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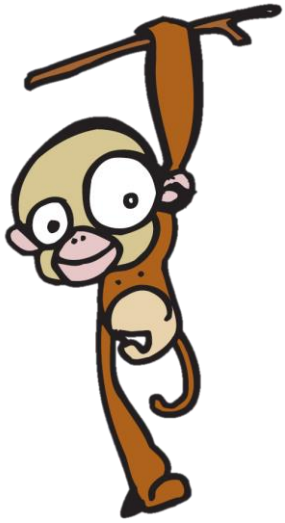

Genomic Advisory Role

Richard Hastings

Consultant Paediatrician, Sherwood Forest Hospitals

What's coming…

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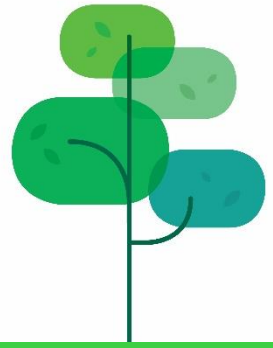
- Who am I and where did I come from?
- Why am I interested in Genomics?
- What I did to increase my knowledge/skills
- What I do now to support my colleagues



My career path…

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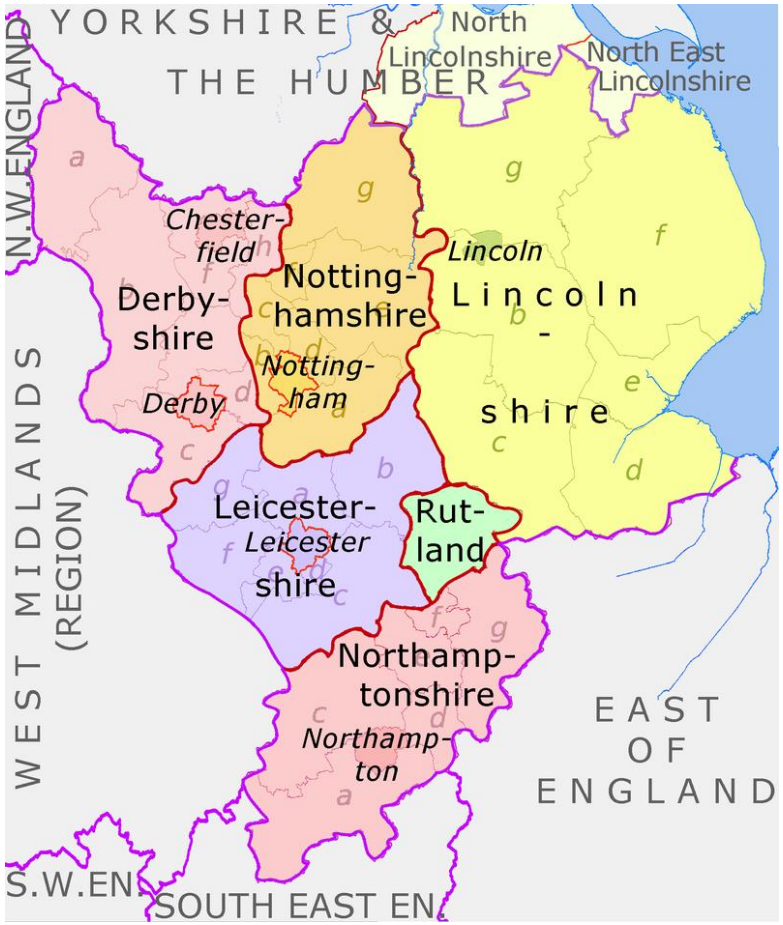
- AKA, a small tour of the East Midlands



My career path…

- 14 year old
- Confused

NUMBER 1

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My career path…

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- 14 year old, uncertain career plans

