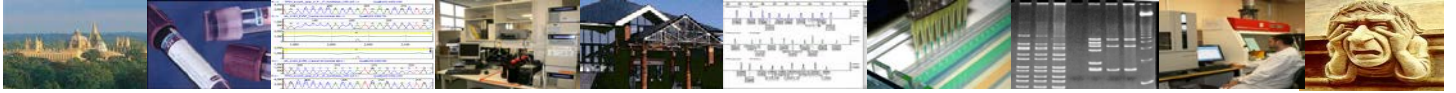


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LI-FRAUMENI SYNDROME– OMIM 151623

INTRODUCTION

Li-Fraumeni Syndrome (LFS) is an autosomal dominant cancer predisposition syndrome. It is characterised by the development of a variety of tumours affecting multiple family members, frequently at an early age of onset. Individuals may be affected by more than one primary tumour. The most common tumour types are soft-tissue sarcomas, osteosarcomas, pre-menopausal breast cancer and brain tumours. The gene associated with Li-Fraumeni syndrome is the *TP53* gene. The lifetime penetrance for mutations in the *TP53* gene is high (93% for women by age 50, 68% for men by age 50). The *de novo* mutation rate for *TP53* is also high; estimated to be up to 20%, Gonzalez et al 2009, J. Med. Genet. 46.

TESTING AND REFERRALS

Referrals are accepted through Clinical Genetics only

Diagnostic:

- Clinically affected patients with a family history of cancer (typically these will fulfil the Chompret criteria)
- Clinically affected patients with young-onset or multiple tumours

Carrier/Presymptomatic/Test for Familial Mutation:

- Relatives of clinically affected patients
- Requests for presymptomatic testing should either be accompanied by details of the known pathogenic mutation in the family or discussed with the laboratory in advance.

Prenatal:

- Prenatal testing is not generally requested
- Prenatal testing must be discussed with the laboratory and arranged in advance.
- Referrals are only accepted from Clinical Genetics and / or Prenatal Diagnosis.

STRATEGY AND TECHNICAL INFORMATION

Molecular testing is undertaken by fluorescent Sanger sequencing of *TP53* exons 2-11, including exon/intron boundaries. Multiplex Ligation-dependent Probe Amplification analysis for large scale deletions and duplications is also undertaken.

Once a pathogenic mutation has been identified in an individual testing for that variant may be offered to at-risk family members.

CLINICAL SENSITIVITY

It is estimated that up to 80% of individuals with LFS have a detectable germline *TP53* mutation [Malkin *et al*, 2011, Genes & cancer 2(4) 475-484]. Mutations are also found in up to 40% of families who have Li-Fraumeni-like (LFL) Syndrome (Varley *et al*, 2003 Hum Mut.21:313-320).

TARGET REPORTING TIMES

Diagnostic:	40 Days
Presymptomatic/Familial Mutation test:	10 Days

N.B Details are correct for the date of printing only – last updated 29/06/2015