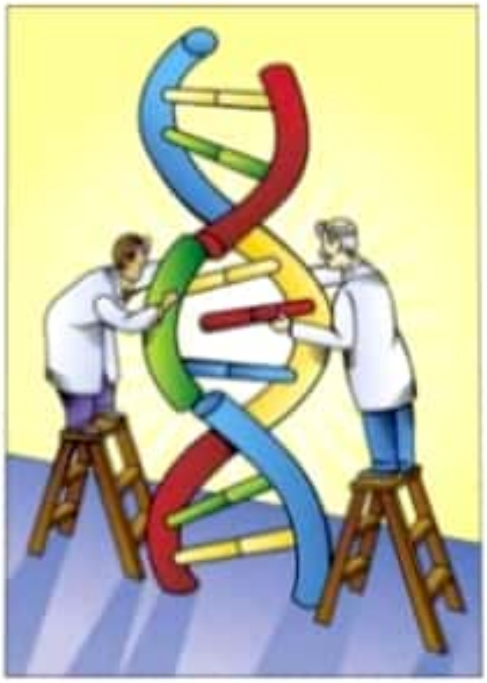
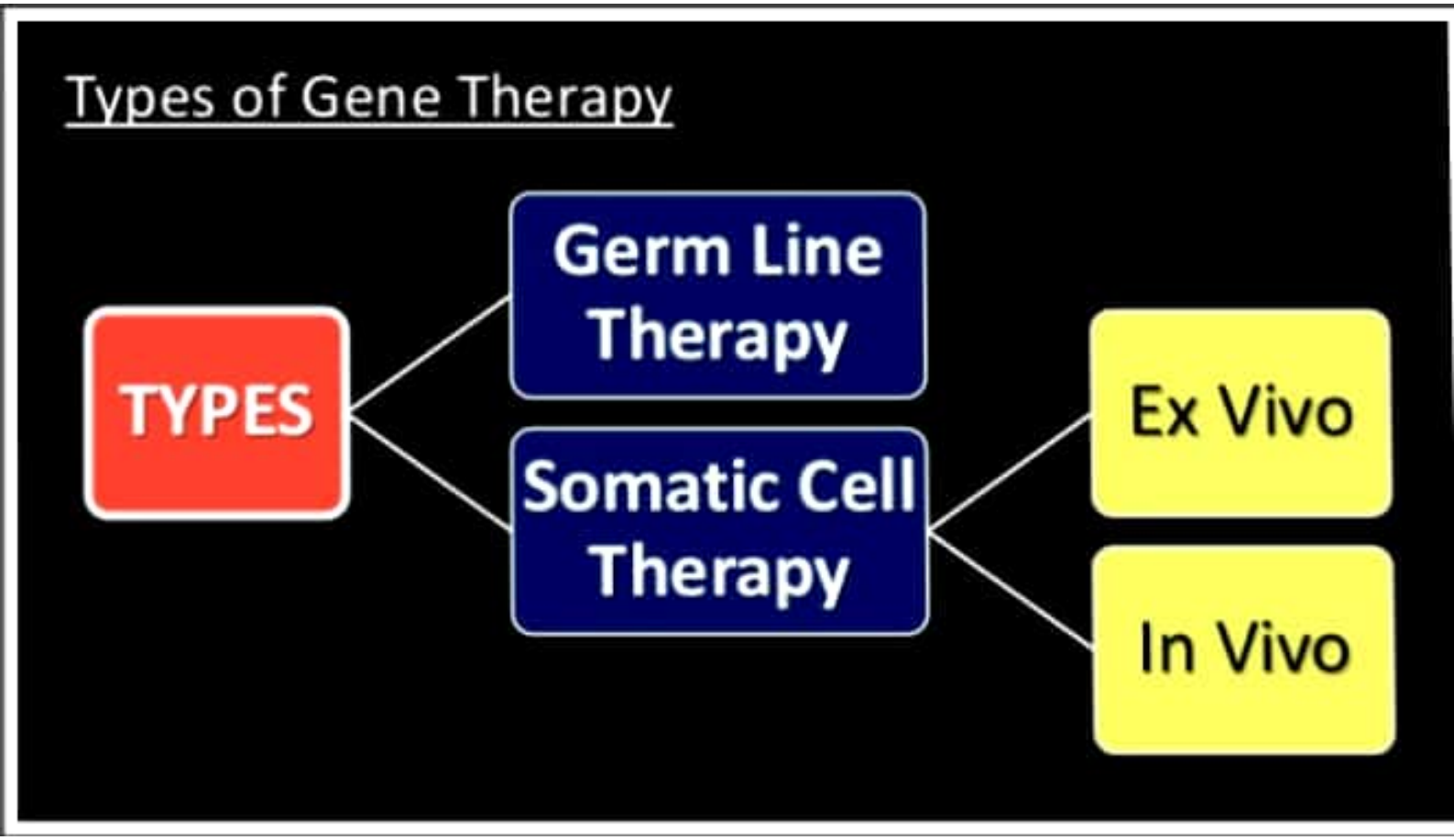
HUMAN GENE THERAPY