My career path…

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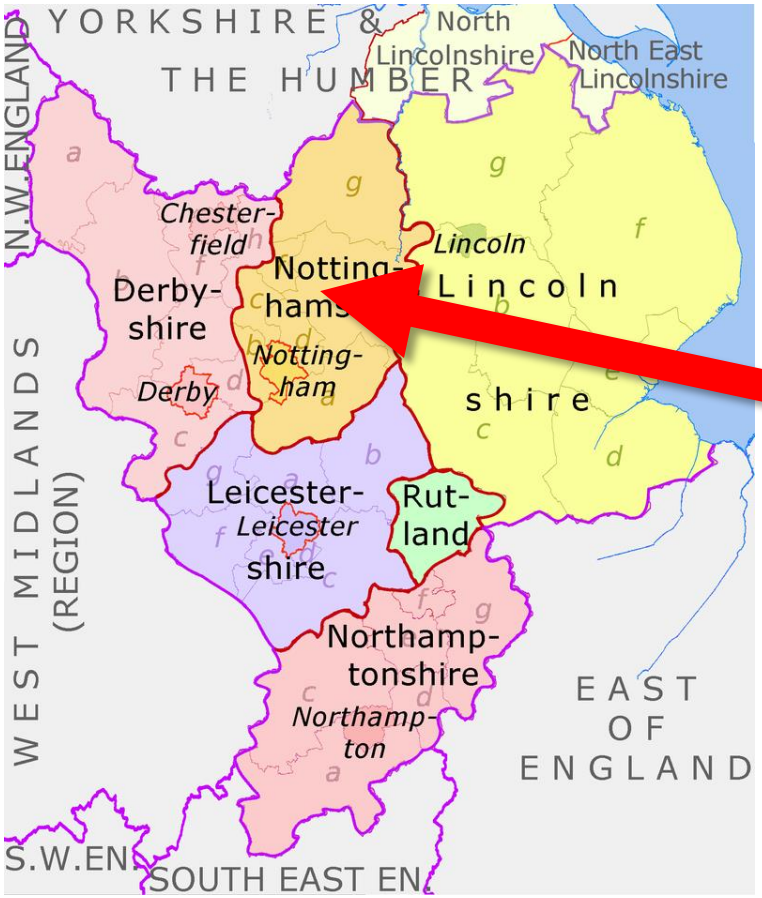
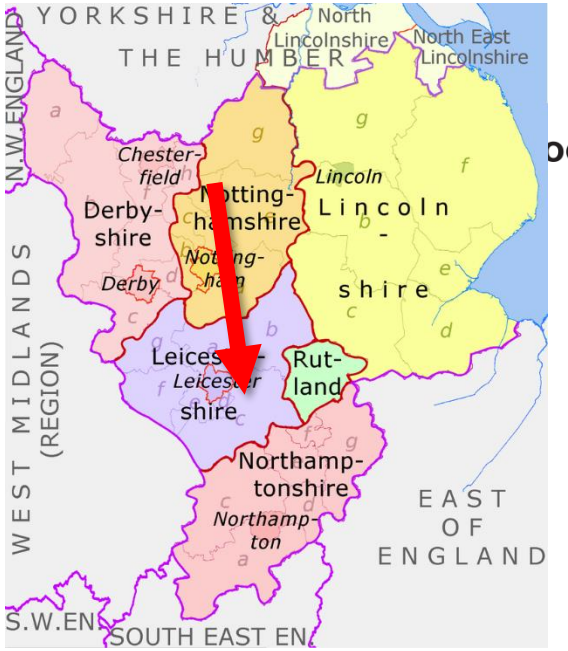
NHS Foundation Trust

- Genetics 1991-1994



My career path…



- Genetics 1991-1994
- PhD 1994-1997

- Post-doctoral research 1997-2004
  - Genetic markers of ageing in CVS cells

NUMBER 2

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A career in **Medicine**!

My career path…

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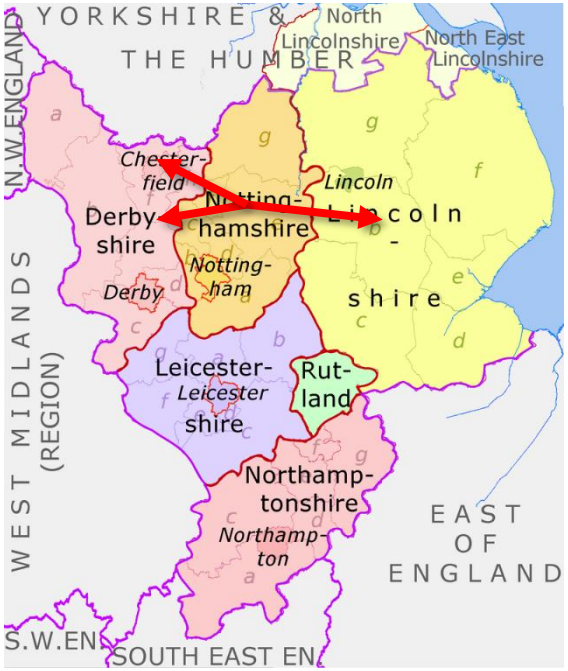
- BMBS 2004-2008

