Supplementary material 1. Additional definitions

Term	Definition
Chimerism	Unlike a single zygote in mosaicism, chimerism is characterized by the fusion of two diverse zygotes, which results in the presence of two genetically unique cell populations similar to mosaicism. It can be discerned cytogenetically and also sometimes clinically.[1] e.g. Tetragametic chimerism
Revertant Mosaicism (RM)	This type of mosaicism involves a rectification of germline variants through somatic events during the stage of meiosis resulting in two distinct cell types. Occurs mainly through spontaneous reversion mutations, mitotic recombination etc. It has been described in EB in the early 2000s, wherein a junctional EB patient had showed reversion to normal patches of skin on hands and upper arms.[2,3]
Chromosomal mosaicism	The coexistence of two or more chromosomally unique cell populations within the same individual.[4]
Pseudo-mosaicism	This refers to the artifacts generated during the processing of samples. Cytogeneticists have designated protocols to distinguish between true and pseudo mosaicism. E.g., During experiments, if one cell shows a structural abnormality, a set of 10 cells from another flask is taken for validation. If no cells in the other flask display the same abnormality, the finding is classified as pseudo-mosaicism.[4]
Confined placental mosaicism (CPM)	This denotes the differences in the chromosomal makeup between the developing foetus and the placenta. The placenta can show aberrations (chromosomal) not present in the fetus.[5]
Epigenetic mosaicism	This refers to differences in gene expression between cells due to epigenetic modifications, such as DNA methylation, histone modifications, or non-coding RNA regulation, rather than differences in DNA sequence. This can lead to differences in phenotype even among genetically identical cells. It plays a role in normal development, X-chromosome inactivation, and various diseases, including cancer and imprinting disorders. [6,7]
Lyonization	An example of epigenetic mechanism which employs the silencing one of X chromosome and the modification of chromatins. As a result, mosaic patches of either abnormal or normal skin appear in female embryos, mostly arranged along Blaschko's lines. E.g. Incontinentia pigmenti, Goltz syndrome, Conradi-Hunermann-Happle syndrome.[6,7]
Didymosis (Twin spotting) Allelic and Non – Allelic	Refers to the occurrence of two adjacent but genetically distinct patches of skin or other tissues due to somatic mutations. It can be classified as allelic or non-allelic based on the underlying genetic mechanism.[8] Allelic - Occurs when both spots result from different mutations in the same gene (allelic mutations) E.g., McCune-Albright syndrome, where postzygotic somatic mutations in the GNAS gene lead to localized café-au-lait macules with adjacent normal skin.

	Non-allelic - Involves mutations in different genes (non-allelic) leading to two distinct but adjacent phenotypic manifestations. E.g., Type 1 segmental mosaicism in neurofibromatosis type 1 (NF1) and epidermal nevus occurring side by side due to independent postzygotic mutations in the NF1 and FGFR3 genes, respectively.
Loss of heterozygosity (LOH)	Refers to the loss of one allele at a specific locus in a cell that originally had two different alleles (heterozygosity). This commonly occurs due to deletions, mitotic recombination, or gene conversion. LOH is significant in cancer genetics, as it can inactivate tumor suppressor genes, leading to uncontrolled cell growth. E.g., In individuals with a germline mutation in one RB1 allele, LOH in the second allele leads to retinoblastoma development. LOH in the NF1 gene can lead to the development of neurofibromas.
Type 1 and Type 2 segmental mosaicism	**Type 1 segmental mosaicism** (T1SM) In this, postzygotic mutations lead to somatic mosaicism, affecting only a segment of the body. There is lower risk of systemic involvement compared to generalized forms. For e.g., in segmental neurofibromatosis type 1 (NF1), CALMs and neurofibromas are localized to a specific body region, and can be taken as an example of T1SM. Consequently, conventional genetic testing in blood would not pick up these variants; instead, cytogenetic techniques and cell assay techniques from skin biopsy of the affected site will identify the mutational variant.[9] **Type 2 Segmental mosaicism (T2SM)** In this, a postzygotic mutation occurs in an individual already carrying a germline mutation, leading to more severe manifestations in affected areas. For E.g., in NF1, plexiform neurofibromas; giant CALMs that may or may not contain neurofibromas; segmentally arranged, tightly packed neurofibromas without hyperpigmentation; plexiform neurofibromas affecting an entire limb - represent examples of T2SM. Here, patients with generalized NF1 develop additional segmental lesions due to a second somatic hit. Lesions present earlier and there is a higher risk of systemic disease transmission to offspring. Other examples include cutaneous leiomyomatosis, glomangiomatosis, Darier disease. [7, 10]
Hypomorphic allele	These are mutations which result only in a partial loss or reduced function of the protein
Gonosomal mosaicism	Refers to mosaicism affecting sex chromosomes (X or Y) and can be present in both somatic and germline (gonadal) cells. Example: 45, X/46, XY mosaicism in Turner syndrome.[11]
Gonadal mosaicism (also known as Germline Mosaicism)	Refers to the presence of a genetic mutation in a subset of an individual's germ cells (sperm or eggs) but not in their somatic (body) cells. This occurs due to a postzygotic mutation during early embryonic development, affecting only the gonadal lineage. Offspring will be affected despite unaffected parents, complicating genetic counselling and recurrence risk estimation. For e.g., osteogenesis imperfecta due to a COL1A1 mutation confined to gonadal cells in an asymptomatic parent.

	Thus, all gonadal mosaicism is not gonosomal mosaicism, but gonosomal mosaicism can include gonadal involvement.
Dominant negative mutation	The expression of mutant protein interferes with activity of the normal (wild type).[12] For e.g., COL7A1 mutations in Dystrophic EB
Haploinsufficiency	Haploinsufficiency occurs when a single functional copy of a gene (i.e.WT/ normal allele) is insufficient to maintain normal function, leading to disease. This typically happens when one allele is inactivated or deleted, and the remaining allele cannot produce enough gene product (protein) to compensate. For e.g., Ehler Danlos Syndrome, cleidocranial dysostosis, some cancers.[13]

EB- epidermolysis bullosa; RM- revertant mosaicism; CPM- confined placental mosaicism; NF1- Neurofibromatosis 1; LOH- loss of heterozygosity; CALM- café au lait macule; WT- wild type

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