A promising future to disease treatment

INTRODUCTION

- Gene therapy is **the introduction of genes into existing cells** to prevent or cure a wide range of diseases.
- It is a technique for correcting defective genes responsible for disease development.
- The first approved gene therapy experiment occurred on September 14, 1990 in US, when **Ashanti DeSilva** was treated for **ADA-SCID**.





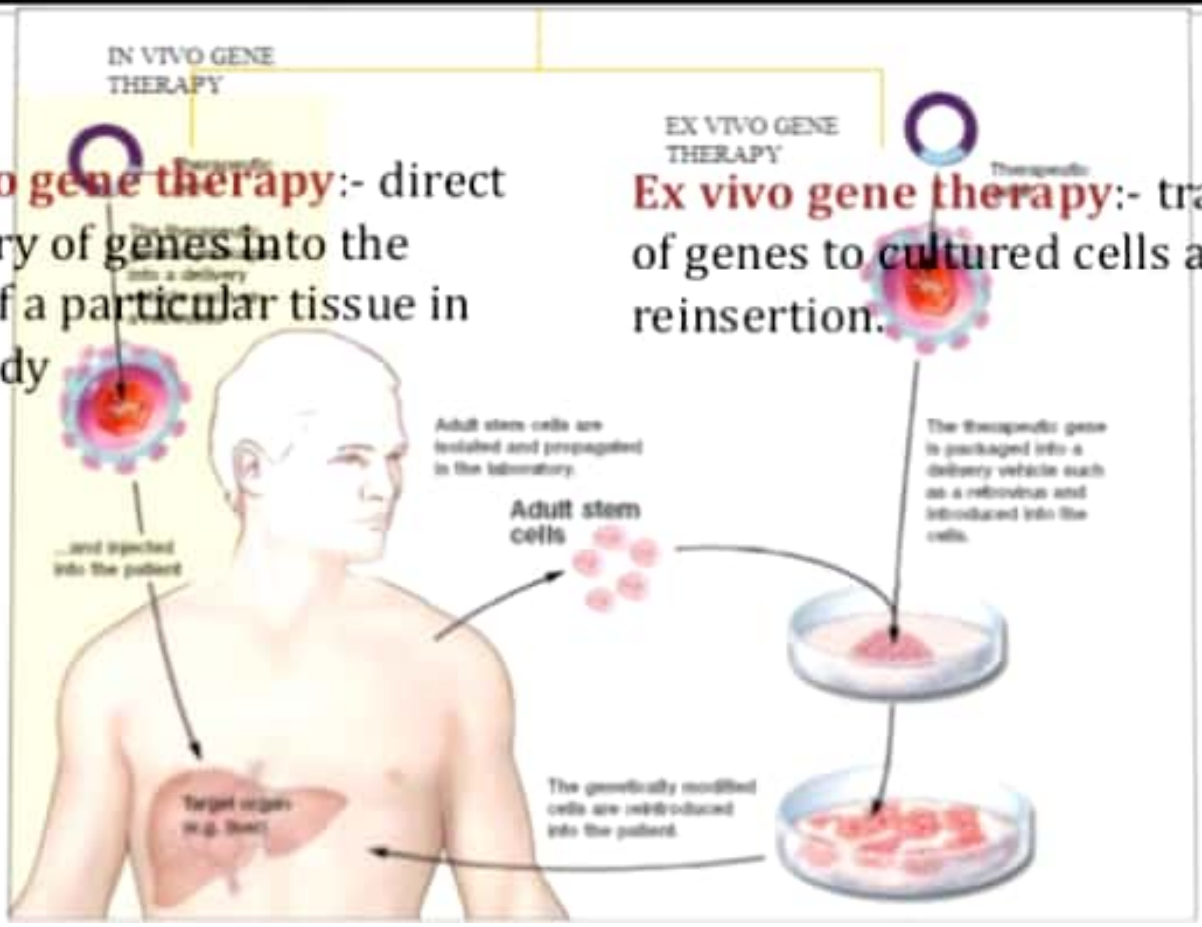
TYPES OF GENE THERAPY

SOMATIC CELL GENE THERAPY	GERM LINE GENE THERAPY
• Therapeutic genes transferred into the **somatic cells**.	• Therapeutic genes transferred into the **germ cells**.
• Eg. Introduction of genes into bone marrow cells, blood cells, skin cells etc.	• Eg. Genes introduced into eggs and sperms.
• **Will not be inherited** later generations.	• **It is heritable** and passed on to later generations.
• At present all researches directed to correct genetic defects in somatic cells.	• For safety, ethical and technical reasons, it is not being attempted at present.

