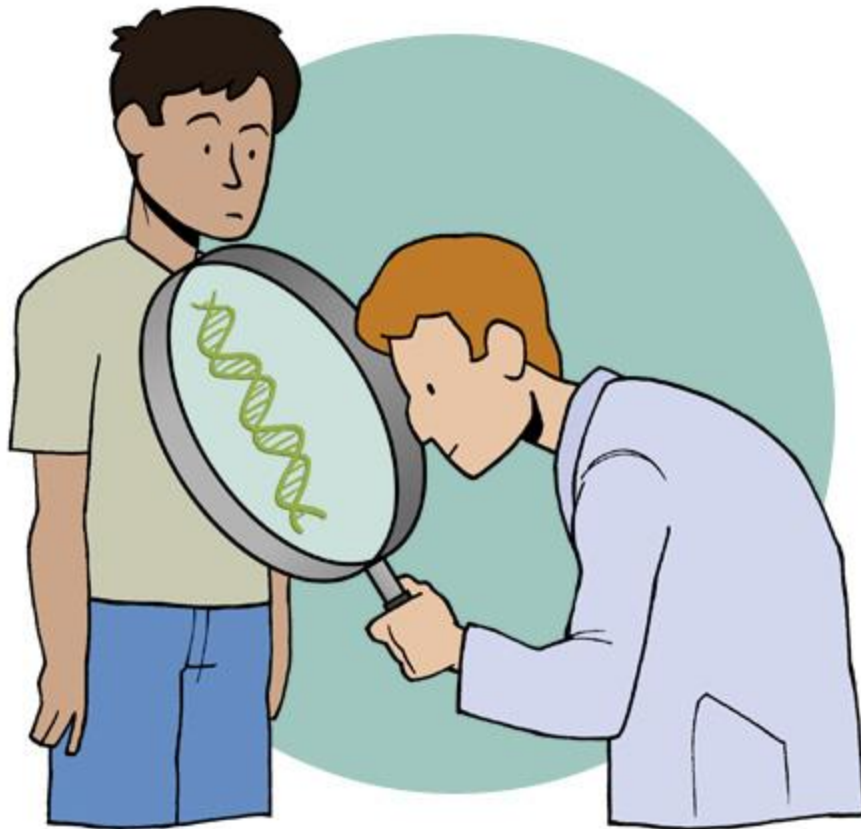




Genetic testing and gene therapy



Genetic Screening

Population screening:

- Newborn
- Heterozygote

Prenatal diagnosis:

- Invasive
- Non-invasive

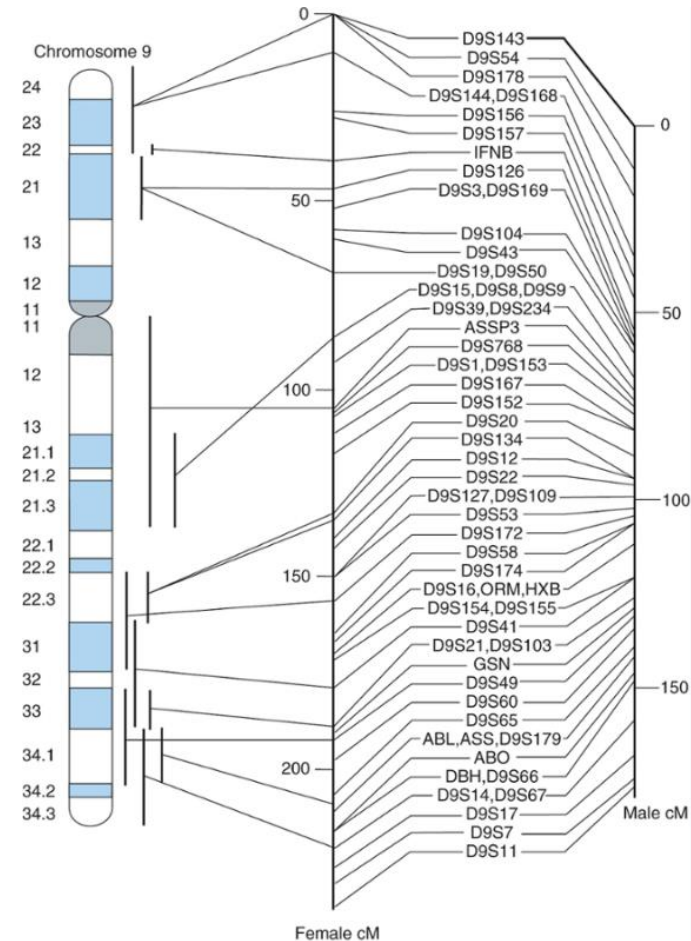
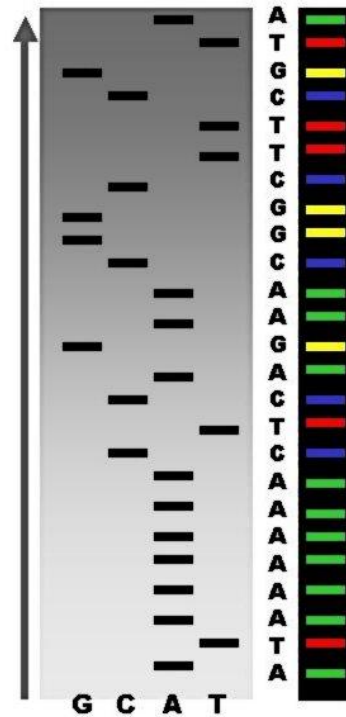
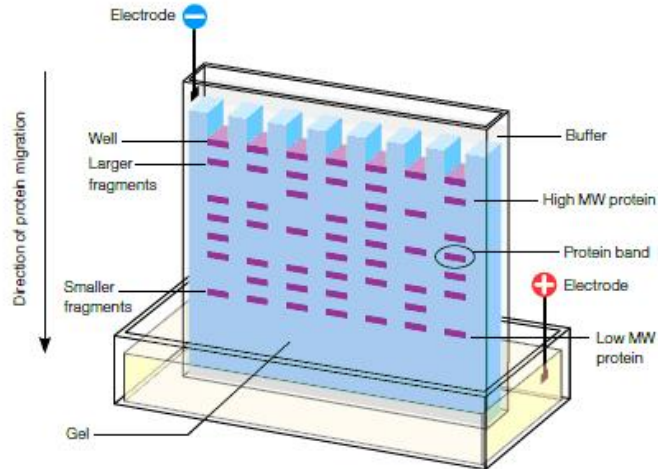
Family screening

