

## Genetic testing for LQTS Information for referring physicians



The Molecular Genetics Laboratory of VCGS Pathology (located on the 10th floor Royal Children's Hospital) is offering genetic testing for Long QT syndrome (LQTS).

### Who can order LQTS gene testing?

Cardiologists with expertise in LQTS and genetic counsellors/clinical geneticists working in association with cardiologists clinically responsible for the patient.

### Who is eligible for genetic testing?

- Patients with a definite or highly probable diagnosis of Long QT syndrome. Cases that fall outside these criteria can be discussed directly with Dr Andrew Davis, Dr Jitu Vohra or Ivan Macciocca (contact details below).
- Relatives from families in which a disease causing mutation has been identified who are seeking predictive or confirmatory testing.

### What should I discuss with the patients before a sample is drawn for genetic testing?

Patients need to be made aware of the advantages and disadvantages of genetic testing. A fact sheet for clinicians that outlines some of the issues to discuss with patients before testing is organised is attached. Patients can be referred to a [clinical genetics service](#) for discussion prior to testing.

### Genetic testing protocol for index cases.

- The coding regions of KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2 and KCNJ2 will be tested by direct sequencing. MLPA (which tests for large gene deletions & duplications) will also be performed on KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2 in all index cases.
- Approximately 75% of cases of definite LQTS will have a mutation identified using this testing procedure.
- A turn around time of approximately 3-4 months is expected.

### Sample requirements:

- For index cases (**mutation detection**): 2 x 5-10mls of EDTA blood:
- For *asymptomatic* relatives from families with a known disease-causing mutation (**predictive gene test**): 2 x 3-5mls EDTA taken on two separate occasions (ie two venepunctures).
- For *symptomatic* relatives from families with a known disease-causing mutation (**confirmatory gene test**): 3-5mls EDTA.

### Shipping details:

Molecular Genetics Laboratory  
VCGS Pathology, Specimen reception  
9<sup>th</sup> Floor, Royal Children's Hospital  
Flemington Road, Parkville, Victoria 3052  
Ph: 03 8341 6275

Blood should arrive within 3 days of collection. If necessary it can be refrigerated but do not freeze.

Processing of samples will not begin until we receive:

- completed referral form including  
Including patient demographics, clinical summary, original or good quality copy ECG, family history
- signed consent form (see attached)

NB: please ensure you use the correct consent for

### Cost:

- Sequencing of KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2 and MLPA of KCNQ1, KCNH2, SCN5A, KCNE1 and KCNE2: \$3500
- Sequencing only of KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2: \$2950
- Brugada Syndrome (SCN5A – sequencing & MLPA): \$1800
- Anderson Syndrome (KCNJ2 – sequencing): \$450
- MLPA (KCNQ1, KCNH2, SCN5A, KCNE1 and KCNE2): \$550
- Testing for a known family mutation (predictive or confirmatory) - \$250

- KCNQ1 (sequencing): \$890
- KCNH2 (sequencing): \$1000
- KCNE1 (sequencing): \$300
- KCNE2 (sequencing): \$300
- SCN5A (sequencing): \$1650

**An invoice will be sent after the test is completed unless otherwise indicated**

### More information:

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Paediatric Electrophysiologist  
Cardiology Department  
Royal Children's Hospital  
Flemington Rd Parkville VIC 3052  
p: 03 9345 5713 f: 03 9345 6001  
andrew.davis@rch.org.au

A/Prof Jitu Vohra  
Adult Electrophysiologist  
Cardiology Department  
Royal Melbourne Hospital  
Parkville VIC 3050  
p: 0412 053 283  
p: 9429 9787 (consulting rooms)  
f: 03 9817 1468  
jitendra.vohra@mh.org.au

Ivan Macciocca,  
Genetic Counsellor  
Genetic Health Services Victoria  
Royal Children's Hospital  
Flemington Rd Parkville VIC 3052  
p: 03 8341 6373 f: 03 8341 6390,  
ivan.macciocca@ghsv.org.au