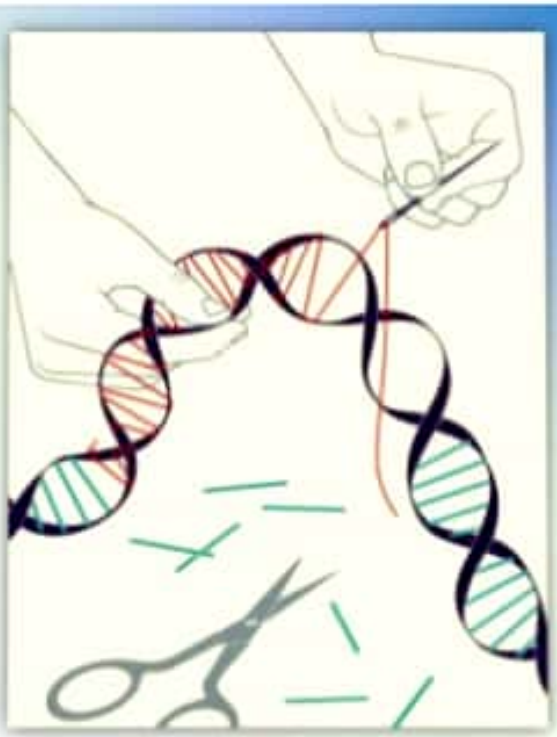
APPROACHES IN GENE THERAPY

In vivo gene therapy:- direct delivery of genes into the cells of a particular tissue in the body

Ex vivo gene therapy:- transfer of genes to cultured cells and reinsertion.



Approaches:



1. **Gene Replacement/Correction**
   – **Replacing** a mutated gene with a healthy copy
   Ex.) Severe Combined Immunodeficiency

2. **Gene Silencing/Gene Interference**
   – **Inactivating** or "knocking out" a mutated gene
   Ex.) Sickle Cell Disease

3. **Gene Augmentation/Gene Addition**
   – **Introducing** a new gene to help fight disease
   Ex.) Parkinson's Disease

4. **"Suicide Gene"**
   – Can cause a cell to kill itself through **apoptosis**
   – Makes cancer cells more **vulnerable** and **sensitive** to anticancer drugs
   Ex.) Solid Tumors

EX VIVO GENE THERAPY

Isolate cells with genetic defect from a patient

↓

Grow the cells in culture

↓

Introduce the therapeutic genes .

