

# Predictive Genetic testing for Inherited Cardiac Conditions in Children

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# Overview

- What is Genetic counselling and predictive genetic testing?
- What ICC's do we commonly offer predictive testing for?
- Genetic Counselling appointment
- Tools used in Genetic Counselling
- Providing results
- Challenges

# What is genetic counselling?

The aims of genetic counselling are to help the individual or family to understand:

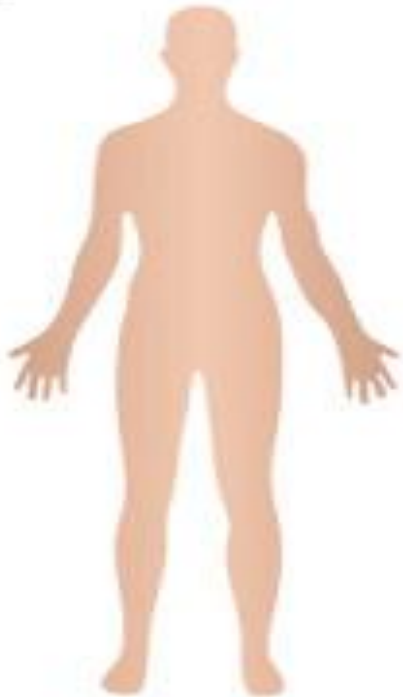
- information about the genetic condition
- the inheritance pattern and risk of recurrence
- options available to them

and helping them to:

- make decisions appropriate to their personal and family situation
- make the best possible adjustment to the disorder or risk.