- Specialty training in Paediatrics



NUMBER 3

My career path…

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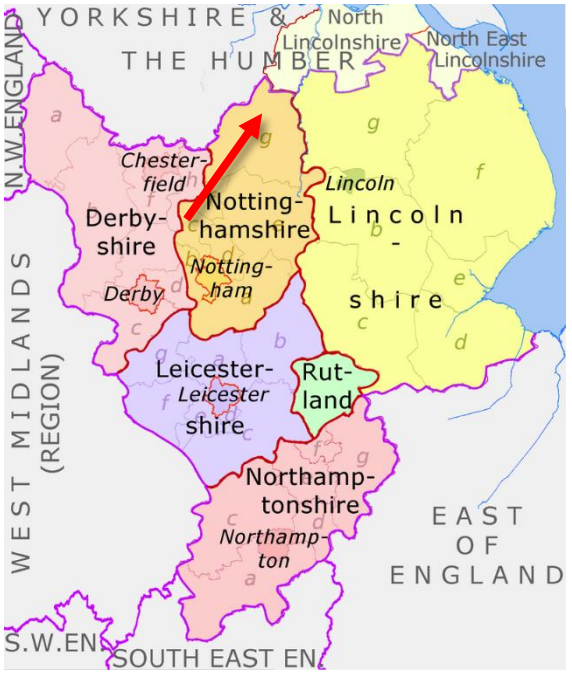
- ST6
- Dr Abhijit Dixit talk
- The Genomic Revolution is coming!
- OOP in Clinical Genetics department
- MSc in Genomic Medicine

My career path…

- CCT and move to East Midlands
- Consultant Paediatrician
- In a Kings Mill Hospital (a DGH)



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NU MBER

Joint clinic

- Took time to organise
- Cases carefully selected by AD
- Pre-clinic by me
- Pre-clinic discussion with AD
- Clinic may or may not be alongside AD
- Improving waiting times
- Challenging me

Why am I interested in Genomics?

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- 1 – I like genetics
- 2 – I like medicine
- 3 – Genomics is a rapidly evolving (and interesting) specialty
- 4 – After a few years as a consultant, you need an interesting new challenge

