Cambridge University Hospitals NHS Foundation Trust

Non-invasive Genetic Testing in Pregnancy: Lessons from Genetic Counselling Practice

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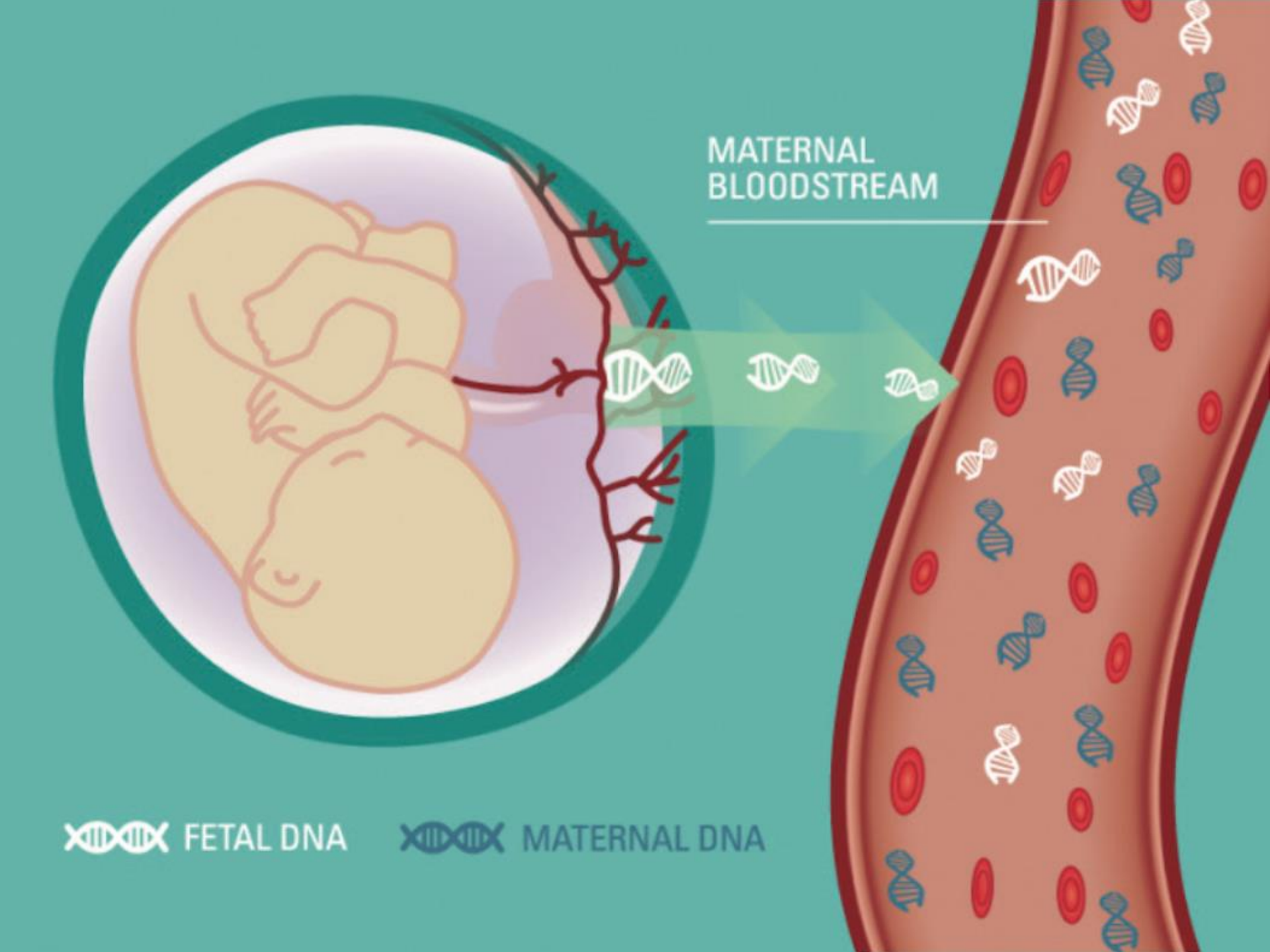
Festival of Genomics
30th January 2020


MATERNAL
BLOODSTREAM
FETAL DNA
MATERNAL DNA

NIPT or NIPD? What's the difference??