Principles?

Screening validation?

Sensitivity/specificity?
PPV/NPV?

Which tools do we use?





Limitations

Test errors

Mutations not disease

Test sensitivity

Psychological implications

Discrimination

Lack of treatment

Other diseases

Direct-to-consumer genetic testing?



Unknown to the rest of the world, members of the scientific community have been making their own babies to order for quite some time now.

Prenatal Diagnosis

AFP screening

Amniocentesis

CVS

Cordocentesis

US, MRI

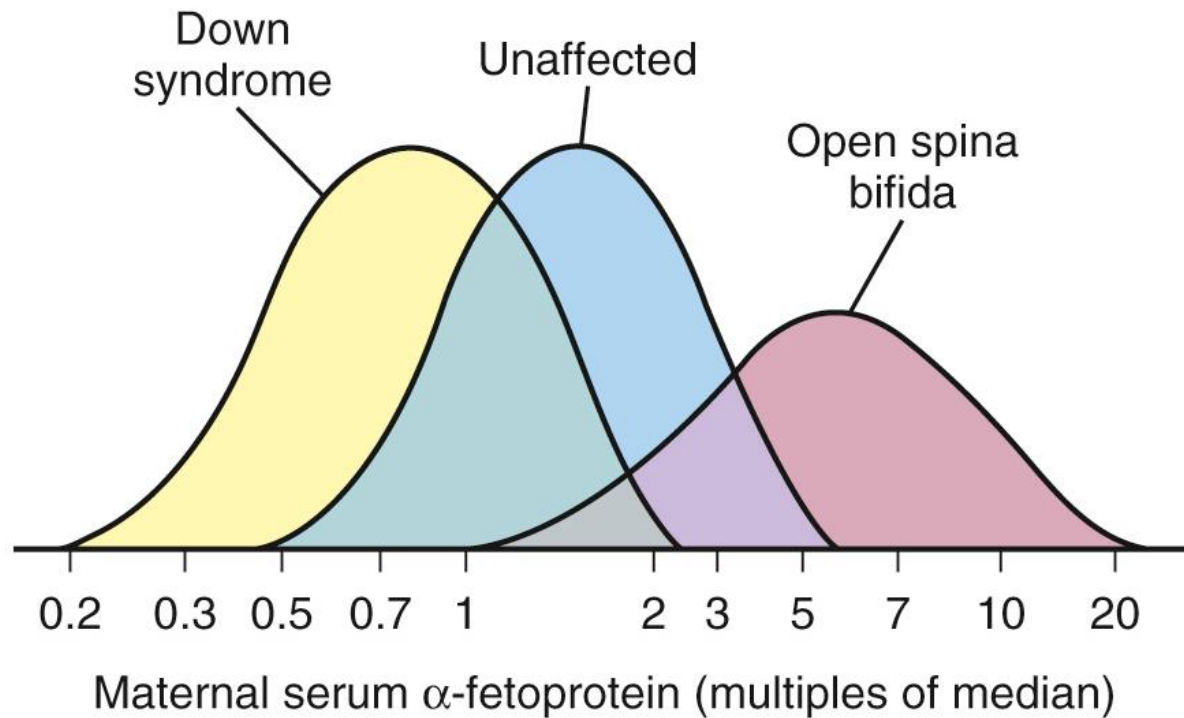
Preimplantation genetic
diagnosis

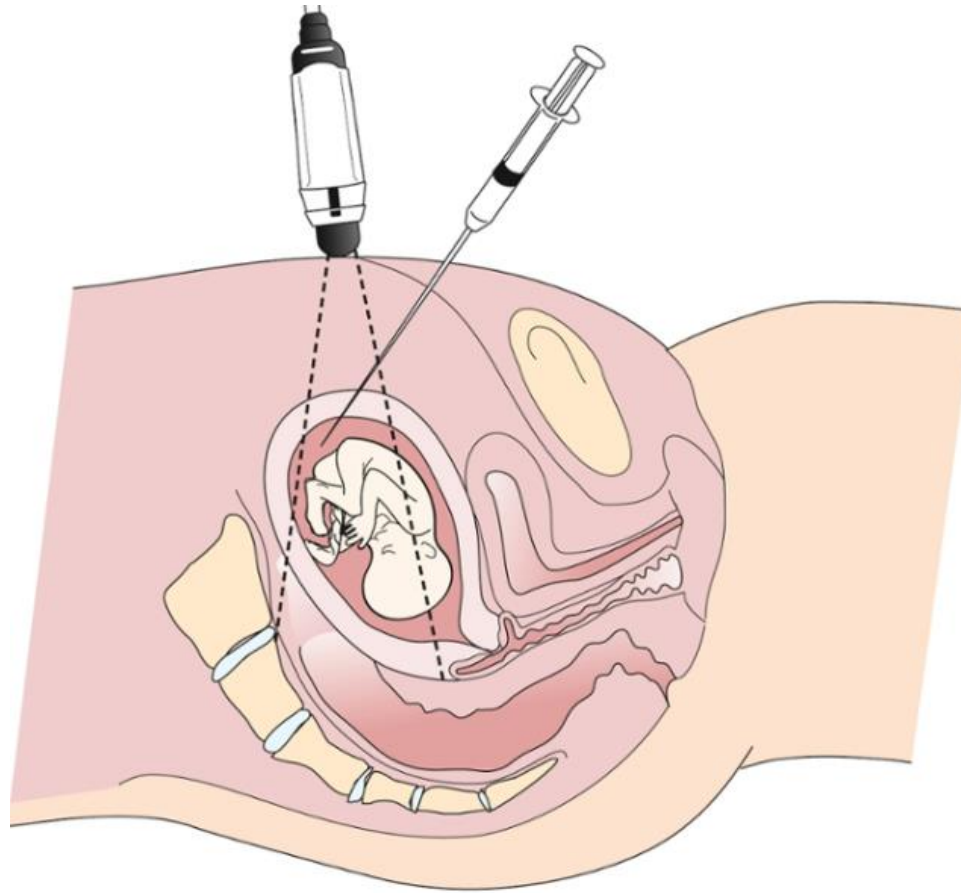
Prenatal Diagnosis

AFP screening:

- Maternal blood
- Amniotic fluid

Fetal DNA circulating in the maternal circulation
(screening) NIPS



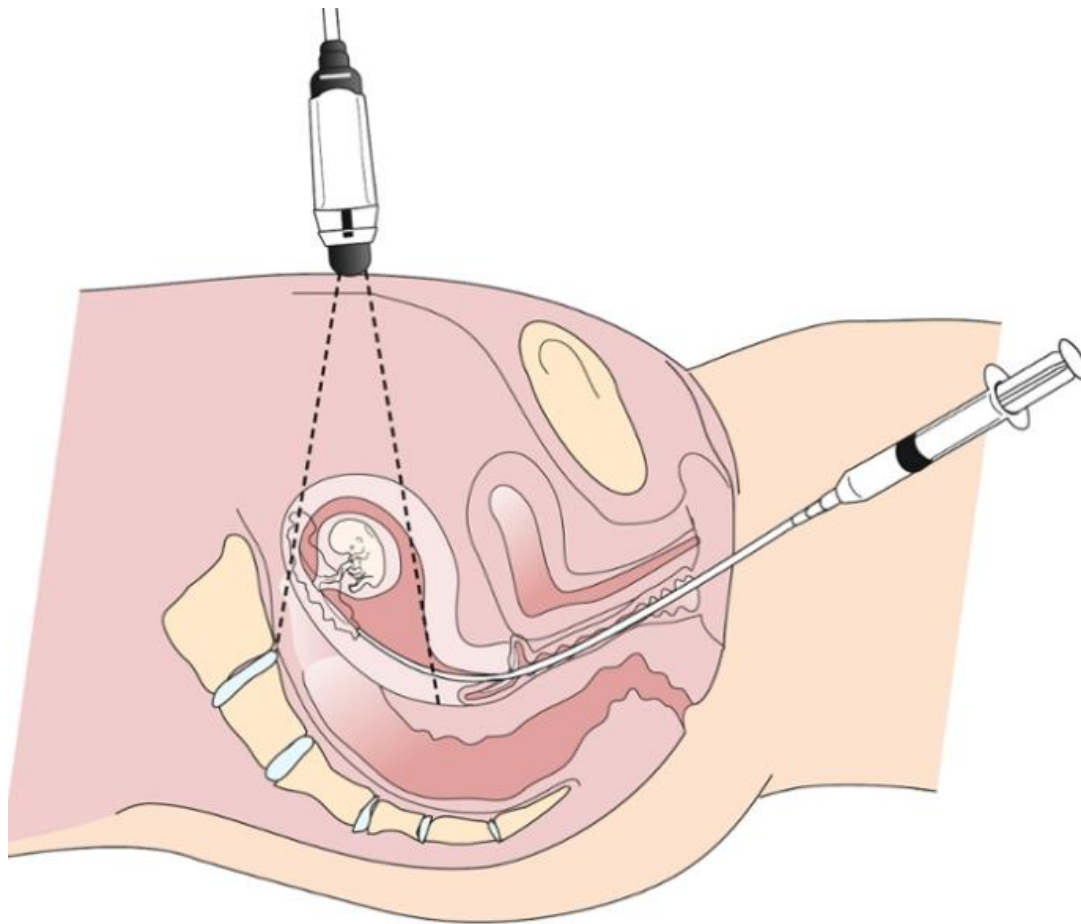


Prenatal Diagnosis

Amniocentesis:

- Mother >35yrs
- Previous child history
- Paternal history
- Family history
- Abnormal screening test

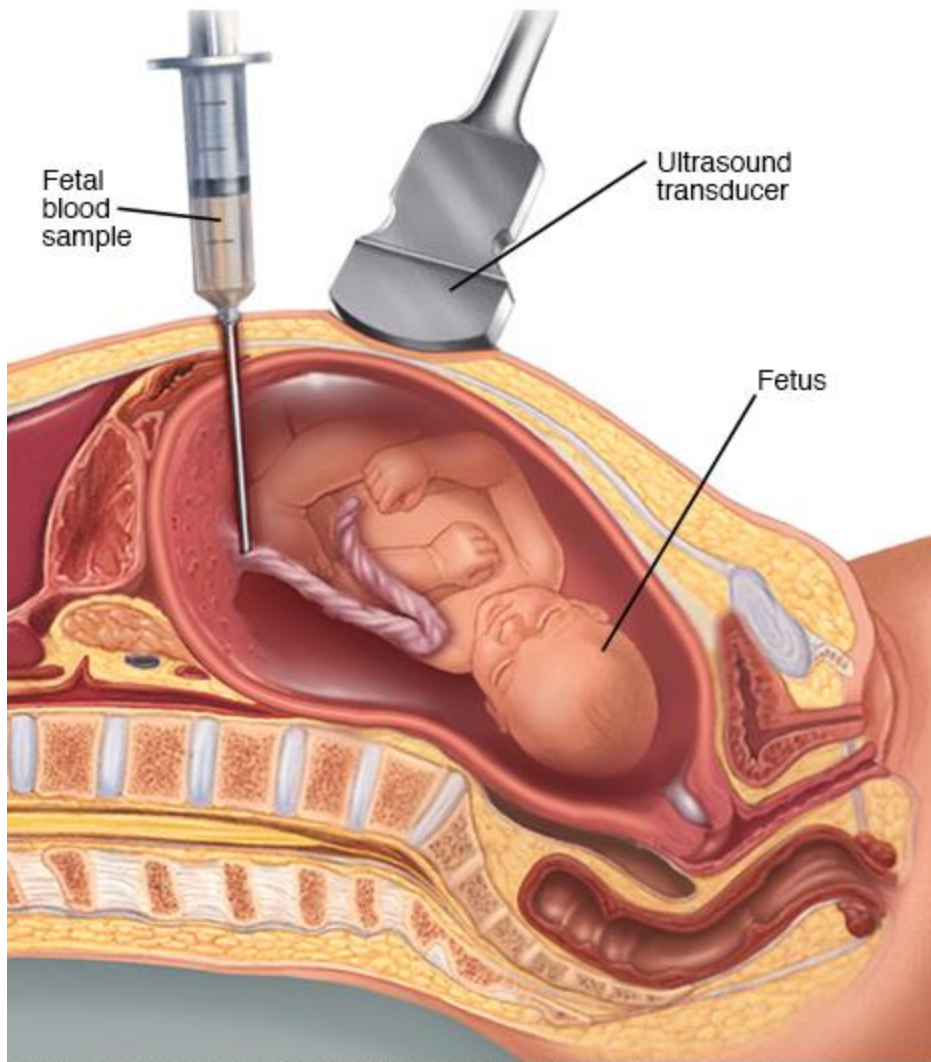
Risks (leakage, infections, fetal loss) rare



Prenatal Diagnosis

CVS:

- Earlier
- Generally safe but higher risk than amnio
- Limb deficiency?
- No amnio AFP measured

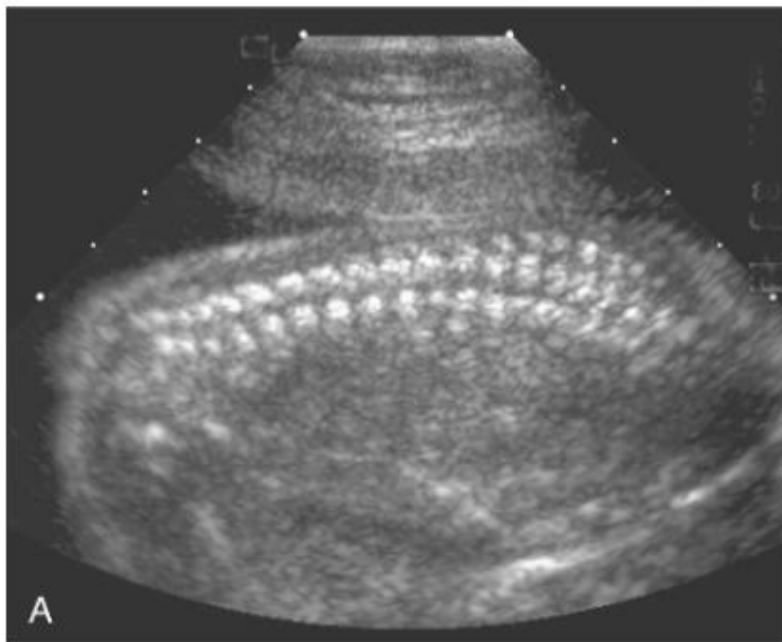


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Prenatal Diagnosis

Cordocentesis:

- aka percutaneous umbilical blood sampling
- Quicker 2-3 days vs 10-12
- US detected abnormality
- Blood disease Dx
- Immune disease Dx



Prenatal Diagnosis

US, MRI:

- Limb problems
- Fetal growth
- Cardiac defects
- Diaphragmatic defects
- ... (see box 13-6)

Prenatal Diagnosis

Preimplantation genetic diagnosis



"The genetic engineers gave him that birthmark as part of a sponsorship deal."

