Unique:
The Rare Chromosome Disorder Support Group

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17th April 2012

Understanding chromosome disorders
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Genetic conditions Unique works with

- Unique works with many thousands of different rare chromosome disorders, some of them literally unique
- Chromosome disorders usually involve loss, gain or rearrangement of genetic material
- In the early 1990s, it was known that at least 1 in every 200 babies was born with a rare chromosome abnormality. New technologies are dramatically increasing the rate of diagnosis of increasingly subtle chromosome changes

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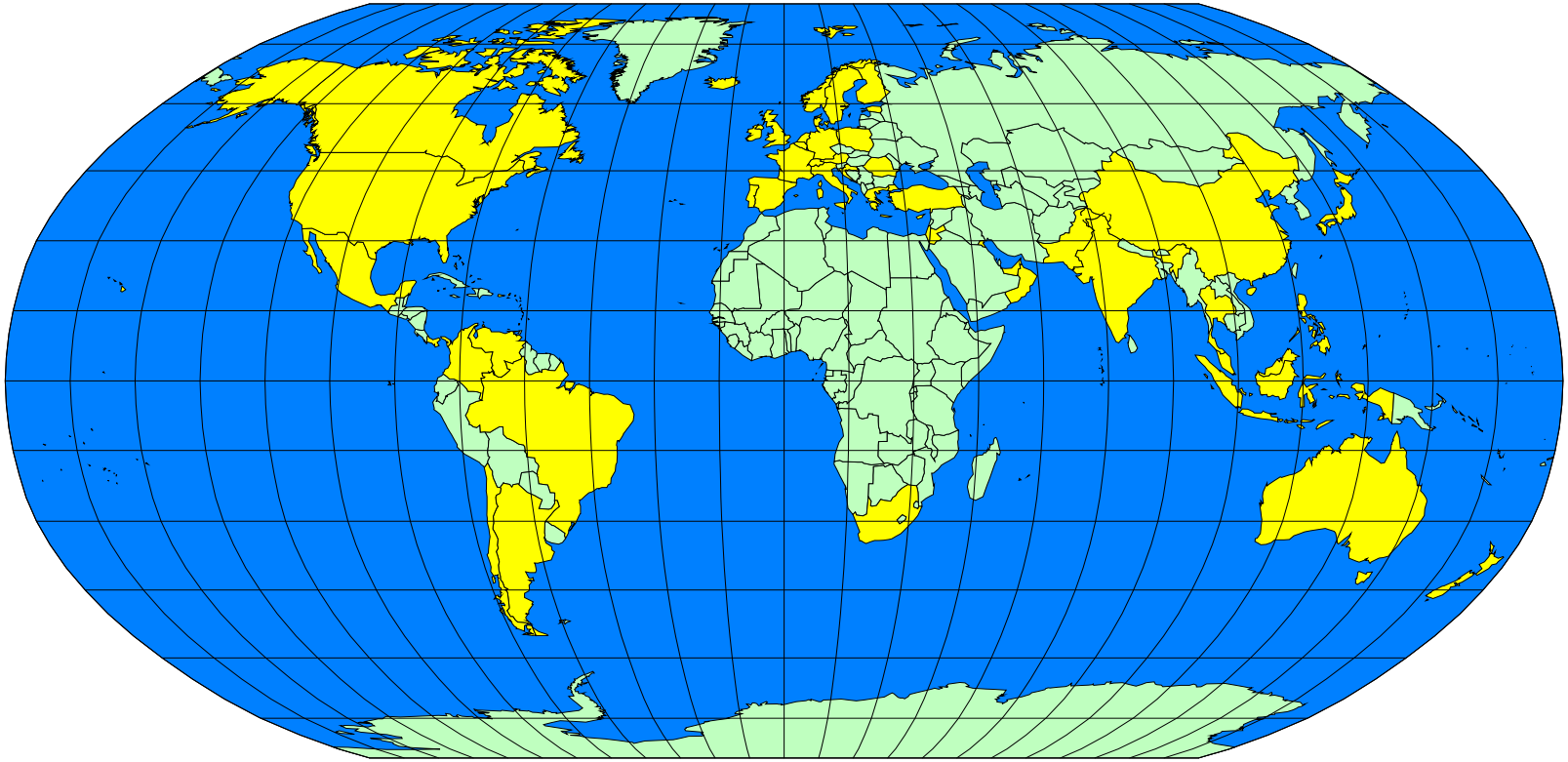
Unique membership worldwide