## What is Long QT syndrome?

- ◆ A patient [fact sheet](#) about Long QT syndrome can be obtained from the Better Health Channel

## Genetic testing

- ◆ The majority of LQTS families have a unique disease causing mutation. For any given family, the first step in the genetic testing process is to identify this unique or “family specific mutation”. This step is called **MUTATION DETECTION** and is performed on an **AFFECTED** person in the family and takes **3-4 months**.
- ◆ Once a mutation is identified in an affected person, unaffected at-risk relatives can be offered testing to determine if they have inherited the family specific mutation. This is called **PRESYMPTOMATIC** (or predictive) testing, and must be performed through a clinical genetics service in order to satisfy National Pathology Accreditation Advisory Council (NPAAC) guidelines. Confirmatory testing of an affected person from a family with a known mutation can be performed by cardiologists or genetics services. Presymptomatic and confirmatory test results take about **4-6 weeks**.

## Interpretation of mutation detection results (from an index case):

- ◆ Our laboratory will test the genes associated with LQT1, 2, 3, 5, 6 & 7. These genes account for approximately 70% of definite LQTS cases.
- ◆ In approximately 3-5% of cases, more than one mutation will be identified in either the same gene (compound heterozygotes/homozygote) or in more than one gene (double heterozygotes). This may influence the genetic risk to relatives of the affected person.
- ◆ There are 3 possible outcomes of genetic testing:
  1. **A disease-causing mutation is identified.** In this circumstance, at risk relatives can be offered presymptomatic testing.
  2. **No mutation is identified.** This is a negative result. The diagnosis of LQTS cannot be excluded and at risk relatives will need to continue to be surveyed. The samples of individuals that receive a gene negative result will be stored and may be tested for other LQTS genes as these genes are set up in the laboratory as resources permit.
  3. **A sequence variation of unknown significance is identified.** In this circumstance, it is standard practice to invite at risk relatives to be clinically evaluated. Those relatives found to be affected can be tested for the sequence variation in the proband to help determine the likely pathogenicity of the sequence variation (co-segregation studies).
- ◆ **At the time of issuing the result, genetic counselling support will be available to both requesting clinicians and families.**

## Ethical and psychosocial issues:

- ◆ **Insurance:** many insurance companies are asking applicants if they have had a genetic test. The genetic test result should not change circumstances for individuals with a definite diagnosis of LQTS, as they would have to declare their affected status. However, it might affect the ability of other relatives to obtain some types of insurance. A fact sheet about insurance and genetic testing is available from the [Investment and Financial Services Association](#) (IFSA).
- ◆ **Psychological impact:** there is very little research on the psychological impact of genetic testing for LQTS. Some individuals may feel distressed, uneasy or guilty about the possibility of having passed on a genetic alteration to their children that could cause LQTS. Genetic counselling is available to those individuals. Counselling of patients will help to understand the potential psychosocial impact on individuals undergoing mutation detection.
- ◆ **Medical aspects:** the presence of a disease-causing LQTS mutation may help guide management but does not enable prediction of disease onset or severity in gene positive individuals in the family. There is considerable variability in disease expression even between individuals in the same family with the same mutation. More information about gene specific management is available through the [Cardiac Inherited Disease Group](#) (CIDG) in New Zealand.

