Inform Network Support

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This booklet was first compiled by Unique (CA) in 2019/20 and reviewed by Dr Jeroen Breckpot (MD PhD), Centre for Human Genetics, Catholic University Leuven, Leuven, Belgium. Version 1.1 2022 (CA)

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Understanding Chromosome & Gene Disorders

Duplications of 5q

rarechromo.org

5q duplications

A 5q duplication is a rare genetic condition that occurs when there is an extra copy of part of the genetic material (DNA) in one of the body's 46 chromosomes - chromosome 5. A duplication is also called a partial trisomy or copy number gain. People have two chromosomes 5, but the extra DNA is found in only one of them.

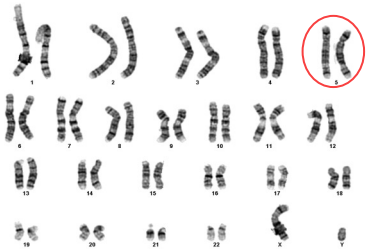
In general, the right amount of genetic material is needed for correct development – not too little and not too much. As with other chromosome disorders, having an extra piece of genetic material may affect development and intellectual abilities, and sometimes health and behaviour. However, the ways and degree to which an individual is affected can vary a lot: how an individual develops and their personality, needs and achievements, depends on a number of factors, including his/her genetic material and the environment in which he or she lives.

Background on chromosomes

Our bodies are made up of trillions of cells. Most of these cells contain a set of around 20,000 genes that carry the set of instructions that tell the body how to develop, grow and function.

Genes are carried in structures called chromosomes, which consist of a complex chemical called DNA. Chromosomes (and hence genes) usually come in pairs, one inherited from the mother and one from the father.

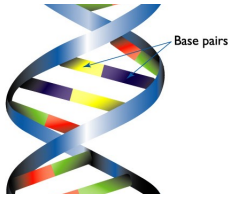
A normal cell in the body has 46 chromosomes that are numbered 1 to 22, approximately from largest to smallest, apart from the sex chromosomes (usually two Xs for a female and an X and a Y for a male).



Chromosome pairs 1-22, X and Y (male). Chromosome 5 pair circled in red

Looking at chromosome 5

Each chromosome contains millions of base pairs of DNA. Base pairs are the chemicals in DNA that form the ends of the 'rungs' of its ladder-like structure. There are millions of base pairs in every chromosome, and they are often counted in millions, where 1 Mb equals one million base pairs. The whole of chromosome 5 has about 181 Mb (181,000,000 base pairs), and approximately 900 genes.



1 base pair = 1 bp
1,000 base pairs = 1 kb
1,000,000 base pairs = 1 Mb

Facebook Groups

Chromosome 5 duplication facebook group (236) - www.facebook.com/groups/1548614302021901/ - This group was created in hopes of connecting with others who have children or themselves with this rare duplication in chromosome 5.

Websites

www.patient.info - information on medical conditions and terms

www.nhs.uk/conditions/ - easy to understand explanations of medical conditions and procedures

www.alextlc.org/ - The Leukodystrophy Charity (Alex – TLC) - offers support and information for all those affected by a genetic leukodystrophy

www.adhdfoundation.org.uk/ - The ADHD Foundation Neurodiversity Charity is the national ADHD charity for the UK, and the largest user-led ADHD charity in Europe

www.griffinot.com/ Griffin Occupational Therapy (GriffinOT) aims to provide affordable, high quality online children's occupational therapy support for educators and parents

DECIPHER

This guide makes use of data generated by the DECIPHER community. A full list of centres who contributed to the generation of the data is available from http://decipher.sanger.ac.uk and via email from decipher@sanger.ac.uk. Funding for the project was provided by the Wellcome Trust.

The DECIPHER database is used by clinicians and researchers to report and share anonymised patient records containing the details of key genetic changes and their associated clinical features. This sharing of information helps to increase the knowledge and understanding of each genetic change and whether it is causal for the clinical features; this improves the quality of advice that can be given to those with the same or similar genetic changes. Patients give their consent to allow their linked-anonymised data to be openly shared. Sharing records openly in a database such as DECIPHER may increase the opportunity for patients with very rare conditions to participate in research or trials of new therapies.

DECIPHER: Database of Chromosomal Imbalance and Phenotype in Humans using Ensembl Resources. Firth, H.V. et al (2009). Am.J.Hum.Genet 84, 524-533 (DOI: dx.doi.org/10/1016/j.ajhg.2009.03.010)

Families say...

❝ My advice to other families would be to take care of each other and know there are as many good times as there are hard times. Don't allow sorrow to remain as the primary emotion. Allow yourself to be sad but also allow yourself to love this beautiful child and experience the moments of joy. Do not blame yourself or drive yourself crazy asking why it happened. Find out what resources are available to assist you. There are many online support groups and Facebook groups that are specific to the chromosome disorder. Reach out to friends and family if possible. ❞

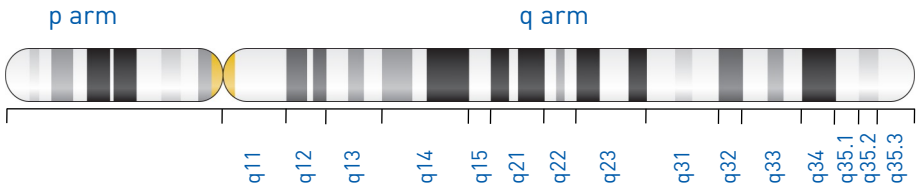
❝ Accept that you cannot fix this. Just love your child and give them the best life you can. ❞

❝ My advice to other families is to not get so caught up on the outcome for the future. Focus on getting support for the whole family. Get respite time as often as you can, especially for date nights with your spouse. When you learn to accept your situation, help those that are still learning. ❞

❝ Use respite services, support workers, take a break and recharge your batteries. Couples need couple time! Other children need uninterrupted time with their parents. Look after your health and make sure you have a contingency plan in place for when you are ill. You are doing a very hard job, no one loves your child more than you but you need to look after yourself first. You have nothing to give otherwise! Use respite services without guilt, take holidays with and without your child, spend time with your other children without your unique child, nurture your marriage. Please. ❞

Chromosomes can't be seen with the naked eye, but they can be stained so that each has a distinctive pattern of light and dark bands when viewed at about 1000 times life size under a light microscope. You can see these bands in the diagram below.

Chromosome 5



Each chromosome has a short (p) arm and a long (q) arm. The bands are numbered outwards starting from the point where the short and long arms meet (the centromere) (marked in yellow). A low number such as q12 is close to the centromere; this part of the arm that is fairly close to the centromere is called the proximal part. A higher number such as q34 is closer to the end of the arm, in the part referred to as distal. The term cen is used to indicate a location that is very close to the centromere, while ter (for terminal) indicates a location that is very close to the end of the p or q arm.

Chromosomal changes

When a sperm and egg cell join they form a single cell. This cell must continuously make copies of itself and all its genetic material (replicate) in order to produce the billions of cells that are necessary for human growth and development. Sometimes during the formation of the egg or sperm cells or during this complicated replication process, parts of a chromosome(s) are lost, duplicated and/or become rearranged. The effect of any chromosomal change varies according to how much genetic material is involved and, more specifically, which genes and/or regions that control genes are included, as well as numerous other factors that we are only beginning to understand.

Sources

The information in this booklet is drawn from the published medical literature and information from *Unique* members. The first-named author and publication date from articles in the medical literature are given to allow you to look for the abstracts or original articles on the internet in PubMed (http://www.ncbi.nlm. nih.gov/pubmed). If you wish, you can obtain most articles from *Unique*. Information gathered from DECIPHER (DatabasE of genomiC varIation and Phenotype in Humans using Ensembl Resources) is open access and can be found at https://decipher.sanger.ac.uk. Eight *Unique* members completed a detailed survey in 2018/19. In addition to this, information has also been drawn from the database records of other members where possible.

Has everyone with a 5q duplication got the same amount of extra DNA?

No. People have very different amounts of extra DNA, and different extra genes. Even where individuals have the same - or very similar - 5q duplication, the effects can vary considerably. Some people have two breaks in the chromosome, with extra material between them: this type of duplication is called interstitial or segmental. Other people have an extra copy of the DNA at the end of the chromosome: this type of duplication is called terminal. In some people the extra DNA runs in the same direction as the rest of the chromosome: this is called a direct duplication, or dir dup. In other people, the extra material runs in the opposite direction: an inverted duplication, or inv dup. Generally, the amount of extra DNA is more important than its direction. Chromosomal duplications are generally less severe than deletions of the same regions.

Is it possible to predict the outcome for a particular duplication?

You may wish to compare your child's duplication with others who have the same or similar duplication, to help understand your child's development. While this may help identify common consequences, it is important to remember that, as mentioned earlier, the same duplication can have different effects on different people and the precise effects of gaining material from a chromosome can vary considerably, even between members of the same family. A child's other genes, environment and unique personality also help to determine their future development, needs and achievements. It is very important to see your child as an individual and not to rely on direct comparisons with others who appear to have the same or a similar duplicated piece of DNA. After all, each of us is unique.

Nevertheless, using the limited data available, attempts have been made by researchers to categorise 5q duplications into groups based on the features associated with duplication of particular 5q bands:

- Category A: proximal duplications involving bands 5q11 to 5q22 are thought to be most commonly associated with a small head (microcephaly); growth delay; a delay in meeting developmental milestones (developmental delay); some degree of learning difficulties/intellectual disability; speech delay or absent speech; low muscle tone (hypotonia); and characteristic facial features, including unusual/low-set ears, a prominent forehead and a nose with a bulbous tip. Occasionally, a heart condition and seizures have been reported. Duplications involving 5q14 are covered in more detail in *Unique*'s guide to 5q14 duplications.
- Category B: distal duplications involving bands 5q31 to 5qter are thought to be most commonly associated with a more severe growth delay;

5q33q34

A boy listed on DECIPHER inherited a ~7 Mb 5q33.3 to 5q34 duplication from a seemingly unaffected parent. He had moderate global developmental delay and some unusual facial features, including a prominent forehead; unusual, low-set ears; and down-slanting eyes.

5q33q35

Unique had one 8-year-old member with a ~ 4.5 Mb 5q33.2 to 5q35.1 duplication. Her mother gave us a description of elements of her daughter's development, following her diagnosis at seven years:

"She was born at full term and weighed 6lb 1oz (2.75 kg). As a baby, she would struggle to gain weight. It would take an hour for her to drink a few ounces of milk and she would become very tired. She has an extremely small head, long fingers and toes, and wide spaces between her teeth.

She has mild scoliosis (curvature of the spine) and pains in her legs, back and feet. She also has Sever's disease (calcaneal apophysitis) (an inflammation of the growth plate in the heel).

Her eyesight is perfect but she is unable to track with her eyes. She does daily exercises, recommended by a physiotherapist, to help her back.

