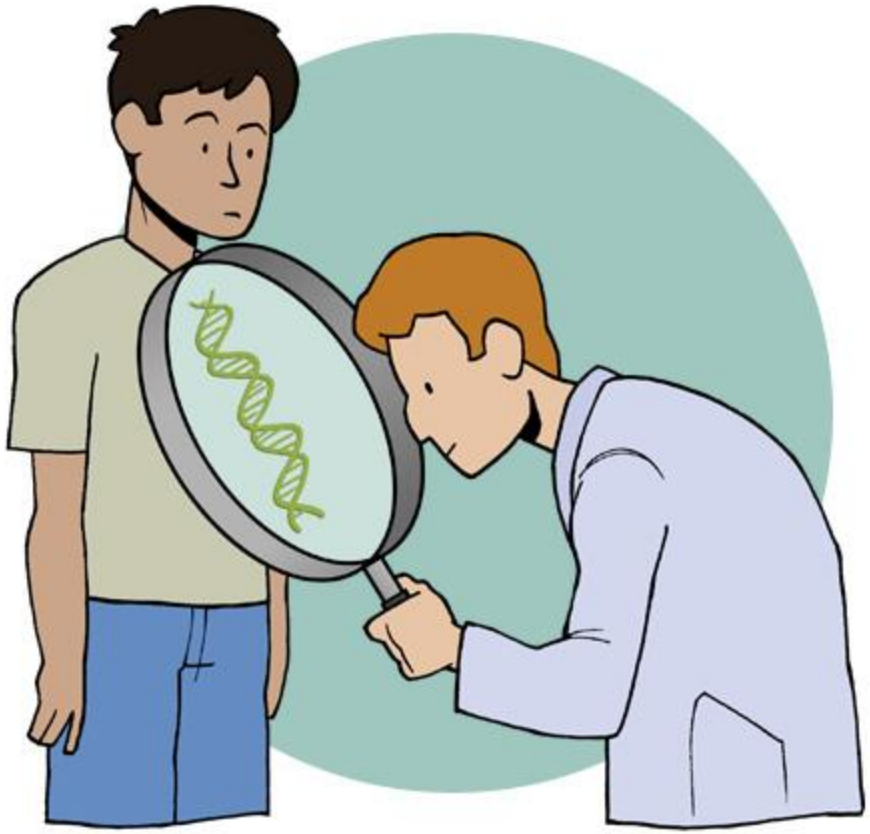
Genetic testing and gene therapy



Genetic Screening

Population screening:
- Newborn
- Heterozygote

Prenatal diagnosis:
- Invasive
- Non-invasive

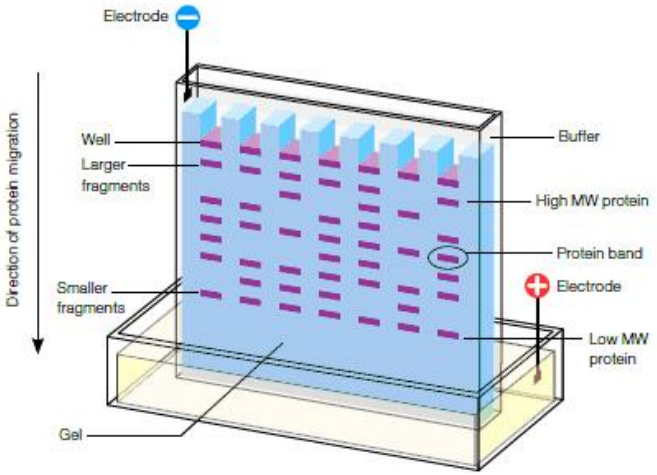
Family screening

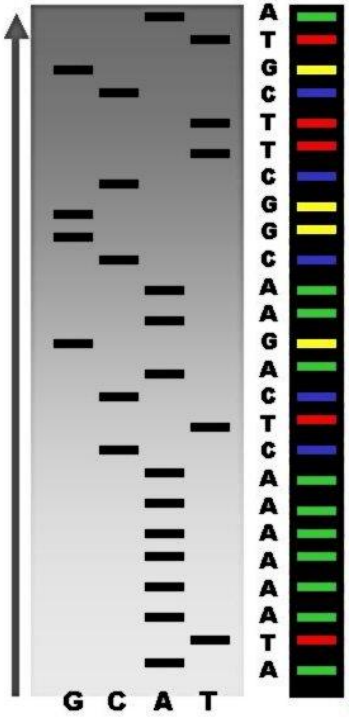
Principles?

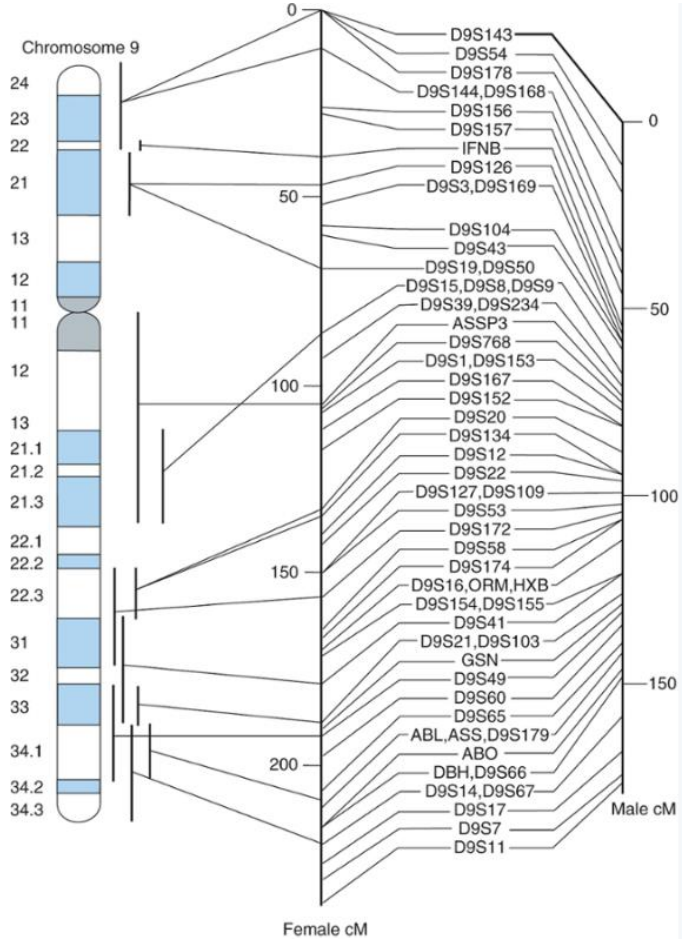
Screening validation?

