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NEWSLETTER

Liverpool Center for Genomic Medicine (LCGM)

OCTOBER 2024

In this edition...

Welcome to this issue of the Genomics Newsletter

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

In this edition we aim to tell you about:

- The role of a Genomic Associate
- A real-life patient story focusing on a family with Fragile X syndrome
- Information about Fragile X syndrome as a condition
- Current research updates
- Genomic charity events
- Exciting new Genomics stories in the news; Vaccine for Lynch syndrome.

Patient Story – James (55 years) and Neil (49 years) have Fragile X syndrome. Siobhan is the sister of James and Neil and their main carer.

1. Siobhan, can you share some of your experience about individuals with Fragile X syndrome?

James and Neil are identical in almost everything they do i.e. they eat a lot when they get upset; it's a big deal when they have tantrums because they want their own way just like a child, but all Fragile X affected adults are different.

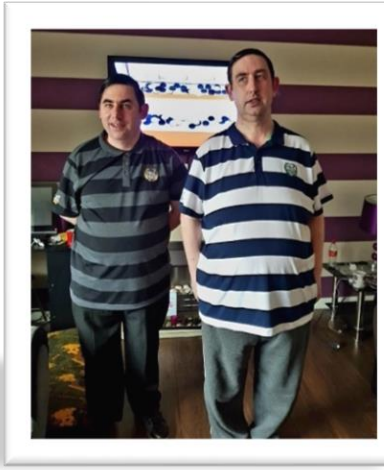
2. Siobhan, you are a carrier of Fragile X. How did you feel once the diagnosis was made? Can you share some of your experience about individuals with Fragile X syndrome? Do you have any advice for others with Fragile X syndrome?

I found out that I am a carrier of Fragile X when I was 8 years old. I didn't understand it fully until I was older, I felt scared not knowing what to expect when having children but one of the worst parts about being a carrier is, you can pass it down to your child /children. I had passed it to my youngest daughter, who had passed it to her daughter.

Fragile X carriers struggle in school and there is not enough help out there for children in mainstream schools. Not enough people are aware of Fragile X carriers; something needs to change for the better to make people aware.

3. Do you have any other thoughts that you would like to share?

Fragile X is biggest cause of autism, I think. If that's the case when people get diagnosed with autism, they should get genetic testing for Fragile X, and I think parents don't get enough help.



Fragile X

What is Fragile X syndrome?

Fragile X syndrome is the **most common identifiable cause of inherited intellectual disability and autism spectrum conditions**. It arises from changes on the X chromosome in the FMR1 gene that normally makes a protein necessary for brain development. Boys are usually more severely affected than girls as they have only one X chromosome. Girls have a second X chromosome, which can compensate for problems with the altered one. However, some girls can be quite severely affected while some boys are only mildly affected.

What causes Fragile X?

The cause is an abnormal DNA expansion just above the tip of the **X chromosome's** long arm. The expansion consists of small repeats of a DNA sequence, which are unstable and can get larger across generations. This means that a child can be more affected than the parent from which they inherited the changed X chromosome.

What is the inheritance pattern for Fragile X?

Fragile X syndrome is inherited in an **X-linked pattern**. Some people are carriers of the condition meaning that they carry an affected X chromosome but do not experience adverse consequences. However, the genetics is more complicated as some people only have a small change, called a 'premutation', in the gene. They too can experience developmental and psychological challenges, but these are usually less marked than when there is a 'full expansion' of the gene. A premutation makes the gene unstable and at risk of developing into a full expansion when passed onto the next generation. If you like to know more about the inheritance pattern, please look at the additional resources listed on the next page.

FRAGILE X SYNDROME - *Continued...*

What is the treatment for Fragile X?

There is **no cure** for Fragile X. Psychological and educational support for children and their families are vital to help them reach their best potential and to maximise their quality of life.

For children with delayed speech and language development, specialised help from a speech and language therapist is important. Sensory issues and coordination difficulties may be helped by an occupational therapist. Hyperactivity and impulsivity may be alleviated by behavioural therapy and in some cases medication. Behavioural therapy can help children who have problems developing relationships, need assistance in developing social skills and need help coping with stressful situations.

