**NHSE Haemostasis Genomics MDT Group - Central and South GLH proforma**

**Please note that this form is not a formal genetics report; the results included in this form may not have been confirmed and should not be used for clinical decision making. A formal report which can be filed in the patient’s notes will follow.**

|  |  |
| --- | --- |
| Surname |  Referring Hospital |
| Forename | Referring Consultant |
| NHS Number | Referring email: *(@nhs.net)* |
| DOB  | Submission date: |
| Gender  | Date of MDT discussion: |
| Local MRN:  | Family ID: |

**Phenotype Summary**

|  |
| --- |
| Suspected Condition: Bleeding Thrombotic |
| Age of bleeding/ thrombosis onset |
| ISTH BAT score (if relevant)  |
| Personal history: |
| Family History: (attach family tree separately) |

Relevant results:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Coagulation** |  | **Thrombosis** |  | **Platelets** |  |
| 1 stage VIII IU/ml |  | Antithrombin IU/ml |  | Plt count |  |
| Chrom VIII IU/ml |  | Protein S IU/ml |  | MPV |  |
| FV IU/ml |  | Protein C IU/ml |  | Film |  |
| FVII IU/ml |  | PT ratio |  | VWF RIPA |  |
| FIX IU/ml |  | APTT ratio |  | **Platelet aggregation** | Normal/ Impaired or Absent |
| FX IU/ml |  | Thrombin time |  | ADP uM |  |
| FXI IU/ml |  | Fibrinogen g/l |  | Collagen ug/ml |  |
| FXIII IU/ml |  | Fib-Ag IU/ml |  | Arachidonic acid mg/ml |  |
| VWF Ag IU/ml |  | INR |  | U46619 uM |  |
| Innov VWF act IU/ml |  |  |  | Adrenaline uM |  |
| VWF CBA IU/ml |  |  |  | Ristocetin mg/ml |  |
| VWF 2N % |  |  |  |  |  |
| Multimers |  |  |  | CLG THROM |  nMol |
| Plasminogen u/dl |  |  |  | CLG COLL |  nMol |
| Fibrinogen g/l |  |  |  | Nucleotide ratio(nmolx10\*9/L) | ATPADP |
| Fib-Ag IU/ml |  |  |  |  |  |

**Variant summary:** (for laboratory scientific staff)

Source of variant identified

|  |  |
| --- | --- |
| OUH diagnostic lab |  |
| Other diagnostic lab | Lab name |
| Research lab | Lab/ Research Study name |

Variant classification and interpretation:

|  |
| --- |
| **Variant 1** |
| **Gene:** |
| **Gene function / pathway:** |
| **OMIM Gene-Phenotype Relationships:** |
| **Phenotype** | **Phenotype MIM number** | **Inheritance** |
|  |  |  |
|  |  |  |
|  |  |  |
| **Variant: transcript, cDNA, coding effect**: **NM\_0000001.1: c. p.****Type of variant:** **Frameshift/ Nonsense / Missense / Canonical splice site / non-canonical splice site****Inheritance: *De novo* /Maternal / Paternal /Bi-parental/ Unknown****Zygozity: Heterozygous / Homozygous / Hemizygous** / **Mosaic****gnomAD constraint scores: missense z= ; LoF pLI = (Recessive)****gnomAD frequency**:**dbSNP:****ClinVar:****GranthamScore**:**Conservation**:**SpliceSitePrediction**:**Functional domain/mutational hotspot:****HGMD / literature**: **Nothing relevant or list below****[1]****[2]****Other comments:****ACGS criteria (assuming the phenotype fits)**: [delete as appropriate & insert weighting]**PVS1** Null variant**PS1** Same amino acid change as a previously established pathogenic variant regardless of nucleotide change**PS2** De novo (both maternity and paternity confirmed)**PS3** Functional studies**PS4** Increased prevalence in affected individuals compared to controls**PM1** Located in a mutational hot spot and/or critical and well-established functional domain (e.g., active site of an enzyme) without benign variation**PM2** Absent from controls (or at extremely low frequency if recessive)**PM3** For recessive disorders, detected in trans with a pathogenic variant**PM4** Protein length changes as a result of in-frame deletions/insertions in a nonrepeat region or stop-loss variants**PM5** Novel missense change at an amino acid residue where a different missense change determined to be pathogenic has been seen before**PM6** Assumed de novo, but without confirmation of paternity and maternity**PP1** Cosegregation with disease in multiple affected family members in a gene definitively known to cause the disease**PP2** Missense variant in a gene that has a low rate of benign missense variation and in which missense variants are a common mechanism of disease**PP3** In silico supports pathogenicity**PP4** Phenotype /family history is highly specific for the disease **PP5** Previously reported as pathogenic but evidence for pathogenicity not provided**BA1** Allele frequency is >5%**BS1** Allele frequency is greater than expected for disorder**BS2** Observed in a healthy adult individual for a recessive (homozygous), dominant (heterozygous), or X-linked (hemizygous) disorder, with full penetrance expected at an early age**BS3** Functional studies show no damaging effect**BS4** Lack of segregation in affected members of a family**BP1** Missense variant in a gene for which primarily truncating variants are known to cause disease**BP2** Observed in trans with a pathogenic variant for a fully penetrant dominant gene/disorder or observed in cis with a pathogenic variant in any inheritance pattern**BP3** In-frame deletions/insertions in a repetitive region without a known function**BP4** In silico: likely benign**BP5** Variant found in a case with an alternate molecular basis for disease**BP6** Previously reported as benign but evidence for pathogenicity not provided**BP7** Synonymous change - no splicing effect in silico AND nucleotide not highly conserved |

For additional variants copy above table and append

**MDT decision:**

|  |  |
| --- | --- |
| **Variant 1** Variant class | Pathogenic / Likely Pathogenic / VUS/ Likely benign / Benign |
| Phenotype Contribution | Full / Partial / Unknown / none |
| CommentsIf partial what aspects are explained? | **Variant specific questions:**Is phenotype relevant?Parental phenotypes known?Clinically actionable / segregation analysis possible?Any functional follow up assays possible? |

|  |  |
| --- | --- |
| **Variant 2**Variant class | Pathogenic / Likely Pathogenic / VUS / Likely benign / Benign |
| Phenotype Contribution | Full / Partial / Unknown / None |
| CommentsIf partial, what aspects are explained? | **Variant specific questions:**Is phenotype relevant?Parental phenotypes known?Clinically actionable / segregation analysis possible?Any functional follow up assays possible? |

**Action:**

|  |
| --- |
| Confirm or DO NOT confirm variants |
| Fully/partially consistent with patient phenotype |
| Report as:Is this a preliminary report and should the case be re-discussed pending further testing? |
| Additional molecular analysis that could be considered: |

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Attendees:

|  |  |
| --- | --- |
| Clinical staff: |  |
| Laboratory staff: |  |

Signatures:

|  |  |
| --- | --- |
| Name of senior laboratory scientist | Electronic signature: |
| Name of MDT chair | Electronic signature: |