NHS
University Hospitals of Liverpool Group

NEWSLETTER

Liverpool Centre for Genomic Medicine (LCGM)

FEBRUARY 2025

In this edition…

Welcome to this issue of the Genomics Newsletter

Welcome to the fourth edition of the Liverpool Centre for Genomic Medicine (LCGM) newsletter, our first newsletter of 2025. Our newsletter aims to provide you with information about our Genomics team, Genomics service developments, interesting patient stories, condition specific information, current research in Genomics and exciting Genomics information in the news.

In this edition we aim to tell you about:

- The role of a Genetics registrar (doctor)
- The career pathway to become a Genetics registrar.
- A real-life patient story focussing on a patient with Wiedemann-Steiner syndrome.
- Information about Wiedemann-Steiner syndrome as a condition
- Current research updates
- Genomic charity events
- Exciting new Genomics stories in the news; Genomics England Generation study, aka Newborn Screening programme in England

Patient Story – Andrew's Story (Widemann-Steiner Syndrome)

Andrew's Story (from his mother):

We were driven by a series of medical issues within Andrew's early months and years. He had 2 inguinal hernias; a heart murmur which turned out to be a PDA; the discovery he had a horseshoe kidney; excessive hairiness; hip socket problem; turned eye. Alongside these health issues were numerous missed developmental milestones. It was our insistence that this collection must be something connected that triggered a GP referral to the paediatrician and subsequently the geneticist even though the GP was doubtful. We were excited to get the referral to the geneticist even though we had no understanding of what would happen, but we hoped they would complete the jigsaw by confirming our concerns and lead to a diagnosis so that we could then access support. Initially the collection of symptoms gave no clear diagnosis of a known condition, (although Noonan syndrome was considered, but eventually ruled out).

We visited for many years through the 2000s and 2010s without conclusion while Andrew's list of issues of health, school learning and life issues became ever longer and more troubling for him and us. Parallel to the genetics visits, we were unsuccessful in obtaining any educational special needs support for Andrew. Despite clear (to us) indications of autism, ADHD and general educational difficulties he remained unsupported in mainstream schooling. Despite positive, hopeful comments from teachers he left school with no qualifications.

Since Andrew's WSS diagnosis he has recently had a number of tests which confirm he has a learning disability which at least proved us right but leaves many questions for us about the capability of educational professionals when faced with cases such as Andrew's when presenting without a formal diagnosis.
We had a mixed range of responses from the paediatricians we saw. One of them was very dismissive and responded to our list of latest concerns with "anything else? there are other people waiting you know" which was devastating to us at the time, but we felt we had to persevere.

We were fortunate to end up in the hands of a geneticist who could only agree that there was something and seemed determined to come up with something. When WSS was first genetically isolated he was straight on it and in 2013 we sent off blood samples but disappointingly for the geneticist and us nothing was found, though he said if you want my opinion WSS is most likely. Without the diagnosis we couldn't access any help for Andrew. Even after Andrew was discharged from paediatrics due to his age, we kept in touch with genetics. In 2023 as part of the 100k genome project and with Siva's conviction that it was WSS Andrew's blood was retested but again showed no positive result for WSS. In 2024 we got news that a retest of the data in the genomic research library was finally positive for WSS.

It has been a long and frustrating journey trying to get a diagnosis for Andrew and has taken a huge amount of determination and perseverance, but it was a huge relief to finally get a diagnosis. We still face many challenges but are hopeful that we will now be able to receive some support.

Widemann-Steiner Syndrome

What is Widemann-Steiner Syndrome?

Wiedemann-Steiner syndrome (WSS) is a rare genetic condition. WSS is named after the two doctors who first described children with features of this syndrome, firstly Dr Hans-Rudolf Wiedemann in Germany in 1989 and then subsequently Dr Carlos Steiner in Brazil in 2000 (Wiedemann 1989, Steiner 2000). The word 'syndrome' comes from a Greek word meaning 'to run together' and is simply used to describe the combination of features which can be seen together in people with a particular condition.

What are the features of WSS?

The main features of WSS are:

- **developmental delay**
- **intellectual disability**
- **short stature**
- **behavioural difficulties**
- **increased body hair (hypertrichosis)**

What is the cause of WSS?

WSS is caused by genetic changes in the ***KMT2A* gene.**

Is there any treatment for WSS?

There is currently **no cure for WSS** since the effects of the genetic change take place during each baby's formation and development. However, knowing this diagnosis means that appropriate monitoring and treatment can be put in place as well as educational support to enable each child with WSS to fulfil their potential. Research is ongoing and, in the future, there may be specific genetic treatments for some of the features of WSS.

Further information:

Rare Chromosome Disorders Support Group *https://rarechromo.org/*

National Widemann-Steiner Syndrome Support Group *https://nwsswarriors.org.uk*

WSS Foundation
Wiedemann-Steiner Syndrome Foundation

CAREERS

Specialist Trainee Registrar – Clinical Genetics

In this issue we highlight the role of a Specialist Trainee Registrar within Clinical Genetics and hear from Dr Rhodri Smith about his career path and experiences in this role.