## Patient referral form

must be completed for any patient having LQTS testing



GENETIC HEALTH | VCGSPATHOLOGY  
Victorian Clinical Genetics Services

### Box 1: Patient demographics

First name: \_\_\_\_\_ Surname: \_\_\_\_\_

DOB: \_\_\_\_\_ Sex: M / F Address: \_\_\_\_\_

Suburb: \_\_\_\_\_ State: \_\_\_\_\_ Postcode: \_\_\_\_\_

Ph: home: ( ) \_\_\_\_\_ business: ( ) \_\_\_\_\_ mobile: \_\_\_\_\_

If less than 18 years, name of parent/guardian: \_\_\_\_\_

Parent phone: home: ( ) \_\_\_\_\_ business: ( ) \_\_\_\_\_ mobile: \_\_\_\_\_

#### Referring doctor details:

First name: \_\_\_\_\_ Surname: \_\_\_\_\_

Address: \_\_\_\_\_

Suburb: \_\_\_\_\_ State: \_\_\_\_\_ Postcode: \_\_\_\_\_

Phone: \_\_\_\_\_ fax: \_\_\_\_\_

Email: \_\_\_\_\_

### Box 2: Patient's clinical details

Age at dx: \_\_\_\_\_

QTc interval = \_\_\_\_\_ ms

12 lead ECG – original or good copy

clinical summary including history and presentation

Exercise test tracing including recovery (if available)

Holter monitor (if available)

Does the patient have a history of:

Syncope

Seizures → (age if known: \_\_\_\_\_)

Aborted cardiac arrest

deafness

Therapy:

ICD → no / yes → if yes, age at implantation: \_\_\_\_\_

PM → yes / no → if yes, age at implantation: \_\_\_\_\_

Medical therapy → no / yes → if yes, please indicate: \_\_\_\_\_

### Box 3: Family history information

Ethnicity of patient's:

Maternal grandmother: \_\_\_\_\_

Paternal grandfather: \_\_\_\_\_

Maternal grandfather: \_\_\_\_\_

Paternal grandmother: \_\_\_\_\_

Where possible, please include a 3 generation family tree, indicating relatives that:

- have been diagnosed with LQTS
- have died suddenly
- have had normal clinical screening

**Please send this form to the Molecular Genetic Laboratory with the blood sample.**

## CONSENT FOR GENETIC TESTING - Adult

(Mutation detection)

I understand that:

- My blood/pathology sample will be used to examine my genetic material and tested for one or more of the genes involved in predisposing to the inherited cardiac arrhythmia syndrome(s) as indicated below:
  - Long QT Syndrome*
  - Catecholaminergic polymorphic ventricular tachycardia*
  - Short QT syndrome*
  - Inherited conduction defects*
  - Brugada syndrome*
- The sample may be examined again in the future when testing for other genes associated with the condition or when new testing methods are introduced into the laboratory.
  - I understand that the onus is on me to ensure that my current contact details are provided to the Victorian Clinical Genetics Services or my referring clinician should I need to be contacted with new information about my testing (PLEASE TICK BOX)
- The testing is completely voluntary and it is possible to withdraw from the testing process at any stage.
- Testing may identify genetic changes (mutations) that may be present in other family members.
- The sample will be stored in the laboratory. It will be stored in good faith but its suitability for future testing cannot be guaranteed. It may be disposed of in accordance with standard laboratory practices or regulatory requirements.

### What are the implications of genetic testing?

I understand that:

- Current genetic testing technology does not detect a mutation in every patient with an inherited arrhythmia syndrome. A gene negative result does not exclude the presence of a mutation in a gene that was not tested. It is also possible that a mutation was missed in one of the genes tested due to the limitations of the testing technology.
- The test may show the presence of a mutation in an inherited arrhythmia syndrome gene and may be used to guide management but it cannot accurately predict when or if cardiac problems may develop. Mutations in inherited arrhythmia syndrome genes cause a high, but not a certain risk of cardiac problems.
- Test results of one individual can change the estimation of risk for other family members who have not requested testing.
- Test results of one individual may affect the ability of family members and/or myself to obtain some types of insurance.

## What will be done with my test results?

I agree that:

- The test results will be held by the Victorian Clinical Genetics Services and my health service provider and will be known by those participating in providing the test.
- Information relating to my testing will not be revealed or made available to any other person/organisation, except with my consent or when disclosure is required by law.
- I agree that the result may also be used, if necessary, to counsel other family members without revealing specific details about me.