# Introduction to genetics



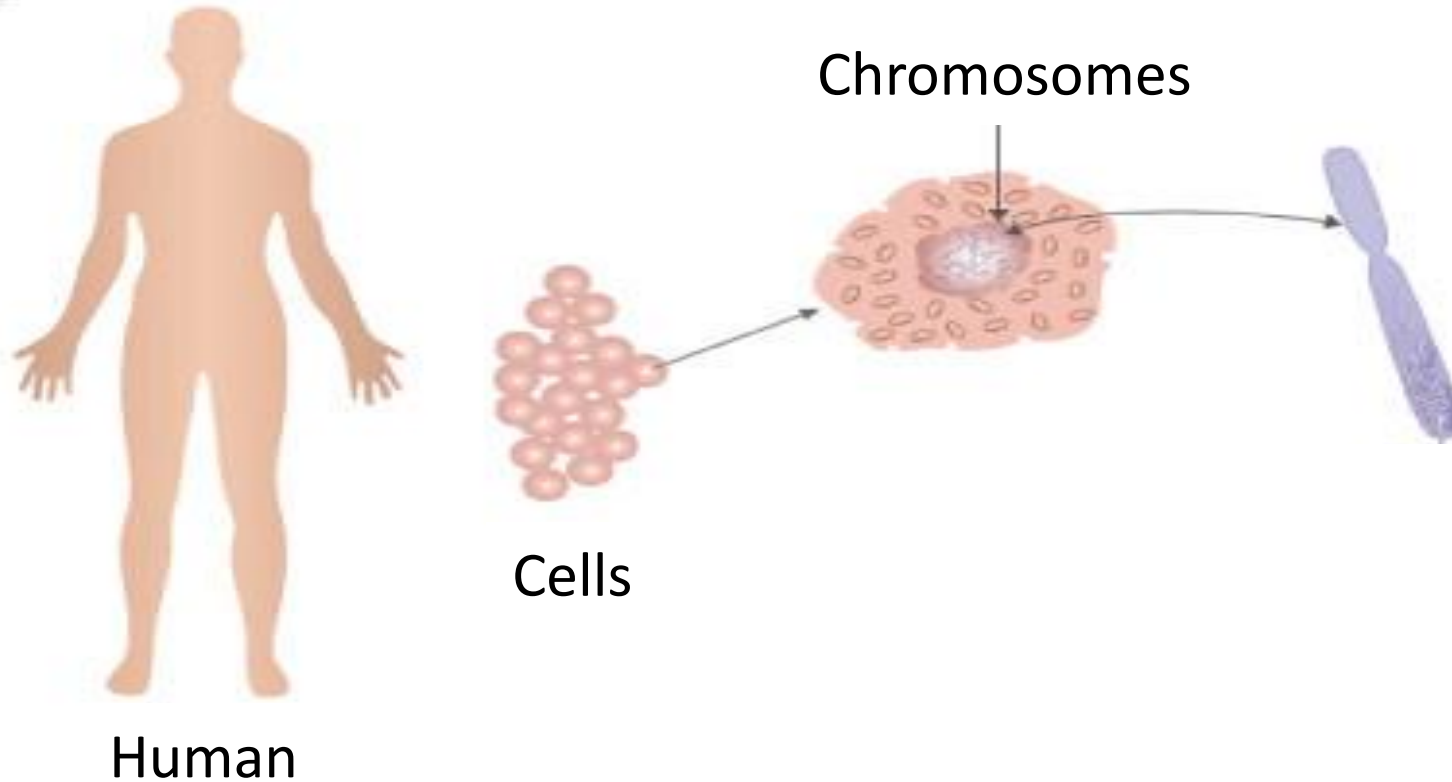
Human



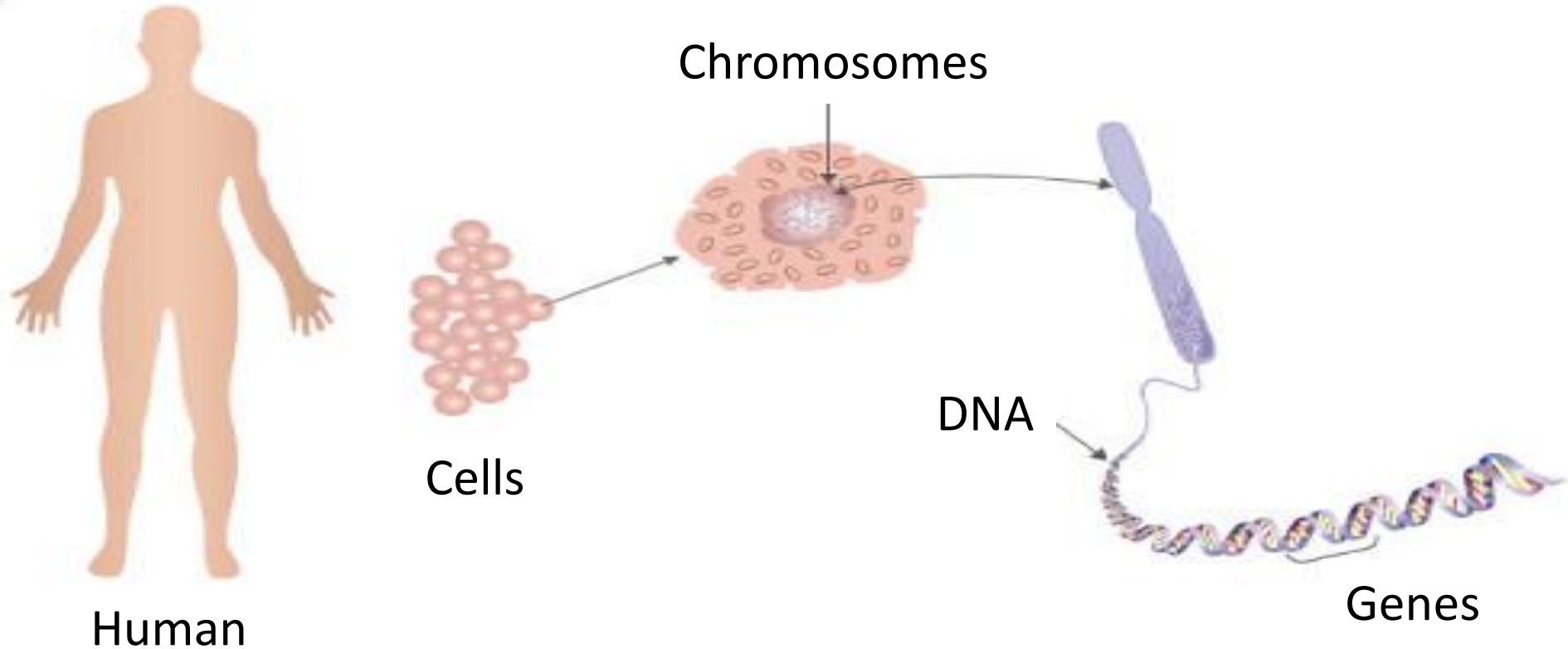