Sensitivity/specificity?
PPV/NPV?

Which tools do we use?







Limitations

Test errors

Mutations not disease

Test sensitivity

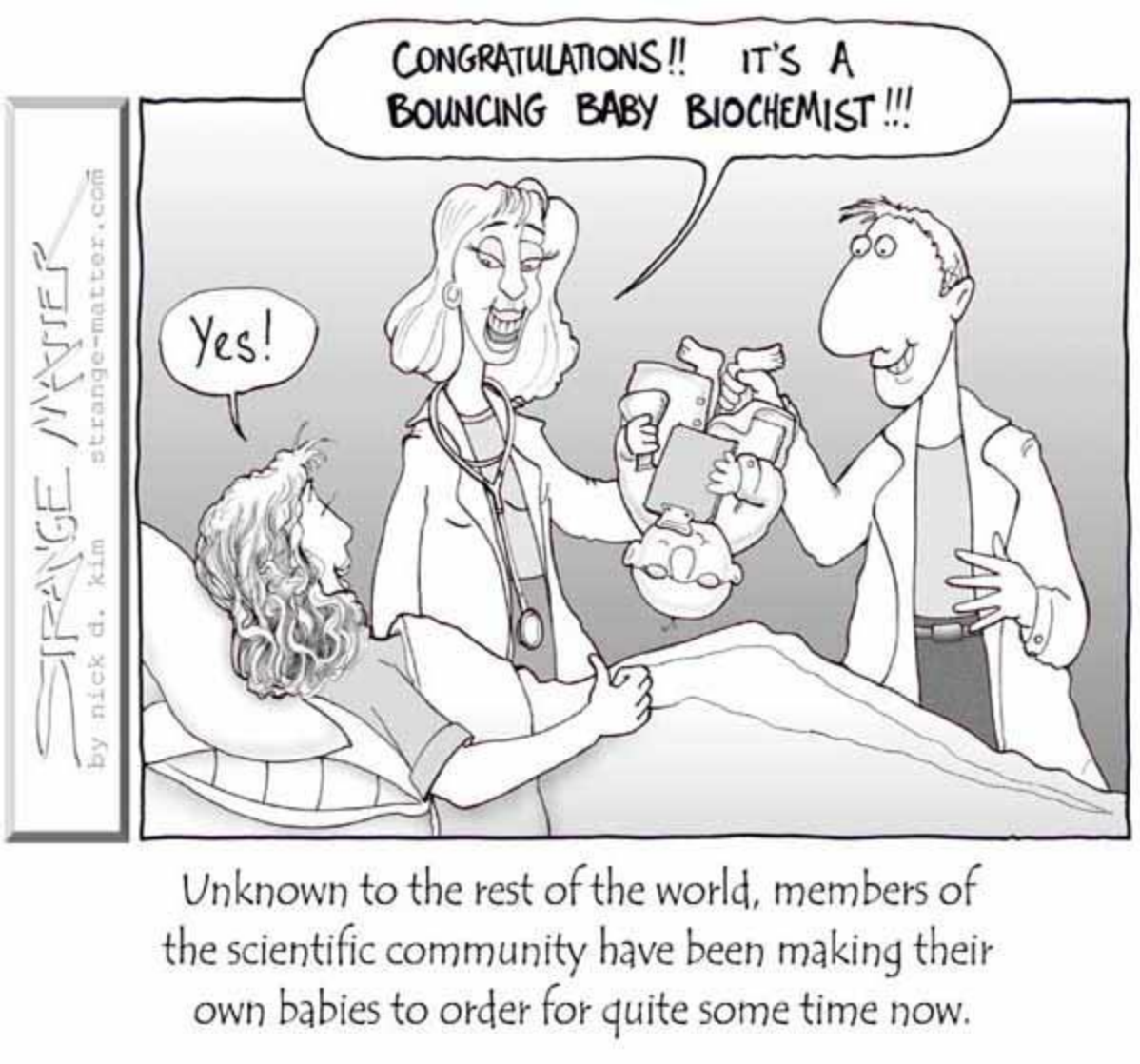
Psychological implications

Discrimination

Lack of treatment

Other diseases

Direct-to-consumer genetic testing?