She has experienced absence seizures and febrile convulsions.

She has premature adrenarche (where the adrenal glands mature and begin to function and release hormones that bring on the early signs of puberty).

She has social difficulties and a poor attention span and has been diagnosed with dyspraxia and sensory processing disorder (SPD)."

5q34q35.1

DECIPHER lists three cases with similar 5q34q35.1 duplications. A girl with intellectual disability inherited a ~7 Mb duplication from a similarly affected parent. Another girl with a similar duplication had global developmental delay and a short stature. In another case, a tiny 673 kb duplication was inherited from an unaffected parent. This individual had a short stature and there were behavioural concerns, including depression.

5q31.1q35.1

In medical literature, a two-day-old baby was described with a 5q31.1 to 5q35.1 duplication, inherited from his mother. He was born with a rare heart condition (an interrupted aortic arch). In terms of appearance, widely-spaced eyes and a broad nasal bridge were noted (Martin 2003).

The descriptions available on the public part of the DECIPHER database are incomplete, but we do know that two people had an unspecified level of intellectual (learning) disability, another an unspecified neurodevelopmental disorder and another had global developmental delay. There were concerns around growth for one of these individuals and behavioural concerns were reported for another. One person is recorded as growing slowly in the womb (intrauterine growth retardation) and having an unusually-shaped face, hyponatremia (low levels of sodium in the blood) and thrombocytopenia (low levels of the cells (platelets) that help blood clot).

Duplications within 5q31 to 5q35.1

In this group there are at least nine people of various ages: one *Unique* member, two in the medical literature and six on DECIPHER (all with no other recorded genomic variant) (Sanchez-Garcia 2001; Martin 2003; DECIPHER; Unique). Information is sparse, but what is known is outlined below.

Note: *Unique* has a separate guide to 5q35 duplications, which may be of interest to families with a duplication including all or part of 5q35.

5q31q32

The DECIPHER database lists two individuals with similar 5q31.1 to 5q32 duplications, with details outlined for one. A boy or man with a ~18 Mb duplication spanning most of bands 5q31 and 5q32 was of short stature and had a relatively small head (microcephaly). We also know that he had intellectual disability and experienced seizures. A minor anomaly of the toes and a sacral dimple were also noted.

5q31q33

There is one report in medical literature of a boy with a *de novo* 5q31.3 to 5q33.3 duplication. The boy had a relatively small head and slight growth delay. He had a prominent forehead; a thin upper lip and down-turned mouth; relatively large, widely-spaced teeth; and was slightly short-sighted. He also had undescended testicles (cryptorchidism). The testicles begin their descent from the abdomen during foetal life and have usually arrived in the scrotum by birth. In a significant number of boys without any chromosome anomaly, that journey is not complete by birth but is completed within the next few months. When descent does not occur, the testicles can be brought down in a surgical operation (orchidopexy) and anchored in the scrotum.

At 32 months, his intellectual and motor development were delayed and considered to be at the level of a 10-month-old. In terms of personality, he was described as a "cooperative, friendly, and timid boy" (Sanchez-Garcia, 2001).

developmental delay and learning difficulties/intellectual disability; microcephaly; a heart condition; anomalies of the hands and feet; a squint (strabismus); and characteristic facial features, including unusual/low-set ears, a skin fold of the upper eyelid covering the inner corner of the eye (epicanthus) and a down-turned mouth with a thin upper lip.

- Category C: more distal duplications involving bands 5q34 to 5qter are most commonly associated with a short stature; some degree of learning difficulties/intellectual disability; delayed puberty; eczema; anomalies of the hands and feet; and characteristic facial features, including a short, receding forehead and high nasal bridge. Since there is an overlap in these features with those associated with microduplications involving only the most distal bands, 5q35.2 to 5q35.3, many of the features associated with category C duplications are thought to be associated with genes localised within the 5q35.2 to 5q35.3 region. *Unique* publishes a separate guide to 5q35 duplications.

(Rodewald 1980; Sanchez-Garcia 2001; Douyard 2006; Zahnleiter 2011; Dikow 2013; Schmidt 2013; Unique)

It is important to stress that these categories serve only as a guide to the features that may be associated with a particular 5q duplication since they are based on a small number of people. Other features have been noted in the medical literature and among *Unique* members with a 5q duplication. Some are known to be generally more common in children with chromosome disorders; others may in fact be unconnected with the chromosome disorder. Just as typically-developing children can experience a number of unforeseen physical and behavioural difficulties, each person with a 5q duplication is unique and can have different developmental and medical concerns.

As with many cases on DECIPHER and in medical literature, some *Unique* members have a 5q duplication alongside another chromosomal anomaly(ies). In all cases, it is only those individuals with a 5q duplication and no other known chromosomal anomaly whose data was used to compile this guide since, for others, the reason for their clinical features may be due to the other chromosomal change(s). This guide may nonetheless be of help to explain some of their features.

The information we have relating to the 5q duplications covered in this guide is extremely limited and therefore provisional, but what is known will be discussed. Many of the duplications are so-called "variants of uncertain (or unknown) significance" (VUS or VOUS), meaning it is unclear whether they are causal of the features mentioned or if there is another cause, such as another as-yet undiagnosed genomic variant. These 5q duplication VUS may be reclassified as either benign (they have no ill effect) or pathogenic (causative of the observed features), as we learn more about them.

Many of the duplications discussed in this guide are tiny microduplications of less than 1Mb. When this guide was compiled, *Unique* had one member with a duplication of the whole 5q arm. He had severe learning disability, autism and sensory processing difficulties.

Genetic tests

With any duplication the amount of duplicated DNA can vary. Duplications that are so small that they are not visible under the microscope using standard techniques are called microduplications (microduplications can vary from a few kilobases to 10 Mb long). Many people who have a microduplication may have previously been told their standard chromosome analysis was 'normal'.

A laboratory technique called FISH (fluorescence *in situ* hybridisation) enables sections of the chromosome to be analysed in more detail and can help detect a duplication. This technique uses fluorescently-labelled pieces of DNA that match the DNA in specific places on a chromosome, so this test will only be offered if there is a suspected abnormality in a specific region of a chromosome.

The more commonly used test nowadays is called chromosomal microarray (CMA) and allows genomic DNA to be analysed in greater detail. An array test can detect very small duplications and deletions even when this diagnosis is not suspected. It will also identify a more precise position on the chromosome for the piece of DNA that has been duplicated, but it cannot show if the new piece of DNA has moved to a different place on the same chromosome or to a different chromosome.

Advances in next generation sequencing (NGS) technologies offer the promise of ever-more accurate diagnoses and understanding of rare chromosome disorders. NGS allows multiple genes; the entire protein-coding portion of all the genes in the genome (whole-exome sequencing (WES)); or even the entire genome (whole-genome sequencing (WGS)), rather than just targeted regions or individual genes, to be sequenced. This allows variation across the entire genome to be assessed and may be particularly useful for detecting microduplications/microdeletions that may be missed by less sensitive microarray analysis.

NGS technologies can also more accurately diagnose low-level mosaicism. Mosaicism occurs when not all cells in the body have the same numbers or arrangements of chromosomes and typically arises after fertilisation. In this case, cells containing a 5q duplication could exist alongside cells with a normal chromosome number and arrangement. Mosaicism is rare, but where it has been reported in medical literature for rare chromosome disorders the outcome of the condition was in some cases milder.

Chromosome test results

The laboratory that finds the 5q duplication will send a report that is likely to read something like one of these examples:

46,XY,dup 5q31.2 dn - This result shows that the expected number of chromosomes (46) were observed. It also shows that an X and a Y

and he is getting a bit of a belly! He is largely toilet trained but still needs a lot of reminding. Accidents are infrequent now and he has been dry at night for a year. He had an inguinal hernia at two-and-a-half months, which was strangulated so required emergency surgical repair. His eczema was bad as a baby but is very limited now and is managed entirely through moisturisers and small quantities of medicated skin creams. At 8 years, he is thriving and is medically well.

His fine and gross motor skills have always been poor and this extends to his swallow reflex. He rolled at six to nine months, sat at 10 months, crawled at 16 months and walked at 21 months. His fine motor use is very immature but developing slowly. At five-and-a-half years, he did not have significant pen control beyond scribbling and at 8 years, he is still mark making rather than writing. He had low muscle tone as a baby but grew out of it by three years.

His other major challenge is his mild learning disability - he is 18-24 months behind his peers. He has had PT and OT assessments/advice in order to secure an education, health and care (EHC) plan. He still has regular OT. He attended a mainstream nursery and preschool and currently attends a special education school. He is good at circle time but less good at small group, adult-led activities and his attention span is poor, which means progression, while happening, is slow. A 1:1 tutor is helping him gain some basic knowledge of maths and literacy.

He started speaking single words confidently at around three years. He has echolalia (repetition of phrases, words or parts of words immediately or almost immediately after they are heard) and his expressive language is good, but masks a significant delay with his understanding of language. In terms of understanding, he's at a three to four-word level, but when directing his own speech he can produce lengthy sentences of around 10 words.

He is charming, funny and a people person. He is reluctant to perform adult-led tasks and suffers from anxiety in group situations of three or more and is reserved and anxious until he is comfortable in a space. He is keen to make friends but struggles to know how to make a start in a new group. He can display challenging behaviour, but almost always when he is very tired. He enjoys being outside in the woods or on the beach. **"** - dup 5q33.2, 8 years

The only other source for information relating to individuals with a duplication involving band 5q33 alone was DECIPHER, where eight people were listed, all with tiny microduplications of less than 0.75 Mb. Two had a 5q33.1 duplication, one a 5q33.1 to 5q33.2 duplication and five a 5q33.3 duplication (all with no other recorded genomic variant). Two had inherited the duplication from a parent, both of whom were seemingly unaffected. The contribution to any features or concerns was uncertain or unknown for five people, but the duplication was believed to be contributory (pathogenic/benign) for two others (Unique; DECIPHER).

Two *Unique* children and one girl listed on DECIPHER had spinal curvature. One had surgery at age 11 for kyphosis and had a tethered spinal cord released at the same time.

Two babies had minor heart anomalies that resolved naturally in babyhood.

Two boys listed on DECIPHER had anomalies of the genitals and there were individual cases of a single kidney; constipation; diabetes; a fatty liver (thought to be linked to diet and lack of exercise); other skeletal anomalies; frequent ear infections; eczema; and café-au-lait patches (Rosenfeld 2011; Unique; DECIPHER).

Duplications within 5q32

When this guide was complied, *Unique* had no members with a duplication involving only 5q32. The only source for information relating to individuals with a duplication involving band 5q32 alone (and with no other recorded genomic variant) was DECIPHER, where six people were listed, all with tiny microduplications of less than 0.7 Mb. Two had inherited the duplication from a parent. The information we have is therefore very limited and there is also no information available on the development of these children. The contribution to any features or concerns was unknown in half of these cases, but the duplication was believed to be contributory (pathogenic/benign) in the others (Unique; DECIPHER).

