

# DECIPHER: A database of genomic disorders

## SUMMARY

New genetic tools are increasingly being used to diagnose chromosomal abnormalities in children with developmental disorders. The DECIPHER database, set up at the Wellcome Trust Sanger Institute, is enabling clinicians across the world to share information about their patients, helping both individual patients and researchers unpicking the basis of human genomic disorders.



## Background

When a young child shows signs of developmental delay, or physical or behavioural abnormalities, paediatricians can often make a diagnosis based on the child's physical appearance or symptoms. If a genetic cause is suspected, karyotype analysis – inspection of chromosomes under the microscope – is usually undertaken to pinpoint chromosomal abnormalities. Often, though, this analysis fails to turn up anything unusual.

In recent years an alternative approach has appeared – DNA microarray analysis. This technique sweeps the entire genome for chunks of DNA that have been duplicated or are missing (so called copy number variation). Currently a diagnosis can be made in around 20 per cent of unexplained cases, a proportion that is expected to rise as the technology becomes more sophisticated.

There is great value in being able to provide parents with a diagnosis. As well as being able to guide clinical care, a diagnosis can be comforting – parents at last have an explanation for their child's condition and can be reassured that they were not in any way to blame. It may also reveal whether they are at risk of having another affected child.

## Advance

DECIPHER (Database of Chromosomal Imbalance and Phenotype in Humans using Ensembl Resources), based at the Wellcome Trust Sanger Institute at Hinxton near Cambridge, was set up to enable clinicians to share information about copy number changes in patients.

It was set up in 2004 by Nigel Carter of the Sanger Institute and Helen Firth, a clinical genetics consultant at Addenbrooke's Hospital in Cambridge. Clinical geneticists from anywhere in the world can register and, having obtained consent from patients and their families, record clinical symptoms and the type of DNA change detected. More than 100 centres worldwide have registered to date.

Dr Carter has pioneered DNA microarray technology used to pinpoint copy number variation while Dr Firth was one of the first to apply the technology in clinical practice. The database also draws on the extensive computing expertise of the Sanger Institute.

## How it's making a difference

For clinicians, identifying a case similar to their patient's own is an important check that a rearrangement is actually causing the symptoms – everyone's genome has some copy number variation, most of it harmless.

Furthermore, global sharing of information can help clinicians to define new syndromes. A small deletion on chromosome 17, for example, was identified in three cases – two from Cambridge and one from Brazil. A similar cluster of cases, this time two from Vancouver, Canada, and one from Cambridge, revealed a new syndrome linked to loss of part of chromosome 14.

As well as revealing which areas of the genome are vulnerable to damaging copy number variation, the database also highlights candidate genes – those within the deletion or duplication that might be causing the clinical abnormalities.

Moreover, chromosomal rearrangements often eliminate several genes, each of which could be having some effect on phenotype. As cases build up, syndromes can be fine-mapped, to identify which of the genes affected are responsible for which aspects of a complex syndrome.

Information is displayed within the Ensembl genome browser, providing access to all the data associated with the region of the genome affected. As understanding of the genome increases, it will also be possible to identify other genomic regions that, while not causing a given syndrome directly, affect how a child develops.

More generally, DNA microarray analysis – pioneered at the Sanger Institute – is beginning to be widely used in clinical practice. Many medical genetic centres are using microarrays as an adjunct to karyotype analysis, but at least one centre has already abandoned karyotypes in favour of microarrays.

## References

<https://decipher.sanger.ac.uk/>

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