Over 9000 member families & professionals representing 10,000+ individuals with a rare chromosome abnormality in 85 countries at March 2012

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Impact on those affected

- A very complex set of symptoms, for example:

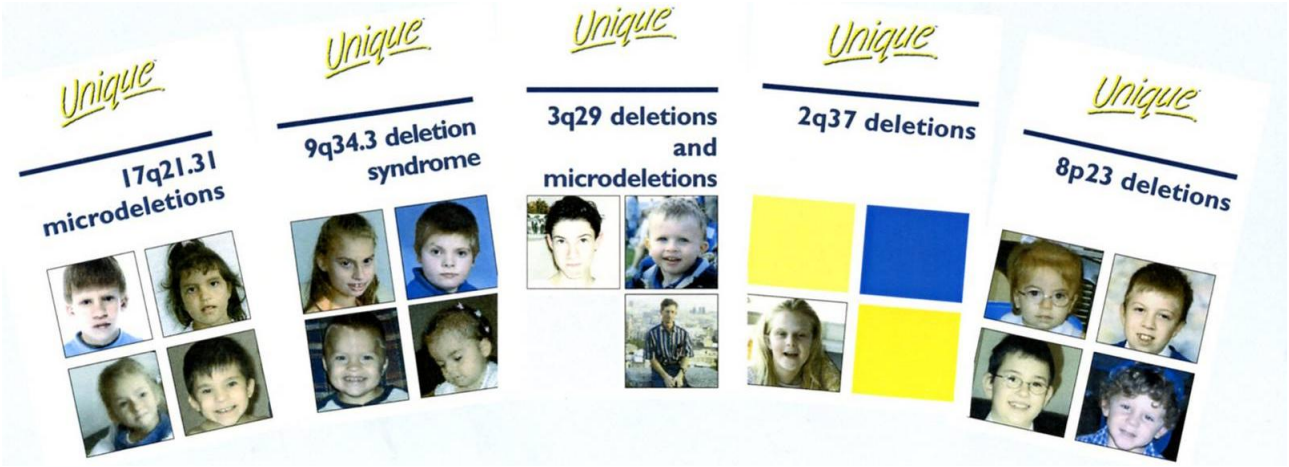
  - learning disability
  - physical disabilities
  - health issues
  - challenging behaviours
  - mental health problems

- All of the disorders we work with are lifelong disorders

- Many are severely life-limiting or even life-threatening

What does Unique do?

- Supports families
- Enables family: family contact
- Enables contact between professionals & families
- Supports professional information & guidance
- Provides syndrome-specific information



- Stimulates research

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Unique's aims and objectives

- Provide information and support to all those affected by and dealing with chromosome disorders
- Relieve the isolation of those affected by a chromosome disorder
- Become an umbrella organisation for all low-incidence chromosome disorders
- **Foster research, including using anonymised information from the database to produce leaflets and identifying medical conditions associated with 'syndromes'**

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Unique Policy and Principles for Potential Research Collaborations

- Details of any ethical approval you have received from suitably accredited internal and/or external bodies
- Details of your research proposal
- A family-friendly information sheet explaining to families the aims of your research
- An open letter to families
- Information on what samples would need to be taken
- A promise to thank participating families and to keep the families informed of progress (or lack of it) made in your research
- Where possible, co-authorship of any published papers arising from work in Unique samples/families or at the very least an acknowledgement in published papers of the help given by Unique, along with the group's contact details.
- Wherever possible, financial assistance to Unique to cover the administrative costs incurred in helping with the research project.