The descriptions available on the public part of the DECIPHER database are incomplete, but we do know that one person experienced sleep disturbance and was considered obese; one had severe intellectual disability, experienced slow growth, had an unusually-shaped face and excessive hair growth; and one had an unspecified anomaly of the heart and the bony plates of her skull closed too soon (craniosynostosis).

Duplications within 5q33

This band is divided into three subbands: 5q33.1, 5q33.2 and 5q33.3.

At the time of writing, *Unique* had one member family with a duplication involving only 5q33.2. The microduplication was diagnosed at two-and-a-half years as a result of global developmental delay and was subsequently found to have been inherited from an unaffected parent. We have a detailed description of his development that was provided by the five-year-old boy's mother.

“ He was born prematurely weighing 4lb (1.8kg). He was jaundiced for three months, which was attributed to breast milk jaundice. He was very slow to establish breastfeeding and had a nasogastric (NG) tube for several weeks. After a month, when we left the special care baby unit (SCBU), he was exclusively breastfed, which continued for five months. We then switched to mixed feeding, followed by formula or milk from eight months. Weaning went well, but he ate a limited diet until five years. His diet is now well balanced

Genome Assemblies

The human genome project, an international effort to sequence the entire human genome and map all of its genes, was announced complete in 2003.
However, there were many gaps in the sequence and mapping data, and scientists have since been working continuously to identify the missing information. When new sequence information is identified, the base pair numbers of each chromosome change slightly and hence the numbers for individual genes and duplications can shift.
Each new version of the genome is often referred to as an 'assembly'. Every few years a new assembly is released. The genetic information you are given will be based on the Genome Reference Consortium (GRC) human (h) genome assembly that was the most up-to-date at the time the test was carried out. Therefore, you may see the DNA sequence referred to as hg19 (human genome 19) (on your child's genetic report it may also be referred to as GRCh37), which was released in 2009, or hg 18, which was released in 2006. The lower the hg number, the earlier the release.
The databases commonly used by clinical geneticists and *Unique* has recently moved to a more recent assembly named GRCh38/hg38, which was released in 2013. Genetic reports will also be altered, so genes and genetic changes may have new base pair numbers.

chromosome were found, so this is a boy or a man. dup means there is a duplication. 5q31.2 shows the part of the chromosome that is duplicated; in this case, the extra material is from the long (q) arm of chromosome 5 in band q31.2 . The duplication occurred dn or *de novo* (as a 'new event'): the parents' chromosomes have been checked and no duplication or other chromosome change has been found so the duplication has not been inherited from either the father or the mother.

arr[hg19] 5q11.2q13.3 (52355412_72399791)x3 This result shows that the analysis used microarray technology (arr). The analysis revealed a DNA anomaly involving 5q11.2 to 5q13.3. The DNA anomaly is identified by its base pair numbers (the points where the change has occurred). In this example, the DNA anomaly lies between base pairs 52355412 and 72399791 (by taking the first number from the second, you can work out that this is 20,044,379 base pairs, or 20.04 Mb). There is an extra copy (x3; the normal copy number is two) so it is a duplication. hg19 tells you which version of the human genome was used for comparison (*see* Genome Assemblies (blue box)).

Why did this happen?

To answer this question, the parents' and affected child's chromosomes need to be tested. What is certain is that, as a father or mother, there is nothing you did to cause the duplication and nothing you could have done which would have prevented it. Chromosome rearrangements affect children from all parts of the world and from all types of background. They also happen naturally in plants and animals. It is no one's fault.

5q duplications are known to be either inherited from a parent or to occur *de*

novo (dn), which means the duplication has occurred as a new event in the child. In many cases, the origin of the duplication may be unknown.

Regardless of the origin of the duplication, as stated above, it is important to know that as a parent there is nothing you could have done to prevent the duplication from happening. No environmental, dietary or lifestyle factors are known to cause 5q duplications. There is nothing that either parent did before, during or after pregnancy that caused the duplication.

Can it happen again?

Where both parents are found to have unaffected ("normal") chromosomes, it is very unlikely that another child will be born with a 5q duplication or any other chromosome disorder. Very rarely (less than 1%), both parents have normal chromosomes by a blood test, but a few of their egg or sperm cells carry a chromosomal change. This is called confined germline (gonadal) mosaicism and it means that parents whose chromosomes appear normal when their blood is tested can have more than one child with the duplication.

In families where the 5q duplication has been inherited from a parent - usually where the duplication is small - the possibility of having another child - either a girl or a boy - with the 5q duplication rises to 50% (1 in 2) in each pregnancy. While the effect of the duplication on the child's development, health and behaviour cannot be reliably predicted, your genetics centre should be able to offer counselling before you have another pregnancy.

If your child with a 5q duplication goes on to have children of their own, the chances of passing on the duplication to their child are 50% (1 in 2) in each pregnancy. Your child's ability to look after their own child is very likely to be closely related to their own learning ability and behaviour.

Are there people with a 5q duplication who are healthy, have no major medical problems or birth defects and have developed normally?

Yes, there are. The effect on development, health and behaviour of some rare chromosome disorders can range from being barely perceptible to being obvious and severe. Even within families, there can be variation between different members of the same family who have the same 5q microduplication.

Some parents of children with a 5q microduplication have the same microduplication but may not have any obvious unusual features or delayed development or may be only mildly affected. We know that if one person is mildly affected or unaffected, others may be more severely and obviously affected.

See *Unique*'s guide to Variable Expressivity & Reduced Penetrance for more details.

her mind is totally active. She appears fine through the day, always on the go and never sits down!" - dup 5q31.2

Growing up

Puberty can be a challenging time for any family. The information we have relating to puberty and 5q31 duplications is extremely limited, but among *Unique* families two boys began puberty at the expected age, or possibly a little early. For one boy, it seems that puberty was proceeding as expected with no real cause for concern, while for the other it seems to have led to changes in behaviour (see comment below). A girl on DECIPHER went through puberty early (precocious puberty). Continence may be the exception rather than the rule and on-going support with daily living tasks to be expected. One teenager was living in a residential home (see comment below).

"He went through full puberty somewhat early, by 11 years. He does not seem to be affected by it." - dup 5q31.2q31.3, 13 years

"Puberty seemed early to me but in line with other boys these days. His behaviour became unpredictable with mood swings for no apparent reason. He lives in a dormitory-type establishment, which he prefers over a group home as there is more activity going on, but is still home most weekends, depending on his behaviour. He loves to go to church, concerts, sports events and watching TV." - dup 5q31.2q31.3, 18 years

Medical issues

Two *Unique* parents told us that their child was susceptible to infections when young, and one was treated for chronic asthma.

While four children experienced seizures, two others were investigated for seizures and another had an abnormal electroencephalograph (EEG). Seizures are caused by a change in electrical activity in the brain. Depending on the part(s) of the brain affected symptoms vary, but include temporary confusion, uncontrollable jerking movements and loss of consciousness or awareness. EEG and video telemetry (video EEG) are medical tests that can be used to measure and record the electrical activity of the brain, and are tools that, when used alongside other tests, can help diagnose the type of seizure experienced. Seizures are often associated with a brain anomaly, including a missing corpus callosum (agenesis of corpus callosum (ACC)), but can occur in children where a brain scan has found nothing unusual. A *Unique* child had ACC but seizures weren't reported.

Some children had anomalies of the eye, although no features were consistent. One child had cortical visual impairment and one had problems with her vision. A boy had eyelid coloboma (where part of the upper or lower eyelid is missing). Several were short-sighted, one had an unspecified visual impairment and a squint (strabismus) and one had astigmatism.

He gets nursing care at home and most of the nurses become very attached because he is such a sweet boy. He is shy around strangers and makes it very clear with vocalisations if he is uncomfortable. People that take the time to get to know him describe him as charming. His teacher and therapists love him. He has been diagnosed with autism but has never had aggressive or harmful behaviour. ” - dup 5q31.2q31.3, 13 years

“ As a child, he was engaging, sociable, laid back. Since adolescence his personality has been unpredictable at times and he has had outbursts of behaviour which are hard to predict or explain. He demonstrates autistic features and atypical catatonia. In the past few years, he's had more and more behavioural issues, but hard to say why as he is functionally non-verbal. He is considered to be on the autistic spectrum and he was treated for ADHD briefly, but I don't think this was a firm diagnosis. When he is upset he will throw furniture but he has never been intentionally aggressive towards a person. He loves music and watching baseball, football etc. ” - dup 5q31.2q31.3, 18 years

“ She has no sense of danger and has sensory dependencies and autistic traits. She is very sensitive to sound so if there are too many noises going on at the same time she becomes very anxious, likewise when things are not done in the same way as before. She is very dependent on routine. If this is changed without her being talked through/shown PECS (if applicable), then she becomes anxious. She is very aware of her surroundings and this makes her attention span very short. ” - dup 5q31.2