Cells



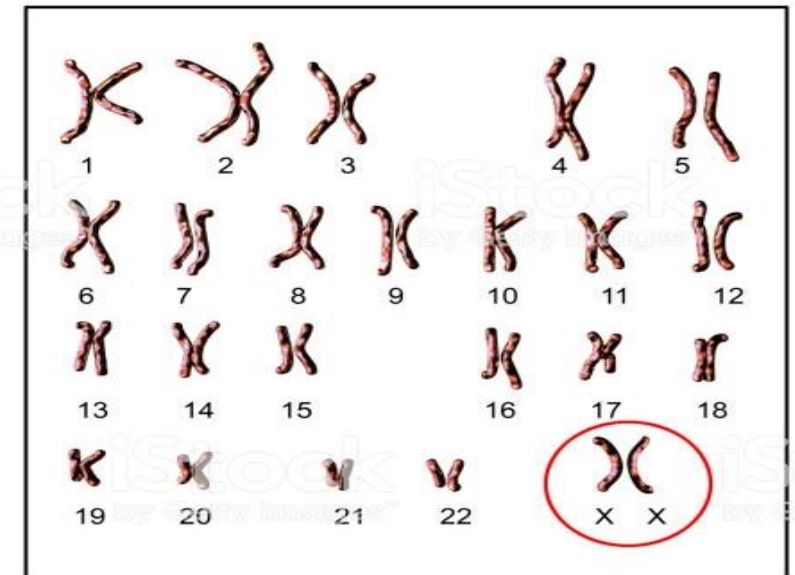
# Introduction to genetics