Some children can be educated in mainstream schools, with support. However, some with more severe intellectual disability, or complicating factors like ASD or ADHD may need special schooling.

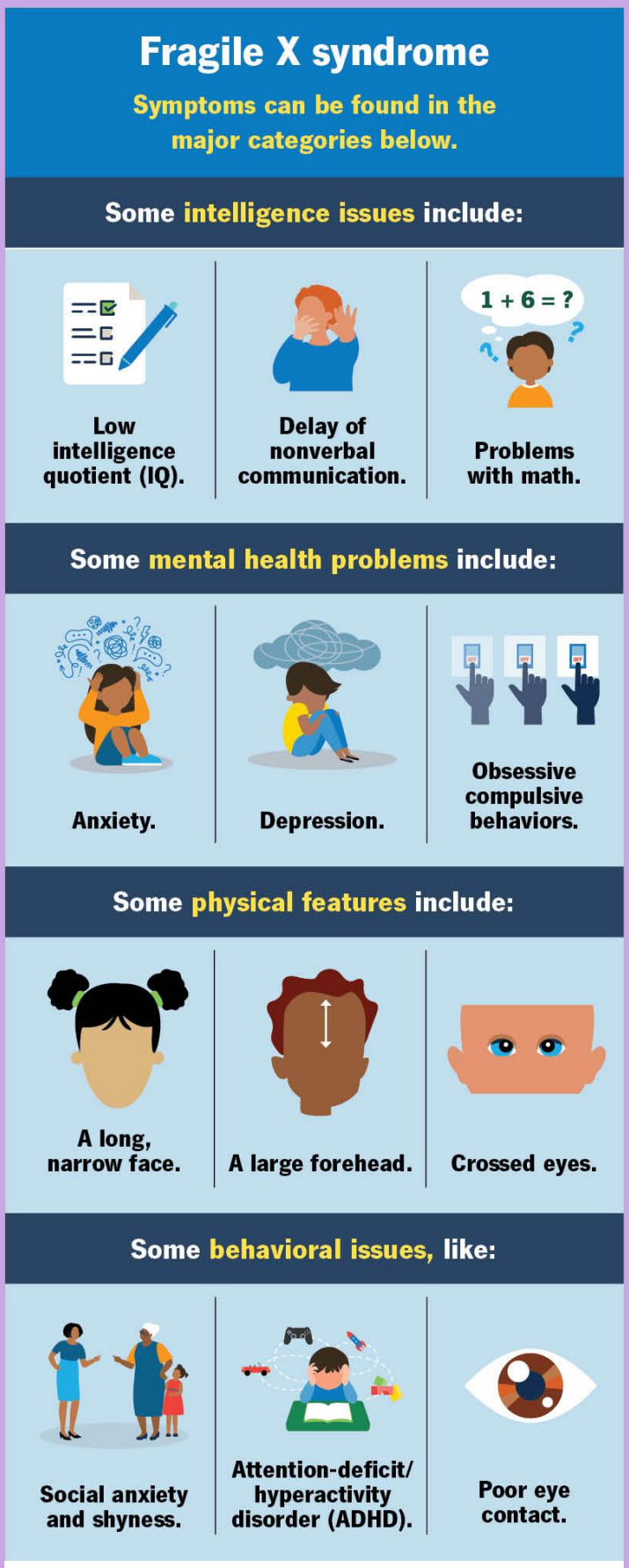
Adults with fragile X syndrome may require support with daily living tasks and may benefit from assisted living arrangements. This is dependent on the degree of intellectual disability.