What I did to improve my knowledge/skills

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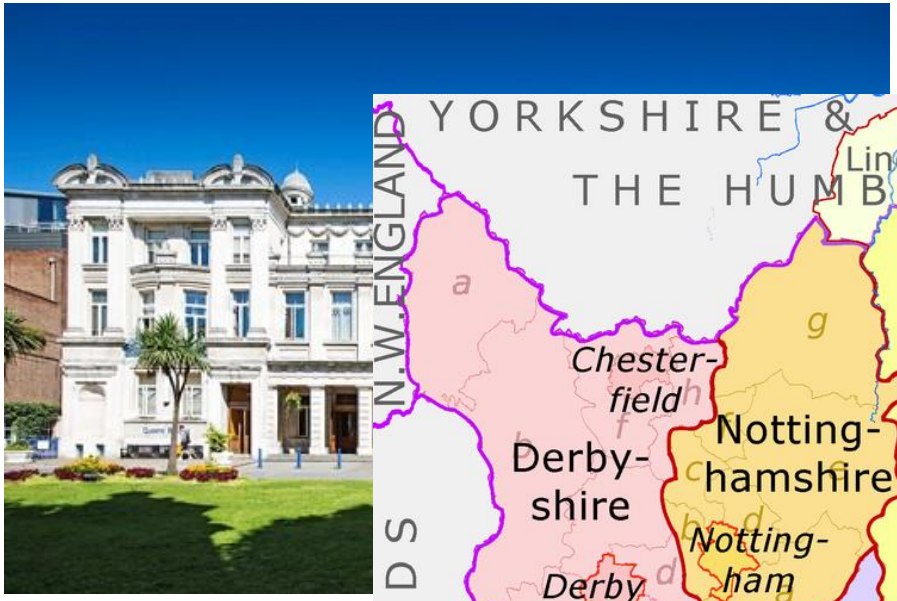
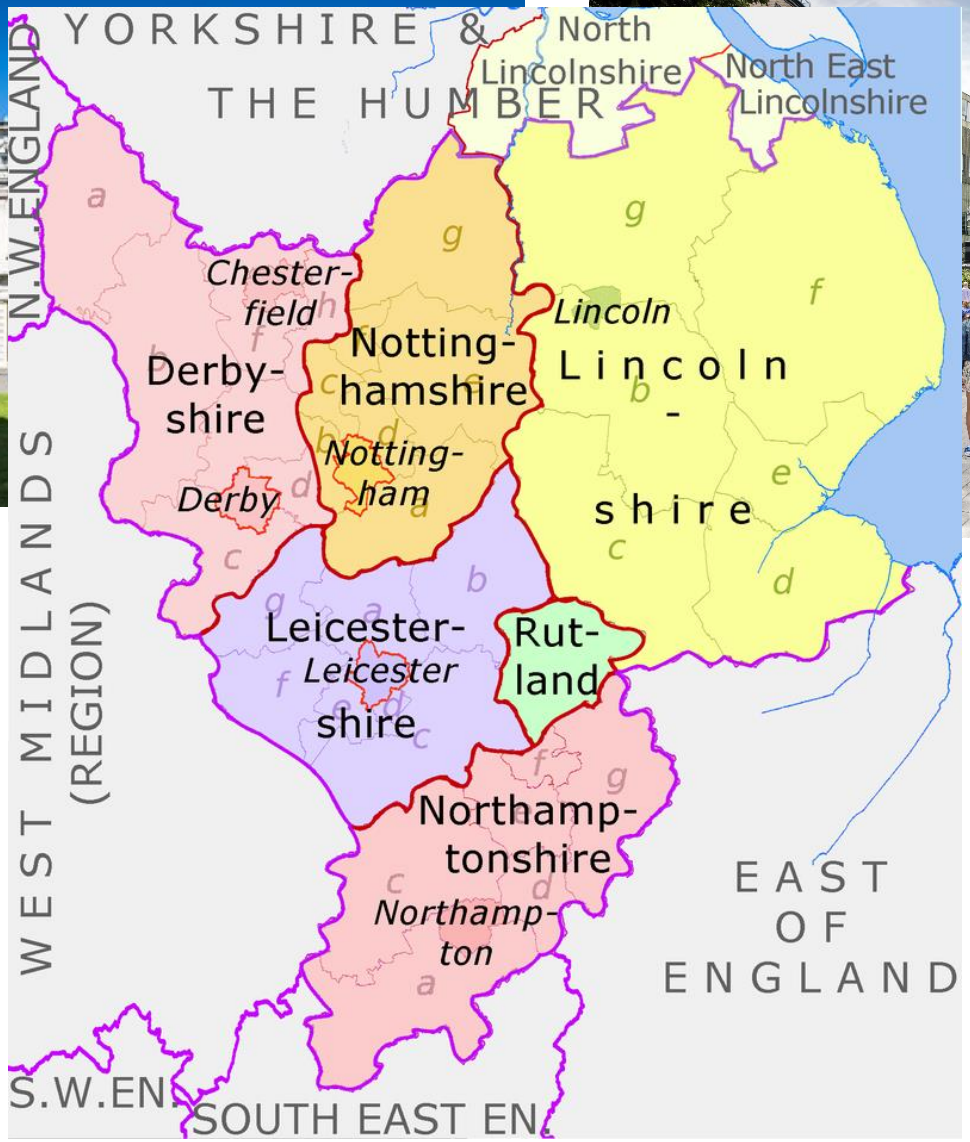
- OOP in clinical genetics (ST7)
  - Included OOH on call in NICU
- MSc Genomic Medicine

Dr Abhijit Dixit (my mentor)





Distance learning!

What did I study?

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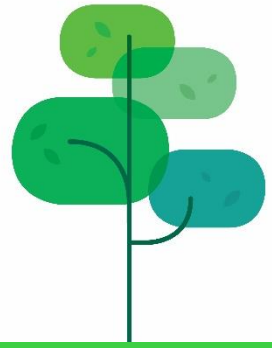
- 2 years – distance (online) learning (funded)

1. Introducing Genomics
2. Pharmacogenomics
3. Inherited diseases
4. Bioinformatics
5. Infectious diseases
6. Research skills
7. Omics
8. Cancer genomics



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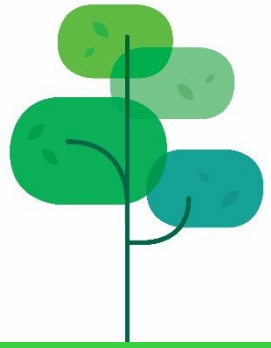
How do I ‘advise’ on Genomics