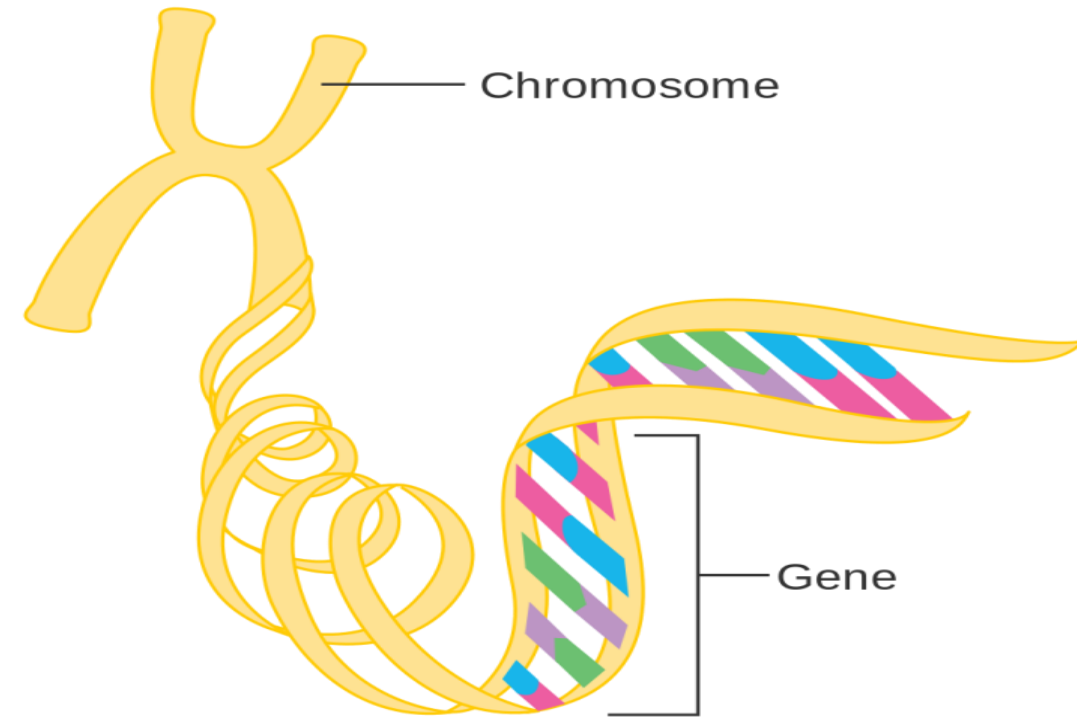
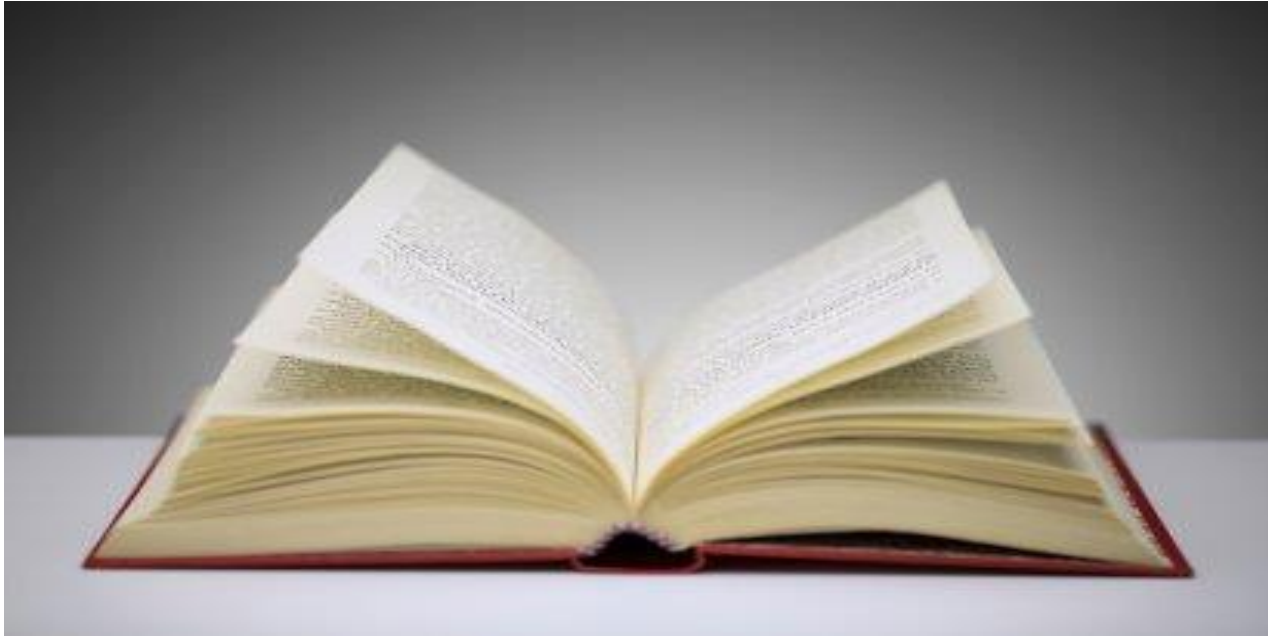
# Introduction to genetics



