MOSAICISM – Complex Patterns of Inheritance 3

Produced by the Centre for Genetics Education. Internet: http://www.genetics.edu.au

Important points

- Mosaicism refers to the situation where individuals have in their bodies a mixture of cells. Some cells may contain the right genetic information while others contain a change in genetic information
- Mosaicism can refer to there being a mixture of cells with some containing the correct chromosome complement while others contain a change in chromosome number or structure
- Mosaicism can also be used to describe a situation where, although the chromosomes look normal, some cells carry a gene with the right information while others contain a faulty copy of the gene
- Without studying every cell in the body (which is impossible), we cannot exclude the possibility that an individual could be mosaic for a chromosomal change or a faulty gene
- When the faulty gene(s) is/are in only some of a woman's egg cells or a man's sperm cells, this is described as ***germline mosaicism*** as the egg and sperm cells are referred to as ***germ cells***
- This situation is also referred to as ***gonadal*** **mosaicism** (since the egg and sperm are produced in the ***gonads***)
- In a situation where a couple has more than one child affected with a condition that is due to a 'dominant' faulty gene, we would normally expect one of the parents to also be affected. When neither are affected, gonadal mosaicism is possible
  - The possibility of mosaicism is frequently the reason that parents cannot be completely reassured a condition affecting their child "will never happen again" in their family
- Genetic counselling will assist in enabling a couple to make an informed decision with the most up-to-date information

Understanding the patterns of inheritance of genetic conditions in families is becoming increasingly complex as discussed in Genetics Fact Sheet 2.

Complex patterns of inheritance

The cells of the body contain the genes or set of instructions for the cell to make all the necessary proteins (chemicals) for our bodies to grow and work normally (see Genetics Fact Sheet 1).

If a gene is changed so that it does not work properly, the gene is described as being faulty (ie. there is a gene *mutation* present). The information contained in the product of the faulty gene is impaired, or is not produced in the right amounts (see Genetics Fact Sheets 4 & 5).

The traditional patterns of inheritance apply to the inheritance of conditions due to changes in a single gene, located on the chromosomes in the nucleus (see Genetics Fact Sheets 8, 9 & 10). Estimating the chance of developing a genetic condition when someone carries a faulty gene is generally straightforward in these individuals.

In some cases, interactions between a person's genetic make-up and the environment means that despite the presence of a faulty gene, the condition does not always develop.

For example, not all women with a faulty breast cancer gene will develop breast cancer (see Genetics Fact Sheet 48). This is described as *incomplete penetrance* of the faulty gene: the gene is present but will not be expressed unless other environmental factors, or changes in other genes, are also present (see Genetics Fact Sheet 11). It is therefore more complex to determine the pattern of inheritance and to estimate the chance for a genetic condition to occur, if a faulty gene is present.

Another example of complex inheritance patterns is the situation where the faulty gene is located in small compartments in the cell called the *mitochondria*, rather than on a chromosome in the cell's nucleus. The pattern of inheritance of conditions due to faulty mitochondrial genes is also known as maternal inheritance and is discussed in Genetics Fact Sheet 12.

This Fact Sheet discusses another example of complex patterns of inheritance, where the genetic change is not present in all the cells of the individual. Instead, they have a mixture of cells containing the correct genetic information, and cells containing the changed information. This situation is referred to as *mosaicism*.

Mosaicism

A person can have some cells in their body in which the chromosome number is different from other cells. The concept of **mosaicism in relation to chromosomes** is discussed in Genetics Fact Sheet 6.

For most people, the genes in **all** the cells in their body will contain the same information, whether they are blood cells, skin cells or cells in other tissues like sperm (in men) and egg cells (in women). Where a parent has a gene change so that the gene is faulty, a child who inherits the faulty gene will usually have the faulty gene copy in all the cells of their body (see *Figure 13.1*).

Some people, however, will have a mixture of cells in their body in relation to their genetic information. Some cells in some body tissues or organs will have the right information in a particular gene(s), and other cells in the same or other tissues or organs will have the gene change(s) (*Figure 13.2*). Just as mosaic tiles on a floor have a mixture of patterns, someone with a mixture of cells containing different genetic information in a particular gene(s) is said to be mosaic for that gene change/ those gene changes.