PUGH



*'It's all your fault,
dad – terrible genes'*

Gene therapy

Somatic cell therapy

Gene replacement therapy

Gene blocking

Gene therapy for non-inherited diseases

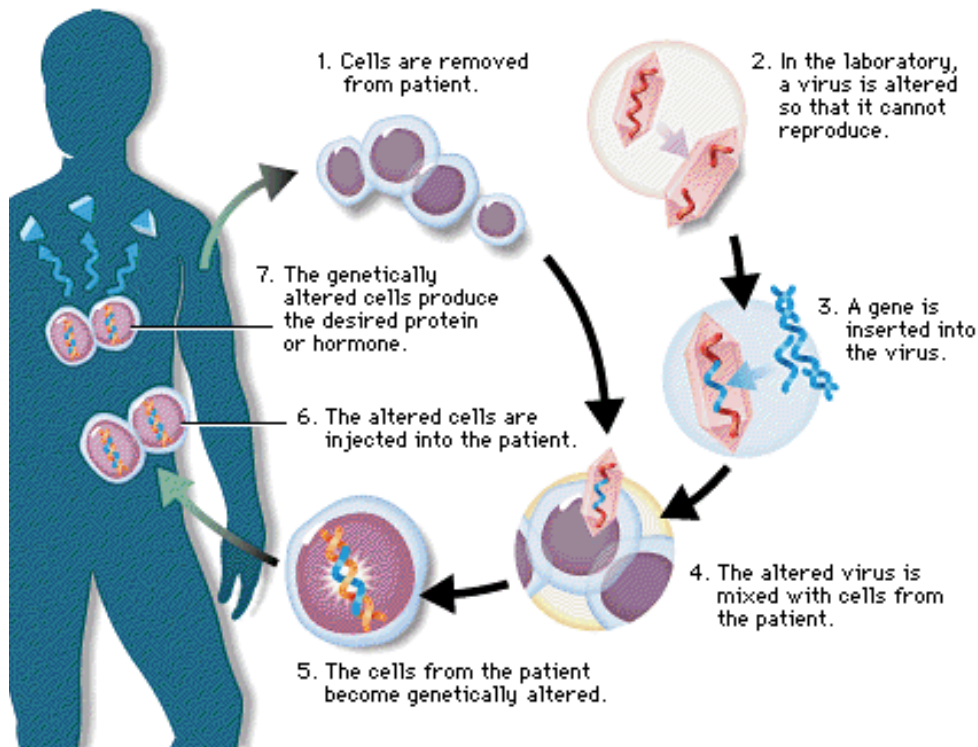
Germline therapy

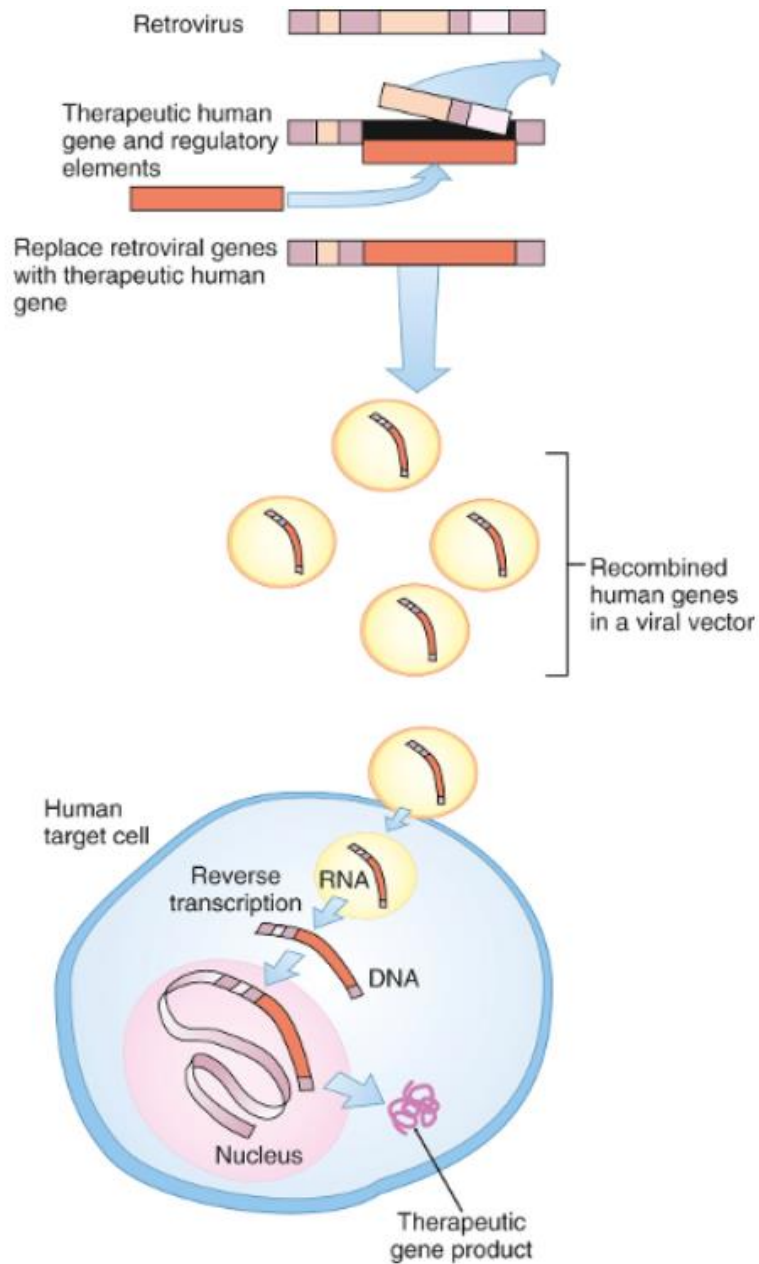
Gene therapy

Somatic cell therapy

Cells should be easily accessible and long lived