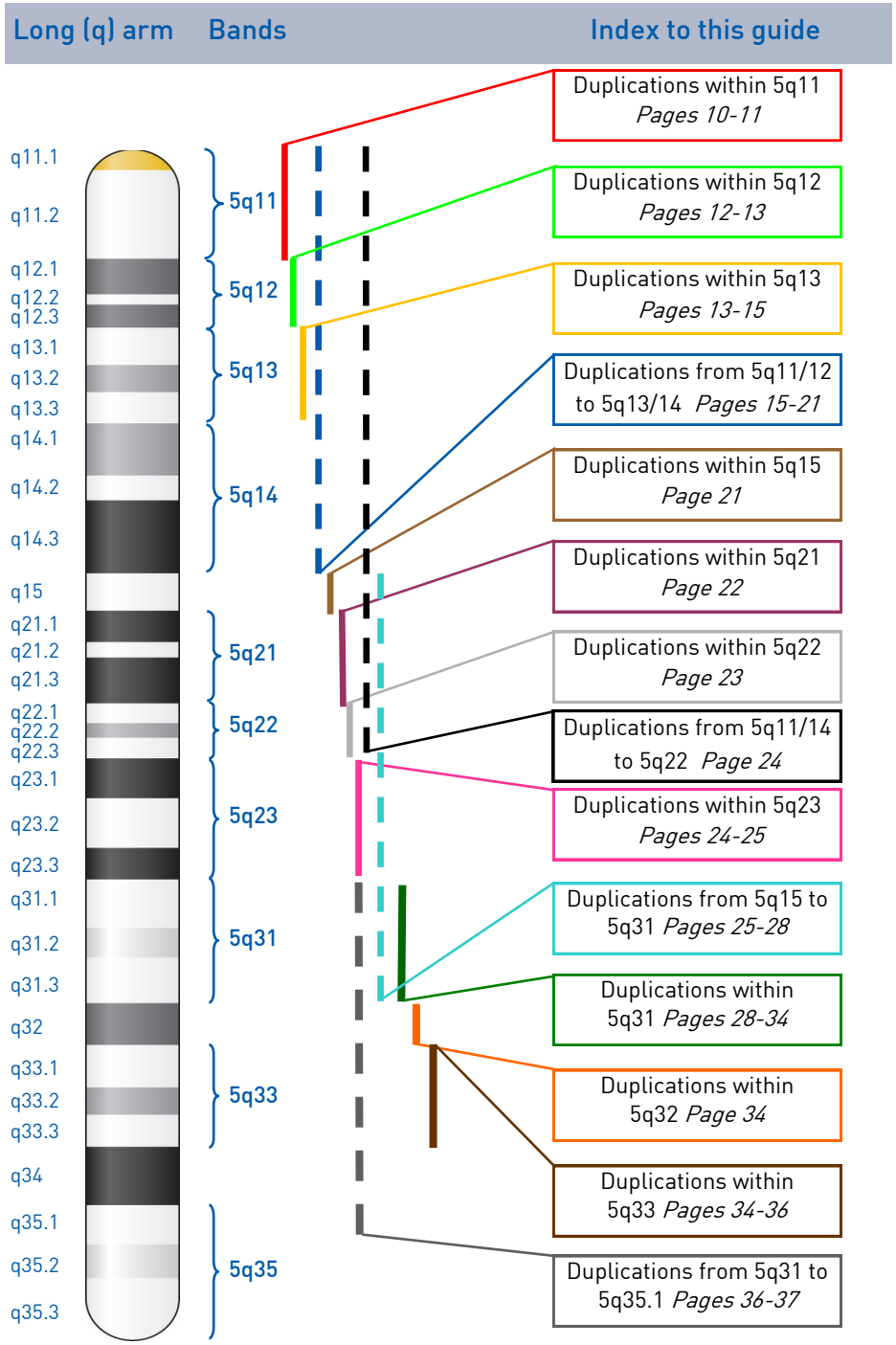
Sleep

Three *Unique* parents told us that sleep was an issue for their child, especially when their child was younger. Medication to help your child sleep may help, including the naturally-occurring hormone melatonin, but such treatments should only be undertaken after consultation with a medical professional. Our Sleep problems in children with chromosome disorders guide, in the “Practical Guides for Families” section of our website, has further information.

“ He has always had sleep issues and didn't sleep through the night until he was almost three years old. He never falls asleep for EEGs even when given sleep medications. He has always been an early riser but has begun sleeping in now that he is a teenager! He takes medications including melatonin, nightly. ” - dup 5q31.2q31.3, 13 years

“ As a baby and young child he definitely had problems with sleep, but eventually outgrew them. He still takes melatonin. ” - dup 5q31.2q31.3, 18 years

“ She doesn't sleep well. We go through spells of using melatonin but she becomes immune after a time. She is very restless through the night, like



Duplications within 5q11

In the most proximal part of the long arm of chromosome 5 is a band known as 5q11. This band is divided into two subbands: 5q11.1 and 5q11.2.

It is difficult to estimate the prevalence of a particular 5q duplication since many people will not have been diagnosed, and many of those who are diagnosed are not reported. We know of at least 20 people with a duplication within this area and with no other recorded genomic variant: three *Unique* members (identical twins who are believed to have the same 5q11.2 duplication and a 10-year-old girl with a 5q11.1q11.2 duplication) and 17 people described on the DECIPHER database (three with a 5q11.1 duplication, 12 with a 5q11.2 duplication and two with a 5q11.1q11.2 duplication) (Unique; DECIPHER). In almost all cases the origin of the duplication was unknown, but two cases listed on the DECIPHER database were documented as being inherited from a parent. In at least one case the parent was seemingly unaffected by the duplication.

The pattern of unusual features is very variable and descriptions are incomplete, particularly in the public part of the DECIPHER database, meaning that no features are known to be consistent for everyone reported. Also, the contribution of the 5q11 duplication to any observed feature is unknown or uncertain in many cases. Apart from familial duplications, each duplication was slightly different.

A *Unique* member with a *de novo* 5q11.1 to 5q11.2 duplication was born at term weighing 7lb 2oz (3.2kg), after an uncomplicated pregnancy. The new-born period was uneventful and she was only diagnosed at the age of six due to difficulties at school with learning and retaining information. Twins with a 5q11.2 duplication received an earlier diagnosis. A girl listed on DECIPHER with a tiny 5q11.2 microduplication grew slowly in the womb and continued to grow slowly after birth.

Overall, it appears that there is no particular "look" associated with babies and children with a 5q11 duplication and a *Unique* parent noted no unusual (dysmorphic) features, but you, or particularly geneticists or doctors, may notice some slight differences. On DECIPHER, features that have been noted include: several instances of unusual or protruding ears; down-turned corners of the mouth; a short, up-turned or broad nose; and a narrow forehead. Two individuals had a cleft (split) in the palate (roof of the mouth) and one had an underdeveloped lower jaw (micrognathia).

A few people had minor anomalies of the hands and feet: a boy had broad palms and feet and there were individual cases of fingers that curved inward (clinodactyly) or were unusually slender or short. One boy had an extra finger (poldactyly) (DECIPHER).

In terms of development, a delay in meeting developmental milestones, such as sitting, walking, hand use and hand-eye coordination, appears to be

was not hard to obtain due to his global delays. He is in an intensive support classroom for special education. The advice I would offer to other parents is be persistent in seeking out the best care for your child. We have encountered amazing teachers and therapists but have also had years where we struggled with classroom situations. His social abilities and tolerance level have improved with age. The iPad is an amazing tool for him, though he only uses it for entertainment rather than communication. He is non-verbal and does not sign or point. He has extremely limited results with PEC cards. We have heard "No" and "Mom" sporadically through the years, but never with real purpose. He uses noises and cries to try and communicate with us. Sometimes it sounds like he is mimicking a sentence, such as "I love you.", by making a similar sound. We believe he understands a lot of the time but is unable to communicate back to us. ” - dup 5q31.2q31.3, 13 years

“ He is now almost 19 and would be in his first year of college if he were typical, but is still attending high school in special classes. He has not learned to read or write. His first words were at ~18 months and at his best he had a vocabulary of perhaps 300-400 words, to the best of my memory, but now he hardly speaks, although being a teenager and the medication he is on may contribute to this. His receptive language is better [than his ability to communicate]. ” - dup 5q31.2q31.3, 18 years

Social, emotional & anxiety disorders

Information is limited, but three *Unique* children and a boy on DECIPHER have had a diagnosis of autism or shown autistic traits. A four-year-old boy in medical literature and a girl on DECIPHER were described as having behavioural/emotional concerns. There is no 'medical test' that can diagnose autism, instead children undergo an autism-specific behavioural evaluation, usually carried out by a specially trained physician and psychologist. The evaluation may be multidisciplinary and include a speech and language therapist as well as an occupational therapist. It is also tailored to the age of the child. Depending on the outcome, further evaluation by a specialist such as a developmental paediatrician, neurologist, psychiatrist or psychologist may be offered.

“ He is a very sweet and loving boy with his family. He loves blowing bubbles, singing, watching television and having his favourite books read to him. He loves to swing at school and we have an adaptive bike that he enjoys when we take him for walks. He has always enjoyed bath time and for us to take him swimming when possible. He does not enjoy a lot of social situations where there are a lot of people and noise. He loves routine and gets very vocal when we have new situations. His older sister is one of his favourite people. He will engage with her and hug her several times a day. He loves his dad and just lights up when he is around. I am his mom and I think he is the most handsome boy in the world. He is affectionate and very responsive with us.

The degree of developmental delay appears to vary, but babies and children may benefit from physical therapy (PT) and occupational therapy (OT) to help overcome these difficulties.

“ He smiled a lot when he was a baby and rolled over when he was seven months old from front to back, but not back to front. He began to sit from around 10 months. He never crawled. At four years he did a type of "frog crawl" to get around (he put both arms out in front of him and then pulled up both legs simultaneously). He could pull up to stand but was not yet standing unaided. He walked (with orthotics) unassisted for the first time when he was five. He did not develop a pincer grasp until he was seven and he still doesn't use his hands with real purpose in fine motor skills. He tends to drop things when they are handed to him. School activities are generally hand over hand and he controls his iPad with his thumb. He began receiving PT and OT when he was 8 months old until present day. He still receives both in school and additional PT at home. He wore orthotics on his legs when he was able to walk with a walker. He is in a wheelchair now with joint contractures in his hips and ankles. ” - dup 5q31.2q31.3, 13 years

“ He could sit well at six months but could not go from lying to sitting until maybe a year. He did not crawl, but scooted around in a sitting position using his feet to pull himself around, and walked at about 23 months. Even now he cannot use a knife and fork together, write, zip clothes or tie shoelaces. He has had chronic hypotonia and prefers to sit with his legs crossed. He frequently sleeps folded in half and is extremely flexible. He received PT and OT for many years. ” - dup 5q31.2q31.3, 18 years

Ability to learn & Speech and Communication

Where we have more detailed information relating to development, it appears that some level of learning difficulty (LD) or intellectual disability (ID) is very likely and may be significant.

We know that at least four *Unique* children had some degree of disability, two described as severe and one profound. Information on the public access part of DECIPHER is incomplete, but six individuals were described as having ID, one profound. This suggests that children are likely to need significant additional support in school and may benefit from attending a special school throughout their education. These children also experienced speech and language delay and some remained non-verbal. A few parents told as that they believed their child could understand (receptive language) more than they could communicate. Where individuals have no speech or very few words, communication may be enhanced through augmentative/alternative communication (AAC). Speech and language therapy was also undertaken by several *Unique* families.

“ He is 13-years-old but tests in roughly the two- to three-year-old range. He has a very specific Individual Education Program (IEP) in the classroom. It

common. Three *Unique* children had developmental delay, although in at least one case this was mild. Another walked independently by two years but benefitted from physical therapy (PT) and occupational therapy (OT). On DECIPHER, one child with an 8.51Mb 5q11.1q11.2 duplication had global developmental delay and one with a tiny 5q11.1 microduplication had low muscle tone (hypotonia) and loose joints. This could be more common since the information on the public part of DECIPHER is limited.

“ She had delayed motor skills and walked at two years. She couldn't do her shoelaces up for a long time, has trouble putting tights on and can't ride a bike very well yet. She is fine holding cutlery and using pens, though. She had OT for a while a year ago, to help with poor motor skills and balance. ” - 10 years

In terms of learning, we only have information for one *Unique* member who, at 10 years, had moderate learning difficulties (LD). Six people on DECIPHER are described as having intellectual disability (ID). In general, the degree of ID was unspecified, but for two the degree was described as moderate.