Additional resources:

https://www.fragilex.org.uk/

https://contact.org.uk/conditions/fragile-x-syndrome/

https://www.cdc.gov/fragile-x-syndrome/



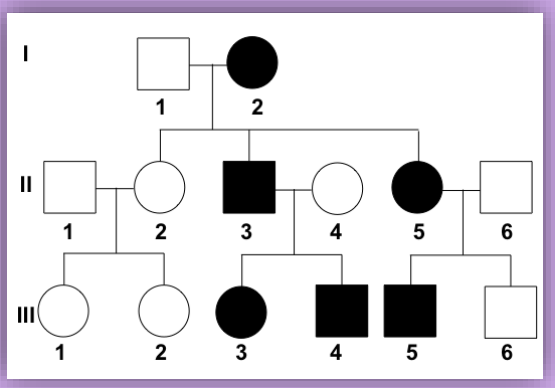
Taken from https://my.clevelandclinic.org/health/diseases/5476-fragile-x-syndrome

CAREERS

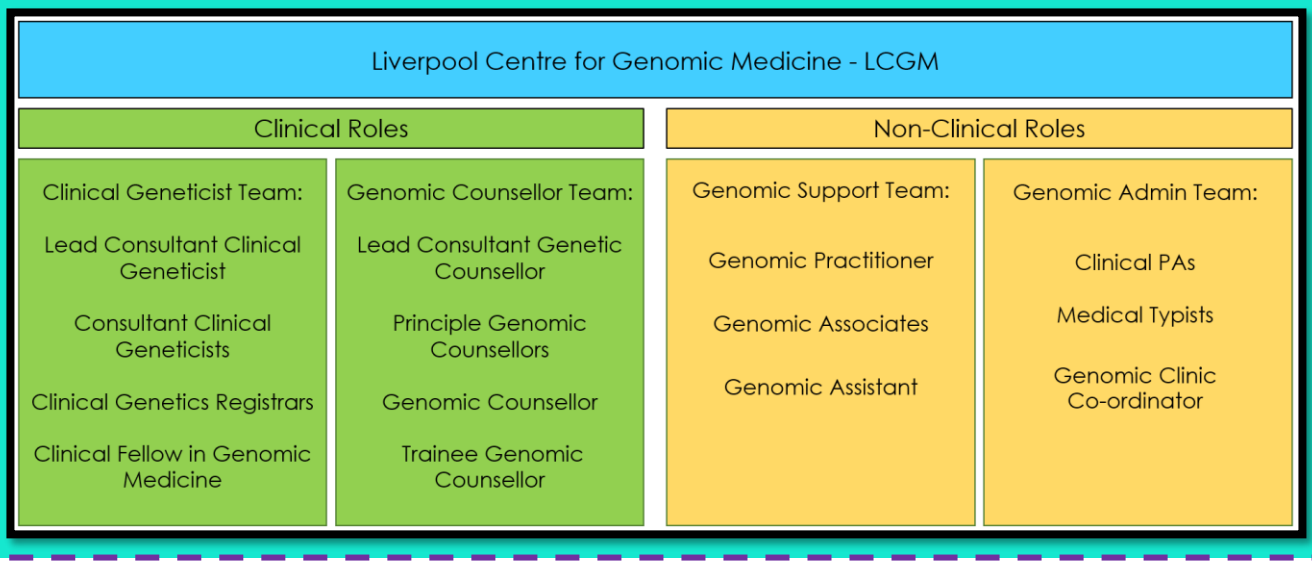
Genomic Associates

The role of a Genomic Associate is to gather information to support the clinical team in advance of patient appointments. Genomic Associates have many responsibilities, including taking and recording family history information using specialist software, gathering information via records from various organisations, such as other NHS hospitals, GP practices, or the National Cancer Registration and Analysis Service (NCRAS).

Pedigree diagrams of a patient's family history is a very useful tool for clinicians that can help to establish inheritance patterns.



The genomic medicine service provided by the LCGM involves the collaboration of many different roles across clinical and non-clinical teams. Some patients may encounter one or more members of each team throughout their patient journey.



CAREERS

Genomic Associates - *Continued*

A massive thank you to Katie Usher, Genomic Associate at LCGM, for sharing information about her role.

How long have you been in your role?

2 years and 4 months.

Did you have any previous experience in genetics or health care?

I had previous experience working in the NHS throughout the Covid Pandemic as swabbing assistant. My only academic experience of Genetics was from when I studied Biology at GCSE. I did however, after learning about this role and prior to my interview, undergo all of the NHS England e-learning modules available that covered aspects of the role such as; how to take a family history and inheritance patterns.

