



Lin is one of a team of scientists investigating the genetics of childhood developmental disorders. The team is sequencing the genomes of 12,000 children with developmental disorders and their parents. They are looking for genetic differences that the families have in common which could be linked to these disorders.

Lin has discovered that one of the children in the study has a mutation that means he is at risk of developing a rare eye cancer called retinoblastoma. She desperately wants to tell the child's parents so that the child can be monitored and treated if there are the slightest symptoms. If the cancer develops, the child could lose an eye, or worse. But the study's strict ethics policy means she is not allowed to share incidental findings like this with the study's volunteers. She has discussed the situation with her colleague Pat, who is adamant that she should stick to what is in the ethics policy.

What should Lin do?

Genetics is so complicated that it's inevitable that we'll find things unrelated to the study that could be important to some of the volunteers. At the moment, we've agreed not to share incidental findings, most of the time we would just be creating anxiety for nothing. Whatever the circumstances, we cannot allow the scientists to make such decisions on their own.

Being part of this study feels like our last hope to help our son – he's had test after test but the doctors haven't been able to give us many answers. They've told us that they will only talk to us about things they find that are connected to his developmental disorder. But if they did come across something else that could be serious, I'd want to know.

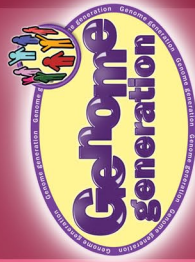
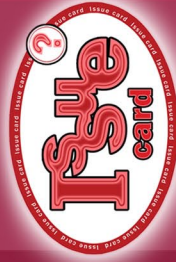
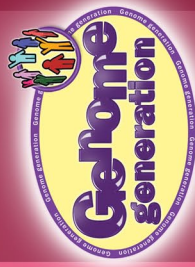
Parent of a child in the study

**John
(Chair of ethics committee)**

Of course I am a bit uncomfortable with not being able to share this information with the parents, but, hard as it may sound, ultimately I do think it is the right thing. Our volunteers are having genetic counselling about their child's developmental disorders through the NHS and we don't get involved in this.

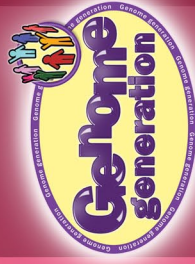
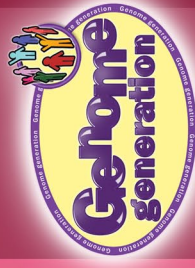
**Pat
(Lin's colleague)**

Lin



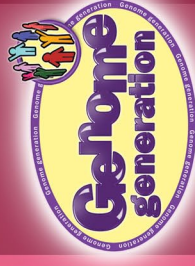
With regards to incidental findings, where should the study draw the line? Should it share all incidental findings with volunteers, just certain findings, or none?

Who should decide what to tell families in the study? Do the parents have the right to know?



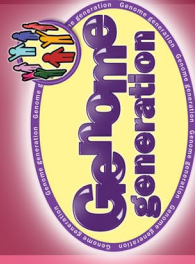
If genetic counselling was provided to all participants about everything their genomes might reveal, it would be very costly and time consuming. Would this compromise the original research?

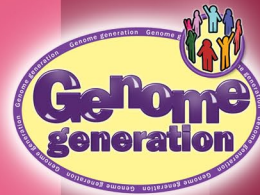
What will be the impact to any siblings of the child in question?



Since incidental findings were not intended to be shared, parents may not have received appropriate counselling to prepare them. How might it affect the parents if the news came out of the blue?

What if the test reveals a false positive? What impact would the unnecessary worry have on parents who are already raising a child with additional care needs?

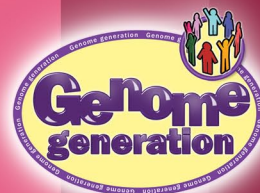




Our genes

Most of the DNA in human cells is packaged into 46 chromosomes, in 23 pairs. Our genes are arranged along these chromosomes and carry the instructions to make molecules, such as proteins. To function properly, each cell depends on thousands of proteins doing the right job, in the right place, at the right time. Our complete set of DNA containing all the instructions required to make us is called a genome.

