correction - changes in the DNA sequence that is responsible for malignant transformation. E.g. removing a mutation in the proto-oncogene or introducing missing tumor suppressor genes
- not all cells can be repaired because the genotype has a multifactorial character

Indirect gene therapy

- introducing new genetic information into a cell (tumor or other type) that leads to the destruction of tumor cells. E.g. introduction of DNA sequences that encode, for example, the stimulation of an antitumor immune response or alter tumor angiogenesis and / or activate an inactive antimetabolite molecule to its cytotoxic activity
- strict ethical criteria, strict selection of patients, the safety of the procedure for both the patient and the nursing staff is considered, the effectiveness of the therapy

Gene Manipulation

It takes place *ex vivo* (outside the whole organism). There are various techniques for introducing a gene into isolated cells:

1. Physical methods

- allow direct insertion of nucleic acid into target cells (microinjection, microprojectiles or electroporation - introduction of a weak electric current into the cell suspension in the presence of the gene to be incorporated into the cell)
- efficiency <1%

2. Chemical methods

- využívají pro inkorporaci genů do buněk např. fosforečnan vápenatý, liposomy (zlepšují průchod přes buněčnou membránu)
- for incorporation of genes into cells are used e.g. calcium phosphate, liposomes (improve passage through the cell membrane)

3. Biological methods

- use viruses as DNA vectors, most common DNA viruses (papovaviruses, adenoviruses, herpes simplex virus) and retroviruses
- transfer efficiency of the required sequence - almost 100%
- other vectors: plasmids - contain multiplied copies of the selected gene, are injected into the bloodstream or directly into the area of tumor growth

- monoclonal antibodies
- *in vitro* proliferating tumor infiltrating lymphocytes (TIL)

TIL after i.v. administration selectively infiltrate postoperative residues of the tumor from which they were isolated. Ex vivo, for example, the tumor necrosis factor (TNF) gene can be integrated into the TIL genome. The TNF gene (part of the TIL genome) is transcribed and the synthesized protein is secreted directly into the tumor tissue, which is destroyed by a necrotic process. Genetically controlled increase in immunobiological activity.

E.g. retrovirus: First, it is genetically modified in vitro. The sequences encoding the viral proteins are removed, leaving only the expression control sequences (LTRs). This is followed by excision of the sequences encoding the production of the product selected for the respective gene therapy. These recombinant retroviruses have the ability to infect cells and incorporate exogenous genes into their genome, but they cannot replicate. An example of gene therapy of this type is the treatment of malignant glioma (a tumor with high mitotic activity) - it does not metastasize and is surrounded by nervous tissue that does not replicate.

E.g. Herpes simplex virus (HSV): Its gene for the enzyme thymidine kinase has been integrated into the genome of the target cell and in it it converts an otherwise inactive dosage form (prodrug) into an active substance with a cytostatic effect.

References

Related Articles

- Tumor Suppressor Genes
- Causes of tumors, carcinogenesis, carcinogens
- Molecular-biological Diagnostics in Oncology

Source

- ŠTEFÁNEK, Jiří. *Medicína, nemoci, studium na 1. LF UK* [online]. [cit. 11.02.2010]. <<https://www.stefajir.cz/>>.