### I consent to a copy of my test result being made available to the following people:

(tick as many boxes as applicable)

- Any family member
- Only to the following individuals (*specify*) \_\_\_\_\_
- My doctor(s) (*specify*) \_\_\_\_\_
- Research group (*specify*) \_\_\_\_\_
- Registry (*specify*): \_\_\_\_\_

In the event of my death, my test results should be released to (*name*) (*address*)

\_\_\_\_\_

### Research:

- I consent to my DNA sample being used for future ethics approved research in cardiac genetics. *If so, tick one of the following:*
  - I want my sample to be anonymised and I do not want to know the results of any research performed, even if the research may provide information relevant to my health
  - I would like to be contacted about the results of any research performed on my DNA sample.

**OR**

- My DNA sample may not be used for research and I do not wish to be contacted regarding research.

**OR**

- I would like to be contacted about any research for which my DNA sample could be used, and I will give consent for the research to be performed (or not) at the time of contact.

Signature of Individual: \_\_\_\_\_

Printed Name: \_\_\_\_\_

Date of Birth: \_\_\_\_\_

Date: \_\_\_\_\_

Health Professional name: \_\_\_\_\_

Health Professional signature: \_\_\_\_\_

## CONSENT FOR GENETIC TESTING – Child/Adolescent

(Mutation detection)

I understand that:

- My child's blood/pathology sample will be used to examine my child's genetic material and tested for one for one or more of the genes involved in predisposing to the inherited cardiac arrhythmia syndrome(s) as indicated below:
  - Long QT Syndrome*
  - Catecholaminergic polymorphic ventricular tachycardia*
  - Short QT syndrome*
  - Inherited conduction defects*
  - Brugada syndrome*
- The sample may be examined again in the future when testing for other genes associated with the condition or when new testing methods are introduced into the laboratory.
  - I understand that the onus is on me to ensure that my current contact details are provided to the Victorian Clinical Genetics Services or my referring clinician should I need to be contacted with new information about my testing (PLEASE TICK BOX)
- The testing is completely voluntary and it is possible to withdraw from the testing process at any stage.
- Testing may identify genetic changes (mutations) that may be present in other family members.
- The sample will be stored in the laboratory. It will be stored in good faith but its suitability for future testing cannot be guaranteed. It may be disposed of in accordance with standard laboratory practices or regulatory requirements.

### What are the implications of genetic testing?

I understand that:

- Current genetic testing technology does not detect a mutation in every patient with an inherited arrhythmia syndrome. A gene negative result does not exclude the presence of a mutation in a gene that was not tested. It is also possible that a mutation was missed in one of the genes tested due to the limitations of the testing technology.
- The test may show the presence of a mutation in an inherited arrhythmia syndrome gene and may be used to guide management but it cannot accurately predict when or if cardiac problems may develop. Mutations in inherited arrhythmia syndrome genes cause a high, but not a certain risk of cardiac problems.
- Test results of one individual can change the estimation of risk for other family members who have not requested testing.
- Test results of one individual may affect the ability of family members and/or myself to obtain some types of insurance.

### What will be done with my child's test results?

I agree that:

- The test results will be held by Victorian Clinical Genetics Services and my child's health service provider and will be known by those participating in providing the test.

- Information relating to my child's testing will not be revealed or made available to any other person/organisation, except with my consent or when disclosure is required by law. I agree that the result may also be used to counsel other family members without revealing specific details about me.

**I consent to a copy of my child's test results being made available to the following people:**

(tick as many boxes as applicable)

- Any family member
- Only to the following individuals (*specify*) \_\_\_\_\_
- My doctor(s) (*specify*) \_\_\_\_\_
- Research group (*specify*) \_\_\_\_\_
- Registry (Specify): \_\_\_\_\_
- No other individual \_\_\_\_\_

In the event of my death, my test results should be released to (*name*) (*address*)

\_\_\_\_\_

**Research**

- I consent to my child's DNA sample being used for future ethics approved research in cardiac genetics. *If so, tick one of the following:*

- I want my child's sample to be anonymised and I do not want to know the results of any research performed, even if the research may provide information relevant to my child's health

- I would like to be contacted about the results of any research performed on my child's DNA sample.