Teach medical students

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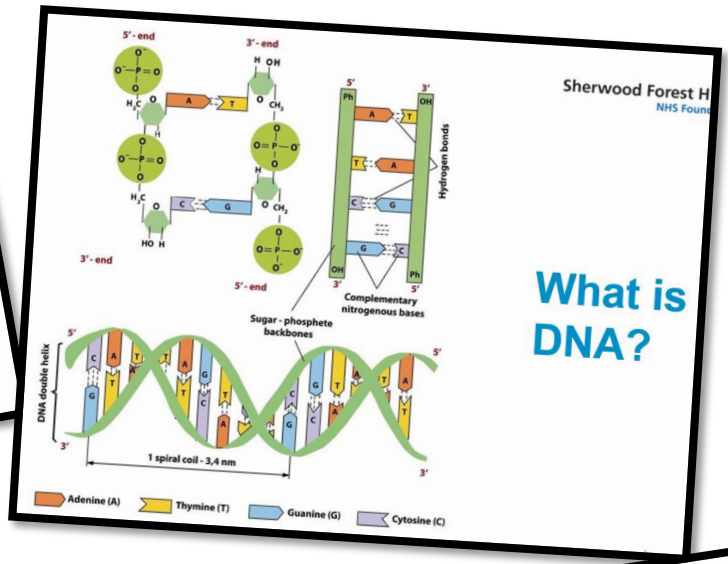
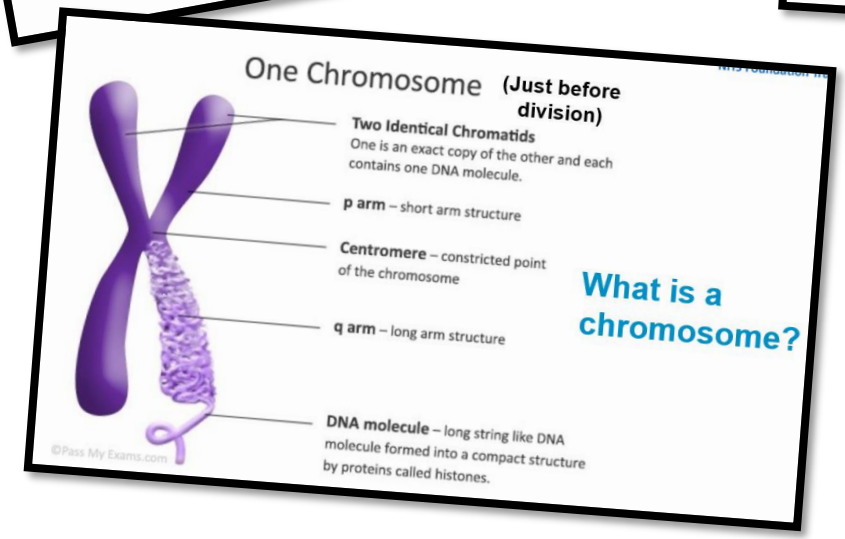
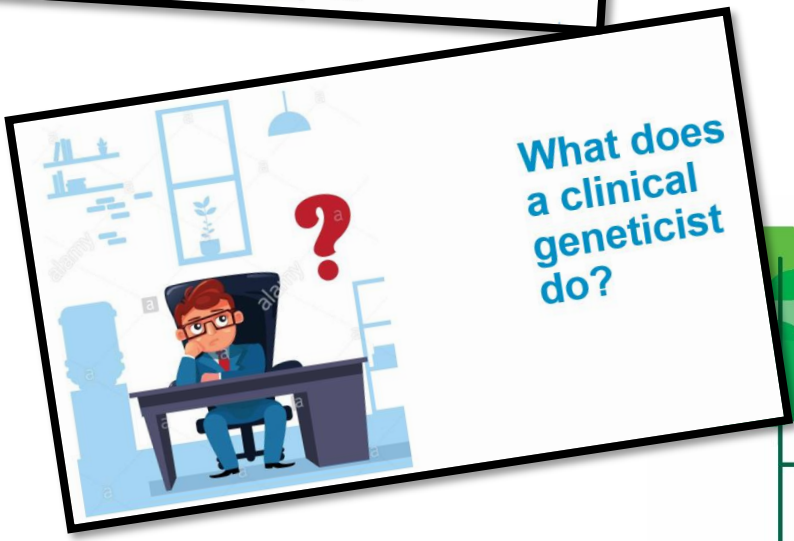
- What is genetics
- What does a clinical geneticist do
- Inheritance patterns
- What is genomics
- Why you should be interested
- What are the basics you need to know
- What tests can we order
- Difficult ethical issues







