NIHR | BioResource

BPD. Bleeding, thrombotic and Platelet Disorders

NIHR BioResource – Rare Diseases study project

Lead Investigator(s): Professor. Andrew Mumford and Professor. Mike Laffan

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Summary

Rare inherited diseases affect 1 in 17 people in the UK and there are an estimated 7,000 different rare diseases and the genetic basis for more than halve have been resolved.

One domain of rare diseases selected for enrolment by the NIHR BioResource are inherited *Bleeding, thrombotic and Platelet Disorders* (BPD). Over the past 5 years the DNA samples from nearly 1200 patients with BPDs of unknown aetiology have been enrolled in the NIHR BioResource and analysed by whole genome sequencing[1]. In addition the DNA samples from another 2,500 patients have been analysed by the ThromboGenomics gene panel test[2]. The new genes for BPD discovered and validated by this joint effort has increased the chance of a patient receiving a molecular diagnosis substantially.

To continue the research and service innovation, you are now invited to enroll your patients with a BPD of *known* or *unknown* aetiology in the NIHR BioResource – Rare Diseases study. This provides a unique opportunity to further expand this national resource and to generate better evidence for the diagnosis and treatment of this group of rare disease patients. Samples from your patient will be deposited for future research in the NIHR National Biosample Centre (at no cost to your hospital) and phenotype information can be entered on a NHS-compliant national database, which is managed by the NIHR BioResource team.

The samples from your patients will NOT be tested by whole genome sequencing or by the gene panel test. If you want a diagnostic test to be performed then please refer a sample to your local NHS Genomics Laboratory Hub[3].

[1] https://www.biorxiv.org/content/early/2019/01/01/507244
[2] https://www.biorxiv.org/content/early/2018/12/21/504142
[3] https://www.england.nhs.uk/genomics/genomic-laboratory-hubs/

Recruitment Criteria

1) Haemostasis disorders > Inherited bleeding and / or platelet disorders

Inclusion

Diagnosis of a rare bleeding and / or platelet disorder*** of known or unknown cause before the age of 50 and following haematological consultation AND family history or consanguineous parents, OR syndromic features (incl. neurodevelopmental, immunological, nephrology, skeletal, hearing, etc.), OR early onset childhood case, OR deficiency of coagulation factor with or without causal coding variants in the corresponding gene.

***Platelet disorder is defined as one or more of the following:

a) Platelet count >400x10^9/L or <100x10^9/L
b) Mean Platelet Volume (MPV) >13 fL AND/OR macrothrombocytopenia, or MPV <7 fL
c) Abnormal platelet morphology, ideally confirmed by high resolution microscopy
d) Abnormal platelet function test, replicated on an independent sample.

Exclusion

1. Acquired bleeding and / or platelet disorders
2. Cases with platelet counts >400x10^9/L and age <30 years must be tested and found to be negative for somatic mutations in JAK2 and CALR
3. Use of prescription or over-the-counter drugs known to be associated with abnormal platelet (function) phenotypes and/or bleeding disorders, including:
    a. Anti-coagulant medications (aspirin, clopidogrel, dipyridamole, etc.);
    b. Non-steroidal anti-inflammatory drugs (incl. COX-2 selective anti-inflammatory drugs)
4. Patients with evidence of an autoimmune or other systemic condition known to affect haemostasis and platelet homeostasis, including:
    a. Autoimmune thrombocytopenia (ITP) responsive to first-line treatment (ITP cases not responsive to first-line treatment are eligible, ***see: the BCA project ('refractoriness first-line treatment for Blood Cell Autoimmunity'***);

    b. Other autoimmune disorders, e.g. SLE
5. Other medical conditions known to be associated with abnormal platelet count and / or volume and / or abnormal platelet function:
    a. Acute viral infection
    b. Bone marrow aplasia
    c. DIC (disseminated intravascular coagulation);
    d. Hepatic failure;
    e. HIV positivity and/or AIDS;
    f. Malignancies, particularly those compromising haematopoiesis;
    g. Splenomegaly;
    h. Uraemia

2) Haemostasis disorders > Venous thrombosis

Inclusion

Unprovoked venous thrombosis (including in pregnancy) occurring before the age of 40, confirmed by imaging and following review by a Haemophilia or Thrombosis Centre haematologist; AND ONE OR MORE OF:

a) Family history of thrombotic events before the age of 40;
b) Consanguineous parents;
c) Syndromic features;
d) Early onset in childhood / adolescence cases before the age of 25 with multiple independent unprovoked thrombotic events.

Exclusion

Acquired thrombotic disorders including:

a) Anti-phospholipid antibodies (anti-beta2-glycoprotein), including during pregnancy;
b) Thrombotic event occurring after trauma/surgical challenge.