# FAQs for mosaicism, ERN-Skin, December 2019

Veronica Kinsler, Olivia Boccara and Jodi Whitehouse, with input from the whole mosaicism leader team

## What are genes?

Genes are a set of instructions. They can be thought of like an instruction booklet, but instead of telling you how to build a set of shelves, or how to make a cake, genes are instructions for how to build a person. Genes are passed on from parents to their children. When the mother and the father’s genes combine, they make a new and unique set of genes for the baby. Usually the baby will only have this one set of genes which are the same throughout the whole body.

## What is mosaicism?

Mosaicism means that there are two sets of genes in one person – one normal set, and one set which is the same except for one faulty gene. This mixture of normal and faulty genes means that some parts of the body develop entirely normally, and some parts abnormally.

## What causes mosaicism?

Mosaicism is caused by a fault occurring to one gene in part of the developing baby in the womb.

## When does the fault in the gene happen?

The fault in the gene can happen at any time during the pregnancy. If it happens earlier in pregnancy it usually causes more problems to the baby than if it happens near the end of pregnancy.

## What is a mosaic disorder?

This is not an exact definition, as it partly depends on size and shape and how common something is. However, in general a mosaic disorder is a medical condition present at birth (even if not visible at birth) which is caused entirely by mosaicism, is rare enough not to be thought of as part of normal human development. Birthmarks which occur very commonly (such as small single congenital melanocytic naevi, small single vascular stains, small single round sebaceous naevi or small single café-au-lait macules) are generally considered to be part of the normal range, not mosaic disorders. Isolated malignant tumours are also specifically excluded.

## Why is there so much variation between people with the same mosaic disorder?

There is often very wide variation between people with the same mosaic disorder diagnosis. Different parts of the body can be affected, and to different extents. This is because it depends when the fault in the gene happened during pregnancy (generally speaking earlier is probably more severe), exactly which part of the developing baby was affected by the faulty gene, and sometimes exactly which fault happens in the gene. As a result, it is best to speak to your doctor about what really applies to you/your child as an individual.

## I am the parent of a child with a mosaic disorder. Will I have another child affected by the same thing?

This is very unlikely to happen. Another child could have the same disorder by chance, but it is very unlikely.

## I am the parent of a child with a mosaic disorder. Did I cause it to happen by something I did in pregnancy?

In general, we think that the fault in the gene arises by chance and is not caused by anything that the parents did or didn’t do.

## I am a person with a mosaic disorder. Will I pass it on to my own children?

This depends on exactly which disorder you have, and sometimes it depends on exactly which faulty gene you have. We have recently published guidelines on this relating to all the diseases listed above (<https://onlinelibrary.wiley.com/doi/epdf/10.1111/bjd.17924> ), and you can ask your own doctor about this.

## What genetic tests are available for mosaicism?

It is possible to have genetic testing done on an area of the body which appears to be abnormal, for example to test a skin biopsy from a birthmark. In a very few mosaic disorders it is possible instead to do a blood test or a cheek swab, but this is unusual, and usually a skin biopsy or other type of tissue biopsy would be required. The genetic tests are available from some specialist centres around Europe, and they are becoming more commonly available.

## Should genetic testing be done for mosaicism?

This depends on the type of mosaic disorder, and it depends on the person themselves. For diagnoses where there is a possibility of passing the condition on to the next generation it is advisable to have a discussion with your doctor who may refer you to a clinical geneticist. In some other conditions having a genetic test can help decide whether there is a treatment available. In general, genetic testing is becoming commoner, and is likely to become more routine for mosaic disorders in the future.

## Where can I get more information on my/my child’s particular mosaic disorder?

On the ERN(https://ern-skin.eu/patient-advocacy/) there is a list of patient support groups in different countries which can often provide more information for patients and families. You can also get more information from your specialist doctors.

## Which other medical tests should I/my child have to look for problems in other parts of the body?

This depends on the type of mosaic disorder, and on the individual patient. In some cases no other investigations will be required, whereas in others some further investigations will be suggested by your doctors. The known associations of each condition have recently been reported (https://onlinelibrary.wiley.com/doi/full/10.1111/bjd.17924).

## Are there any treatments available for mosaic disorders?

This depends on the type of mosaic disorder, and on the individual patient. Recently doctors have started to try to use “targeted therapies” for mosaic disorders. These are usually medicines which are targeted at the faulty gene, or the effects of the faulty gene. Depending on the exact mosaic disorder there may or may not be treatments available, and depending on your/your child’s age and severity of problems the medicines may or may not be suitable for you. It is always ok to ask your doctor about whether any targeted therapies are available for your particular mosaic disorder, as more of these are being developed and tested over time. Moreover, there are several standard treatments available for the possible complications of specific mosaicisms.

## Should mosaic disorders be looked after by a specialist?

In general we would advise that patients with a mosaic disorder affecting the skin should be seen by a skin specialist who understands mosaic disorders. A list of EU specialists is available on the ERN website, and there are also many other specialist centres within the EU which may not be a member of the ERN. It may be that after an initial consultation the specialist recommends that you/your child are seen by local doctors, or they may recommend that you continue under a specialist centre. This will depend on the mosaic disorder and on each individual patient.

## **Which diagnoses are mosaic disorders affecting the skin?**

**Vascular malformations**

Capillary malformation

Venous malformation

Lymphatic malformation

Arteriovenous malformations

Mixed vascular malformations

Blue rubber bleb syndrome

**Vascular tumours**

Congenital haemangioma

Kaposiform haemangioendothelioma

Tufted angioma

**Naevi**

Congenital melanocytic naevus

Sebaceous naevus (including papiloomatous pedunculated sebaceous naevus)

Keratinocytic epidermal naevus (including ILVEN)

Hair follicle naevus (naevus comedonicus)

Connective tissue naevus (including collagenoma, elastoma)

Becker naevus

Linear syringocystadenoma papelliferum

Porokeratotic eccrine and ostial dermal duct naevus

Woolly hair naevus

Straight hair naevus (likely mosaic)

**Complex syndromes**

McCune-Albright syndrome

Proteus syndrome

*PIK3CA*- associated overgrowth spectrum (including CLOVES, MCAP, CLAPO and others)

Congenital melanocytic naevus syndrome

Generalised lymphatic anomaly/Gorham-Stout disease

Sturge-Weber syndrome

Phakomatosis pigmentokeratotica/Schimmelpenning syndrome

Other keratinocytic epidermal naevus syndromes (including FGFR3-related and KRAS-related)

Phakomatosis pigmentovascularis (various types)

Extensive or atypical dermal melanocytosis

Speckled lentiginous naevus syndrome

Fine and whorled Blaschko-linear macular hypopigmentation (including Hypomelanosis of Ito)

Fine and whorled Blaschko-linear macular hyperpigmentation (including naevoid and whorled hypermelanosis)

Segmental odonto-maxillary dysplasia

Happle-Tinschert or Curry-Jones syndrome

Vabres syndrome

Encephalocraniocutaneous lipomatosis syndrome

Phylloid hypermelanosis

Phylloid hypomelanosis

PHACE syndrome (likely mosaic)

**Mosaic versions of diseases which are usually seen affecting the whole body**

Mosaic neurofibromatosis type I (localised or generalised)

Mosaic Legius syndrome

Mosaic tuberous sclerosis

Mosaic dominant dystrophic epidermolysis bullosa

Naevoid epidermolytic hyperkeratosis