OR

- My child's DNA sample may not be used for research and I do not wish to be contacted regarding research.

OR

- I would like to be contacted about any research for which my child's DNA sample could be used, and I will give consent for the research to be performed (or not) at the time of contact.

**Signatures:**

*Parent/Guardian:*

Name: \_\_\_\_\_ DOB: \_\_\_\_\_

Signature: \_\_\_\_\_ date: \_\_\_\_\_

*Child/Adolescent:*

Name: \_\_\_\_\_ DOB: \_\_\_\_\_

Signature: \_\_\_\_\_ date: \_\_\_\_\_

*Health Professional name & signature:* \_\_\_\_\_

## CONSENT FOR *PRESYMPTOMATIC* or *CONFIRMATORY* GENETIC TESTING (Adult)

I understand that:

- My blood/pathology sample will be used to examine my genetic material and tested for the specific gene alteration known in my family to predispose to the inherited cardiac arrhythmia syndrome stated below:
  - Long QT Syndrome (*gene symbol:* \_\_\_\_\_)
  - Catecholaminergic polymorphic ventricular tachycardia (*gene symbol:* \_\_\_\_\_)
  - Short QT syndrome (*gene symbol:* \_\_\_\_\_)
  - Inherited conduction defects (*gene symbol:* \_\_\_\_\_)
  - Brugada syndrome (*gene symbol:* \_\_\_\_\_)
- Only the family specific mutation will be tested therefore the test will not reveal all possible mutations that may occur in the genes tested.
- The testing is completely voluntary and it is possible to withdraw from the testing process at any stage.
- Testing may identify genetic changes (mutations) that may be present in other family members.
- The sample will be stored in the laboratory. It will be stored in good faith but its suitability for future testing cannot be guaranteed. It may be disposed of in accordance with standard laboratory practices or regulatory requirements.

### What are the implications of genetic testing?

I understand that:

- The test may show the presence of a mutation in an inherited arrhythmia syndrome gene and may be used to guide management but it cannot accurately predict when or if cardiac problems may develop. Mutations in inherited arrhythmia syndrome genes cause a high, but not a certain risk of cardiac problems.
- Test results of one individual can change the estimation of risk for other family members who have not requested testing.
- Test results of one individual may affect the ability of family members and/or myself to obtain some types of insurance.

### What will be done with my test results?

I agree that:

- The test results will be held by Victorian Clinical Genetics Services and my health service provider and will be known by those participating in providing the test.
- Information relating to my testing will not be revealed or made available to any other person/organisation, except with my consent or when disclosure is required by law.
- I agree that the result may also be used to counsel other family members without revealing specific details about me.

**I consent to a copy of my test result being made available to the following people:**

(tick as many boxes as applicable)

- Any family member
- Only to the following individuals (*specify*) \_\_\_\_\_
- My doctor(s) (*specify*) \_\_\_\_\_
- Research group (*specify*) \_\_\_\_\_
- Registry (Specify): \_\_\_\_\_
- No other individual \_\_\_\_\_

In the event of my death, my test results should be released to (*name*) (*address*)

\_\_\_\_\_

**Research:**

- I consent to my DNA sample being used for future Clinical Research and Ethics Committee approved research in cardiac genetics. *If so, tick one of the following:*
  - I want my sample to be anonymised and I do not want to know the results of any research performed, even if the research may provide information relevant to my health
  - I would like to be contacted about the results of any research performed on my DNA sample.

**OR**

- My DNA sample may not be used for research and I do not wish to be contacted regarding research.

**OR**

- I would like to be contacted about any research for which my DNA sample could be used, and I will give consent for the research to be performed (or not) at the time of contact.

