

# How to treat a genetic disease (XLMTM) ?

## 1- Pharmacology:

symptoms

*better knowledge of the disease: novel molecules  
(high-throughput drug screening)*

## 2- Cell therapy:

*myoblasts*

*stem cells*

## 3- Gene therapy:

*transfer of genes into skeletal muscle*

## 2- Regenerative cell therapy:

Transplantation of either differentiated or stem cells in tissues/organs

### Differentiated cells

Cell that has a **specific** morphology and function in a given tissue (myoblast, neuron, epithelial cell, hepatocyte ...)

#### Example:

- Transplantation of autologous **myoblasts** in patients with **myopathies** (Duchenne, facio-scapulo-humeral dystrophy...)
- Transplantation of embryonic neurons in the brain of patients with Huntington's disease

### Stem cells

They are **undifferentiated** cells with self-renewal capacities that are able to differentiate into multiple cell types

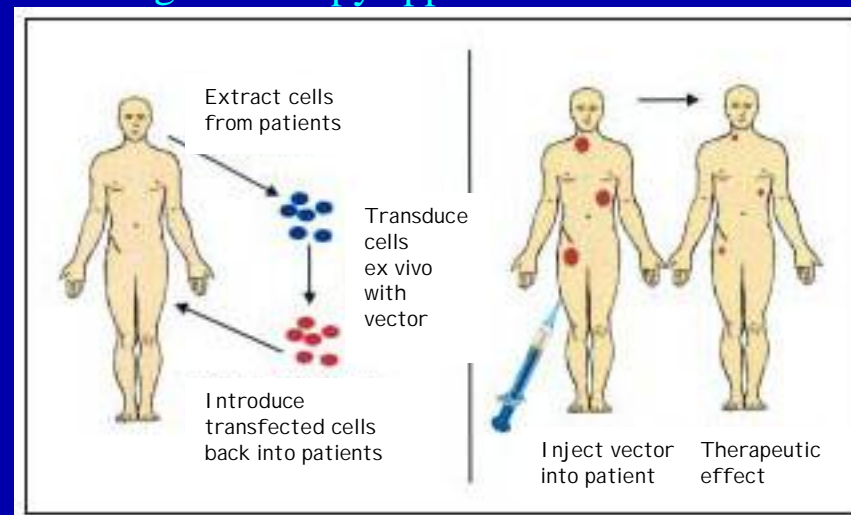
#### Example:

- Transplantation of **stem cells** originating from bone marrow in patients with **myocardial infarction**

### 3- Gene therapy:

Therapeutic approach that involves **delivery** of **nucleic acid** to a **somatic** cell to correct a debilitating condition, relieve suffering, and extend life. It does not cause a change in the germ line of the individual, so any genetic corrections are not passed to successive generations

#### Current gene therapy approaches



Gene therapy in patients with **severe combined immunodeficiency (SCID)** or bubble-boys (France, 2002)  
= hematopoietic stem cells  
Correction of **junctional epidermolysis bullosa (JEB)** (Italy, 2006)  
= epidermal stem cells

Gene therapy in a patient with an inherited **retinal degeneration**, Leber's congenital amaurosis (London, 2007)  
= retina

## Method:

- Non-viral method:**
- naked DNA (no toxic, small efficacy)
  - oligonucleotides
  - lipoplexes (+ lipids) and polyplexes (+ polymers)

- Viral vectors:**
- retrovirus (RNA)
  - adenovirus (DNA)
  - adeno-associated virus, **AAV** (DNA)

Ongoing gene therapy studies in a mouse model of the disease

Vector: AAV-Mtm1