Teach Colleagues

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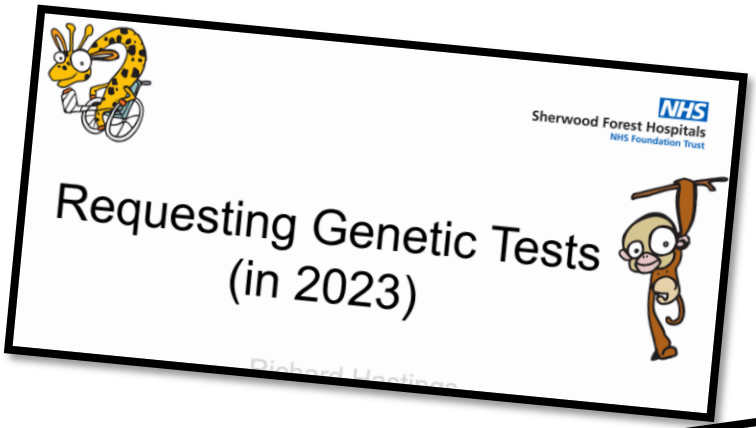
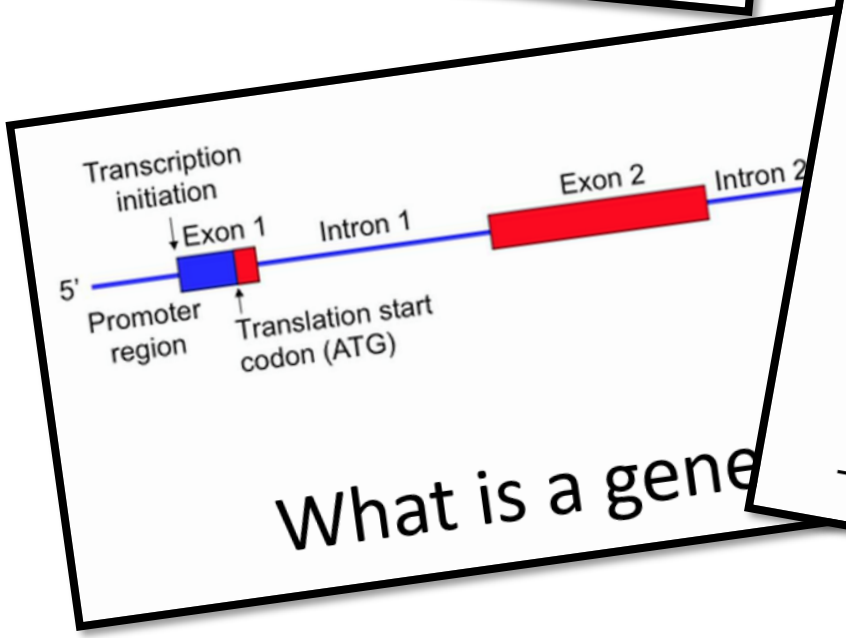


- Basic biology lesson – quick whizz through
- Explain types of test
- Explain how to choose the right test
- Explain how to request a test
- Explain consent for testing
- Discuss results of test
- Useful resources



Mainstreaming

IMPORTANT

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- **You** need to:
  - Consider which type of test is appropriate...
  - ...And decide which test to request
  - Know how to request the test
  - Be able to consent appropriately
  - Understand the report

How to guides…

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Requesting a genomic test (non-WGS)

24 March 2022 10:13

Look at this webpage for lots of inform
https://www.eastgenomics.nhs.uk/for-

This guide is a summary of the informa
If any of the links in this document do r
It would be helpful if you could let Rich

Overview (details of each s

1. Look in test directory to see if a g
2. Review the testing criteria within
3. Ensure the test is a non-WGS par
4. Fill out the referral form.
5. Fill out the record of discussion w
6. Send the sample and referral for
7. File the record of discussion in th
8. Wait for results.

Requesting a genomic test (WGS)

24 March 2022 14:17

Look at this webpage for lots of information:
https://www.eastgenomics.nhs.uk/for-healthcare-professionals/genomic-tests/rare-and-inherited-diseases/genome-sequencing/

This guide is a summary of the information that is obtained at the webpage above.
If any of the links in this document do not work then please contact Richard.