When the faulty gene(s) is/are in only some of a woman's egg cells or a man's sperm cells, this is described as ***germline mosaicism***

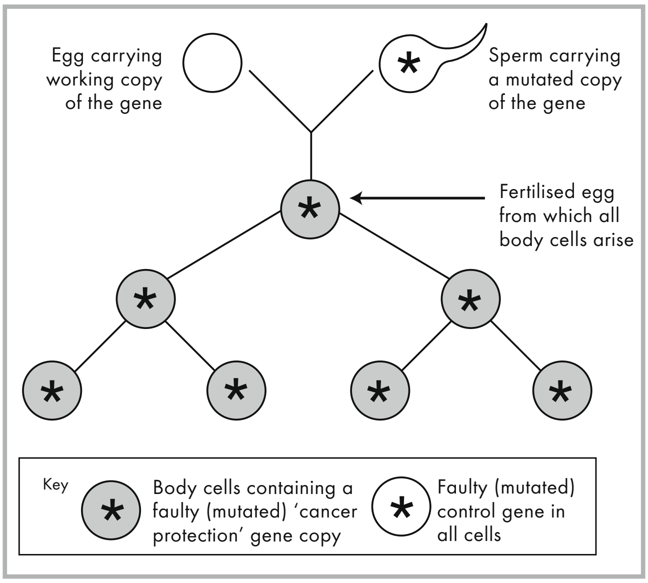

Figure 13.1. *A faulty gene will usually be present in all the cells arising from the fertilised egg*

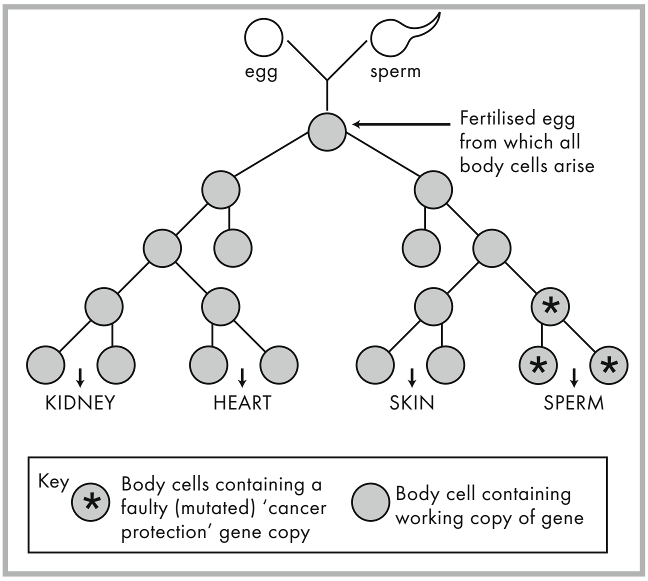

Figure 13.2. *The faulty gene copy is only in the sperm cells. The man is mosaic for the faulty gene. Since the sperm cells are in the 'germ cells', the man has germline mosaicism for the faulty gene.*

as the egg and sperm cells are referred to as ***germ cells*** (*Figure 13.2*). This situation is also described as ***gonadal* mosaicism** since the egg and sperm are produced in the ***gonads***.

Without studying the genes in every cell in the body (which is impossible), we cannot always be certain that someone is not mosaic for a gene change.

What are the indications that a person is mosaic for a faulty gene?

For a faulty gene to cause a problem, its product must have an impact on the cells of the tissue or organ in which it is present. For example, if the gene contains information for a protein or gene product that is important for brain function, but the faulty gene copy is only in the lung cells where the protein is not important, the person will not have the condition.

A person may therefore have the faulty gene detected in their blood cells but not show any signs of the condition if the faulty gene is not in the cells of tissues or organs where the faulty gene product would have an impact. In rare cases, this may explain the variability of symptoms in people with the same genetic condition. It is, however, impossible to study the genes in every cell in the body, and so we cannot always be certain if someone is mosaic for a faulty gene.