A Specialty Registrar (StR) is the working title held by doctors in their ST training programme.

Rhodri is an ST3 in Clinical Genetics in Liverpool with his previous training in GIM and rheumatology all within adult medicine and the Mersey region. Prior to medicine he gained a BSc in Genetics at University of Cardiff, before completing an MSc in Genetic Epidemiology at the University of Sheffield and then a PhD in the Genetics of Psoriasis within the ARC Epidemiology Unit at the University of Manchester, during which time he published several papers and presented his work at international meetings. Following his PhD, Rhodri returned to Cardiff to take a postdoctoral role researching the genetics of schizophrenia before deciding to pursue a career in medicine, graduating from the University of Liverpool, in 2016.

I have not taken the most typical route into clinical genetics, but I am glad that I did. I have always held a keen interest in genetics and went on to do a degree in the subject from school before going on to do a masters, PhD, and post doc in various aspects of human genetics.

It was only then that I decided that a career in medicine was for me and so I undertook a degree in medicine at Liverpool University.

After I had completed my foundation training, I took a year to evaluate things (F3 year) before I started my ACF in rheumatology, aspiring to be a clinical academic in rheumatology which would complement my previous career as a scientist looking at genetics of autoimmune disease. I was enrolled onto run through training in rheumatology and general internal medicine and we were the first year of the Internal Medicine Training programme too, and I completed my MRCP membership exams during this time as well.

CAREERS

Specialist Trainee Registrar – Clinical Genetics - *Continued*

A massive thank you to Dr Rhodri Smith, ST3 in Clinical Genetics at LCGM, for sharing information about his role.

I was always aware of clinical genetics from an early stage but for some reason that I will never really understand, had not really considered it as a career until later in my ACF training at the start of IMT3.

However, as I investigated the role of a clinical geneticist more, I became increasingly convinced this was a career for me, and so I contacted my local genetics service who invited me to join them for some multi-disciplinary meetings and sit in on some clinics too, which I was able to do sporadically as my rota allowed.
Having been inspired by what I saw, I decided that I would apply for Clinical Genetics training.

Having a PhD and an academic publication record in genetics I felt that I had a strong application but was not successful on my first application attempt, following interview.

After a period of reflection, I realised that I clearly did not have the experience in clinical genetics to give myself a chance in an interview for a discipline that is increasingly competitive.

Feeling that I needed more on the job experience if I was to give myself a chance of success, I resigned my training position as an ST4 in rheumatology and GIM registrar, to take up a fixed term fellowship in clinical genetics where I had my own clinic and undertook a similar role to a junior registrar.

Resigning my training post was a big decision, and one I presided over for a considerable length of time, not only for my own career aspirations, but also because I was no spring chicken and had a young family with three children under 5 to think of too. Nonetheless with support of my family and colleagues I took this leap of faith, and with the experience gained from my fellowship, I was successful with my second application the following year. I am now coming to the end of my first year of training (ST3) and have absolutely no regrets regarding the decisions I made and would certainly encourage anyone who is considering clinical genetics as a career to get in contact with their local department to explore things further.

RESEARCH STUDIES

In this edition, we have summarised information about two on-going research studies. We have included details about the aim of these research studies, who can take part and what taking part in the research study would involve.

RAS-MAPK

We want to know more about how the gene changes that are responsible for CFC, NS and CS result in the problems that people with these conditions may have. People with each of these conditions can have similar problems to one another, and this is because all of the disorders involve changes in the way that a particular pathway, called the RAS-MAPK pathway, works in the cells of the body. Affected people may have a wide variety of problems including

Aim of the study	Who can take part?	What does it involve?
This study aims to identify what particular features individuals with these conditions have, so that they can be most effectively managed.	Patients with germline disorders of the RAS-MAPK pathway including: • Noonan syndrome • Costello syndrome • Patients with features of cardio-facio-cutaneous syndrome	Completion of consent form and giving permission for research team to look at medical records.

RESEARCH STUDIES – *Continued*

AIP

Most tumours that start in the pituitary gland are adenomas which are non-cancerous (benign). Some pituitary tumours make extra hormones that can cause symptoms. They are sometimes called neuroendocrine tumours. Very rarely, several members of the same family have a pituitary gland tumour. We know from research that there can be a gene that is abnormal in some of these families. Researchers want to study this and other genes to understand more about how these tumours develop. In this study, they will take blood samples from people who have a pituitary gland tumour, and from other family members.

Aim of the study	Who can take part?	What does it involve?
Identify genes that play a part in the development of pituitary gland tumours. Participation in the study is voluntary and patient can withdraw from study at any time.	Individuals of any age with a diagnosis of an endocrine tumour (e.g. pituitary tumour/ paraganglioma)	Consent Form, Completion of questionnaire and small blood sample (if no stored DNA is available)

LATEST NEWS

Generation Study

Genetic study to test babies for 200 conditions

A hospital has begun testing hundreds of babies for genetic conditions as part of a "world-leading" study into rare illnesses.