# Chromosomes



# Diagnostic testing





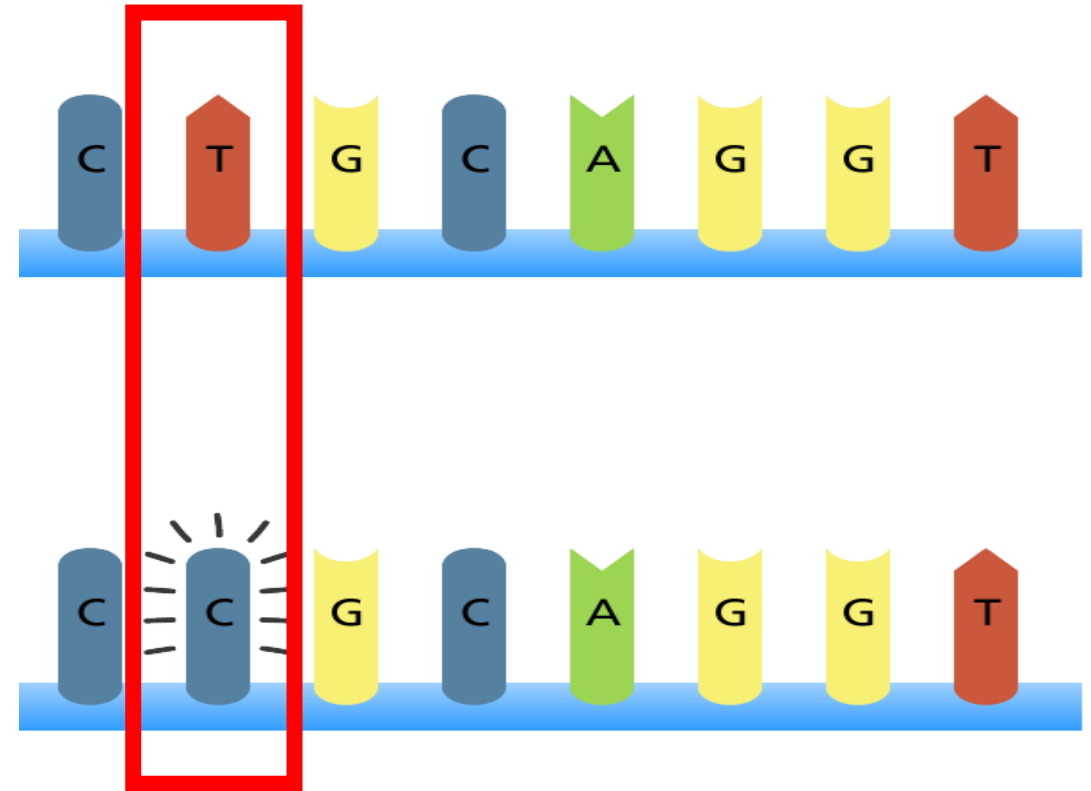
# Possible test results

Positive-  
pathogenic  
variant

Uninformative-  
no variants  
identified

Variant of  
uncertain  
significance  
(VUS)

# Predictive testing



# Predictive Genetic testing

- A predictive genetic test can provide information about whether or not someone will develop or is likely to develop a specific condition, usually at a later stage in life- *Genetic Alliance UK., 2020*
- If there is a known **pathogenic variant** in a family then at risk relatives can have a predictive genetic test to see if they have inherited that variant or not.
- Predictive genetic testing only looks for the variant identified in the family. It **DOES NOT** look at other genes/variants.

# Predictive Genetic testing in children

- British Society for Human Genetics., 2010 - unless testing has current medical benefit, it should be deferred until a child is old enough to make her/his own decision
- Cascade predictive genetic testing in ICC's can assist with:
  - early diagnosis
  - initiation of preventative treatment, protecting individuals from arrhythmic events and potentially improving cardiac outcome.
- Determining the optimal time to perform predictive genetic testing in children is complex and involves balancing the ethical principles of beneficence, nonmaleficence, autonomy, and informed consent.

# Predictive genetic testing for ICC's at the Liverpool Centre for Genomic Medicine

- No UK consensus on predictive testing for ICC's
- UK centres are doing things differently
- This can be tricky if relatives live elsewhere in the UK

# What conditions?

- Hypertrophic Cardiomyopathy (HCM)
- Dilated Cardiomyopathy (DCM)
- Arrhythmogenic Cardiomyopathy (AVC)
- Long QT syndrome (LQTS)
- Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)
- Brugada Syndrome

