GENETIC TESTING FOR BONE MARROW FAILURE SYNDROMES

Bone Marrow Failure Syndromes are a group of blood disorders that happen when our bone marrow is not working correctly. Bone marrow is where all our blood cells (red, white and platelets) are made. It is the spongy centre found in our major bones.

What causes bone marrow failure syndrome(s)?
Bone marrow failure syndromes (BMFS) happen when our bone marrow does not make enough working blood cells. BMFS are caused by changes in our genes.

What are genes?
Genes are made up of strings of DNA found in our bodies. DNA contains the code, or specific instructions, to make every person unique. Many genes provide the instructions for creating new blood cells and how they should work. Changes in these genes (also called 'variants' or 'mutations') can lead to BMFS.

How can a gene change happen?
Changes within our genes can be ‘acquired’ or ‘inherited’.

Acquired gene changes (variants):
These variants are caused by environmental factors (like exposure to high levels of radiation) or happen just by chance. They develop over time in a person in their bone marrow and/or lymph nodes.

Inherited gene changes (variants):
These variants are may be inherited (passed on) from a biological parent, or may have happened as a new genetic change at the time of conception. They can predispose someone to developing a BMFS at a younger age.

Is there a test for gene changes?
Knowing the exact genetic cause of a bone marrow failure syndrome can help your doctor decide on your treatment and management options. The ‘Inherited Bone Marrow Disorders’ panel test, examines 37 genes for variants known to cause inherited BMFS.
Your doctor may ask you to do this test for one or more of the following reasons:

- Your bone marrow disorder symptoms are suspected as being associated with an inherited genetic cause.
- You have a family history of bone marrow disorders, blood problems, cancer or immune issues.
- Your condition first started at a younger age
- Siblings or other family members are being considered as donors for an allogenic stem cell transplant (bone marrow transplant).
- An acquired cause for your bone marrow disorder is suspected (such as aplastic anaemia) and your doctor would like to exclude an inherited cause.

Sometimes the exact genetic cause is unable to be found. If it is found, it may have other implications for you and/or your family.
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| “Pathogenic” or “likely pathogenic” variant identified | • The underlying germline cause for BMFS is identified and can guide how your doctor manages the condition.  
• Family members can be tested to determine their personal health risk and screening options, even if they have no symptoms.  
• For those planning a pregnancy, options may be available to avoid passing on the condition.  
• Can inform decision making about the suitability of a family member to act as a bone marrow donor. |
| Variant of “uncertain significance” identified. | • The variant may or may not be the cause for the BMFS.  
• We may contact you and your doctor for more information.  
• We may recommend family member testing to determine the possible significance of this variant.  
• Sometimes it is not possible to know the significance of a variant. |
| “No variants” identified. | • No variants thought to be connected to BMFS are identified.  

More information when **no variants** are identified:  
* If your doctor suspects an inherited cause, other genetic testing options may be available.  
* If your doctor suspects an acquired cause, the chances of an underlying inherited cause is significantly reduced. |

Sometimes we need to test another DNA sample to confirm a genetic result. This may mean having another blood sample, cheek swab (buccal) or a small piece of skin tissue (biopsy) taken.

Please speak to your doctor if you have any questions about your results, treatment or care. If you or your family would like more information about genetic testing, please contact our Genetic Counsellors via email on: ibmdenquiries@petermac.org