Bristol Genetics Laboratory

North Bristol NHS Trust

Thrombophilia / Factor V Leiden & Prothrombin Mutation Analysis

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Sample Required:
Adult: 5mls blood in EDTA

Samples should be accompanied by a FULLY completed request form (available as download at www.nbt.nhs.uk/genetics or from the laboratory).

Please include details of test, family history, address and POSTCODE, NHS number, referring clinician and unit/hospital.

Consent and DNA Storage:

All genetic testing requires consent. It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.

DNA is stored from all patients unless consent for this is specifically denied.

Stored samples may be used for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

- The prothrombin 20210G>A (c.*97G>A) mutation in the factor II gene (OMIM 176930) is the second common inherited clotting abnormality in Caucasians, with a carrier frequency of 2% in the UK (1 in 50 is a carrier). Heterozygous carriers of this mutation have a two- to three- fold increased risk of thrombosis and up to 1.3- fold increased relative risk for pregnancy complications.
- Thrombophilia is an increased tendency to form blood clots due to a congenital or acquired defect. Protein C, protein S and antithrombin deficiencies and factor V Leiden and prothrombin mutations have all been associated with increased risk for deep vein thrombosis and pulmonary embolism (VTE) and pregnancy complications.
- The factor V Leiden deficiency (OMIM 227400) is caused by the c.1691G>A p.(Arg506Gln) mutation in the factor V gene (OMIM 612309) and is the most common hereditary thrombotic risk factor in Caucasians, with a UK carrier frequency of 4% (1 in 25 is a carrier). Heterozygous carriers of the factor V Leiden mutation have a three- to five- fold increased risk of VTE and there is also a two- to three- fold increase in the relative risk for complications during pregnancy.

Service offered

- Real-Time PCR is used to detect the factor V Leiden c.1691G>A p.(Arg506Gln) and the prothrombin 20210G>A (c.*97G>A) mutations.

Referrals

- Referrals are usually via the local Haematology department or via Consultant Specialists. Referrals from GPs are accepted provided it is clearly demonstrated on the referral form that they meet one of the criteria listed below.

Diagnostic Testing is considered in patients with:

1. Unprovoked venous thromboembolism before the age of 40 years.
2. Recurrent unprovoked thromboembolism.
3. Thrombosis in unusual sites.
4. Patients with unprovoked venous thromboembolism and pregnant women, whose first degree relative meets one of criteria 1-3.
5. Women with unexplained foetal loss or >3 spontaneous early miscarriages.
6. VTE associated with use of oral contraceptives or hormone replacement therapy
7. Unexplained skin necrosis.
8. Neonates and children with purpura fulminans.

Predictive/Carrier Testing: Following clinical assessment, testing is indicated in certain cases for first degree adult relatives of patients with a history of VTE.

Please note:

1. It is not recommended to routinely test asymptomatic relatives of patients with low risk of thrombophilia (factor V Leiden or G20210A variants).
2. Testing of asymptomatic relatives of patients with high risk of thrombophilia (such as deficiency of antithrombin, protein C or S) should only be considered in selected thrombosis-prone families.
3. Testing of asymptomatic individuals under age 16 is only considered for females seeking oral contraception with a first degree relative with a proven genetic risk factor or relative meeting the criteria 1-3 above.
4. Testing of relatives where the affected family member has not undergone genetic testing or no results are available reduces the utility of the test and is not recommended

Quality

- BGL participates in the UK NEQAS for Blood coagulation scheme for Molecular Genetics of Thrombophilia for this service.

Clinical Advice

- If clinical discussion is required we would recommend contact with Dr Alastair Whiteway, Consultant Haematologist (Tel: 0117 414 8401).

References

1. Middeldorp S et al 2008 British Journal of Haematology, 143, 321-335
2. Baglin T et al 2009 British Committee for Standards in Haematology
3. http://www.bcshguidelines.com/pdf/ThrombophiliaGuideline_101209.pdf

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