Non-invasive prenatal testing (NIPT) and non-invasive prenatal diagnosis (NIPD) both involve the analysis of cffDNA from a maternal blood sample.

- NIPT: **screening** test, commonly used for aneuploidy testing. An invasive test will still be necessary to confirm an abnormal result
- s diagnostic and an invasive test is not
  sult
- planned (for couples with high risk
  t in first trimester)
- NIPD has been slower

harmony™ PRENATAL TEST *performed in the UK*

NIFTY™

serenity

progenity® Prepare for life.

the IONA® test non-invasive prenatal screen: safe, fast, accurate

natera® Conceive. Deliver.

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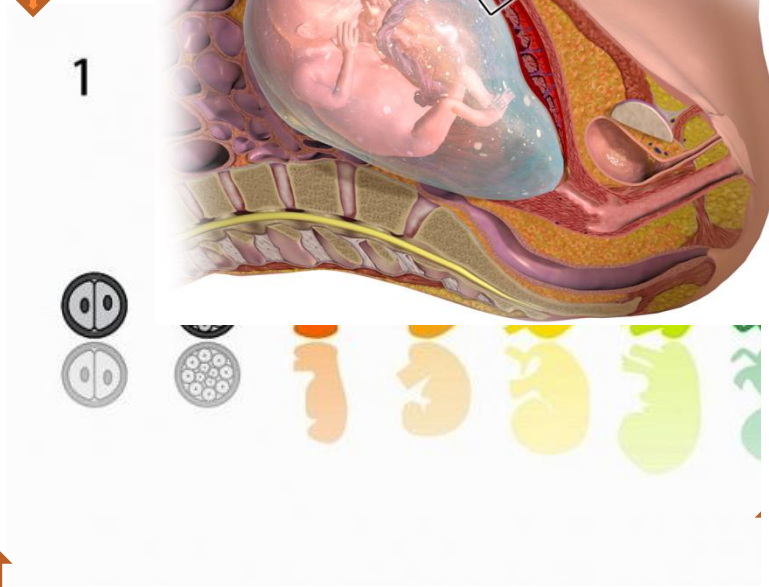
UK Genetic Testing Network (UKGTN) approved NIPD for:

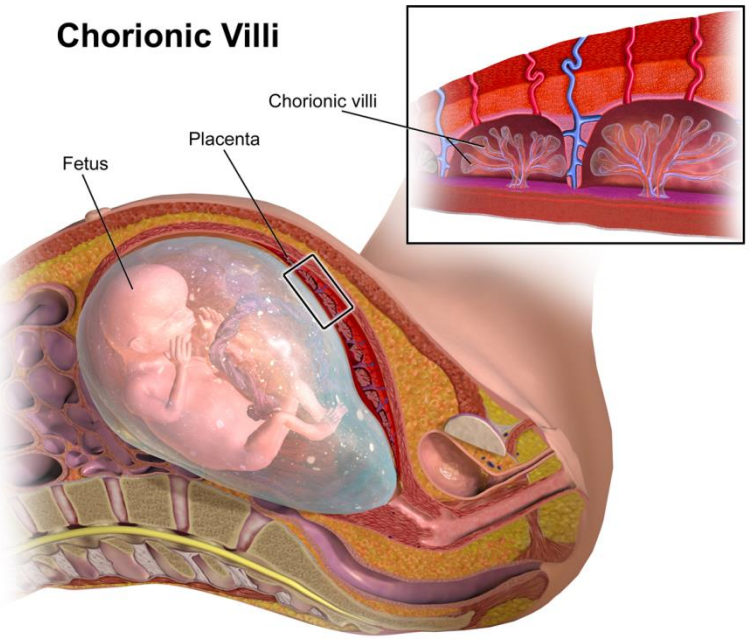
- ✓ **Fetal sex determination:**
  - DMD (X-linked)
  - Haemophilia A and B (X-linked)
  - CAH (AR – management)