↓

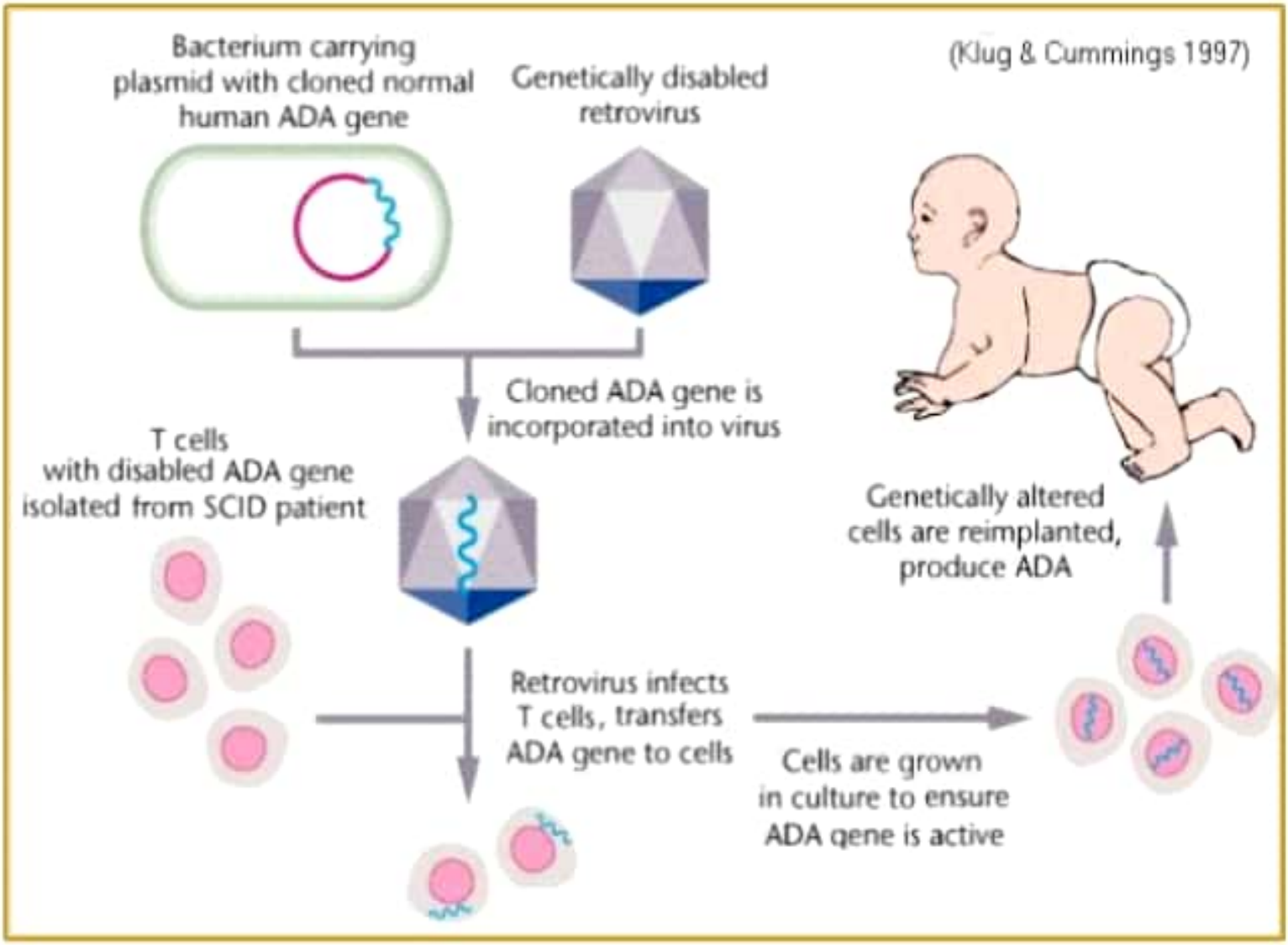
Select genetically corrected cells and grow.

↓

Transplant the modified cells to the patient.

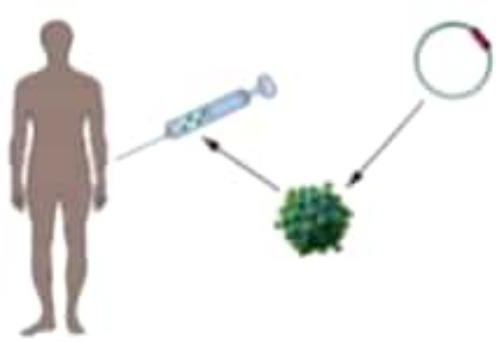
EXAMPLE OF EX VIVO GENE THERAPY

- 1st gene therapy – to correct deficiency of enzyme, **Adenosine deaminase (ADA).**
- Performed on a 4yr old girl Ashanthi DeSilva.
- Was suffering from **SCID- Severe Combined Immunodeficiency.**
- Caused due to defect in gene coding for ADA.
- Deoxy adenosine accumulate and destroys T lymphocytes.
- Disrupts immunity , suffer from infectious diseases and die at young age.



IN VIVO GENE THERAPY

- Direct delivery of therapeutic gene into target cell into patients body.
- Carried out by viral or non viral vector systems.
- It can be the only possible option in patients where individual cells cannot be cultured in vitro in sufficient numbers (e.g. brain cells).



- In vivo gene transfer is necessary when cultured cells cannot be re-implanted in patients effectively.

EXAMPLE OF IN VIVO GENE THERAPY

-Therapy for cystic fibrosis

- In patients with cystic fibrosis, a protein called **cystic fibrosis transmembrane regulator (CFTR)** is absent due to a gene defect.
- In the absence of CFTR chloride ions concentrate within the cells and it draws water from surrounding.
- This leads to the accumulation of sticky mucous in respiratory tract and lungs.
- Treated by in vivo replacement of defective gene by **adenovirus vector** .