Bristol Genetics Laboratory is a UKAS accredited medical laboratory No.9307.

North Bristol NHS Trust

CALR exon 9 mutation analysis in MPN

Contact details:
Bristol Genetics Laboratory
Pathology Sciences
Southmead Hospital
Bristol, BS10 5NB
Enquiries : 0117 4146168
Email: nbn-tr.geneticsenquiries@nhs.net

Head of department:
Eileen Roberts FRCPath

Principal Clinical Scientist (Oncology Genomics):
Chris Wragg FRCPath
Christopher.Wragg@nbt.nhs.uk

Service Lead:
Rebecca Wragg
Rebecca.Wragg@nbt.nhs.uk

Sample Required:
Adult: 3-5ml 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.

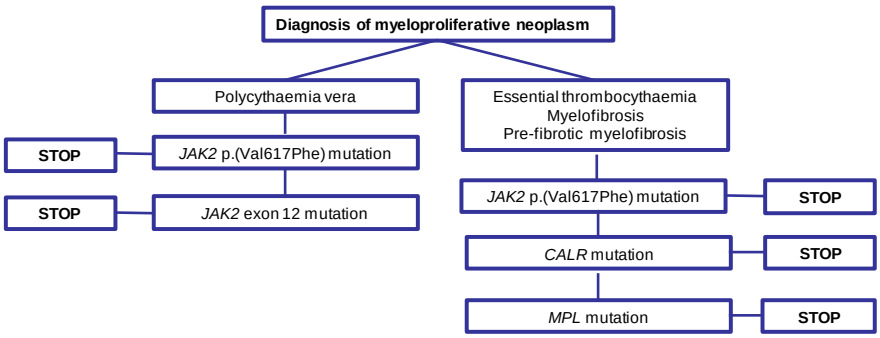
Consent and DNA Storage:
All genetic testing requires consent. It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.

Stored material from all referrals may be retained for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

- Acquired mutations in the *JAK2* and *MPL* genes are an established finding in myeloproliferative neoplasms (MPN).
- The majority of patients with Essential Thrombocythaemia (ET) and Primary Myelofibrosis (PMF) will have a *JAK2* V617F mutation (50-60%).
- A further 5~10% of *JAK2* V617F-negative ET and PMF patients possess a mutation in exon 10 of the *MPL* gene.
- The remaining third of patients have neither of these mutations.
- Several studies (Klampfl *et al.,* 2013; Nangalia *et al.,* 2013) have identified recurrent mutations in exon 9 of the *CALR* gene in patients with MPN. These mutations have been found to arise in patients with ET (67%) and PMF (88%) with non-mutated *JAK2* V617F and *MPL*. As such, *CALR* mutations have been described as being the second most frequent mutation, after *JAK2,* in MPN.
- Patients with *CALR* mutations have a lower white cell count, lower haemoglobin level, higher platelet count and a longer overall survival than patients with *JAK2* mutations so it is important that patient testing algorithms take *CALR* mutation status into account (see algorithm below).
- Currently, 36 mutations have been identified within exon 9 of the *CALR* gene in patients with MPN. The most common mutations are Types 1 and 2 which consist of a 52bp deletion and 5bp insertion respectively.

British Committee for Standards in Haematology diagnostic criteria for ET have recently been updated to include testing for *CALR* mutation



Service offered

- The Bristol Genetics Laboratory (BGL) is part of the Bristol Haemato-oncology Diagnostic Service (BHODS) and has access to a full range of complementary pathology services.
- Testing for mutations in exon 9 of the *CALR* gene is carried out on genomic DNA using a simplex PCR and analysis on the Beckman Coulter CEQ8000.

Quality

- BGL takes part in a sample exchange scheme with other UK Genetics laboratories in the absence of a formal UK NEQAS EQA programme for this test.

Target reporting time: 14 calendar days

For up-to-date prices please contact the laboratory

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