**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) | ATP  ADP |
| 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 |
| Comments  If 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 |
| Comments  If 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: |

**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.**

Attendees:

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

Signatures:

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