Proliferating cells are useful to ensure integration of new genetic material





Gene therapy

Gene replacement therapy

Viral vectors (transduction)

Non-viral vectors

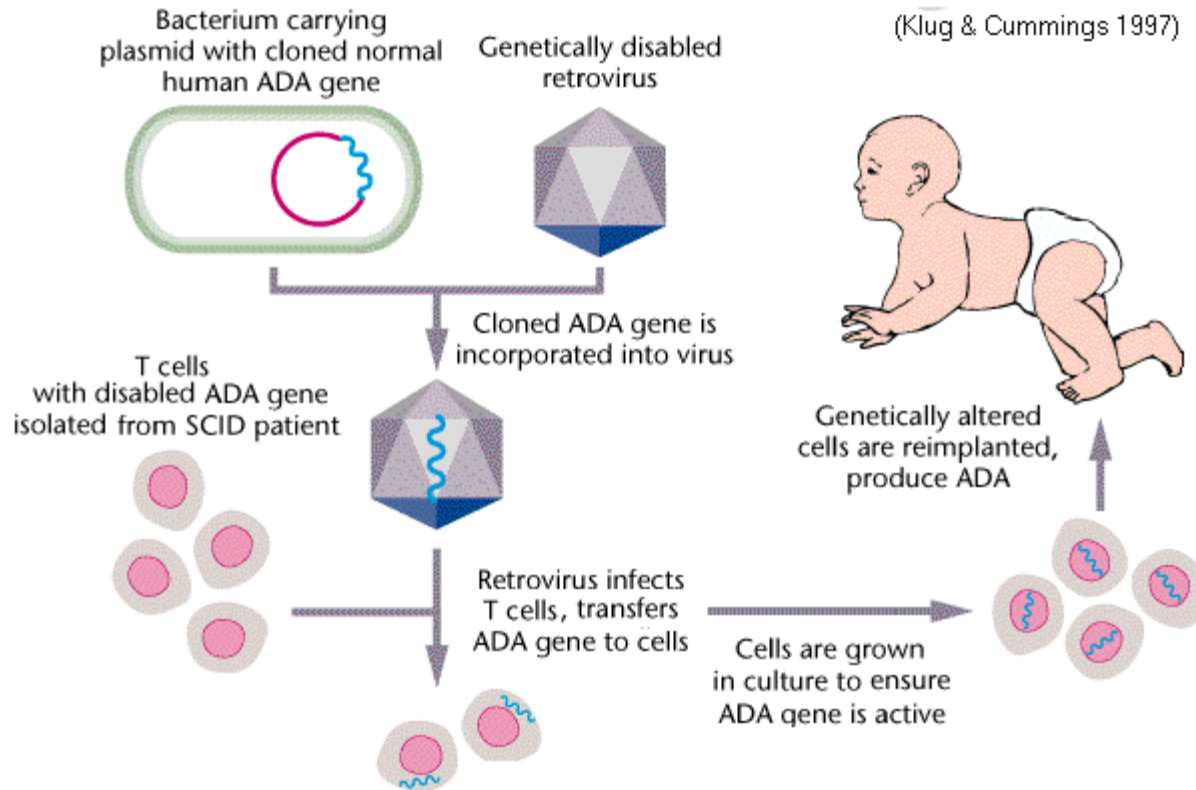
Gene therapy

Retroviral treatment of SCID

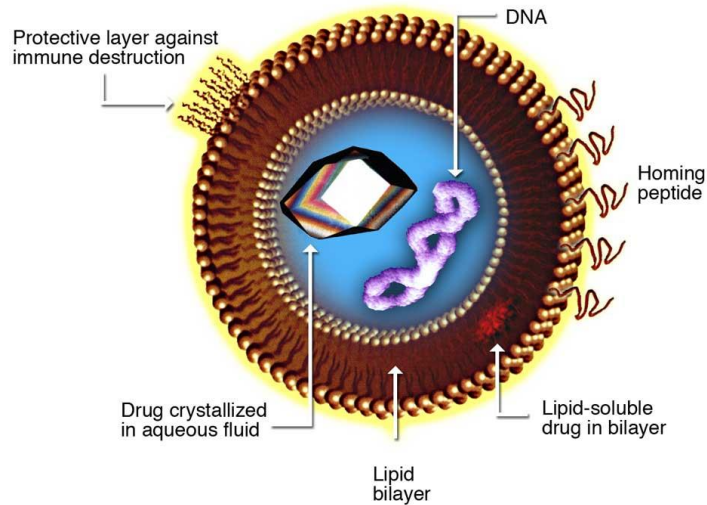
- Lymphocytes
- BM stem cells

Integration requires nuclear membrane dissolution during proliferation (advantages/disadvantages?)