What are some of the main tasks involved in your role?

Mainly we talk to patients or the parent/guardian of patients to gather their family histories over the phone. This helps the Genetic Counsellor or Clinical Geneticist assess their family history and build an accurate risk assessment so that the correct care or eligible testing can be offered. Other tasks involve; requesting genetic test reports, medical records and liaising with the Clinical Genetics team to ensure all information is gathered prior to clinic.

CAREERS

Genomic Counsellors - *Continued*

How would you say your role fits into the clinical care for patients?

Often, we are the first point of contact for patients. Our role is administrative and not clinical, but it is a good opportunity for clinical questions to be noted prior to the clinic appointment. Our role is important as it involves clinical note taking, which must be accurate to be assessed appropriately by the clinicians. Our role is also important to get an understanding of how the patient or parent/guardian is dealing with the referral emotionally or whether there are any safeguarding concerns.

What do you enjoy most about your job?

I enjoy the problem-solving aspects that can come with some information requests, like tracking down records from somewhere out of area. Mainly I enjoy speaking with people, listening to them, and feeling as though I am supporting them through their patient journey.

What do you find most challenging about the role?

In a way, the things I enjoy about my role can become the most challenging aspects as well. Sometimes it can take a long time to track down records. It can be difficult when patients become upset over the phone, as there is only so much help you can offer. But often patients are grateful even if it just involves listening and empathising with them.

Do you have any hobbies outside of your role?

I am a part-time artist. I mainly draw animal portraits, which I use coloured pencil to create. I also enjoy running in my spare time.

Next edition: Clinical Geneticist

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.

GENPROS

Analysing outcomes after prostate cancer diagnosis and treatment in carriers of rare germline mutations in cancer predisposition genes (GENPROS) study

This study's main objective is to investigate whether Prostate Cancer patients who carry a rare germline mutation, such as BRCA2, have shorter cause specific survival compared to non-carriers.

Aim of the study	Who can take part?	What does it involve?
To evaluate prostate cancer treatment outcomes in men with prostate cancer who are also known to have rare germline mutations (mutations in the DNA that are present from birth) in genes thought to be involved in the development of prostate cancer.	Men diagnosed with prostate cancer and have undergone genetic testing and are either- 1. known carriers of germline mutations associated with prostate cancer risk 2. known non-carriers of mutations in the genes below	Minimal involvement for participants. May be contacted for follow up for up to 10 years to update details, stored DNA samples used but if unavailable silva sample kit can be sent to participant's home.

Associated Genes

BRCA1	BRCA2	ATM	CHEK2	HOXB13
MLH1	MSH2	MSH6	PMS2	EPCAM

For more information about GENPROS research study, please visit http://genpros.icr.ac.uk/

RESEARCH STUDIES – *Continued*

An Outpatient study of speech, language and communication abilities in children with genetics conditions study

This study's main objectives are-

1. Characterise the communication abilities of children with recently discovered genetic causes of intellectual disability (ID).
2. Create an online information resource detailing the communication profile/communication deficits for each genetic condition.

Aim of the study	Who can take part?	What does it involve?
The information this project produces will help families, doctors/nurses and educators better understand the needs for communication interventions in children affected by these genetic conditions.	1. Children between 2-15 years old 2. Children able to engage in some form of communicative behaviour 3. Pathogenic variant in one of the genes newly associated with 100K / DDD project (examples of some of these variants are below)	All study involvement is remote. The below activities are co-ordinated by University of Sheffield with parents/ caregivers and £25.00 voucher is provided for participation. 1. Parents/caregivers complete questionnaires about their child's speech and communication. 2. Children complete speech and language assessments via video call with a researcher. 3. Parents/caregivers of children who communicate non-verbally will complete an interview via video call with a researcher. 4. Parents/caregivers record a short video of themself and their child doing an activity at home.