- ✓ **Single gene disorders:**
  - *Dominant conditions* - inherited paternally or arising de novo: Achondroplasia & Thanatophoric dysplasia, Apert syndrome.
  - *Recessive conditions*: CF, SMA
  - *X-linked conditions*: DMD

Preimplantation Genetic Diagnosis



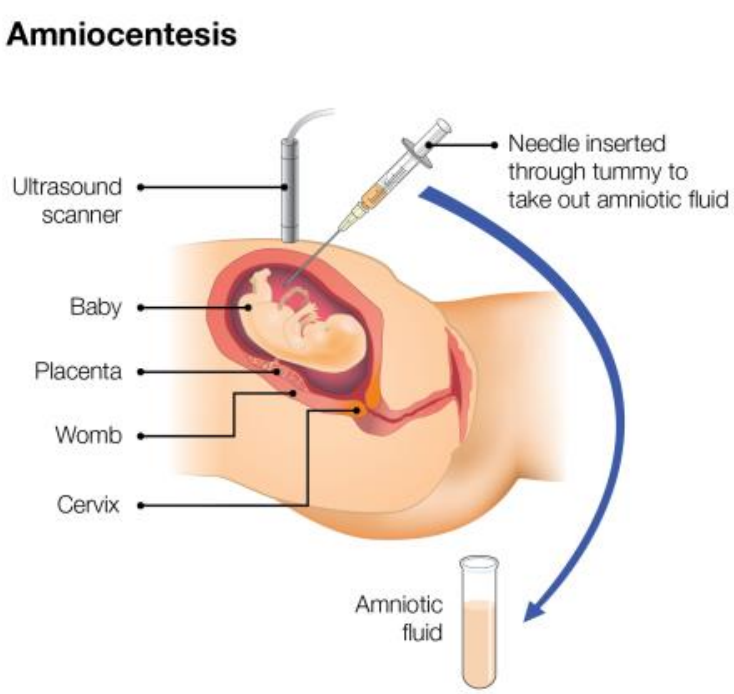
Chorionic Villus Sampling



Umbilical Cord Sample

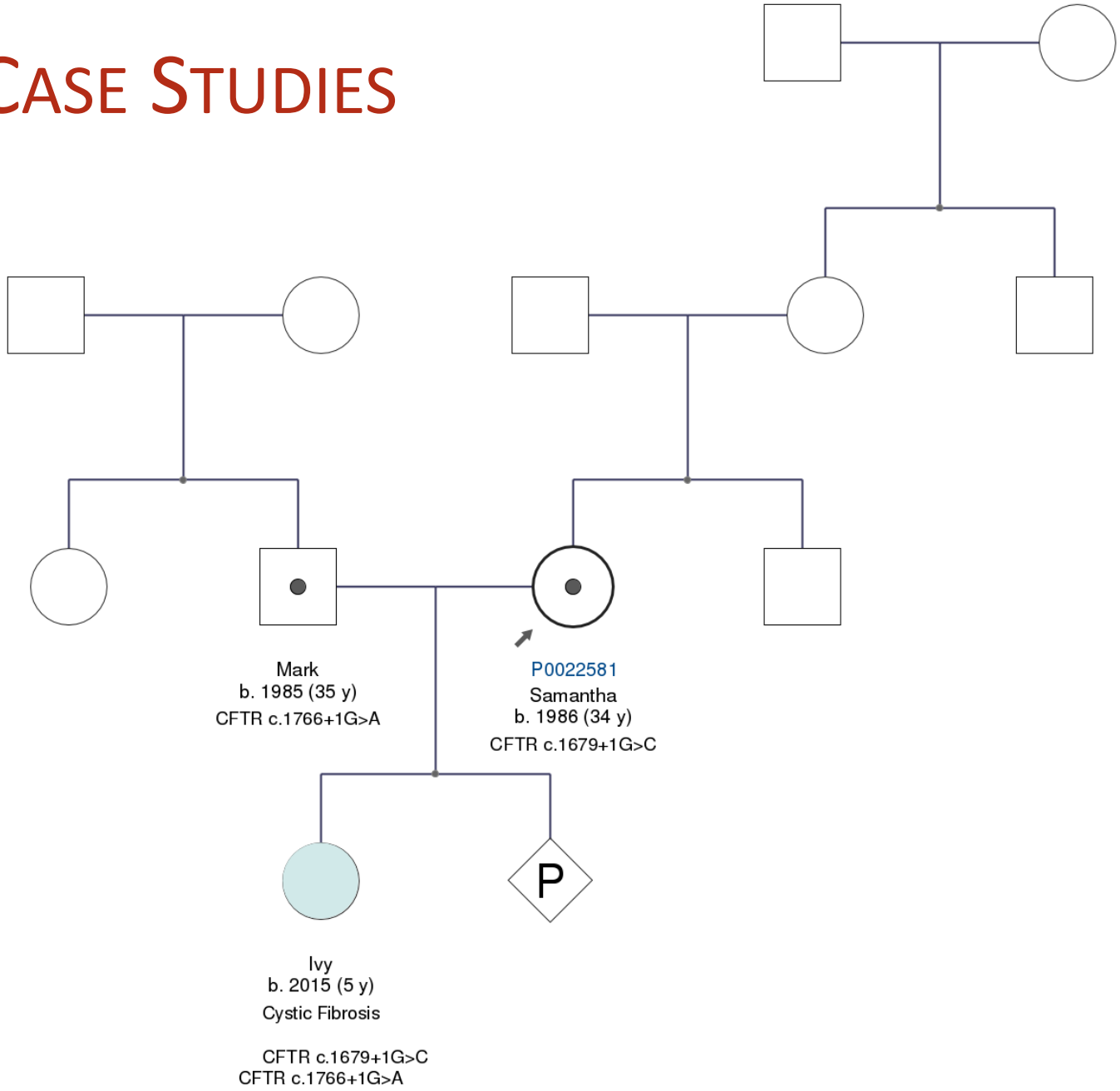
Confirmed gene mutation or chromosome anomaly

