Genetic Testing

DNA is continuously damaged. This is normally not a problem because our proteins repair the damaged DNA. However, patients with FA have a congenital defect as a result of which the DNA is repaired less well than normal. Alterations (mutations) in over twenty different genes can cause FA.. These genes code for proteins that function in a biochemical pathway, the so-called Fanconi anaemia (FA) pathway, to repair the DNA. FA patients have a defect in one of these proteins, as a result of which the pathway no longer functions correctly.

These genes are described by their complementation groups, of which the most common are FANCA, FANCC and FANCG. However many of the other groups are also seen in patients in the UK. There are different characteristics associated with each complementation group, hence the reason why it is important to understand which group a patient belongs to.

Most FA genes are inherited in a recessive manner. We have two copies of every gene, one inherited from our mother and one inherited from our father. A carrier is someone who has one normal copy of a gene and one copy with a mutation in a specific gene. If they have children with another carrier, with a mutation in the same gene, then there is a 1 in 4 chance that the baby can inherit both copies of the mutated gene.

The following answers have been provided by Dr Marc Tischkowitz, University Reader and Honorary Consultant in the Department of Medical Genetics at Cambridge.

From an FA parents' perspective what is the benefit of genetic testing?

There are several reasons why parents (and patients) can benefit from genetic testing:-

1) Some very rare FA complementation groups can cause an increased risk of cancer in carriers.

   These are:

   - FANCD1 (BRCA2) - breast, ovarian, pancreatic, prostate
   - FANCN (PALB2) - breast, pancreas, possibly ovarian, possibly gastric

- FANCJ (BRIP1) - ovarian
- FANCO (RAD51) - ovarian
- FANCS (BRCA1) - breast, ovarian

If FA is due to one of these genes then the parents and possibly other family members will need appropriate surveillance.

2) If the parents are planning further children and would like to consider their reproductive options (prenatal testing, preimplantation genetic diagnosis). A genetic diagnosis is desirable for prenatal testing (PNT) and essential for preimplantation genetic diagnosis (PGD).

3) Testing of other family members may be useful and is very important if there is consanguinity. i.e. blood relatives marrying each other.

Will my doctor/FA Consultant support this testing?

These days mutation analysis should be considered a routine part of the work up of a child with FA. This is recommended in the UK FA Standards of Care document which was written through consensus by a wide range of consultants.

Is Genetic Testing expensive?

Genetic testing costs a few hundred pounds and is a one-off test. Genetics centres are specialist commissioned (i.e. paid for centrally by the NHS not locally by the GP). Routine testing can take some time (several months or longer), but it can sometimes be done more quickly if there is an urgent need.

Do I need only to know the complementation group or should I expect to have more comprehensive genetic mutation analysis?

This depends on what you want the information for and what the complementation group is.

Mutation testing should be done in addition to complementation group analysis

1) if you are considering PND or PGD;

2) if there is consanguinity in the family and other family members wish to be tested;

3) if the complementation group is one of the genes listed above.

Where is the Genetic Testing undertaken?

Several labs in the UK offer this including Leeds, Sheffield and Bristol. In reality it does not matter where the test is done as clinical genetic centres are very used to sending samples to different labs on a routine basis.

All genetic testing should be done through your local genetic centre which can be found here: http://www.bsgm.org.uk/information-education/genetics-centres/
Most centres also do clinics in local hospitals so you may not have to travel far to see a genetics specialist. All centres will accept referrals from your GP or specialist.