Example associated variants

KMT2A	DRYK1A	SYNGAP1	ADNP	TRIP12
ANKRD11	SETD5	ARID1B	EP300	MED13L

For more information about this research study, please visit
Speech, language and communication abilities in genetic conditions - Health Research Authority (hra.nhs.uk)

LATEST NEWS

Advances in vaccine for Lynch Syndrome

Vaccine hope for cancer risk genetic disorder

Researchers hope a vaccine could teach the immune system of someone with Lynch syndrome to destroy cells

Storm Newton
PA Media

10 September 2024

Oxford scientists are aiming to develop a vaccine for people with a genetic condition that increases their risk of a number of cancers.

Lynch syndrome is caused by a mutation in the gene that fixes mistakes in DNA when it is copied, which can lead to uncontrolled cell growth.

People with the condition have a higher risk of developing cancers of the bowel, womb, and ovaries.

About 1,100 bowel cancer cases in England each year are caused by Lynch syndrome and the condition is thought to increase the lifetime risk of the disease by 80%.

Researchers from the University of Oxford could potentially design a vaccine that teaches the immune system of someone with the disorder to recognise and destroy cells before they become cancer.

As part of the project - known as LynchVax - scientists will analyse cells from Lynch syndrome patients that are showing signs of becoming cancerous.

They will use their findings to determine which parts of a pre-cancer cell can be attacked by the immune system and if a vaccine approach is likely to work.

You may wish to look at
Lynchvax: Vaccine hope for cancer risk genetic disorder - BBC News
for the full article.

LATEST NEWS

Lynch Syndrome

What is Lynch Syndrome?

Individuals with Lynch syndrome have an increased lifetime risk of a variety of cancers, most commonly colorectal cancer or endometrial cancer, as well as ovarian, pancreaticobiliary, gastric, small intestinal, brain, urinary tract, skin and other cancers. The exact risks depend on the underlying genotype.

Affected individuals usually have a family history of bowel cancer and other Lynch syndrome-related cancers.

Lynch syndrome — Knowledge Hub (hee.nhs.uk)

The facts about Lynch syndrome

Our bodies are made up of millions of cells, each one containing our DNA, all the genes (or, to use a common metaphor, all the instructions) each of us needs to grow and function. Lynch syndrome is caused by alterations in one of a handful of genes that control how cells repair DNA damage. In some cells, these alterations can result in DNA damage building up until it affects other genes that control growth, increasing the risk of cancer.

Around 1 in 400 people in the UK (approximately 175,000 to 200,000 people) are estimated to have Lynch syndrome. Less than 5% of them (around 10,000 people) have been diagnosed.

Lynch syndrome is estimated to cause around 1,300 bowel cancer cases in the UK every year, roughly 3% of the total. Up to 7 in 10 people with the condition will develop bowel cancer in their lifetime, many of them before they turn 50.

People with Lynch syndrome also have an above average risk of developing endometrial cancer, ovarian cancer, stomach cancer, gallbladder cancer, prostate cancer and cancers of the urinary tract, among other cancer types.

Information taken from Work starts on a cancer vaccine for people with Lynch syndrome - Cancer Research UK - Cancer News

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
Oesophageal Atresia (OA) & Tracheo-Oesophageal Fistula (TOF): Adult and family information seminar	16th November 2024	Warrington

For more information, click the link: https://tofs.org.uk/

Bardet-Biedl Syndrome (BBS) UK Annual General Meeting	Saturday 9th November 2024 @10am – 12pm	Online – Via Zoom

For more information, click the link: Registration open for the BBS UK Annual General Meeting on 9th November 2024. - BBS UK

Who are Huntington's Disease Youth Organization (HDYO) and what do they do?	25 November 2024 @7 pm - 8pm	Online

For more information, click the link: Huntington's Disease Association - Who are Huntington's Disease Youth Organization (HDYO) and what do they do? (hda.org.uk)

Red Cross first aid workshop	9th December 2024 @1pm – 2:30pm	Online

For more information, click the link: Huntington's Disease Association - Red Cross first aid workshop (hda.org.uk)

To find more information about events please visit geneticalliance.org.uk

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SCAN ME

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

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