Leukemia like disease due to random integration of vector near proto-oncogene activating it



Liposome for Drug Delivery

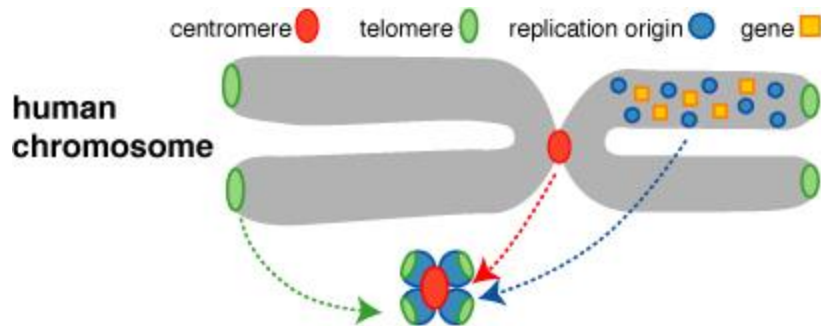


Gene therapy

Gene replacement therapy

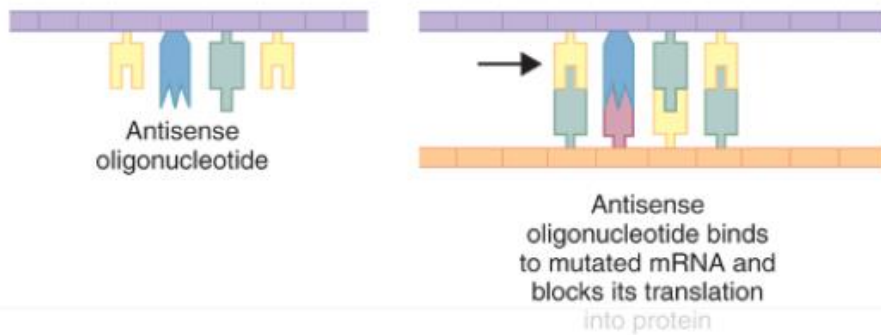
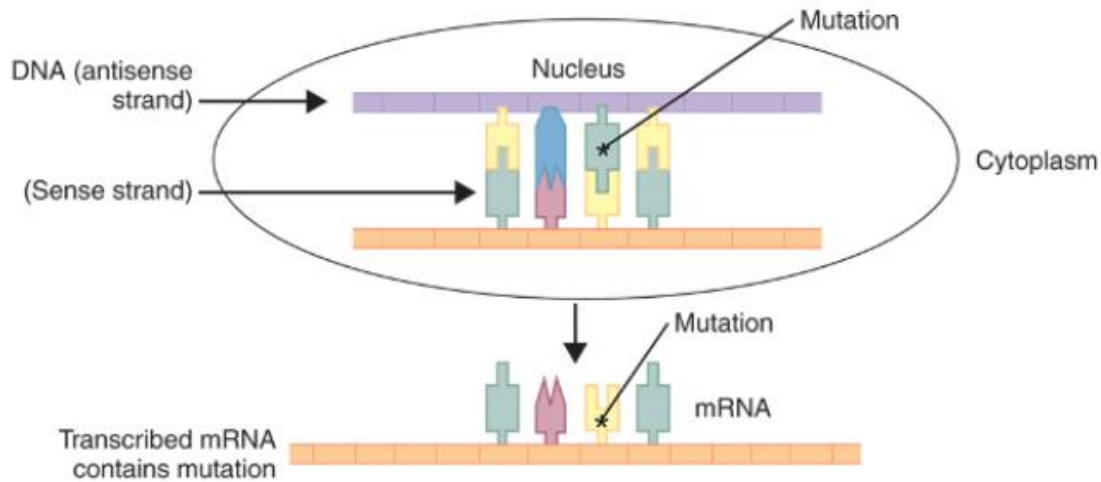
Viral vectors (transduction)

Non-viral vectors



HAC(human artificial chromosome)

- Constructed artificially in cultured human cells.
- Constructed by minimum DNA elements for the maintenance of chromosome function
- Enable gene introduction of desired sequences