Prenatal Diagnosis

AFP screening

Amniocentesis

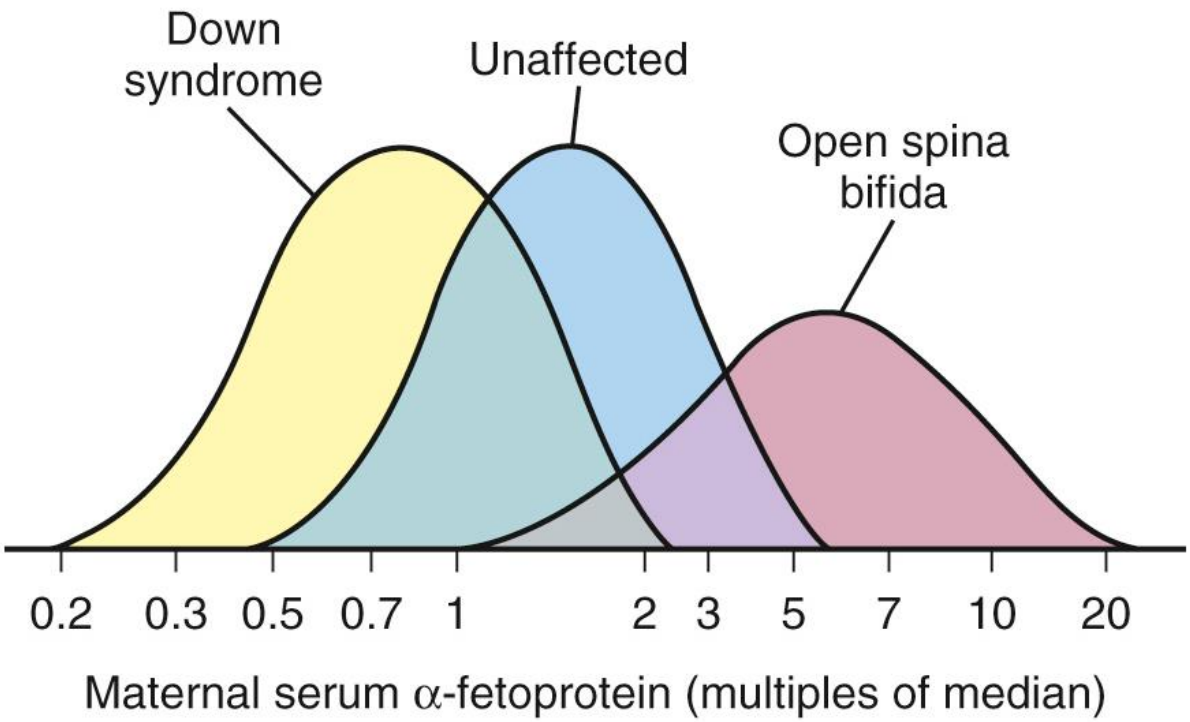
CVS

Cordocentesis

US, MRI

Preimplantation genetic diagnosis

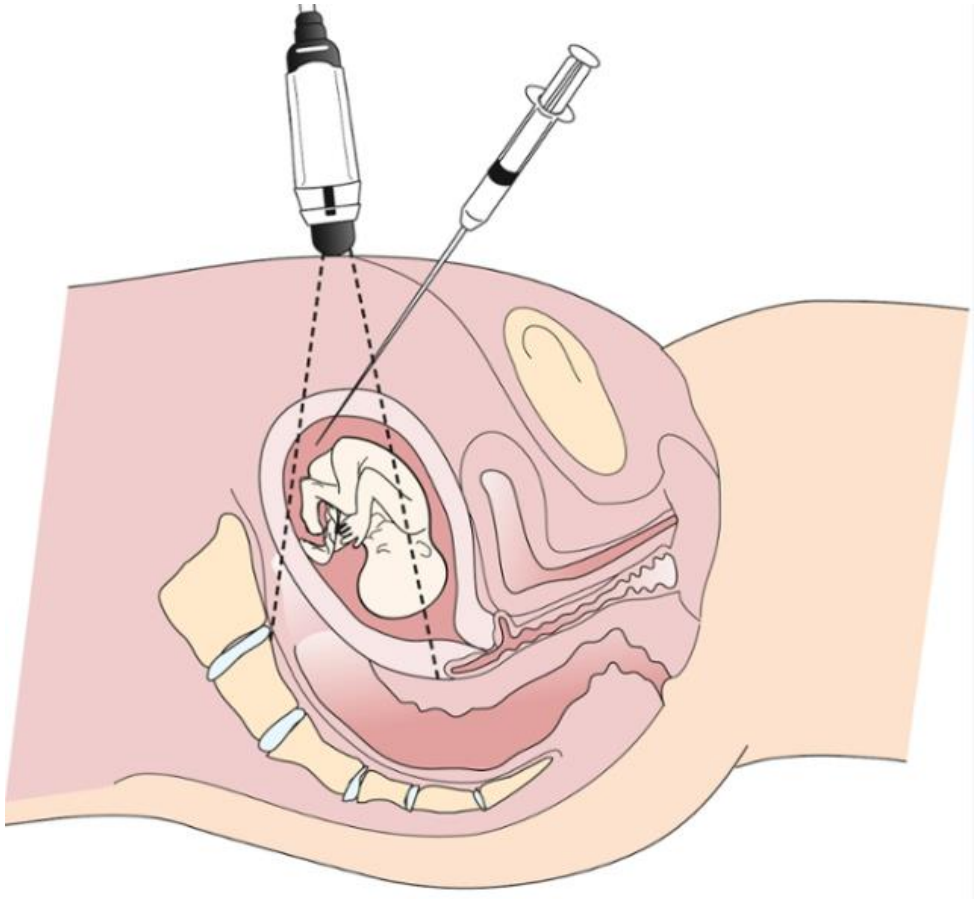
Prenatal Diagnosis



AFP screening:

- Maternal blood
- Amniotic fluid

Fetal DNA circulating in the maternal circulation (screening) NIPS

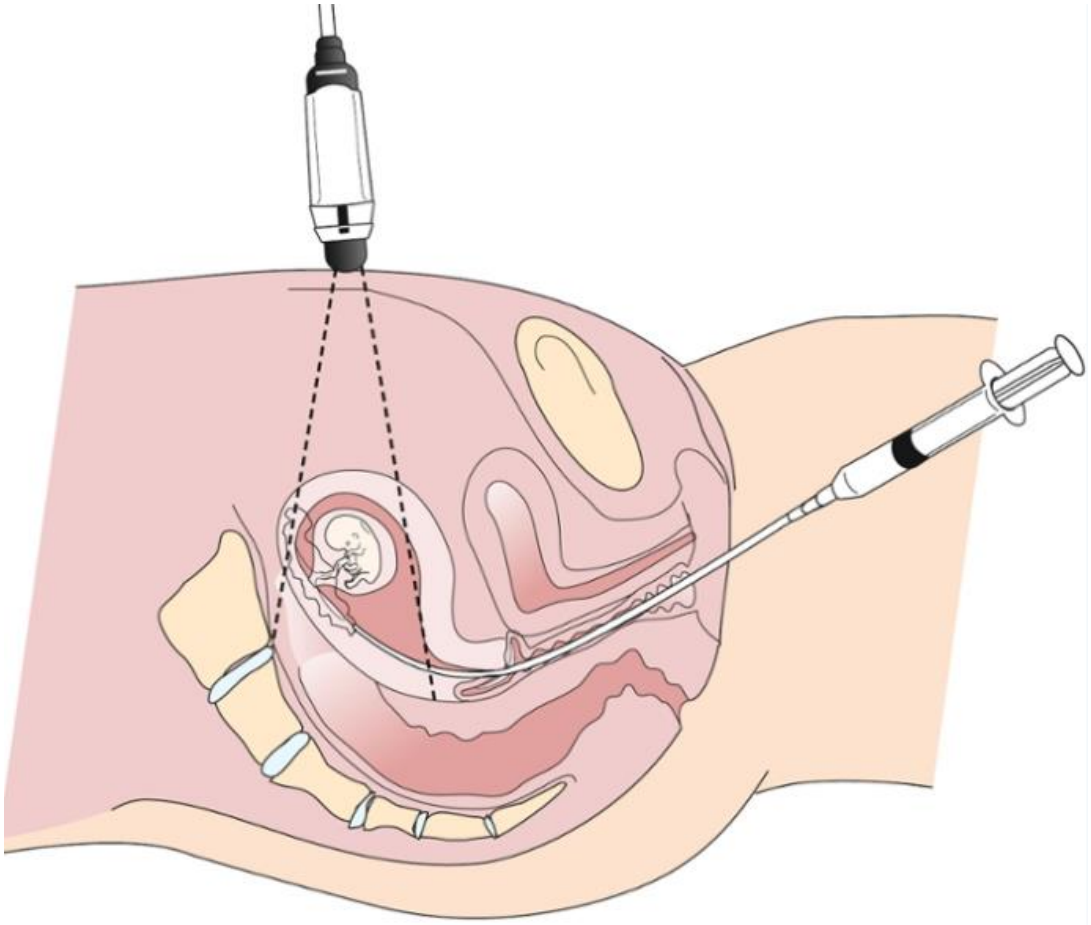


Prenatal Diagnosis

Amniocentesis:

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

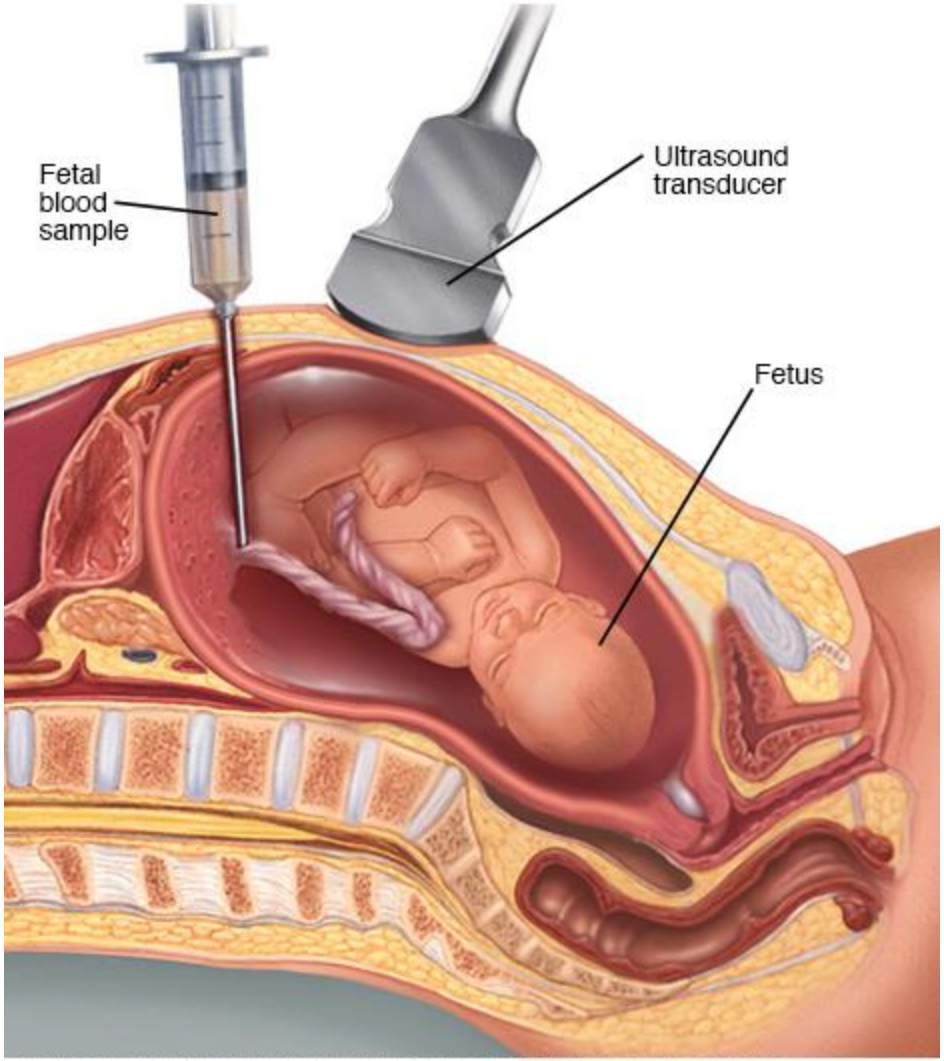
Risks (leakage, infections, fetal loss) rare



Prenatal Diagnosis

CVS:

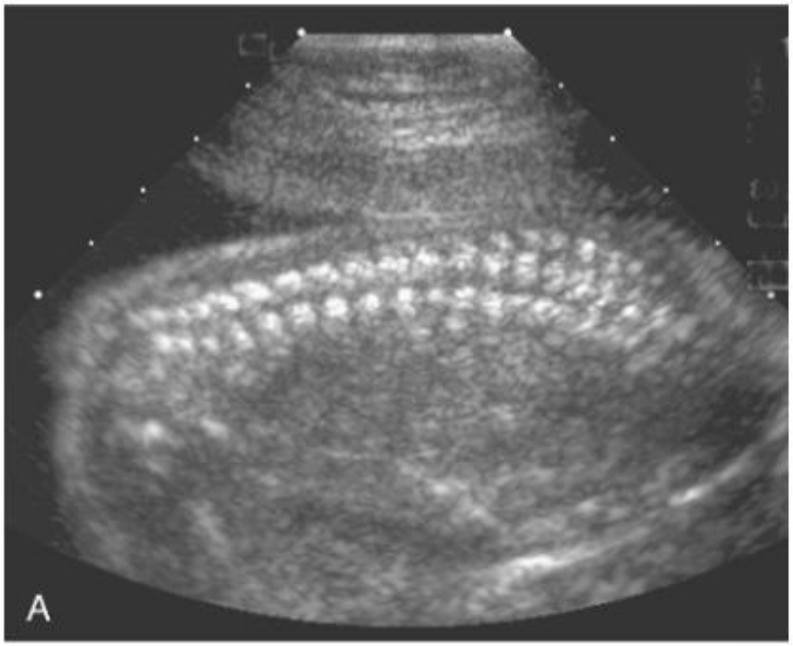
- Earlier
- Generally safe but higher risk than amnio
- Limb deficiency?
- No amnio AFP measured



Prenatal Diagnosis

Cordocentesis:

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



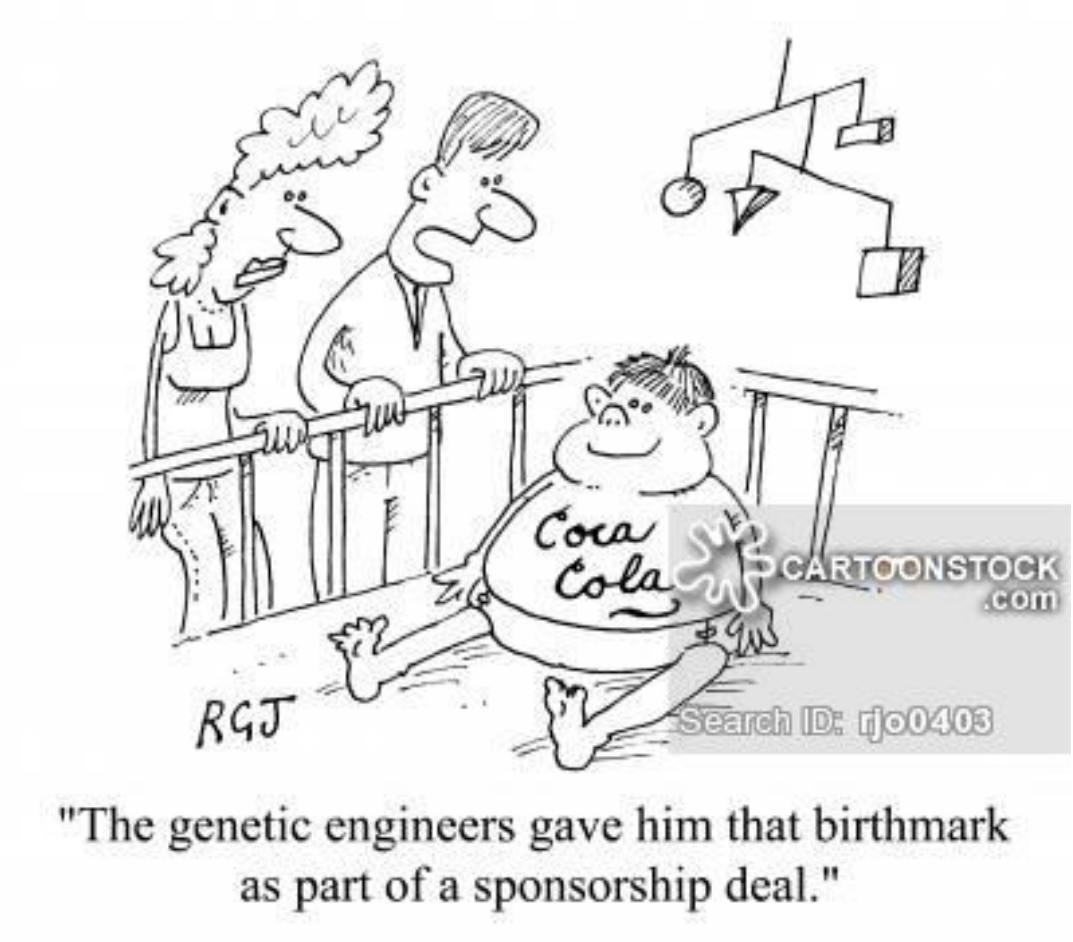
Prenatal Diagnosis

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."