# Hypertrophic Cardiomyopathy (HCM)

- Predictive test usually offered around 10 years of age

The European Society of Cardiology's position statement and the Australian and New Zealand guideline recommend deferring predictive genetic testing until after 10 years of age for these conditions when the likelihood of onset is higher, cardiac screening is recommended and assent may be possible *Ingles Jet al.; CSANZ Cardiac Genetic Diseases Council Writing Group. Guidelines for genetic testing of inherited cardiac disorders. **Heart Lung Circ.** 2011; 20:681–687. doi: 10.1016/j.hlc.2011.07.013*

# Dilated Cardiomyopathy (DCM)

- Predictive testing offered in childhood
- Work with family around timing



# Arrhythmogenic Ventricular Cardiomyopathy (AVC)

- Discussion with family

The European Society of Cardiology's position statement and the Australian and New Zealand guideline recommend deferring predictive genetic testing until after 10 years of age for these conditions when the likelihood of onset is higher, cardiac screening is recommended and assent may be possible *Ingles Jet al.; CSANZ Cardiac Genetic Diseases Council Writing Group. Guidelines for genetic testing of inherited cardiac disorders. Heart Lung Circ. 2011; 20:681–687. doi: 10.1016/j.hlc.2011.07.013*

# Long QT

- From birth
- Cord blood sample if possible

A consensus statement by the Heart Rhythm Society and the European Heart Rhythm Association recommends offering predictive genetic testing as early as infancy for children at risk of long QT syndrome (LQTS) because of possible early onset of the condition and because the result may directly impact medical management with the initiation of  $\beta$ -blocker therapy. Ackerman MJ et al.. HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies this document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). **Heart Rhythm**. 2011; 8:1308–1339. doi: 10.1016/j.hrthm.2011.05.020

# Catechloaminergic Polymorphic Ventricular Tachycardia (CPVT)

- Predictive testing offered in early childhood
- Work with family around timing

# Brugada

- Test as late as possible in childhood
- If familial variant not detected- will still request ajmaline

# Pre Genetic Counselling clinic appointment

Telephone/video appointment with parents to discuss:

- Timing of testing
- Family experiences
- What does the child know
- Terminology used
- Siblings
- Blood sample/saliva sample- when not in COVID 19 pandemic

# Genetic Counselling appointment

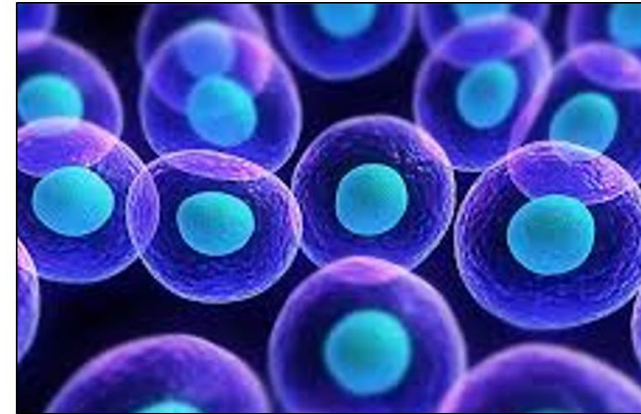
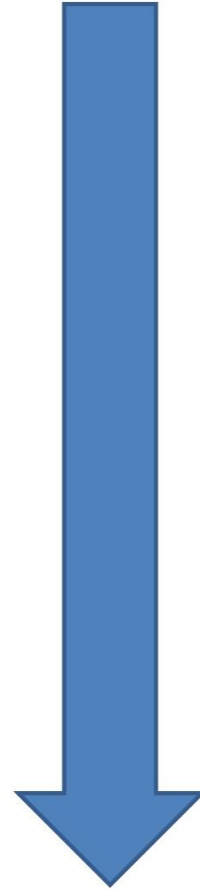
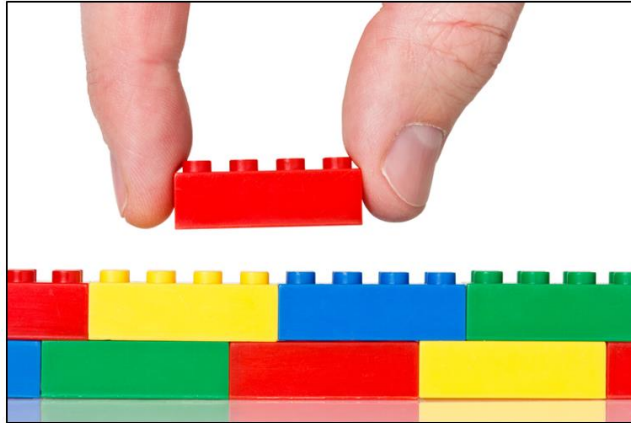
- What does the child know
- Overview of condition, genetics and inheritance
- What it means if they have/haven't inherited the gene alteration
- Insurance
- Career
- Lifestyle
- Siblings
- Support groups/friends
- Reproductive options
- Consent/assent