Overview (details of each step below)

1. Look in test directory to see if a genomic test for your indication is available.
2. Review the testing criteria within the directory.
3. Ensure the test is a WGS panel (there is an alternative guide for non-WGS testing).
4. Do consent training if not already completed.
5. Fill out the Order form - rare disease WGS
6. Fill out the record of discussion with each member of the family who is submitting a sample.
7. Fill out the YP assent form if appropriate.
8. Send the sample to the lab.
9. Email the order form and record of discussion forms as detailed below.
10. File the record of discussion in the medical notes.
11. Wait for results.

Familiar with GTD

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R441 Unexplained death in infancy and sudden unexplained death in childhood

Testing Criteria

1. Sudden death in child less than 18 years that remains unexplained after the standard investigation protocols including post mortem AND
2. DNA available from proband and both biological parents for trio WGS analysis OR
3. DNA available from proband and one biological parent only

Where in Pathway

After standard SIDS/SUDC protocol including post mortem have been completed. Following specialist MDT discussion of patients that may be suitable for WGS (including eg. pathology, designated doctor for child deaths, clinical genetics as appropriate). Consent will need to be obtained from family.

Requesting Specialties

- Clinical Genetics
- Paediatrics

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Dermatology
- Neonatology

Promote use of R14

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Part I. Acutely unwell children

R14 Acutely unwell children with a likely monogenic disorder

Testing Criteria

Acutely unwell children with a likely monogenic disorder

For more detailed guidance for R14 outlined in "Guidance Document – Rapid Genome Sequencing for NICU-PICU Referrals" please contact your local Genomic Laboratory Hub.

Where clinical features and/or non genetic investigations are pathognomonic of a single gene disorder, no test is available and molecular testing is required urgently to guide management, R14 may be requested.

Promote Consent Training

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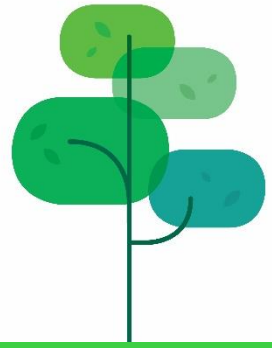
- Chromosomal microarray for low birth weight
- (due to placental insufficiency)
- Incidental finding of 2p16.3 deletion
  - Associated with ID, SL delay, ASD and seizures



Act as an interpreter

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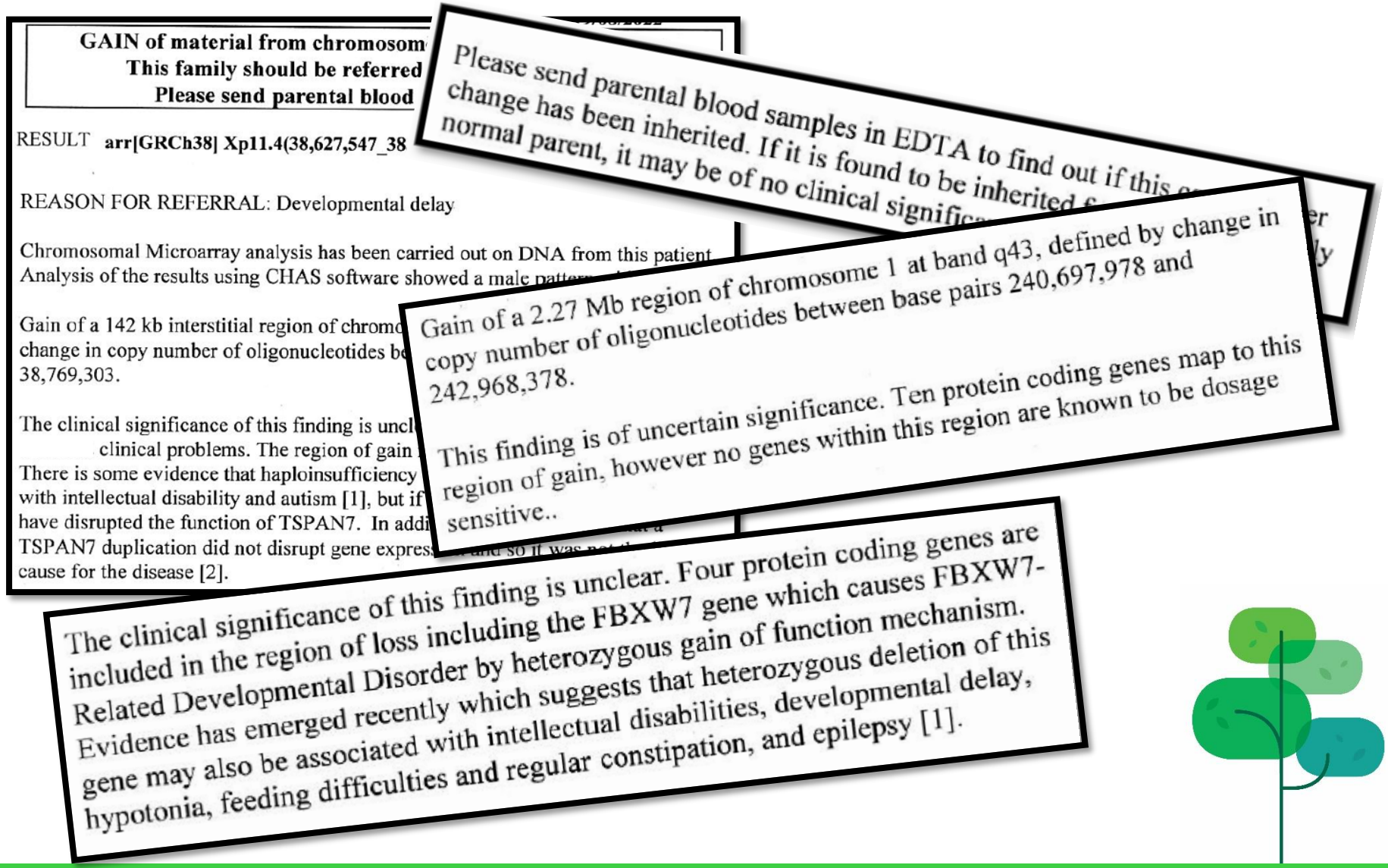