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

Gene therapy

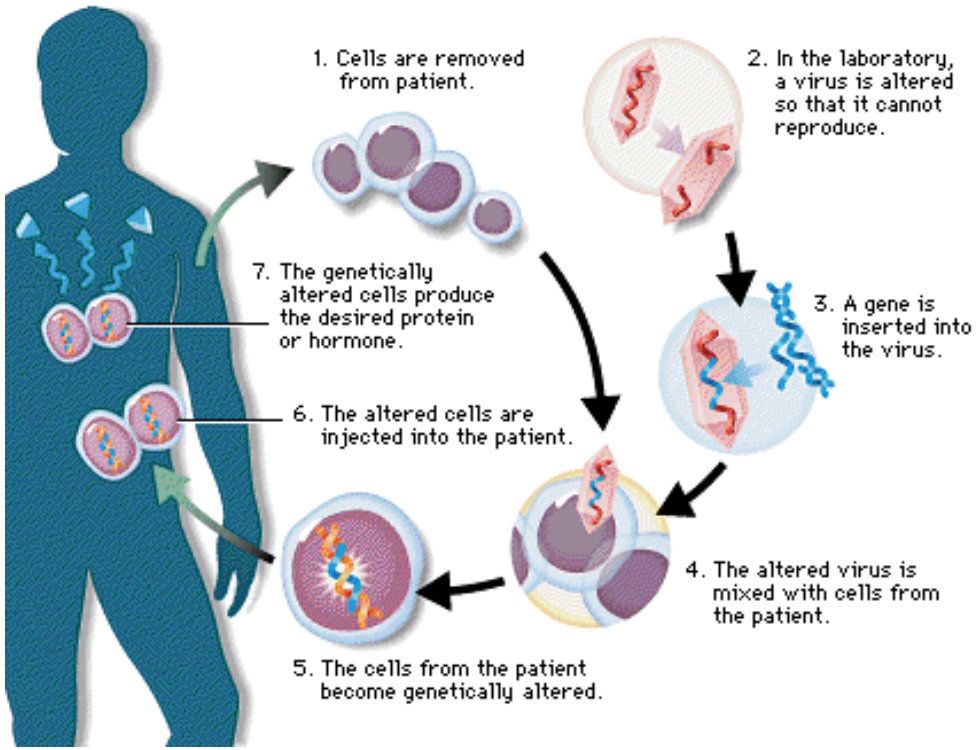
Somatic cell therapy

Gene replacement therapy

Gene blocking

Gene therapy for non-inherited diseases

Germline therapy

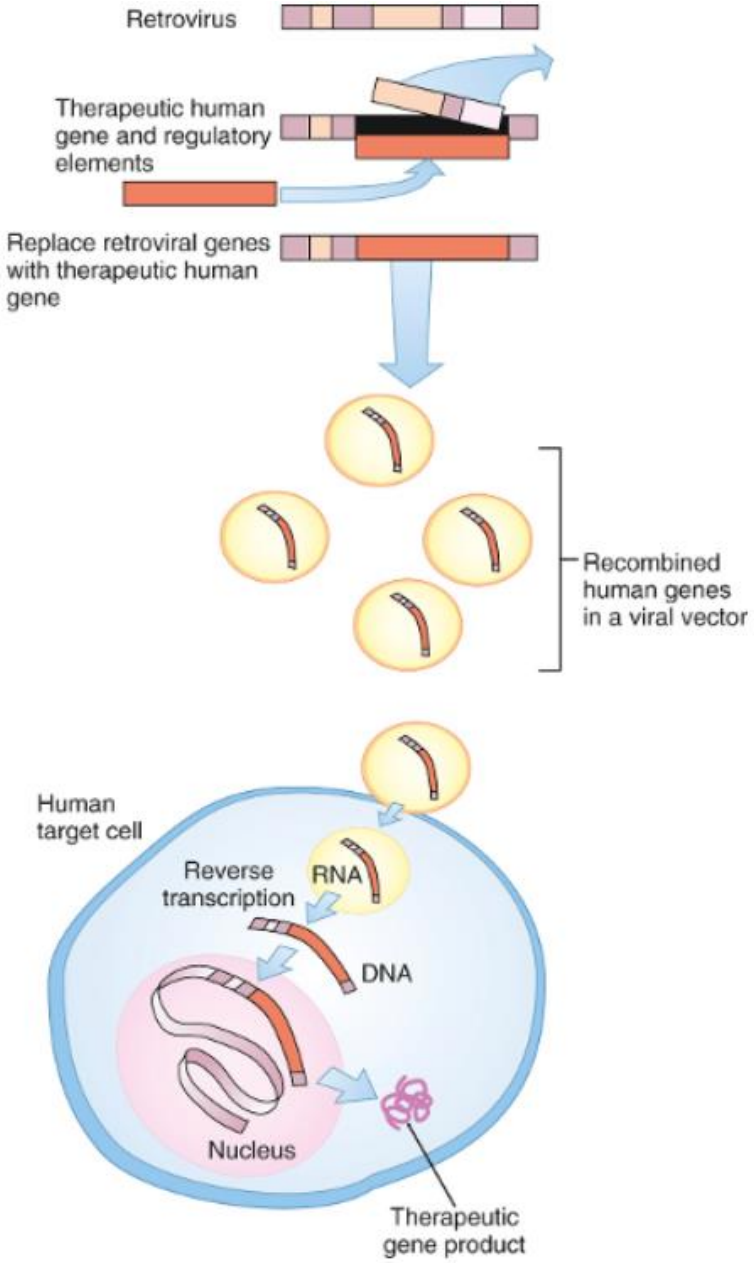


Gene therapy

Somatic cell therapy

Cells should be easily accessible and long lived

Proliferating cells are useful to ensure integration of new genetic material

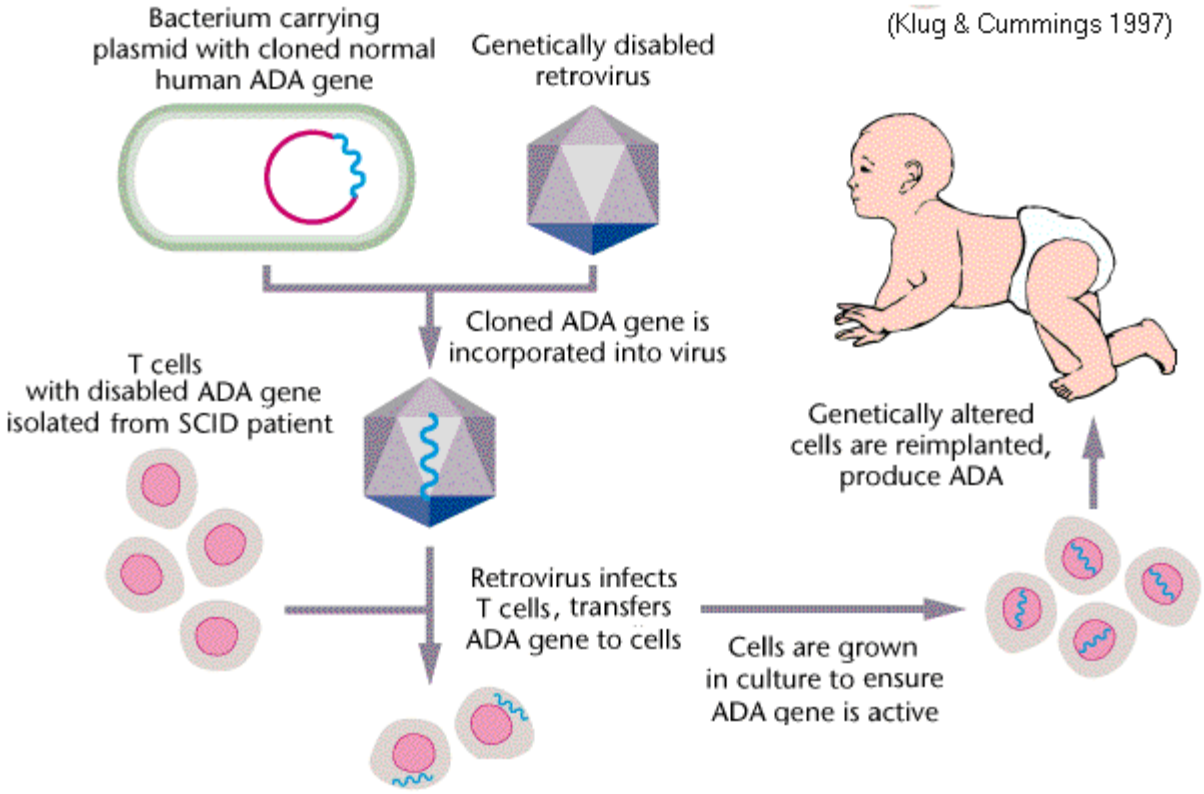


Gene therapy

Gene replacement therapy

Viral vectors (transduction)