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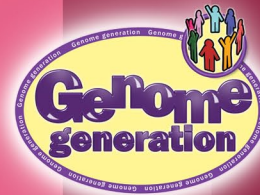


Gene mutations

A mutation is a permanent change in the DNA sequence. Mutations come in a number of different forms and can change the functioning of our genes. Some mutations may lead to a difference in the amount, or structure, of a protein produced by specific genes. Some mutations may switch genes on at the wrong time. This may prevent a protein from doing its job, or it might change the way it does its job.

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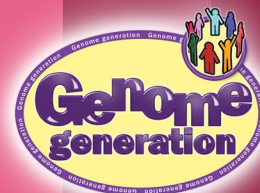




What are developmental disorders?

The term 'developmental disorder' describes a whole range of childhood problems, including issues with growth, birth defects, and learning and behavioural problems. Some are associated with deleted sections of specific chromosomes, but for many more, the underlying genetic cause is unknown.

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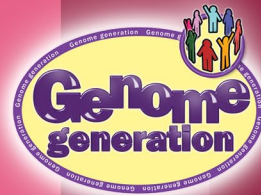


What is retinoblastoma?

Retinoblastoma is a rare childhood cancer of the retina in the eye. It occurs in children under the age of five when growth of the retina is at its fastest. In the UK, 40-50 cases are identified each year. Although the cancer can be fatal, UK treatment has a 98% success rate.

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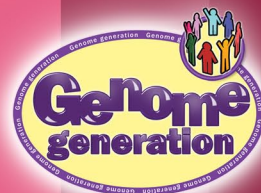
The *RB1* gene

Retinoblastoma is caused by mutations in the *RB1* gene; both copies of *RB1* must carry a mutation for the cancer to develop. 90% of people with mutations in both copies of the gene will develop the disease. Affected individuals are likely to develop tumours in both eyes and have a higher risk of cancer in other areas of the body in adulthood.

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Genetic tests for retinoblastoma

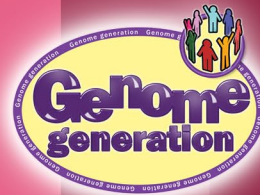
There are three types of genetic tests for retinoblastoma:

- Comparing genes from different family members to identify the altered version.
- Looking for visible changes to chromosome 13 (where the gene is located).
- Looking for changes in the *RB1* gene itself. This can be a lengthy process. Even with careful study the test only picks up 90% of mutations.

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Incidental findings

Genome analysis for any condition will always produce incidental findings. On average, each person's genome contains around 100 different things of interest. Ethicists have calculated that counselling someone through all of this would take around five hours.

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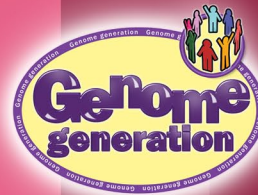


Treatment for retinoblastoma

Retinoblastoma is diagnosed and monitored through eye examinations which are usually carried out under general anaesthetic. Treatments range from laser therapy, to removal of the tumour from the affected eye(s). Families with the disease are offered specialist genetic counselling to help them through the complex decisions they face.

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False positive tests

Genetic tests are used to predict disease but they are not 100% accurate. If evidence of genes that can cause disease is found, the result is said to be positive. If the relevant genes are not found, the result is said to be negative. Occasionally, false results occur when genes are present but not detected (false negatives) or shown to exist when they do not (false positives).

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Our DNA

Our bodies are made up of around 50 trillion cells. Most of these cells contain a person's genetic information within a long molecule called DNA (deoxyribonucleic acid). This DNA contains the genetic information that we inherit from our parents.

DNA is made up of specific sequences of letters or bases that encode instructions on how to make proteins. These bases [Adenine (A), Guanine (G), Cytosine (C) and, Thymine (T)] are lined up along two strands of DNA. The DNA is coiled into a double helix structure that resembles a twisted ladder.

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