“ At 10 years, my daughter is working at the level of a five-year-old in reading, writing and maths. She was statemented and now has an EHC plan. As she's getting older the gap between her and her peers in school is widening, so we have now got to make the decision about whether to keep her in a mainstream school. We have visited special schools, which are not suited to her, and we have considered home-schooling, but still haven't made a definite decision. ”

DECIPHER records three diagnoses of autism, an autism spectrum disorder (ASD) that is associated with impaired social skills; problems with communicating; and a need to carry out repetitive and restrictive behaviours, interests and activities, from which an individual derives comfort. Three other individuals had demonstrated challenging behaviours, including aggression and self-harm. A *Unique* member showed no behavioural issues and was described by her mother as “very caring and loving. She is well behaved and she knows right from wrong. No behavioural issues whatsoever“.

In terms of medical issues, these appear to be limited. Three people on DECIPHER are listed as having seizures and another had an abnormal electroencephalograph (EEG) scan, a medical test that can be used to measure and record the electrical activity of the brain. One boy with a 5q11.2 microduplication had an abnormality of the scrotum (the pouch of skin containing the testicles). A girl with a 5q11.2 microduplication had an under-developed optic nerve. A boy with a 5q11.2 duplication had septo-optic dysplasia, which is characterised by a diagnosis with two or more of the medical conditions optic nerve hypoplasia (underdevelopment), midline brain abnormalities and pituitary gland abnormalities. Another individual listed on DECIPHER had an abnormality of the eyelid.

Duplications within 5q12

This band is divided into three subbands: 5q12.1, 5q12.2 and 5q12.3. At the time of writing, *Unique* had only one member with a *de novo* 5q12.1 to 5q12.3 duplication, who was diagnosed at three years. A further 16 people were listed on the DECIPHER database (10 with a 5q12.1 duplication, two with a 5q12.3 duplication, three with a 5q12.1q12.3 duplication and one including a tiny amount of 5q11.2 extending into 5q12.1, all with no other recorded genomic variant). The information we have is therefore very limited and there is also less information available on the development of these children (Unique; DECIPHER).

In almost all cases the origin of the duplication was unknown, but six cases listed on the DECIPHER database were documented as being inherited from a parent. In two cases, we know that the parent was seemingly unaffected by the duplication, while in another case the parent had similar features to the child. With one exception, each of the duplications is slightly different and the description of features is very variable and incomplete. No features are known to be consistent for everyone reported and the contribution of the 5q12 duplication to any observed feature is unknown or uncertain in many cases.

There appear to be no consistent facial features associated with 5q12 duplications, with only the occasional mention of subtle facial features: a girl with a 5q11.2q12.1 microduplication had unusual ears and a wide nasal bridge; a girl with a 5q12.1 microduplication had a short nose with a depressed nasal bridge; a boy with a tiny 5q12.1 had an unusually large head (macrocephaly); a boy with a 5q12.1q12.3 microduplication had a high hairline and fine hair, a long gap between the nose and lip (philtrum) and a prominent forehead; and another boy with a 5q12.1q12.3 microduplication had a receding chin and held his mouth open. There are only two mentions of anomalies of the hands and feet: two boys had feet that turned inwards (one wore special shoes and tailor-made insoles); a girl had slender fingers (DECIPHER; Unique).

In terms of development, a boy with a 5q12.1q12.3 duplication had low muscle tone (hypotonia), loose (hypermobile) joints and a delay in reaching his motor skills from birth, but at four years his parents felt his intellectual ability was unaffected. An individual with a tiny 5q12.1 microduplication showed a delay in reaching developmental milestones and another boy with a 5q12.1q12.3 duplication had low muscle tone. Four individuals on the DECIPHER database had intellectual disability, but no further details are recorded.

“ He has had developmental delay from birth. For the first 1.5 years there was probably a most significant difference in his physical development. But eventually he managed to sit up, to stand up, to walk. Was late to reach milestones such as holding up his head and fell over a lot (he used to fall and

intrauterine growth retardation (IUGR) and low levels of amniotic fluid (oligohydramnios). Following her birth, she appeared to be healthy other than a low birth weight and slight club foot. She also had trouble gaining weight and was of short stature.

“ He had high Apgar scores so we did not know there was a problem. He rejected breastfeeding at three months due to severe acid reflux and threw up frequently. He cried frequently and didn’t sleep through the night and didn’t nap. I tried formula, soy and goat milk, but nothing helped. He was finally diagnosed at one year with severe acid reflux and began taking Prevacid. He also had a heart murmur that resolved at six months. He still disliked formula but loved baby food when he began eating solids. ” - dup 5q31.2q31.3

“ He had significant trouble with sleeping. He was very sociable, but physically placid. He had trouble with breastfeeding at first, in retrospect likely due to low muscle tone and/or apraxia. Once he learned to breastfeed, we continued past a year. ” - dup 5q31.2q31.3

Appearance

As for appearance, there is not enough information to say whether a particular “look” is associated with duplications in these bands, and we only have detailed descriptions for two children. Both had some degree of facial asymmetry, where the sides of the face don’t mirror each other exactly, unusual ears and a broad/prominent forehead. Similarly, in medical literature one child also had a triangular-shaped face with a pointed chin, slight facial asymmetry, unusual ears, a relatively small head (microcephaly) and mild flattening of the mid-facial area. Two girls listed on DECIPHER had deep-set eyes and an unusual head shape (Rosenfeld 2011; DECIPHER).

There were a few reports of unusual features of the hands and feet, but these are not consistent. They include curved fingers (clinodactyly) and short fingers and toes. One *Unique* members had flat feet (pes planus).

Development: sitting, moving, walking (gross motor skills) & hand use and coordination (fine motor skills)

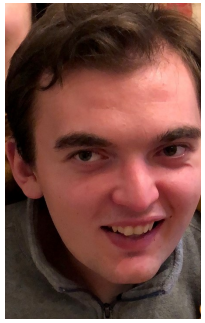
Information provided by *Unique* members suggests a delay in reaching developmental milestones, such as holding the head up and sitting, is to be expected (see below). There are also records of global developmental delay on DECIPHER and in the case reported in medical literature. It appears that fine motor skills, such as holding a bottle or cup and getting dressed, may be particularly affected in some children, which means they may take considerably longer to reach for and grab toys, hold a bottle or cup and dress themselves. We know that several babies and children had low muscle tone (hypotonia), which can make them feel floppy as babies and also contribute to feeding difficulties in the new-born period. A few also had loose, hypermobile joints, which can also contribute to mobility difficulties.

5q15 to 5q31 duplications

There is one report of an individual with a large 5q15q31 duplication who had learning difficulties; a short stature; a small head; and unusual facial features, including high eyebrows, low-set/unusual ears and a small mouth with thin lips (Osztovics & Kiss 1982).

Duplications within 5q31

5q31 is divided into three subbands: 5q31.1, 5q31.2 and 5q31.3. It is difficult to estimate the prevalence of a particular 5q duplication since many people will not have been diagnosed, and many of those who are diagnosed are not reported. We know of at least 25 people with a duplication within this area (and with no other recorded genomic variant): six *Unique* members (one with a 5q31.1 duplication, two with a 5q31.2 duplication and three with a 5q31.2q31.3 duplication);18 people described on the DECIPHER database, where very little detail is publicly accessible (two with a 5q31.1 duplication, seven with a 5q31.2 duplication, three with a 5q31.3 duplication, two with a 5q31.1q31.2 duplication; three with a 5q31.2q31.3 duplication; and one with a 5q31.1q31.3 duplication); and one in medical literature with a 5q31.2q31.3 duplication (Rosenfeld 2011; Unique; DECIPHER).



Aged 2.5 & 18 years

In almost all cases the origin of the duplication was unknown or *de novo*, but four cases listed on the DECIPHER database were documented as being inherited from a parent. Each of the duplications is slightly different and the descriptions of features is very variable and incomplete. No features are known to be consistent for everyone reported and the contribution to any observed feature is unknown or uncertain in many cases.

In three cases, *Unique* parents told us that initial genetic testing came back as "normal", but repeated tests later in childhood revealed the 5q31.2q31.3 microduplication.

Pregnancy & the new-born period

Information is limited, but two *Unique* babies with similar 5q31.2 to 5q31.3 duplications went to term and weighed 6lb 13oz (3.09kg) and 7lb 6oz (3.35kg) at birth. One mother felt that her baby moved less in the womb than his sister. Both babies experienced some degree of feeding difficulty, including difficulties with breastfeeding and reflux, and later constipation. Their parents also told us that they experienced sleeping difficulties. The mother of another baby with a 5q31.2q31.3 duplication was followed by the high-risk team for the duration of her pregnancy due to complications that included

was not able to protect himself by stretching out his arms), as he was struggling to keep his balance. With intensive PT two or three times a week, until he was about two-and-a-half years old, he did manage to catch up with these delayed skills. He still struggles at four years, as his upper body is not strong and he does not have much strength in his arms. When he runs, it takes a lot of effort and he wobbles to the sides a bit and sometimes trips over, but does not hurt himself as much as he has learned how to fall. He started to speak quite early, at about 18 months. At the age of two he spoke in sentences. He is bilingual. In general, his mental development is good at four years and we do not think it is affected in any way. At four years he is dry during the day but not at night, so he is still in pads at night. He is still not as good with his fine motor skills, but this improved when he started at nursery a year ago. Now, he just loves to do lots of crafts using scissors, pencils, stickers and glue. **"**

In terms of behaviour, three individuals on DECIPHER are recorded as demonstrating challenging behaviours, while one also had an autism diagnosis. A boy would sometimes get frustrated if he couldn't achieve something like putting on or taking off his clothes himself, but was described as "a sensitive, loving and happy child".

Medical concerns appear to be rare. There are two records of anomalies affecting the heart, including an atrial septal defect (ASD) (hole in the heart); one record of hydrocephalus (a build-up of fluid in the brain, which may not require treatment if the pressure rebalances spontaneously); a record of unspecified seizures; a double hernia (where an organ or fatty tissue pushes through a weak spot in a surrounding muscle or tissue) that was corrected surgically; one report of an under-developed optic nerve; and an unspecified abnormality of the skin. One baby who inherited a 5q12.1 microduplication needed to be tube-fed at birth and was later classified as obese. She also had an unspecified brain anomaly, seizures, a low platelet count (thrombocytopenia) and scoliosis (curvature of the spine) (Unique; DECIPHER).

Duplications within 5q13

5q13 is divided into three subbands: 5q13.1, 5q13.2 and 5q13.3. When this information was compiled, *Unique* had one member with a 5q13 duplication. In medical literature, a boy who had inherited a 1.1Mb 5q13.2q13.3 duplication from his mother (Balikova 2010) and a 20-month-old boy with a larger 10Mb 5q13.1q14.1 duplication (Zou 2010) were described, but most of the information we have is derived from the public part of DECIPHER where descriptions will be partial, thereby limiting the information that can be provided. There is also less information available on the development of these children.

