

THE CHANGING LANDSCAPE OF PAEDIATRIC GENOMICS
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NHS
 Great Ormond Street Hospital for Children

THE CHANGING LANDSCAPE OF PAEDIATRIC GENOMICS

- Importance of a genetic diagnosis for children
- Evolution of genomic analysis
- Paediatric genomic mainstreaming
- Cell free DNA analysis
- Gene therapy
- Personalised cancer pathways
- The Generation study
- Resources for genomics education

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IMPORTANCE OF A GENETIC DIAGNOSIS IN CHILDREN

Genomic medicine has the potential to save costs and improve quality of care by targeting treatment, maximising benefit and reducing side effects. For patients with rare diseases, it can shorten their 'diagnostic odyssey' helping to identify therapeutic options faster and improve outcomes.
 – Sally Davies CMO 2016

I want another child but without any answers it seems like such a gamble.
 SWAN UK member

The scale of rare diseases
 In the UK alone that equates to approximately 3.3 million people.
 1 in 17 people will suffer from a rare disease at some point in their lives.

Only a quarter of rare diseases have had their molecular basis defined, meaning many risk being undiagnosed and therefore untreated.

THERE ARE AT LEAST **6,000** RARE DISEASES
 Many rare diseases (approximately 80%) are of genetic origin.

30% of rare diseases severely affect children.

Genomics in Paediatrics

RARE DISEASE **GENETIC ALLIANCE** **Uniqe**

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EVOLUTION OF GENOMIC ANALYSIS

Chromosome DNA

Likely a heterozygous variant

The 100,000 Genomes Project

NHS National Genomic Test Directory Testing Criteria for Rare and Inherited Disease

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NATIONAL TEST DIRECTORY

TESTS PAEDIATRICIANS CAN REQUEST:

- R222 NF1
- R28 Congenital malformation/dysmorphism - microarray
- R29 Intellectual disability
- R377 Intellectual disability - microarray
- R47/R48 Angelman/Prader Willi syndrome
- R49 Beckwith-Wiedemann syndrome
- R53 Fragile X
- R89 Hypotonic infant
- R70 SMA type 1
- R147 Growth failure in early childhood
- R149 Severe early-onset obesity
- R67 Monogenic hearing loss
- R24 Achondroplasia
- R73 Duchenne Muscular Dystrophy
- R88 Severe microcephaly
- R222 NF1
- R137 Congenital heart disease - microarray
- R135 Paediatric/syndromic cardiomyopathy

TESTS THAT CAN BE REQUESTED WITH CLINGEN APPROVAL:

- R14 - Rapid Exome Sequencing (Exeter)
- R27 - Congenital malformation and dysmorphism super panel

Legend:

- Array (copy number variants)
- MLPA (single/partial gene deletion/dup)
- STR (short tandem repeats)
- Other (methylation | linkage | DLX)
- Single gene sequencing
- Small panel or WES
- WGS

<https://www.england.nhs.uk/publication/national-genomic-test-directories>
<https://nhs-gms-panelapp.genomicsengland.co.uk/>

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PAEDIATRIC GENOMIC MAINSTREAMING

PAEDIATRICIAN

LABORATORY SCIENTISTS

GENETIC COUNSELLOR

CLINICAL GENETICIST

MDT

EVOLVING ROLE OF THE PAEDIATRICIAN

- Facilitating genomic testing
- Seeking informed consent
- Understanding key aspects of genomic reports
- Managing a genomic diagnosis
- Working with genomic specialists

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CELL FREE DNA ANALYSIS

NON-INVASIVE PRENATAL DIAGNOSIS (NIPD)

PRECISION MEDICINE IN ONCOLOGY

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GENE THERAPY

LEBER CONGENITAL AMAUROSIS (RPE65)

LUXTERNA

SPINAL MUSCULAR ATROPHY (SMN1)

ZOLGENSMA
[Nusinersen (Spinraza)]
[Risdiplam (Evrysdi)]

METACHROMATIC LEUKODYSTROPHY (ARSA)

LIBMELDY

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PAEDIATRIC CANCER

Whole genome sequencing for children

An information guide for parents, carers and families.

