

Mosaicism describes the presence of two or more populations of cells with different genotypes in one individual that have developed from a single fertilized egg. This article reviews the various clinical presentations of mosaicism associated with hereditary cancer syndromes and the challenges in providing patients and their families with appropriate genetic testing, as well as provides recommendations for cancer presentation and early detection. Management of mosaicism is based on personal and family history, along with genetic testing results.

#### AT A GLANCE

- Newer technologies and more widespread use of genetic testing have resulted in the detection of more cases of mosaicism.
- Recommendations for care are made following careful review of the patient's personal and family history and discussion with the laboratory; additional testing may be needed to further clarify the meaning of the results.
- Oncology nurses should communicate with the genetics professional to obtain a clear understanding of the rationale behind the recommendations for care, as well as implications for testing in other family members, to ensure comprehensive care and psychosocial support for the patient and his or her family.

#### KEYWORDS

mosaicism; Li-Fraumeni syndrome; juvenile polyposis syndrome; genetic testing

#### DIGITAL OBJECT IDENTIFIER

10.1188/17.CJON.428-432

# Mosaicism

## Implications for genetic counseling and medical management

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**A**lthough the idea that all cells in the body contain an identical genetic component (genotype) may be a tempting one, the reality is that cells often differ genetically. Mosaicism refers to the occurrence of two or more genetically distinct populations of cells having developed from a single fertilized ovum (Machiela & Chanock, 2013). When a mutation occurs in a single cell after conception (postzygotic mutation), this leads to an individual having a mixture of cells, some with the mutation and some without (see Figure 1). Mosaicism can affect any cell or tissue from the developing embryo through adulthood. A mutation may be confined to only a subset of cells or may be present in multiple tissues and/or organs (Nussbaum, McInnes, & Willard, 2016). Mosaicism has been studied extensively in oncology because tumor initiation, maintenance, and evolution are mediated by the sequential acquisition of genetic variants in single cells (Vijg, 2014).

Gonadal or germline mosaicism is the occurrence of two or more genetically distinct cell populations present in the egg or sperm (Fernández, Torres, & Real, 2016). This phenomenon can result in de novo mutations (an alteration in a gene present for the first time in one family member as a result of a mutation in a germ cell or the fertilized egg). When the mutation is present in egg or sperm cells (germline mosaicism), the mutation can be passed on to an individual's offspring. Somatic mosaicism is the occurrence of two or more genetically distinct cell populations exclusively in somatic cells.

When mosaicism is detected only in cells from adult tissues, it is often impossible to determine when the genetic event leading to mosaicism occurred. An individual who is mosaic for a somatic mutation may or may not show the clinical signs (phenotype) of the disorder caused by that mutation (Vattathil & Scheet, 2016). Because of the exponential rate of growth during embryonic development, somatic mutations must occur early to have expression of phenotypic effects over large portions of the body (Freed, Stevens, & Pevsner, 2014).

Technological advances have resulted in the detection of genetic mosaicism (Biesecker & Green, 2014). When genetic testing reveals mosaicism for a specific mutation, determining what proportion of cells and tissues have this mutation, as well as the impact on cancer risk and whether this mutation could be transmitted to offspring, can be difficult (Cohen, Wilson, Trinh, & Ye, 2015). The following cases illustrate how mosaicism can lead to challenges in genetic counseling and medical management.

#### Case Study 1

E.W., a 61-year-old woman, was referred for genetic counseling because of a maternal history of breast cancer (see Figure 2) and underwent genetic testing. Results demonstrated that she was “apparently mosaic for a pathogenic variant in *TP53*: *TP53*c.916 C>T, p.Arg 306Ter (R306X),” meaning that some, but not all, of the cells had this *TP53* mutation. Interpretation of results included the following: The *TP53* mutation was a somatic, not inherited,