The *Unique* member with a *de novo* 5q13.3 duplication was born at full-term, weighing 8lb 10oz (3.9kg) with no apparent concerns in the new-born period other than being jaundiced. There were no difficulties related to feeding. She

had plagiocephaly (where the head appears flattened on the back or side) and congenital torticollis (where the head is held tilted to one side), a slightly enlarged tongue, but no other unusual (dysmorphic) facial features. As for her development, she made steady progress, reaching her milestones in the usual order, albeit slower than a typical child, and had had PT and OT since six months. She rolled both ways at 8 months, sat up at 9 months, fed herself finger foods at 10 months, went from lying down to sitting up on her own at 11 months, crawled a little at 12 months, pulled herself up to standing and cruising furniture at 14 months, crawled proficiently at 15 months, held her own bottle at 17 months, began to stand on her own for a few seconds at 18 months, and stood alone for a minute and took a few steps on her own at 20 months. At 21 months she was constantly moving. At 12 months she had increased muscle tone (hypertonia) but at 21 months she had slightly low muscle tone (hypotonia). A happy, friendly, unfussy child who laughed and smiled easily, she was very sociable, loved music, singing and playing with water, and slept well. She did demonstrate some sensory-seeking behaviours. There were no major health concerns but she was susceptible to colds, respiratory infections and an excessive build-up of fluid in the ears that was treated with grommets (a small ventilation tube) inserted into the eardrum. She had annual check-up for a Still's (innocent) heart murmur, which is relatively common in babies and children and often resolves naturally. She also had a high pain threshold and two small red birthmarks (hemangioma). Her teeth were slow to come through and erupted in an unusual order.

"Speech is her weakest area. She has no words or babbling but makes constant vowel and consonant sounds with inflections. Receptive speech (understanding) is much better than expressive speech at 21 months. She has had speech therapy since 12 months." - dup 5q13.3

The mother and son with a 1.1Mb described by Balikova had some of the features associated with branchio-oculo-facial syndrome (BOFS) (OMIM 113620), which were thought to be caused by duplication of the *FOXD1* gene (located in 5q13.2), including prematurely grey hair around the forehead in the mother and branchial cysts (swellings) in the cervical (neck) area in the son. Both also had a mild degree of intellectual disability. The boy experienced feeding difficulties in the new-born period and had low muscle tone, a curved fifth finger (clinodactyly) and mild developmental delay (Balikova 2010).

A 20-month-old boy with a 10Mb duplication spanning 5q13.1 to 5q14.1, inherited from his mother (who had a three-way balanced translocation), was described as having mild developmental delay. He began crawling at 9 months, was able to sit without support at 11 months and began walking at 12 months. Speech/language were also delayed and his weight and height measurements were below the 3rd centile, indicating restricted growth. He was born with a small hole in the heart (atrial septal defect (ASD)), which had

experienced seizures for which they took medication. Two children in medical literature had heart anomalies, although no concerns were reported on DECIPHER or by *Unique* parents. One was born with persistent ductus arteriosus (PDA), while the other had multiple anomalies, including ventricular hypertrophy and hyperkinesias. A boy had spasticity (where the muscles remain contracted for long periods making them feel stiff, heavy and difficult to move) and had a squint (strabismus). A girl was totally deaf at birth but by seven months appeared to have a limited sense of hearing. She was also diagnosed with cortical blindness (partial or complete loss of vision despite a normal appearance of the eyes) soon after birth, but at seven months was able to track with her eyes, although not consistently. She also benefited from artificial tears to help moisten her eyes as her eyelids were unable to close completely (lagophthalmos) (Giardino 2004; Arens 20014; DECIPHER: Unique).

5q15 to 5q21/q23 duplications

We know about at least six people with a 5q15 to 5q21 duplication. A father with a 5q15q21 duplication was reported to have no unusual features, aside from epilepsy. His identical twin daughters inherited the duplication but had quite different features. One had complex cardiac anomalies and abnormalities of the kidneys; the other had a cleft plate and a duplicated (extra) ureter (collecting system) from one kidney. On DECIPHER two individuals with a 5q15 to 5q21.1 microduplication had a cleft palate and global developmental delay, respectively, although the contribution of the duplication to these features was uncertain. A boy with a larger ~8.5 Mb 5q15 to 5q21.3 duplication, which was inherited from an unaffected parent, was born with meningocele (where the protective membranes around the spinal cord (meninges) push out through the spine); an inguinal hernia (where an organ or fatty tissue pushes through a weak spot in a surrounding muscle or tissue, in this case located in the inner groin); proportionate short stature; brachycephaly (where the skull is shorter than average); a thumb that was broad and placed closer to the wrist than is typical; and unusually large ears (Li 1998; DECIPHER).

Two people in medical literature had a 5q15 to 5q23 duplication and highlight the difficulty in predicting the outcome for a particular 5q duplication. A 4.5-year-old girl with a *de novo* 5q15 to 5q23.2 duplication had moderate developmental delay and was non-verbal. Her head was small and she had subtle unusual facial features including a prominent forehead, broad nose, unusual ears, skin folds covering the inner corner of the eye (epicanthic folds) and a protruding tongue. A boy with a similar 5q15 to 5q23.1 duplication had mild to moderate motor and intellectual delay, but normal head size and growth. He had large, low-set ears; a protruding lower lip; a long space between the nose and lip (philtrum); small genitalia; and low muscle tone (hypotonia). The only shared feature was a broad nose (Mowat 1999; Douyard 2006).

eyebrows; drooping upper eyelids (ptosis); and a short nose with a broad nasal tip were consistent features, with minor anomalies of the feet. Both sisters had a small head (microcephaly) and for both slow growth continued throughout childhood. Their mother also had a short stature. The younger sister was found to have several heart conditions: atrial and ventricular septal defects - sometimes called a hole in the heart - as well as a pulmonary stenosis, where the pulmonary valve is too small, narrow, or stiff. Both sisters had motor and learning development at the lower end of the "normal" range and needed additional help at school, while their mother struggled with learning (Zahnleiter 2011).

A three-year-old boy and his six-year-old half brother were born after uneventful pregnancies with a 5q22.1q23.2 duplication inherited from their mother. All three had a short stature to a varying degree, although none had a small head. Both boys had high arched eyebrows, thin lips, a small mouth and a short nose with a broad nasal tip. The two half brothers had a mild to severe developmental delay - the older brother had ID and attended a special school. Both brothers also had speech delay and had speech therapy (Schmidt 2013).

5q22/23 to 5q31 duplications

At least 10 people are recorded as having a duplication spanning 5q22/5q23 to 5q31, including five *Unique* members (Giardino 2004; Arens 20014; DECIPHER: Unique).

One girl with a large 15.2 Mb duplication, inherited from her father and spanning almost the whole of the 5q23 and a tiny bit of 5q31.1, is listed on DECIPHER and was described as having ID and delayed speech and language delay.

A few *Unique* babies were premature and were tiny at birth. At least two babies had difficulty feeding, including reflux, colic and difficulty digesting milk. One benefitted from special, prescribed formula milk.

In terms of appearance, a few minor unusual features were reported, including a sloping forehead, low-set or unusual ears, widely-spaced eyes, a small or receding jaw, a flat nasal bridge, short fingers and fused toes. Several children were reported to have slow growth and a few had a small head, although this may be a more common feature.

Information is limited, but a degree of developmental delay, difficulty with learning and delay in speech and language development may be relatively common. A few *Unique* children were minimally– or non-verbal. Where individuals have no speech or very few words, augmentative/alternative communication (AAC) can enhance communication and reduce frustrations. *Unique* parents used words like loving, engaging and sociable to describe their child. Several children had autistic tendencies and one had a diagnosis of attention deficit hyperactivity disorder (ADHD).

Medical concerns appear to be rare. Enlargement of the ventricles in the brain (ventriculomegaly) was reported for one child. Two children

closed spontaneously without treatment. Dysmorphic features included a mildly "sunken" breastbone (pectus excavatum (funnel chest)); small head (microcephaly); a high arched palate; low-set ears; a broad nasal bridge; and minor anomalies of the hands, including short thumbs and a mildly curved fifth finger (Zou 2010).

Sixteen individuals were listed on the DECIPHER database (four with a 5q13.2 duplication, three with a 5q13.2q13.3 duplication, seven with a 5q13.3 duplication, one with a 5q12.3q13.2 duplication and one involving 5q13.3 extending into 5q14.1, all with no other recorded genomic variant). In some cases, the origin of the duplication was unknown, but in two cases the duplication was listed as *de novo*. In seven cases the duplication was documented as being inherited from a parent; in at least two cases the parent was seemingly unaffected by the duplication. With two exceptions, each of the duplications is slightly different and the description of features is variable and incomplete. No features are known to be consistent for everyone reported, and the contribution of the duplication to any observed feature is unknown or uncertain in many cases. In terms of these individuals, only a few unusual (dysmorphic) features were noted. Two had an "unusual facial shape", one had an over-bite (retrognathia) and one had a wide mouth. A boy with a 5q12.3q13.2 duplication had a curved fifth finger (clinodactyly) and overlapping toes. There are only two mentions of global developmental delay on DECIPHER. Learning and speech appear to be the more affected areas: four individuals are known to have had a degree of learning difficulty or intellectual disability, while three were documented as experiencing speech and language delay. One child had autism and two demonstrated autistic traits. A boy listed had ADHD, while another demonstrated unspecified behaviours. As for health, there appear to be few concerns. One person experienced seizures and another had an unspecified anomaly affecting the nervous system. Another had failure to thrive and experienced stridor, where breathing is unusually noisy and high pitched.

Duplications from 5q11/12 to 5q13/14

In this group there are at least 13 people of various ages: three *Unique* members, six in medical literature and four on DECIPHER, all with no other recorded genomic variant (Yip 1989; McGillivray 1990; Rojas Martinez 1990; Breslau-Siderius 1993; Barbosa Melo 2011; DECIPHER; Unique).

Pregnancy & Birth

Information is limited, but babies may be born slightly small. A *Unique* member with a 30 Mb *de novo* 5q11.1q14.1 duplication weighed 6lb 1oz (2.7kg)) at birth. Scans during pregnancy revealed that his bladder was enlarged and he was born with mild jaundice. In medical literature, a baby with a 5q11.2q13.1 duplication had a birth weight of 6lb 3oz (2.8kg), while there was evidence of reduced fetal movements during pregnancy for a baby with 5q11q12.1 mosaicism who weighed 6lb 1oz (2.75kg) at birth.

Feeding difficulties, including reflux and constipation, have been reported, mostly in babies and younger children, and were experienced by at least two *Unique* babies.