The purpose of this guide is to give information about a whole genome sequencing (WGS) test which is being offered to your child as part of diagnosis for cancer, suspected cancer and non-cancerous (benign) tumours.

Information in this guide should be used to supplement professional advice specific to your circumstances. If you have any questions, it is important to ask your child's medical team.

Why consider a WGS test?

The results may help us to understand:


- why your child has developed their tumour or cancer
- what type of tumour or cancer your child has and check that they are on the correct treatment plan
- how WGS may be used in treatment planning for the future
- whether your child has a gene which might increase their risk of developing other cancers in the future
- whether other family members may have a greater risk of developing cancer

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GENERATION STUDY

Newborn Genomes Programme

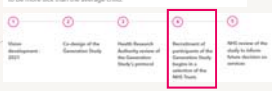
Defining the NHS embedded Generation Study



We are using whole genome sequencing to look for changes in genes linked to more than 200 rare conditions. The conditions we test for:

- Usually appear in the first few years of life
- Can be improved if caught early
- Can be treated through the NHS in England

These conditions have different types of symptoms, but can all cause someone to be more sick than the average child.



Collecting the sample

Getting results

Conditions we test for

Benefits and risks

The test includes:

- Well known conditions** like Cystic Fibrosis.
- Rarer known conditions** like Smith Syndrome and Diamond Blackfan Anaemia.
- Normal conditions** that affect growth and development, like genetic Hypothyroidism and Growth Hormone Deficiency.
- Blood conditions** that affect red blood cells like Sickle Cell Disease, or blood clotting like Haemophilia.
- Immune system conditions** that increase someone's risk of life-threatening infections, like Severe Combined Immune Deficiency (SCID).
- Metabolic conditions** that affect the body's ability to process certain substances and remove toxins, like Phenylketonuria.

The test does not include:

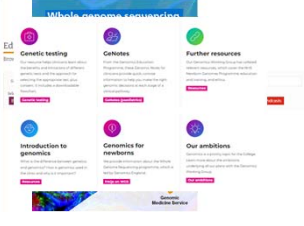

- Abilities** such as food allergies, hay fever, eczema, or autism.
- Neurodiversity** like Autism, ADHD, ADD, and Dyslexia.

Visit: ge-newborns@genomicsengland.co.uk

Genomic Resources

USEFUL RESOURCES:



- > Your local Genomic Laboratory Hub: <https://www.norththamesgfh.nhs.uk/healthcare-professionals/ordering-whole-genome-sequencing/>
- > NHSE Genomics Education Programme (GEP): <https://www.genomicseducation.hee.nhs.uk/education/>
- > RCPCH Genomics landing page: <https://www.rcpch.ac.uk/key-topics/genomics>


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- > Gene panels information: <https://panelapp.genomicsengland.co.uk/>

TIER TWO



Knowledge Hub
Extend your learning with this encyclopedia of resources, designed to support your understanding of genomics in medicine.

Conditions
Core concepts
Technologies
Genomics in action

22q11.2 deletion syndrome
22q11.2 deletion syndrome (also known as DiGeorge syndrome and velocardiofacial syndrome) is a highly variable multiplex genetic condition associated with learning difficulties, congenital heart defects, facial abnormalities, immunodeficiency and hypocalcaemia.

Fanconi anaemia
Fanconi anaemia is a heritable bone marrow failure syndrome caused by problems with the body's chromosomal repair systems. Patients have a variety of diagnostic features and a progressive reduction in the production of normal blood cells in the bone marrow.

Autosomal dominant inheritance **Genomic imprinting**

Microarray (array CGH)
Microarray is a high-resolution genome-wide screen for copy number variants.

Whole genome sequencing
Whole genome sequencing (WGS) involves the sequencing of all 2.9 billion base pairs of the human genome, including both coding and non-coding regions.

How to complete a test order form for WGS
Test order forms are request forms that contain demographic and phenotypic information about the patient and specify which genomic test is required. There is a separate form for whole genome sequencing and this resource will guide you through how to fill it in.

@genomicsedu #GenomicsConversation

Genomics Education Programme NHS England



THANK YOU & QUESTIONS
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NHS Great Ormond Street Hospital for Children NHS Foundation Trust