Free DNA

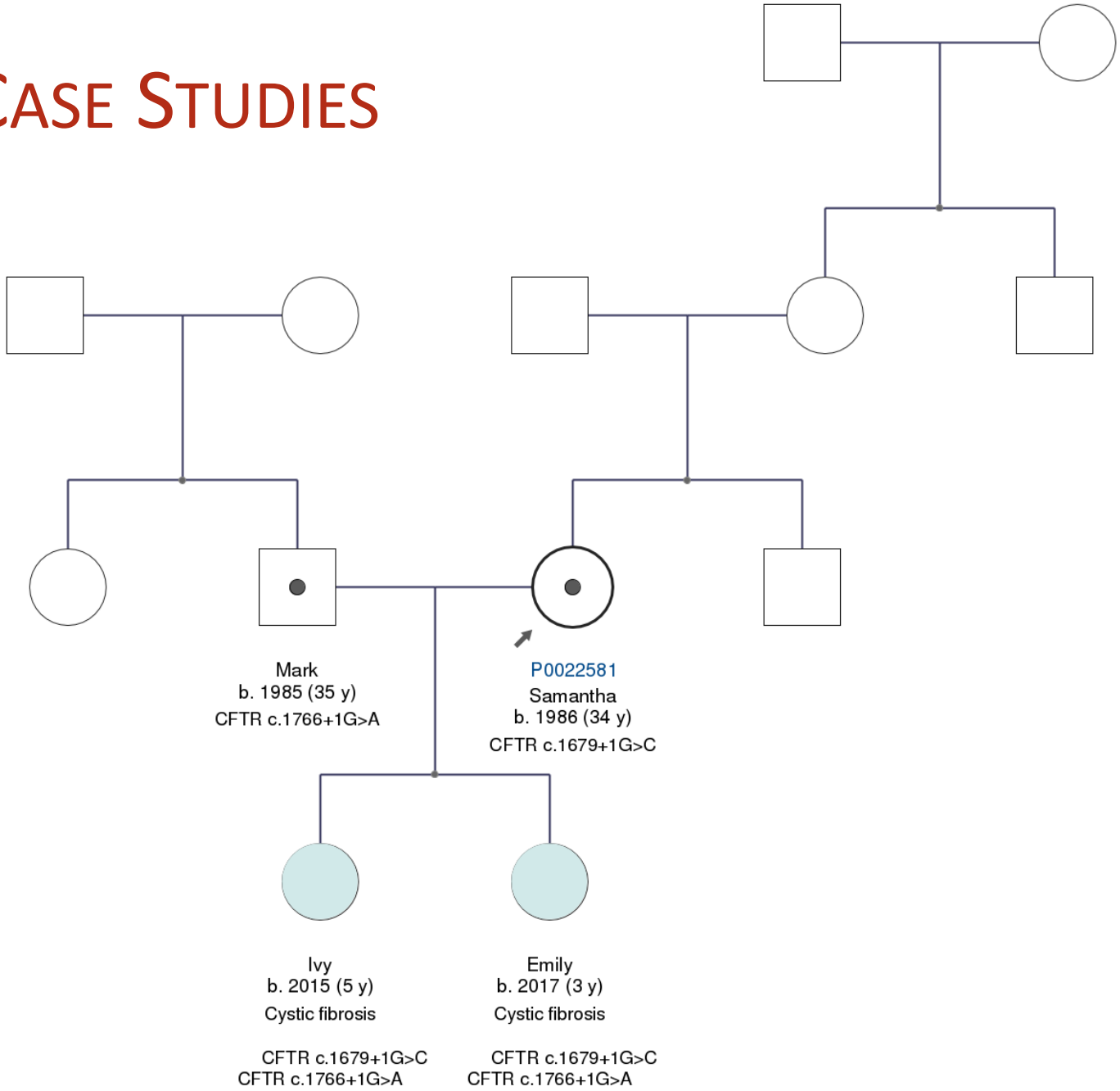


Newborn Screening

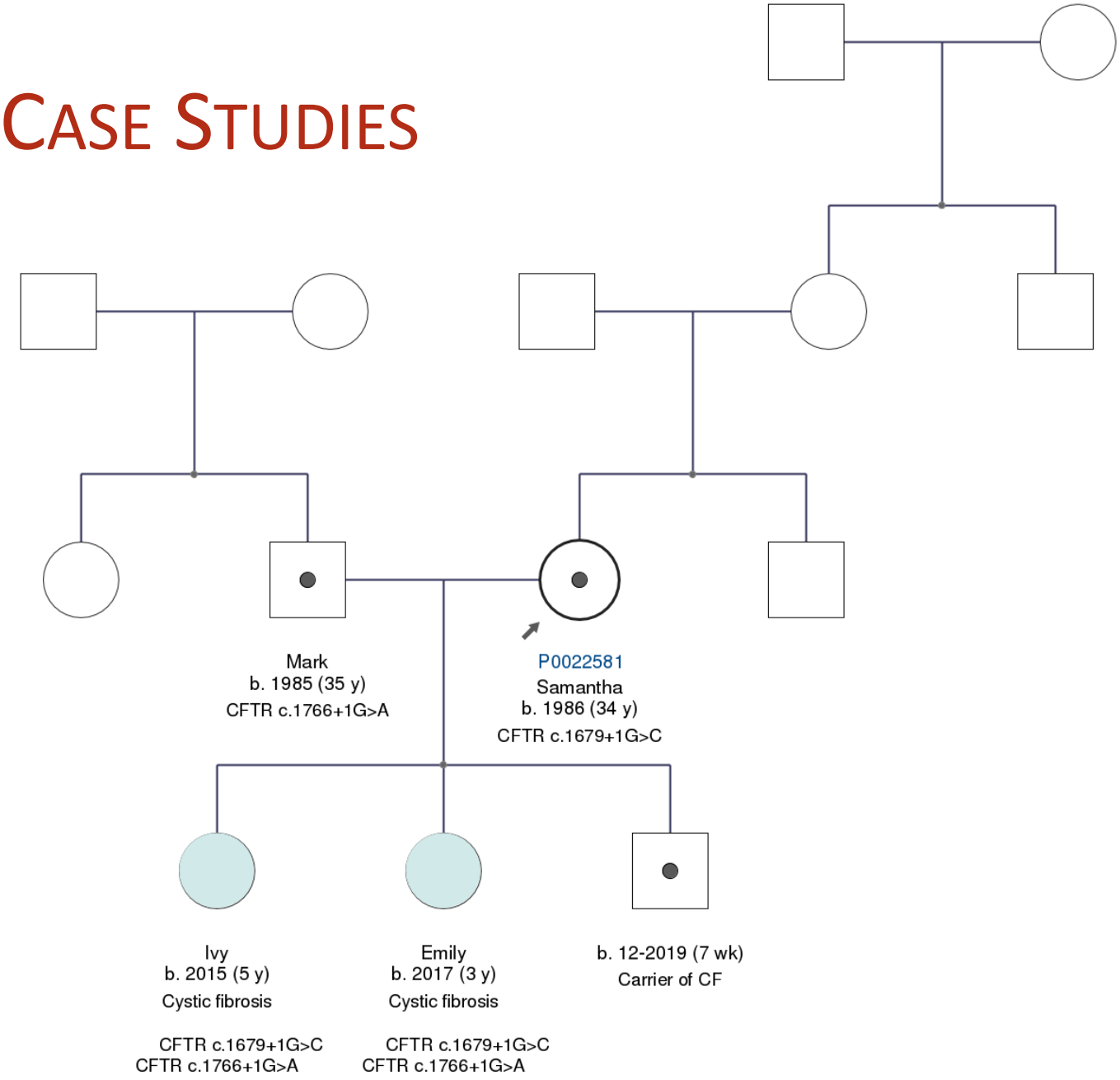
Case Studies



Case Studies



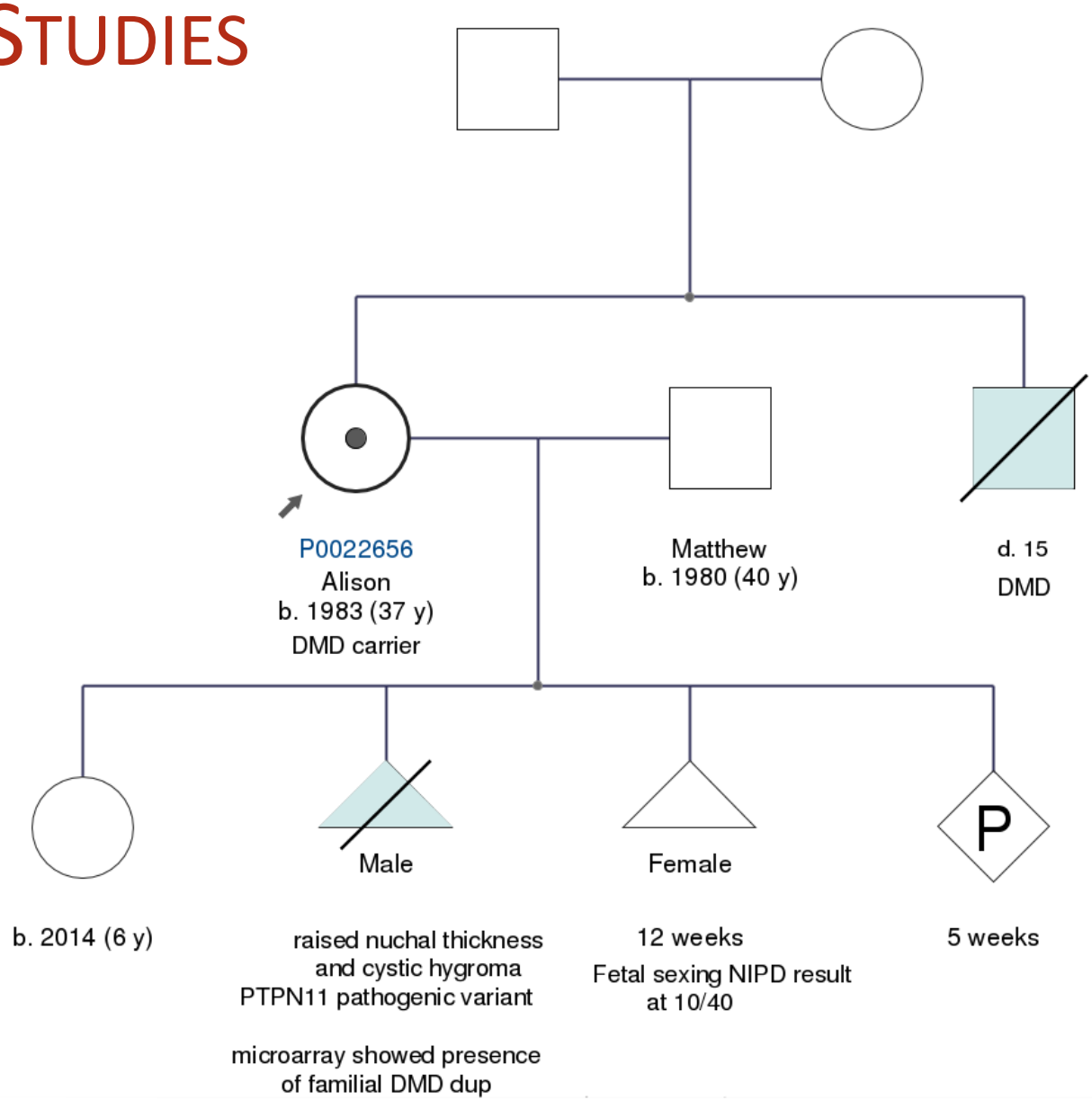
Case Studies



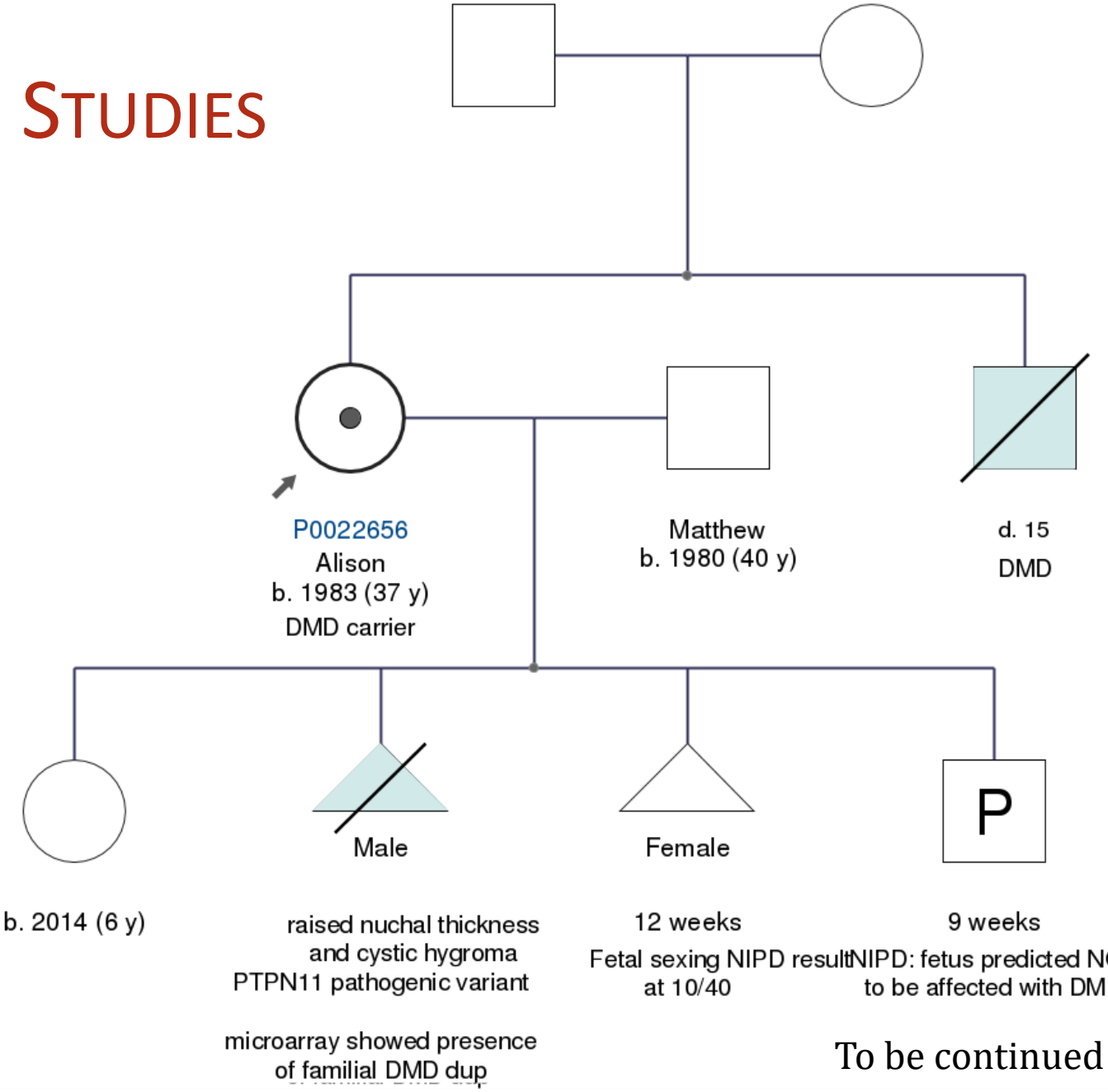
Learning points

- Technology rapidly changing
- Couples have to be empowered to contact Clinical Genetics team early to access testing
- Importance of pre-test counselling
- Easier test but the same possible implications
- Demand for micro-management - close links with midwifery teams essential