Non-viral vectors



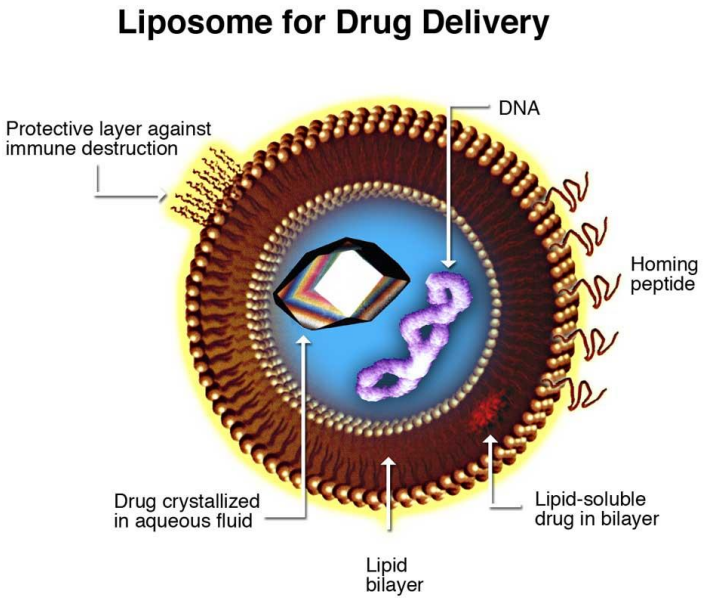
Gene therapy

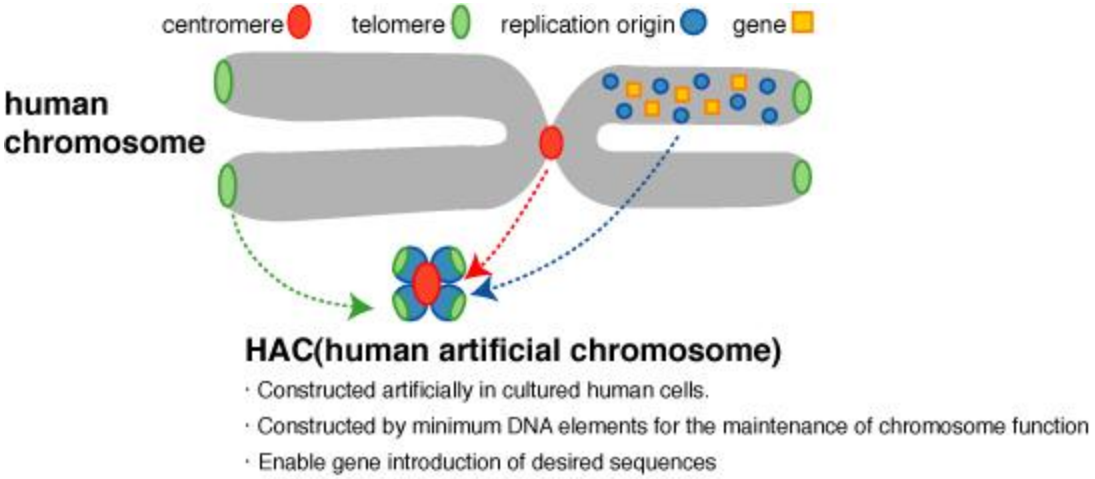
Retroviral treatment of SCID

- 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





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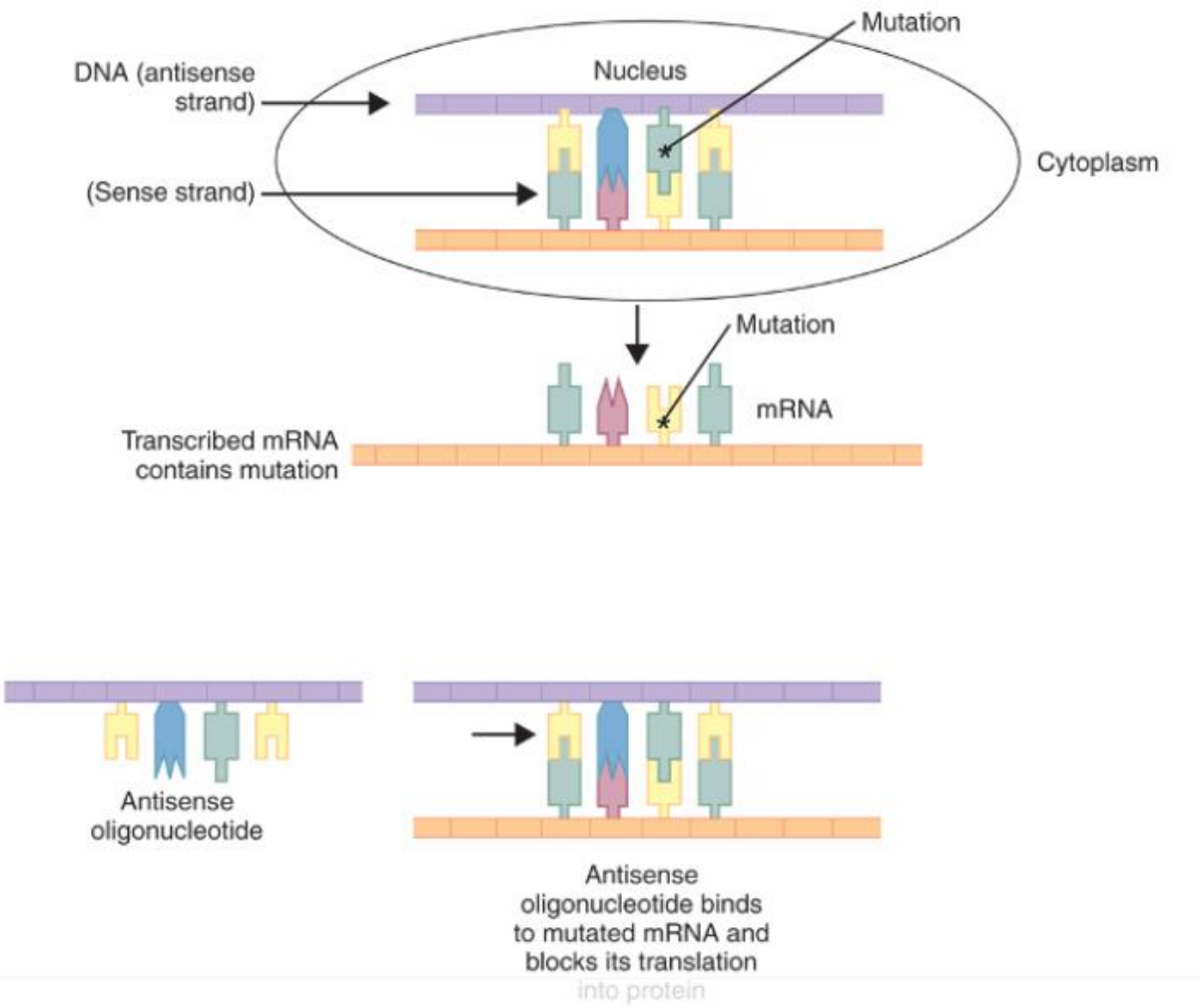
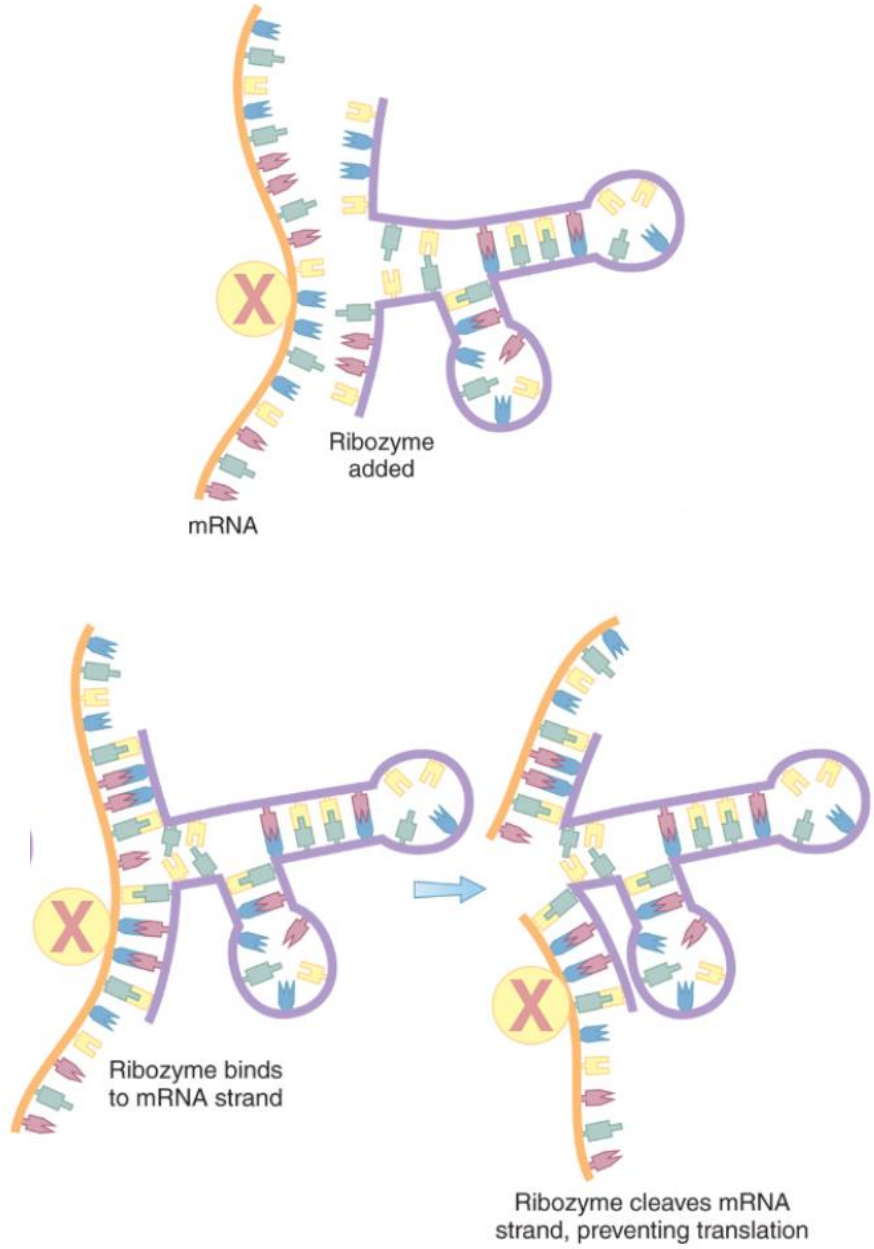