Signature of Individual: \_\_\_\_\_

Printed Name: \_\_\_\_\_

Date of Birth: \_\_\_\_\_

Date: \_\_\_\_\_

Health Professional name: \_\_\_\_\_

Health Professional signature: \_\_\_\_\_

## CONSENT FOR *PRESYMPTOMATIC* and CONFIRMATORY GENETIC TESTING (Child/Adolescent)

I understand that:

- My child's blood/pathology sample will be used to examine my child's genetic material and tested for the specific gene alteration known in my family to predispose to the inherited cardiac arrhythmia syndrome stated below:
  - Long QT Syndrome (*gene symbol:* \_\_\_\_\_)
  - Catecholaminergic polymorphic ventricular tachycardia (*gene symbol:* \_\_\_\_\_)
  - Short QT syndrome (*gene symbol:* \_\_\_\_\_)
  - Inherited conduction defects (*gene symbol:* \_\_\_\_\_)
  - Brugada syndrome (*gene symbol:* \_\_\_\_\_)
- Only the family specific mutation will be tested therefore the test will not reveal all possible mutations that may occur in the genes tested.
- The test may show the presence of a mutation in an inherited arrhythmia syndrome gene and may be used to guide management but it cannot accurately predict when or if cardiac problems may develop. Mutations in inherited arrhythmia syndrome genes cause a high, but not a certain risk of cardiac problems.
- Testing may identify genetic changes (mutations) that may be present in other family members.
- The sample will be stored in the laboratory. It will be stored in good faith but its suitability for future testing cannot be guaranteed. It may be disposed of in accordance with standard laboratory practices or regulatory requirements.

### What are the implications of genetic testing?

I understand that:

- Alterations (mutations) in inherited arrhythmia syndrome genes cause a high, but not a certain risk of cardiac problems. The test may show the presence of a mutation but it cannot accurately predict when or if cardiac problems may develop as a result.
- Test results of one individual can change the estimation of risk for other family members who have not requested testing.
- Test results of one individual may affect the ability of family members and/or myself to obtain some types of insurance.

### What will be done with the test results?

I agree that:

- The test results will be held by Victorian Clinical Genetics Services and my child's health service provider and will be known by those participating in providing the test.

- Information relating to my child's testing will not be revealed or made available to any other person/organisation, except with my consent or when disclosure is required by law. My child's result may be disclosed to him/her in the future, by appropriate health care professionals, if the test information will influence his or her medical management.
- I agree that the result may also be used to counsel other family members without revealing specific details about me.

**I consent to a copy of my child's test result being made available to the following people:**

(tick as many boxes as applicable)

- Any family member
- Only to the following individuals (*specify*) \_\_\_\_\_
- My doctor(s) (*specify*) \_\_\_\_\_
- Research group (*specify*) \_\_\_\_\_
- Registry (Specify): \_\_\_\_\_
- No other individual \_\_\_\_\_

In the event of my death, my child's test results should be released to (*name*) (*address*)

**Research**

- I consent to my child's DNA sample being used for future Clinical Research and Ethics Committee approved research in cardiac genetics. *If so, tick one of the following:*
  - I want my child's sample to be anonymised and I do not want to know the results of any research performed, even if the research may provide information relevant to my child's health
  - I would like to be contacted about the results of any research performed on my child's DNA sample.

**OR**

- My child's DNA sample may not be used for research and I do not wish to be contacted regarding research.

**OR**

- I would like to be contacted about any research for which my child's DNA sample could be used, and I will give consent for the research to be performed (or not) at the time of contact.

**Signatures:**

*Parent/Guardian:*

Name: \_\_\_\_\_ DOB: \_\_\_\_\_

Signature: \_\_\_\_\_ date: \_\_\_\_\_

*Child/Adolescent:*

Name: \_\_\_\_\_ DOB: \_\_\_\_\_

Signature: \_\_\_\_\_ date: \_\_\_\_\_

*Health Professional name & signature:* \_\_\_\_\_