Case Studies



Case Studies



To be continued…

Some points to consider

- Couples need to be aware of possible technical issues and inconclusive results
- [illegible] with uncertainty
- Cost implications
- [illegible] to test for
- Clinic established
- "Work up" time needed [illegible] and empowerment

2 gestational sacs

Insufficient informative markers

Insufficient cffDNA

Recombination

Multiple pregnancies

SNP in primer site

Missed miscarriage

Future Considerations

- Just another pregnancy blood test?
- Teaching, training and integrated working between Clinical Genetics and Fetal Medicine departments
- Moving towards WGS
  - WES/WGS for NIPD to assist in diagnosis along with scans
  - results much earlier
  - uncertain or incidental findings
- Commercial NIPD testing for low risk pregnancies
  - no pre-test counselling?
  - no “lived experience”?
  - implications for other relatives?

Clinical Chemistry 66:1
53–60 (2020)

Mini-Reviews

Noninvasive Prenatal Diagnosis of Single-Gene Diseases: The Next Frontier

Elizabeth Scotchman,[1] Natalie J. Chandler,[1] Rhiannon Mellis,[1,2] and Lyn S. Chitty[1,2*]

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Cambridge University Hospitals NHS Foundation Trust

Thank you

- Genetic Counsellors of Addenbrooke's Hospital, Cambridge
- Clinical scientists from the Genetic Laboratory Hubs offering clinical NIPD
- Fetal medicine and midwifery teams across East of England region.
- Patients and their families

Any questions?

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