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Research Projects

Development of materials to help families explain to their child about a sex chromosome abnormality

Professor Dorothy Bishop; Dr Gaia Scerif; **Ms Prisca Middlemiss**; Dr Karen Melham; Dr Diana Wellesley; Dr Debbie Shears, Department of experimental Psychology, University of Oxford

2 year project funded by **Nuffield Foundation: Grants for Research and Innovation**

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Research Projects

As a conduit between families and research groups:

- Parent questionnaire on Triple X (University of Colorado, Denver. USA)
- 1p36 deletion syndrome behaviour study (Professor Chris Oliver, University of Birmingham, UK)
- Phelan-McDermid syndrome behaviour study (Professor Chris Oliver, University of Birmingham, UK)
- 1p36 deletion syndrome in adults and adolescents (Cincinnati Children's Hospital, Ohio, USA
- Research into learning and behavioural problems in children with copy number variations (CNVs) (University Hospital of Wales, Cardiff, UK)
- 22q11.2 duplications (The Hospital for Sick Children, Toronto, Canada)

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Research Projects

Advisory boards:

- **DDD (Deciphering Developmental Disorders)**
  The aim of the DDD study is to advance clinical genetic practice for children with developmental disorders by the systematic application of the latest microarray and sequencing methods while addressing the new ethical challenges raised. www.ddduk.org

- **EACH study: Evaluation of Array Comparative genomic Hybridisation in prenatal diagnosis of fetal anomalies**
  Lead by Professor Stephen Robson, Newcastle University

- **Predictive genetic testing of children for adult onset conditions**
  Lead by Dr Ingrid Holme, University of Southampton

- **Incidental findings in genetic tests**
  Lead by Gillian Crawford, University of Southampton

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Study Days

- Opportunities for families and professionals to learn from each other
- The first chance in a lifetime for most families to meet others in their own situation
- Further stimulus to research
- The chance for older families to share longer-term outcomes
- A platform for professionals to update their knowledge
- Spread of information beyond the study day

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Study Days

Study days we have run:

- Triple X
- XYY
- 1p36 deletion syndrome
- 2q37 deletions
- 4q deletions
- 8p23 deletions
- Kleefstra syndrome (9q34 deletions)
- Pallister-Killian syndrome


XXY study day report

Families with a daughter with Triple X syndrome – a single extra X chromosome – met experts and researchers at a study day in Oxford, UK in September 2007. They heard what is already known from research conducted on girls and women with Triple X who were recruited in the 1960s and they were invited to tell researchers from the Sex Chromosome Trisomy study group what they would like the new study, launched this summer in the UK, to focus on. The findings from the study day will help to sharpen the focus of the study, which is looking at behaviour and learning in girls and boys aged between 4 and 16 with Triple X, XYY and XXY (Klinefelter syndrome).

Genetics of Sex Chromosome Trisomy: Professor Pat Jacobs

Pat Jacobs, Professor of Human Genetics at the Wessex Regional Genetics Laboratory, told families that they owed both the study day and the Sex Chromosome Trisomy study to the fact that she had shared a long taxi ride with Helen Clements, who runs the UK Triple X support group, and her daughter Megan and realised how little we in Britain were doing for both girls with Triple X and boys with XYY (an extra Y chromosome).

What is that blob?

Professor Jacobs then took families back to the 1950s, before chromosomes were identified, when an astute microscopist noticed a blob in the nucleus of cells in females but not in males (Slide 1). By analogy with the fly Drosophila, scientists assumed that the blob was two X chromosomes. However, in the early 1960s, Professor Jacobs looked at the chromosomes of a woman with Triple X and saw not one, but two blobs. What was then to be revealed was that when humans have two X chromosomes only one is fully working and the second one curls up on the edge of the cell to form a blob. That is true however many extra X chromosomes a person has. So a single blob was the second of two X chromosomes and a nucleus without a blob had only one X chromosome. To discover how many X chromosomes someone has, you count the blobs and add one.

Professor Jacobs then moved on to the six newborn studies that form the basis of almost everything that is known about children and adults with a sex chromosome trisomy. In the early 1960s, all babies born at six centres worldwide – in Denmark, Scotland, two centres in Canada and two in the US – had a blood sample taken and their chromosomes analysed. From a total of some 60,000 babies it was found that each of the three sex chromosome trisomies - Triple X syndrome, XYY and XXY - occurs at a rate of around 1:1000 sex matched newborn babies. But what has happened before birth? She reminded families that not all babies are born alive, some miscarry (15-25 per cent of clinically recognisable pregnancies) and a very much smaller number (around one per cent) are stillborn. Looking at the three groups of babies with

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Future research

- Increasing sensitivity of testing (array CGH and next generation sequencing) will result in an increase in diagnosis of rare chromosome disorders

- More research is needed to determine in more detail the impact of these smaller chromosome changes

Any Questions?

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