Germline mosaicism (mosaicism in sperm cells and egg cells)

A faulty gene may not be present in the blood cells, but is in the germ cells (egg or sperm cells). An indication that this is possible is when a couple have several children with a condition that is due to a 'dominant' faulty gene located on one of the numbered chromosomes (an autosome) but neither parent is affected with the condition (see Genetics Fact Sheet 9 for more information about autosomal dominant inheritance).

- When parents have one child with a condition that is due to an autosomal 'dominant' faulty gene but neither parent has the faulty gene on a blood test, it is usually assumed that the gene change in the child occurred due to a new or spontaneous change in the egg or sperm at, or shortly after conception
- When however, they have a second child with the same condition, the chance of the condition occurring again because of another spontaneous change in the same gene is highly unlikely
- The explanation may be that one of the parents is mosaic for the faulty gene in their egg (in the mother) or the sperm (in the father)

What can be done if there are indications that one of the parents is mosaic for a faulty gene in their egg or sperm cells (germline mosaicism)?

A number of genetic conditions have been described, where a change occurs in a gene in the germ cells ie. the egg cells of a woman or the sperm cells of a man.

This is seen, for example, in cases of neurofibromatosis type 2 (NF2) (see Genetics Fact Sheet 52).

- NF2 is a rare genetic condition that is primarily characterised by benign (non-cancerous) tumours of the nerves that transmit sound impulses from the inner ears to the brain. Associated symptoms and findings typically occur in adolescence or adulthood
- The condition is due to having a faulty copy of the *NF2* gene and the pattern of inheritance is autosomal dominant (see Genetics Fact Sheet 9)
- If a man or woman has germline mosaicism for *NF2*, they have a mixture of sperm or egg cells – some containing the faulty *NF2* gene copy and others containing the working *NF2* gene copy. They do not have an *NF2* faulty gene in any other cell in the body

- Therefore, he or she does not have NF2. They have no signs or symptoms associated with the condition; and their parents, uncles and aunts, cousins and grandparents and more extended family members do not have NF2
- Since some of their sperm or egg cells have a faulty copy of the *NF2* gene, there is **a chance** that their child will inherit a faulty copy of the *NF2* gene and will usually develop the condition. Estimating what that is for the parents is complex For example:
- If a mother has an autosomal dominant condition, it would be expected that on average half (50%) of her egg cells would contain the working copy, and half (50%) the faulty gene copy. There is therefore a 50%, or 1 in 2 chance of passing on either the faulty copy, or the working copy of the gene to each of her children
- On the other hand, if a woman has mosaicism for the gene change in her egg cells, it would be likely that **less** than 50% of her egg cells would carry the faulty gene. In other words, the chance of passing on the faulty gene to a child is less than 50%. This is lower than the chance of a woman affected with the condition passing on the faulty gene copy but it is not possible to provide a more accurate risk assessment

Testing in pregnancy to determine the presence of the faulty gene may be possible. For more information about prenatal testing options see Genetics Fact Sheet 17C. Testing of the embryo in association with assisted reproductive technologies (ART) including *in vitro* fertilisation (IVF) may also be possible (see Genetics Fact Sheet 18).

Genetic counselling may be helpful in assisting a couple with making an informed decision with the most up-to-date information available (see Genetics Fact Sheet 3).

Other Genetics Fact Sheets referred to in this Fact Sheet: 1, 2, 3, 4, 5, 6, 8, 9, 11, 12, 17C, 18, 48, 52

Information in this Fact Sheet is sourced from:

Harper P, (2004). *Practical Genetic Counselling*. London: Arnold

Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD) [online].Available from: http://www.ncbi.nlm.nih.gov/omim/ [Accessed June 2007]

Read A and Donnai D. (2007). *New clinical genetics*. Bloxham, Oxfordshire:Scion publishing

Edit history

June 2007 (1st Ed)

Author/s: A/Prof Kristine Barlow-Stewart and Gayathri Parasivam

Acknowledgements this edition: Dr Anne Turner