Gene therapy

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

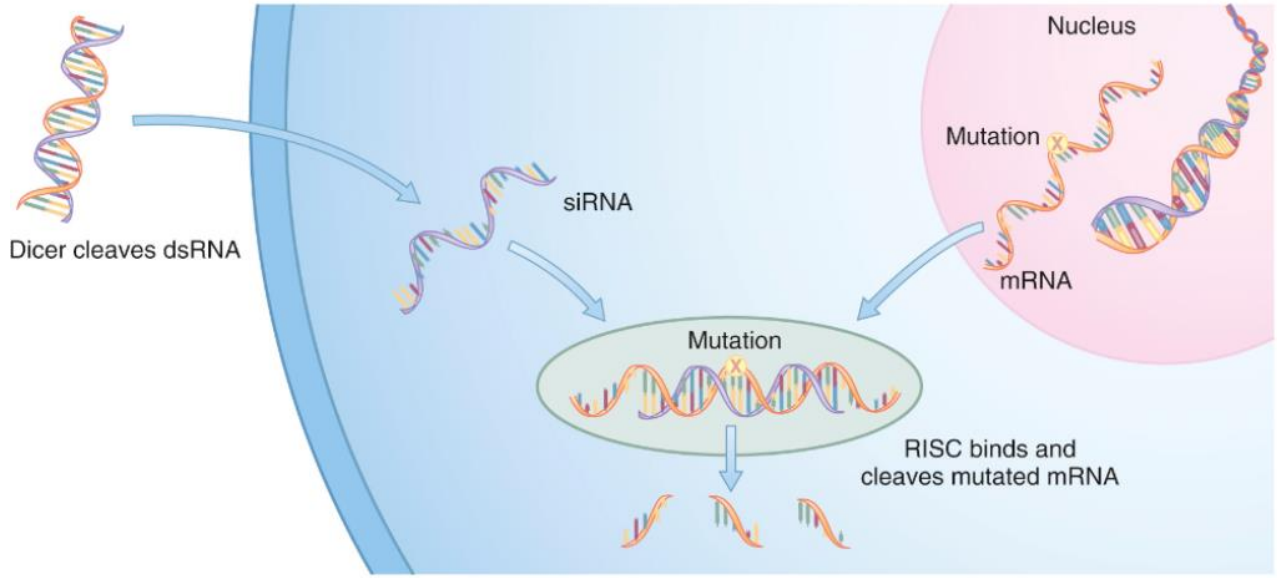
Gene blocking

Antisense therapy

Ribozyme therapy

RNAi

e.g. KRAS, BCR-ABL



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

Gene therapy

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