Midwife Georgie, who is expecting her first baby in April, was the first person in Leeds to be recruited for the genetic study and took the first sample from a baby.

The study will test babies for more than 200 rare genetic conditions and could enable people to benefit from earlier diagnosis and treatments.

Georgie said having the test would "hopefully give me peace of mind when my baby is born and help future generations too".

BBC News 11/01/2025

What is the Generation Study?

The Generation Study is a research study that will **sequence the genomes of 100,000 newborn** babies. It will use a technique known as **whole genome sequencing (WGS) to analyse the genetic codes of newborns,** to look for a defined set of treatable rare genetic conditions. The study is being carried out by Genomics England in partnership with the NHS.

What does the Generation study aim to do?

The study has three key aims:

1. **Identify rare conditions in babies earlier.**
2. **Enable research.**
3. **Explore the risks and benefits of storing an individual's genome over their lifetime.**

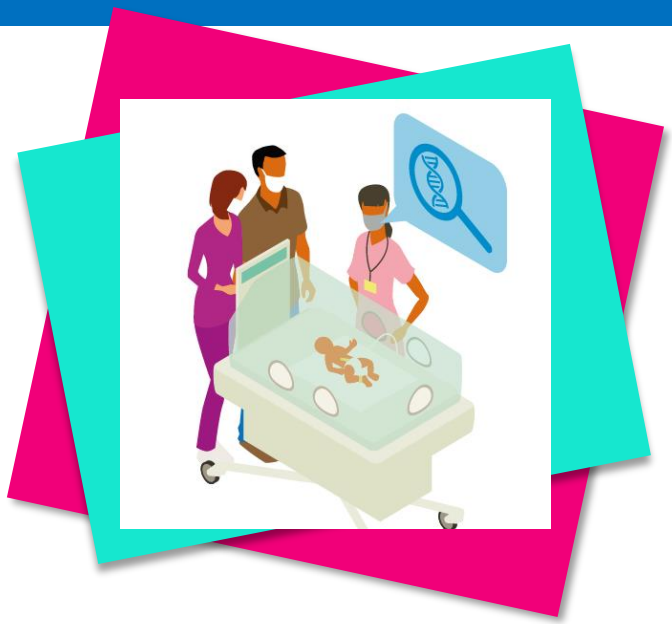
When did the Generation Study begin?

The Generation Study **began in 2024**, and the study is currently scheduled **to run until March 2025.**

You may wish to look at
https://www.bbc.co.uk/news/articles/cnvqyeyqn4do for the full article.

LATEST NEWS

Generation Study



Where will the babies' genome be stored?

For those that do consent, any data collected is **securely kept in the National Genomic Research Library**, where it can be accessed by approved researchers. This data is de-identified, meaning babies' identities will not be visible to researchers.

How is this different to NHS newborn screening?

The NHS already offers newborn blood spot screening (the 'heel prick' test) to all babies when they're about 5 days old. This already well-researched NHS service tests for 9 rare, treatable conditions.

Parents will **still be offered the heel prick test for their baby**, which the NHS recommends.

Where will the babies' genome be stored?

For those that do consent, any data collected is **securely kept in the National Genomic Research Library**, where it can be accessed by approved researchers. This data is de-identified, meaning babies' identities will not be visible to researchers.

What if parents change their minds?

It is completely okay if parents change their mind after sequencing. Parents **can withdraw from their child from the study at any point** before their child turns 16, and their data will be removed from the National Genomic Research Library. When the child is around 16 years old, they will be asked to give their own consent for the study.

What conditions will be screened for?

The study uses a single sample to look for changes in genes linked to about 200 rare conditions. The test includes:

- **Well-known conditions** like Cystic Fibrosis.
- **Lesser-known conditions** like Barth Syndrome and Diamond Blackfan Anaemia.
- **Hormonal 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.

You may wish to look at https://www.generationstudy.co.uk/ for further information.

EVENTS

In this edition, we have summarised some events upcoming in the UK in the table below. These events are either in person or on online.

EVENT	WHEN	WHERE
How NF2 Affects me – The Exhibition	24th February 2025	Carrington Street, Nottingham

For more information, click the link: rarediseaseday.org/event/how-nf2-affects-me-the-exhibition/

Rare Disease Day 2025	28th February 2025	Everywhere!

For more information, click the link: geneticalliance.org.uk/event/rare-disease-day-2025/

Genetics Matters 2025 – A Rare Disease Day event	2nd March 2025	Discovery Museum, Newcastle Upon Tyne

For more information, click the link: rarediseaseday.org/?post_type=event&p=101257

Undiagnosed Children's Day 2025	25th April 2025	Everywhere!

For more information, click the link: geneticalliance.org.uk/support-and-information/swan-uk-syndromes-without-a-name/undiagnosed-childrens-day/

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SCAN ME

https://www.liverpoolwomens.nhs.uk/our-services/liverpool-centre-for-genomic-medicine-lcgm/

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