"At birth, he was slightly jaundiced but didn't require treatment. Feeding and crying was the main difficulty for the first five months. We were told he had moderate reflux, but his symptoms were severe. He didn't like to eat and it was a challenge to get even a couple of ounces of formula down. He was prescribed Prevacid and Neocate formula to help with symptoms." - dup 5q11.1q14.1

Appearance

As for appearance, there is not enough information to say whether a particular "look" is associated with duplications in these bands. We do know that more than half of those described had low-set or unusual ears and widely-spaced eyes, while roughly one third had a prominent forehead and/or a large or prominent nose. Other unusual features are less consistent but include: a small head; a round face; downwards- or upwards-slanting eyes; skin folds at the inner corner of the eye; curved eyelashes; thin or unusual eyebrows; a small mouth; a thin upper lip; a wide, open mouth; and a small or receding jaw.

Babies may have unusual features of the hands and feet, but these are not consistent. Observed features include curved fingers (clinodactyly) and short fingers and toes. All three *Unique* members had flat feet (pes planus).

Some children and adults had reduced growth and a proportion were overweight for their height.

Development: sitting, moving, walking (gross motor skills) & hand use and coordination (fine motor skills)

Babies and children are typically delayed in reaching their developmental milestones and benefit from early intervention with occupational therapy and physiotherapy. For some the delay is mild - one *Unique* member rolled at 2 months, sat at 8 months and walked at 18 months - but others may be more severely affected. Some benefit from the use of orthotics such as support boots to help increase mobility, or may require a wheelchair for a period of time or for longer distances. Underlying low muscle tone (hypotonia) appears to be common and is associated with difficulties in carrying out gross and fine motor skills.

"As a toddler, she spent some time in a wheel chair and benefited from orthotics. She has low muscle tone but, at 16 years, she manages very well. She walks well but is often unsteady." - dup 5q11.2q13.3

"He is poorly co-ordinated with fine motor tasks and some gross motor tasks, but is getting much better." - dup 5q11.1q14.1 - 7 years

minor anomalies of the hands and feet; proptosis (a bulging eyeball); and Wolff-Parkinson-White syndrome (a relatively common heart condition that causes the heart to beat abnormally fast for periods of time due to an extra electrical connection in the heart), were reported.

It should be noted that duplication of the *LMNB1* gene, which is located in band 5q23.2 (at position 126,112,314 – 126,172,721 (genome assembly GRCh37/hg19); 126,776,622-126,837,020 (genome assembly GRCh38/hg38)), is one of the known causes of a very rare neurological disorder called autosomal dominant adult-onset demyelinating leukodystrophy (ADLD) (OMIM #169500). Duplication of *LMNB1* alone is sufficient to cause ADLD, although it has also been associated with larger duplications. As the name suggests, the main symptoms of ADLD usually become apparent in adulthood when an affected individual reaches their forties or fifties. In ADLD, there is a gradually increasing loss of white matter within the central nervous system (brain and spinal cord), which means symptoms get progressively worse over time. Symptoms include problems with movement, speech, vision, hearing, balance, the ability to eat, personality/behavioural changes and cognitive impairment (in some). Where an individual has a duplication affecting expression of the *LMNB1* gene, they should be monitored appropriately so that they can receive the appropriate support (Meijer 2008; Giorgio 2013; Dai 2017; The Leukodystrophy Charity (Alex - TLC) www.alextlc.org/).

Duplications within 5q15 to 5q31

In this group there are at least 26 individuals of various ages. All had a duplication within 5q15 to 5q31 and involving more than one band: five from *Unique*, six listed on DECIPHER and 15 in medical literature. Most of these duplications were unique, although some were inherited. All had no other recorded genomic variant (Osztovics & Kiss 1982; Evans 1984; Li 1998; Mowat 1999; Arens 2004; Giardino 2004; Douyard 2006; Zahnleiter 2011; Schmidt 2013; DECIPHER; Unique).

5q21q22 duplications

On DECIPHER, a boy or man with a 5q21.3q22.1 microduplication had intellectual disability (ID), although the contribution of the duplication was uncertain.

5q22q23 duplications

Seven people had a duplication involving 5q22 and 5q23, all recorded in medical literature. Overall, it appears that common features were short stature, some degree of developmental delay and learning difficulty (LD), a small head (microcephaly), a heart condition and characteristic facial features (Evans 1984; Zahnleiter 2011; Schmidt 2013).

A 9-year-old and her 13-year-old sister, with a 5q22.1q23.2 duplication inherited from their mother, grew slowly in the womb and were born small. In terms of their appearance, large, low-set ears; thin lips; highly arched

Duplications from 5q11/14 to 5q22

The information we have about these 5q duplications is extremely limited. In medical literature, a girl with a 5q11q22 duplication and two girls with a 5q13q22 duplication were described (Jalbert 1975; Kessel & Pfeiffer 1979; Gilgenkrantz 1981). Consistent features included developmental delay; absent speech; curvature of the spine (scoliosis); a small head (microcephaly); low muscle tone (hypotonia); and unusual facial features, including a prominent forehead, a bulbous nose and unusual ears. Two had a heart condition, in one case a ventricular septal defect (VSD) and the other hypoplasia of the ascending aorta. A boy with a 20Mb 5q14.3q22.1 duplication listed on DECIPHER had a specific learning disability, a small head and displayed autistic behaviours.

Duplications within 5q23

This band is divided into three subbands: 5q23.1, 5q23.2 and 5q23.3. At the time of writing, *Unique* had no members with a duplication involving only 5q23. The main source for information relating to individuals with a duplication involving band 5q23 alone (and with no other recorded genomic variant) was DECIPHER, where 23 people were listed, all but four with tiny microduplications of less than 0.5 Mb. The information we have is therefore very limited and there is also less information available on the development of these children. With the exception of two cases, all duplications were unique. Thirteen people had a 5q23.1 duplication, six a 5q23.2 duplication, one a 5q23.1q23.2 duplication and three a 5q23.3 duplication. Seven had inherited the duplication from a parent, and in at least one case the parent was seemingly unaffected. The contribution to any features or concerns was uncertain or unknown for nine people, but the duplication was believed to be contributory (pathogenic/benign) for at least 11 people (Unique; DECIPHER).

The descriptions available on the public part of the DECIPHER database are incomplete, but we do know that seven people were described as having cognitive impairment or intellectual (learning) disability, two with speech and language delay, one with conductive hearing impairment, and two with global developmental delay. A few were described as having unusual facial features, including an unusual face shape and a pointed chin. Two people demonstrated autistic behaviours, while two had unspecified behavioural concerns. Two others were affected by ataxia (a group of neurological disorders that affect balance, coordination and speech), one of whom also experienced seizures. Individual cases of an EEG abnormality; multiple enchondromatosis (a rare disorder that causes benign (not cancerous) growths of cartilage in the bones); recurrent infections; short stature; strabismus (a squint); myopia (short-sightedness); arthralgia (pain in the joints); insensitivity to pain; hypogonadism (when the gonads e.g. testes and ovaries, produce little or no sex hormones); telangiectasia ("spider veins");

Ability to learn

Some level of learning difficulty (LD) or intellectual disability (ID) is very likely, but the degree is really quite variable and how much support with learning is needed may only become apparent over time. The information we have suggests that individuals have experienced difficulties ranging from mild to severe.

Three *Unique* children had some degree of ID, including a teenager with an IQ of 42. A seven-year-old had the cognitive age of a three years. Information from medical literature is incomplete, but a 35-year-old woman with a mosaic 5q11.1 to q12.1 duplication was reported to have had mild LD throughout her life. An adult with a 5q11.2 to q13.3 duplication was judged to have typical development in terms of motor skills and learning, but his academic performance was reported to be below average. His uncle with the same duplication is described as having experienced difficulties with his education. Two individuals with duplications listed on DECIPHER spanning 5q11 to 5q13 had unspecified ID (McGillivray 1990; Barbosa Melo 2011; DECIPHER; Unique).

Where difficulties are milder, the best school placement may not be obvious and, depending on local provision, a child may start in a mainstream (regular) setting with support and move to a special environment as the need for extra therapies and input becomes more apparent. Others may benefit from a special school throughout their education, in order to better access the curriculum and develop to their full potential.

"At 16 years, she is just beginning to read and her writing is still at about the level of a three-year-old. She loves science, colouring and painting (and keeps within the lines) and her art/craft abilities are good. She also enjoys music, dancing, drumming and performing. She is very confident with a good sense of rhythm. She goes to music and dance classes and learns new routines and communicates well with others.

Between the ages of three and 10 she attended specialist schools. She was then home educated for two years. This went very well and I would encourage others to give it a try. When she was almost 12 she was enrolled in a mainstream school with a special learning unit. She was there for two years but that style of learning did not suit her at all. She now attends a specialist high school with pupils varying in ability from moderate to profoundly disabled.

She has become more and more able over time with a loving, supportive home and being given opportunities to do the things she loves." - dup 5q11.2q13.3

"He was in a regular day care from 9 months to three years. At three years, he entered a delayed pre-kindergarten programme for half a day and attended day care the other half. At age four, we moved him to a special day

care that included pre-kindergarten. At five years, we moved him to his current special therapy school. He receives 32 hours of ABA (applied behavioural analysis) therapy/week at this private school. His receptive language has really blossomed. He is now able to follow simple directions and we feel that he is understanding a lot of what is being said. " - dup 5q11.1q14.1 - 7 years

Speech

For many, speech is likely to be affected to some degree. Four children were confirmed to have had speech delay and four others remained minimally– or non-verbal. For one child, speech was only affected as the result of problems with hearing. An assessment by a speech therapist should be able to identify your child's specific difficulties allowing regular therapy sessions tailored to your child's areas of need. Speech therapy has proved beneficial to many *Unique* families. Similarly, hearing concerns should be acted on early.

Where individuals have no speech or very few words, communication can still be successful through augmentative/alternative communication (AAC) e.g. Makaton, signing, gesture, facial expression, Picture Exchange Communication System (PECS) and iPad communication.

" Speaks very well and her only speech impediment is due to her hearing loss. She always makes sense and is very confident. " - dup 5q11.2q13.3, 16 years

" He can repeat words and say about 10 words independently; he understands more than he can express. He will speak in phrases of two to three words, mostly when prompted e.g. "I love you" and "Hi mama". He can use an AAC device and we are slow figuring out how to help him learn to use it. " - dup 5q11.1q14.1, 7 years

Personality

Unique parents told us that their children were positive, affectionate, charming and sweet-natured. Children and teenagers enjoyed a range of activities, often relishing music and dance.

Tiredness, stress or not being able to communicate their needs could lead to challenging behaviours, such as aggressive/bad temper outbursts, stubborn refusal and self-harmful behaviours. Children seemed to enjoy socialising, but could also be over-friendly with strangers, requiring close monitoring.

