

Checklist

- Blood samples collected:
20ml in EDTA
5ml Lithium Heparin.
- Consent Form completed and signed.
- Service Agreement completed and signed.
- WCH Request Form completed and signed (including provider number).
- All samples and paperwork sealed in IMVS Path-o-Pack.

Samples should be kept at room temperature at all times and transported to the laboratory within 24 hours of collection where practicable.

Clinical enquiries:

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Laboratory enquiries:



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Genetic Testing for Retinoblastoma for Clinicians



South Australian Familial Cancer Service

Introduction

Retinoblastoma is caused by inactivation of both alleles of the retinoblastoma susceptibility gene, RB1.

The hereditary form of the disease results from a germline mutation in one RB1 allele being transferred from parent to child as an autosomal dominant trait. A new germline mutation may also occur in one RB1 allele during the formation of the sperm from which the child develops. The mutation in the second allele occurs somatically in one or more retinal cells. Approximately 90% of people with a germline mutation develop a mutation in the second RB1 allele in a retinal cell and develop retinoblastoma.

In the non hereditary of the disease, the mutations in both alleles are somatic.

Identification of a germline mutation in RB1 has a number of advantages. The presence of a mutation identifies children at increased risk of developing another retinoblastoma or other cancers in later life. Relatives who are at increased risk of developing the disease can be tested for the same mutation to determine if they need screening. Conversely, if the germline mutation is not found in an at-risk relative no further ophthalmic surveillance is required and the emotional and financial costs of unnecessary surveillance can be avoided.

RB Susceptibility Gene Testing

Germline mutations in the RB1 gene can be detected utilizing current techniques in approximately 80% of people with familial or bilateral disease and in 10% of sporadic unilateral cases.

Testing is conducted under the auspices of the South Australian Familial Cancer Service at the Institute of Medical and Veterinary Science, Adelaide.

Turnaround time for testing

Analysis of the RB1 gene is a lengthy process requiring a number of stages. The first step involves screening the promoter and 27 exons of the gene for any small insertions, small deletions or single base substitution mutations by direct DNA sequencing. At the same time a sample is sent to the Women's and Children's Hospital in Adelaide for analysis by Fluorescent In-Situ Hybridization (FISH) for the detection of whole gene deletions and insertions. Failure to detect a causative mutation after this initial screen necessitates the use of Fluorescent Multiplex PCR technique to test for other large scale deletions and rearrangements.

Most results are available within 2-3 months. If more detailed testing is necessary, it may take 3-4 months to issue a report.

Detection of an identified mutation can be extended to presymptomatic testing in other family members. The testing takes approximately 4 weeks to complete.

Results

A full report will be issued on the outcome of testing. Please indicate on the IMVS Request Form if additional reports are required to be issued to other specialists involved in the case.

Identification of a mutation in the RB1 gene serves to aid both the genetic counselling process and in early clinical management.

Procedure for testing

1. Collect 20 ml fresh blood in EDTA **and** 5ml fresh blood in Lithium Heparin. Please ensure that all samples are kept at room temperature at all times including transportation to the laboratory.
2. Ensure that a *Consent Form* from a Family Cancer Clinic accompanies each of the samples to be tested. We require that informed consent be obtained and documented. (A suitable consent form is available from the laboratory if required).
3. Complete the Women's and Children's Hospital *Request Form*, paying particular attention to include your provider number. **Do not send the samples or form to the Women's and Children's Hospital.**
4. Complete the *Service Agreement Form* indicating that funding can be guaranteed.
5. Place all paper work and samples in the IMVS Path-o-Pak and complete the IMVS Request Form on the front.
6. Forward to the laboratory within 24 hours of collection where practicable.