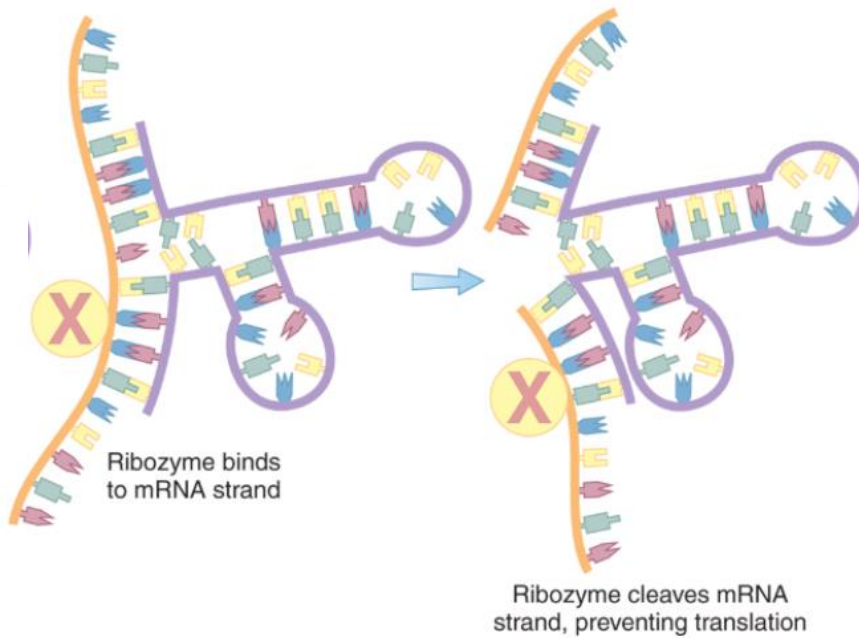
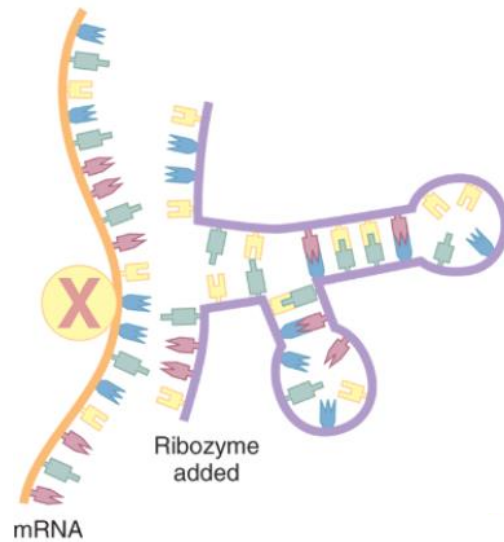


Gene therapy

Gene blocking

Antisense therapy

e.g. blocking KRAS in pancreatic and colon cancer and inducing exon skipping in DMD



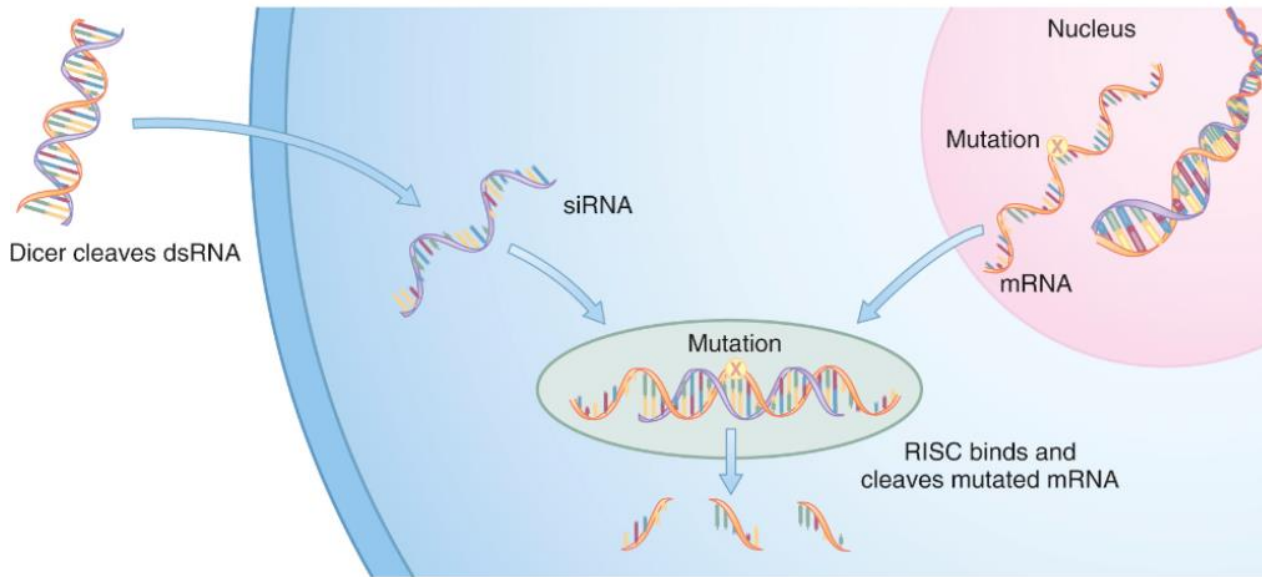
Gene therapy

Gene blocking

Antisense therapy

Ribozyme therapy

e.g. anti-HER2



Gene therapy

Gene blocking

Antisense therapy

Ribozyme therapy

RNAi

e.g. KRAS, BCR-ABL

PUGH



*'It's all your fault,
dad – terrible genes'*

Gene therapy

Somatic cell therapy

Gene replacement therapy

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Germline therapy

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Gene therapy

Somatic cell therapy

Gene replacement therapy

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Gene therapy for non-
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Germline therapy