Social, emotional & anxiety disorders

Several children have had a diagnosis of autism, including one *Unique* child who also had a diagnosis of attention deficit hyperactivity disorder (ADHD), and two individuals listed on DECIPHER. Where a parent believes that their child may have a specific disorder - such as an ASD or ADHD - they should consult their general practitioner/paediatrician who can refer them to a

Duplications within 5q22

This band is divided into three subbands: 5q22.1, 5q22.2 and 5q22.3. In this group there are at least 13 people with a duplication involving 5q22 alone and with no other recorded genomic variant (four *Unique* members and 9 people listed on DECIPHER). Two had a 5q22.1 duplication, seven a 5q22.2 duplication, one a 5q22.3 duplication and three a duplication involving 5q22.1 and 5q22.2. Each of the duplications is slightly different, even when the band numbers are the same, and the details we have are extremely limited. Three of the people listed on DECIPHER are known to have inherited the duplication from a parent. In at least one case the parent appears to have been unaffected. The contribution of the duplication to any observed feature was stated as unknown or uncertain in many cases (DECIPHER; Unique).

A *Unique* boy with a ~1 Mb 5q22.3 microduplication grew slowly in the womb, was born prematurely at 27 weeks and was diagnosed with growth delay and failure to thrive. He had gastro-oesophageal reflux disease (GERD/GORD), where feeds frequently and forcefully return up the food pipe from the stomach. At 27 months, he had constipation and was diagnosed with malabsorption, where the body is not able to fully absorb all the nutrients from the food that is consumed. He had global developmental delay, with hypotonia (low muscle tone) and hypermobile joints, and was considered non -verbal, although he had about 15 words between signing and speaking.

A *Unique* boy with a 5q22.2 duplication had trouble with walking and benefitted from leg braces. He also had a larger than typical head size (macrocephaly).

On DECIPHER, two individuals experienced seizures. Three others had a behavioural disorder, one with unusual fear/anxiety-related behaviour and depression, although it was unclear whether this was related to the 5q22 duplication. There were also individual reports of intellectual disability (ID), neonatal hypotonia, and obesity and a short stature, including a boy with a tiny inherited 5q22.2 duplication who was described as having an autism diagnosis with high cognitive abilities. Cases of global developmental delay (with a regression in development over time); problems with coordination and tight (contracted) Achilles tendons; a specific learning difficulty; and absent speech, were also documented. As with many other cases in this guide, the contribution of this duplication to these features was uncertain.

Note: A fourth *Unique* member with a 0.67Mb 5q22.1q22.2 microduplication was described as "bubbly, happy go lucky, pleasant, friendly, easy-going and positive". He had developmental delay, a moderate learning disability, speech delay, an autism spectrum disorder (ASD), dyspraxia and possibly ADHD. He was also overweight and, at the age of 15 years, when this guide was being produced, was found to also have a mutation in the *SIM1* gene on chromosome 6, which is linked to severe obesity and other features. The degree to which this mutation may contribute to his obesity and other features can therefore not be determined (El Khattabi 2015).

Duplications within 5q21

This band is divided into three subbands: 5q21.1, 5q21.2 and 5q21.3. In this group there were 16 people (three *Unique* members, two people in medical literature and11 people listed on DECIPHER): six with a 5q21.1 duplication, one with a 5q21.2 duplication, five with a 5q21.3 duplication, one with a duplication involving 5q21.1 and 5q21.2 and three with a duplication from 5q21.1 to 5q21.3, all with no other recorded genomic variant. Each of the duplications is slightly different, even when the band numbers are the same, and the details we have are extremely limited. We do know that in at least five cases the duplication was inherited from a parent, at least three of whom appear to have been unaffected, including a baby boy with a maternally-inherited 5q21.1q21.3 duplication who was diagnosed with the 5q duplication following prenatal testing. His mother appeared to have been unaffected by the duplication and was only diagnosed when both parents were tested following detection of the duplication in the fetus. At six months, the baby boy appeared also to be unaffected, but his development continued to be monitored (Chen 2020; DECIPHER; Unique).

A *Unique* member with a 5q21.1 duplication reached all her developmental milestones on time, except for speech (she was not talking at nearly three years). Due to parental concerns, an evaluation for autism revealed that she scored very highly in daily living skills, but her social skills and eye contact were impaired and she was diagnosed with autism. She also had sensory processing disorder (SPD). A child with SPD finds it difficult to process and act upon information received from the world around them through their senses e.g. sound, touch. This makes carrying out everyday tasks and responding to different environments challenging. Her parents found that "brushing", which may be recommended as part of a sensory therapy programme, was sometimes beneficial.

One *Unique* member with a 5q21.2 duplication had global developmental delay and was not walking at two-and-a-half years.

On DECIPHER, three people had learning (intellectual) disability, one described as moderate, and one had impaired language development. Two people experienced (unspecified) seizures, one had a severe hearing impairment and one had a small head (microcephaly). Two individuals displayed autistic traits or had an autism diagnosis.

behavioural or clinical psychologist to undergo assessment.

An uncle and his nephew described in the medical literature were both diagnosed with schizophrenia, but it should be noted that these appear to be the only cases. Schizophrenia is a mental health condition that causes a range of different psychological symptoms, including hallucinations (hearing or seeing things that do not exist) and delusions (believing in things that are untrue). Schizophrenia can be treated using a combination of medical treatments, such as antipsychotic medicines, and psychological interventions, such as cognitive behavioural therapy. Both the nephew and uncle appear to have responded well to medication. See also *Unique*'s guide to Behaviours.

"She is very sociable and friendly. She can be overly affectionate inappropriately and needs supervision in public situations. When she came to live with my family (as an eight-year-old) she was very aggressive and self destructive. There would be outbursts many times a day. Over time this behaviour diminished and now there are no issues at all." - dup 5q11.2q13.3, 16 years

"He is charming, sweet-natured, funny (he has a contagious laugh) and mostly happy, unless he can't communicate his needs. He is always on the go, very active, never stops until it is time to sleep. He loves basketball, reading books, music and going to places. He is very affectionate and loves to give kisses and get attention from people. He does not know how to self-entertain and has no interest in toys, but occasionally he will find a toy that makes some type of repetitive sound and use it obsessively, until he decides he doesn't want it anymore. He would rather get attention from a person 100% of the time.

He has been diagnosed with autism and intellectual disability. He is mainly non-verbal. He has had some self-injurious behaviour, but it has not been severe and at this age it is very minimal, if not absent. He didn't have any interest in other kids until aged five to six years. He also takes medication for ADHD." - dup 5q11.1q14.1, 7 years

Sleep

Several *Unique* parents mentioned that getting to or staying asleep could cause sleep disturbance, especially when their child was younger. The naturally-occurring hormone melatonin, which can help synchronise the body clock, was used successfully by one child, but such treatments should only be undertaken after consultation with a medical professional. Our Sleep problems in children with chromosome disorders guide, in the "Practical Guides for Families" section of our website, has further information.

Medical concerns

In terms of general health, among *Unique* members the picture was mixed.

Some parents told us that their child was susceptible to respiratory infections, asthma and/or ear infections, particularly as a baby or young child, as is the case for many children with a chromosome disorder. Major health concerns don't appear to be common or consistent, but a few children had on-going health conditions, including, in one case, those associated with curvature of the spine.

Two *Unique* children experienced a degree of hearing loss, which in one case affected speech development. Both needed treatment with aeration tubes (grommets) and while one child needed surgery to correct damage to the eardrum caused by frequent ear infections, another had an adenoidectomy to help with symptoms.

Eyesight problems have also been reported. Two children had ptosis (drooping of the upper eyelid so the eye is not fully open), one requiring surgery; two *Unique* children were long-sighted, one of whom also had astigmatism (where the eyeball is rugby ball-shaped rather than round like a football, which can lead to blurred vision) and uncontrolled eye movements (nystagmus). An individual listed on DECIPHER had a squint (strabismus).

Slight dental abnormalities are not unusual in children with chromosome disorders, and one child had over-crowding while another two individuals in medical literature had unspecified dental anomalies. One *Unique* child had "no problems since the age of 8 and perfect teeth". Two *Unique* children had a high/arched palate.

Among *Unique* children excessive drooling (sialorrhea) was common. Drooling can happen without excessive saliva production if there is difficultly keeping the mouth closed or there is an inadequate mechanism or rate of swallowing, as is sometimes the case with neurological conditions such as cerebral palsy and ID. Various treatment options are available and medication may be prescribed if necessary.

A *Unique* boy with a 5q11.1q14.1 duplication had a Chiari malformation type 1, where the lower part of the cerebellum extends below the large hole at the base of the skull, without involving the brainstem. He also experienced kidney reflux and had a very large bladder. A toddler had an unspecified urinary tract defect.

A boy with a 5q11.2q14 duplication had cardiac anomalies (an atrial septal defect (ASD) and valvular pulmonic stenosis) (Breslau-Siderius 1993). Two men in medical literature had a small penis and a boy had small testicles that were undescended at birth (cryptorchidism). One also had small testes and low testosterone levels that were increased after human chorionic gonadotropin (CG) injection (McGillivray 1990).

Growing up

Information is extremely limited, but toilet training is likely to be very delayed and may not be possible for all. We know that one girl went through puberty at the expected age and coped well with the associated changes.

Experiences of adulthood are likely to vary considerably and will depend on many factors. These include the level of any LD/ID, possible on-going medical concerns and improvements in early intervention. A 35-year-old woman with a mosaic 5q11.1 to q12.1 duplication had succeeded in finishing a professional course, although it appears that she had difficulty holding down a job. She also had a son who had not inherited the duplication.

As mentioned earlier in this guide, the DECIPHER database has cases of unaffected parents who carried a 5q duplication in this region, which they passed on to their child. These parents are likely to have only been diagnosed as a consequence of their child's investigation and would have otherwise been unaware of their duplication.

"At 16, she loves many activities such as dancing, drumming, movies, listening to and making music, family gatherings, ten pin bowling, live music and theatre if there is music involved. There is nothing she particularly does not enjoy. She is bubbly, confident, positive, affectionate and thrives on routine and familiar people. She works in the cafe at school and has learned many new things there." - dup 5q11.2q13.3

Unique has a separate guide to 5q14 duplications, which may be of interest to families with a duplication including all or part of 5q14.

Duplications within 5q15

At the time of writing, the only source for information relating to individuals with a duplication involving band 5q15 alone (and with no other recorded genomic variant) was DECIPHER, where 10 people were listed, all but three with tiny microduplications of less than 0.5 Mb and all unique. Four children had inherited the duplication from a parent and in at least one case the parent was seemingly unaffected. The contribution to any features or concerns was uncertain or unknown for seven people, but the duplication was believed to be contributory (pathogenic/benign) for three people.

The descriptions available in the public part of the DECIPHER database are incomplete, but we do know that one person was described as having cognitive impairment; another, with a 240kb duplication, had learning (intellectual) disability and demonstrated autistic behaviours, but completed his schooling and obtained a driving licence; one had hyperactivity and mild intellectual disability; one had global developmental delay and an autism diagnosis; one person had unspecified behavioural concerns; one had growth delay; and one had an unspecified hearing abnormality and had an autism diagnosis.