GAIN of material from chromosom
This family should be referred
Please send parental blood

RESULT arr[GRCh38] Xp11.4(38,627,547_38

REASON FOR REFERRAL: Developmental delay

Chromosomal Microarray analysis has been carried out on DNA from this patient
Analysis of the results using CHAS software showed a male patter

Gain of a 142 kb interstitial region of chromo
change in copy number of oligonucleotides be
38,769,303.

The clinical significance of this finding is uncl
clinical problems. The region of gain
There is some evidence that haploinsufficiency
with intellectual disability and autism [1], but if
have disrupted the function of TSPAN7. In addi
TSPAN7 duplication did not disrupt gene expres
cause for the disease [2].

Please send parental blood samples in EDTA to find out if this
change has been inherited. If it is found to be inherited
normal parent, it may be of no clinical signific

Gain of a 2.27 Mb region of chromosome 1 at band q43, defined by change in copy number of oligonucleotides between base pairs 240,697,978 and 242,968,378.

This finding is of uncertain significance. Ten protein coding genes map to this region of gain, however no genes within this region are known to be dosage sensitive..

The clinical significance of this finding is unclear. Four protein coding genes are included in the region of loss including the FBXW7 gene which causes FBXW7-Related Developmental Disorder by heterozygous gain of function mechanism. Evidence has emerged recently which suggests that heterozygous deletion of this gene may also be associated with intellectual disabilities, developmental delay, hypotonia, feeding difficulties and regular constipation, and epilepsy [1].

(Take home message)

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Create network with local Clinical Genetics Service

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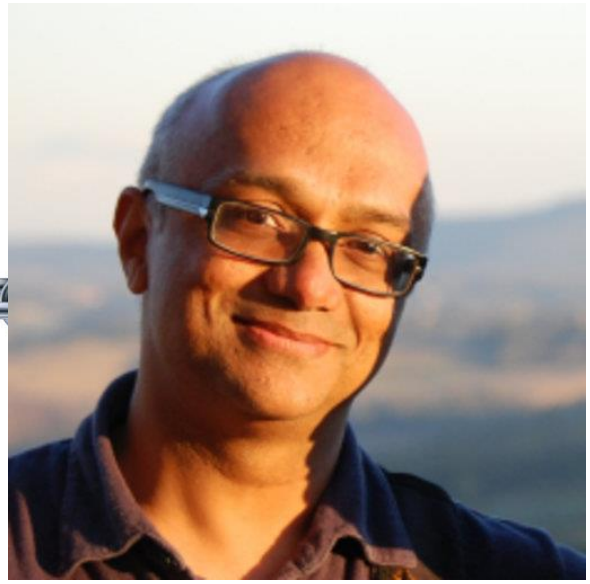

Paediatrics

Clinical Genetics

Act as a liaison

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NHS Foundation Trust