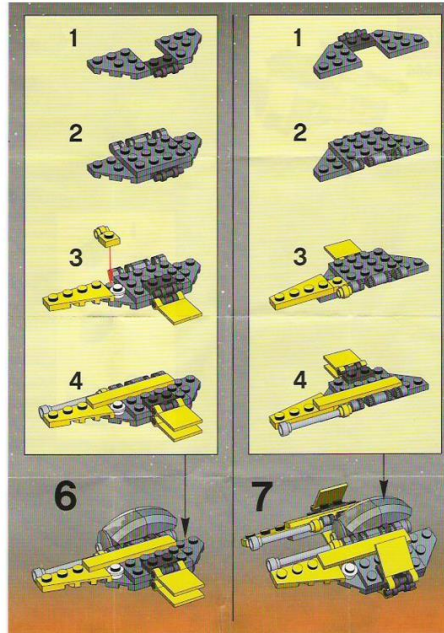
# Myth busting

- It only affects girls
- I am the eldest so I will have inherited it
- All the boys in the family have got ICD's
- It skips a generation

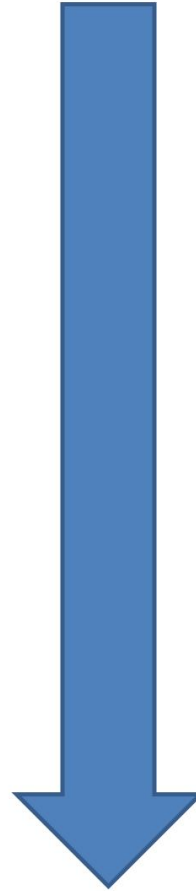
# Tools used in Genetic Counselling clinic







Each step within the set of instructions makes a part which the millennium falcon needs to work.



Each gene within our DNA makes a protein which our bodies need to work.

## Adult consent form

Please initial what you agree to:

### Testing Now

1). I agree to the analysis of the sample for: \_\_\_\_\_

☐

### Sample Storage

2). I agree to the sample being stored in case future checks or tests are needed

☐

### Further Testing

3). I am happy for further diagnostic tests on the stored sample to be undertaken without being contacted

☐

### OR

4). I would like to be contacted before further tests are done on the stored sample if new tests become available

☐

### Sharing Results

5). I agree that information and test results may be shared to help other family Members.

☐

Please confirm your agreement by adding your signature to this form below:

Signed .....  
(Patient/Parent)

Date .....

## Paediatric assent form

### Childs assent

Do you understand the reason for this test? Yes/No

Do you agree to this test? Yes/No

Have you asked all the questions you wanted to? Yes/No

Signed .....  
(Patient)

Date .....

# Results

- Predictive test result take ~4 weeks
- Who will provide results
- Type of appointment
- If siblings are tested who will receive results first
- Timing of results- are they near exams/Christmas?

# Challenges

- Relatives tested in another centre
- No contact with the child
- Testing siblings at the same time
- Parents not wanting to tell the children what the test is for

# Referrals

- Children – Genetic Counsellors at Liverpool Centre for Genomic Medicine based at Liverpool Women's hospital

[lwft.clingen@nhs.net](mailto:lwft.clingen@nhs.net)

- Adults- Genetic Counsellors at Liverpool Heart and Chest hospital

# Questions?

