Journal for Research in Applied Sciences and Biotechnology

www.jrasb.com

ISSN: 2583-4053

Volume-2 Issue-2 || April 2023 || PP. 259-267

https://doi.org/10.55544/jrasb.2.2.37

An Overview of Differences Between Types of Chimeras and Their Impact on Humans

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www.jrasb.com || Vol. 2 No. 2 (2023): April Issue

Received: 07-04-2023	**Revised:** 28-04-2023	**Accepted:** 08-05-2023

ABSTRACT

Chimera has several important definitions that are common to each other, where he is known a single creature that is made up of two or more separate populations of genetically unique cells that originated from various zygotes. Definition can be interpreted as cells from one person might appear in another individual in a process known as chimerism. These cells may be incorporated into the parenchyma or they may circulate. Chimeras are divided into several types depending on several factors such as the percentage of chimera cells in the body of the organism neighborhood, origin, or other reasons, which includes microchimeras, natural human macro-chimeras and man-made chimeras. Chimeric cells in human can arise from three significant sources, namely originating from gestation, blood transfusions, and transplants.

Keywords- Human natural chimeras, Microchimerism, Chimera, Chimerism, Fusion chimeras.

I. BACKGROUND

The term "chimera" alludes to a legendary monster composed of several animal parts. The chimera is described in Greek mythology as a fearsome, fire-breathing hybrid creature that resided in Lycia, Asia Minor, and was created from the pieces of three separate animals: a lion, a snake, and a goat. Figure 1 shows a lion with a goat's head sprouting out of its back and a tail that ends in a snake's head.

A chimera is a single creature that is made up of two or more separate populations of genetically unique cells that originated from various zygotes engaged in sexual reproduction. Chimeras may be found in a wide variety of organisms, including plants, animals, and microorganisms. The term "mosaic" refers to an organism in which all of the distinct cell types originated from the same zygote. Chimeras are made up of at least four different types of parent cells (two fertilized eggs or early embryos fused together). Because of this, each population of cells maintains its unique identity, resulting in an organism with a diverse assortment of tissues (Schlitt et al.,1998; Polejaeva and Mitalipov., 2013).

Figure 1: Chimera: An individual organ (Shrivastava *et al*.,2019).

In 1953, the first human chimera was discovered. Since Antiquity, the meaning of the word "chimera" has changed. A fantastical monster originally denoted by the term "chimera," but in contemporary medicine the term refers to a biological being made up

Journal for Research in Applied Sciences and Biotechnology

www.jrasb.com

ISSN: 2583-4053

Volume-2 Issue-2 || April 2023 || PP. 259-267

https://doi.org/10.55544/jrasb.2.2.37

of cells or tissues of several genotypes. However, this expression has a variety of distinct meanings depending on the field. A chimera is a hybrid embryo composed of cells from different individuals. In the field of molecular genetics, a chimera consists of two DNA molecules, either from two different persons or from two different chromosomes on the same individual's genome. In genetics, however, the term "chimera" is used to describe hybrids between different species, such as the mule (a female horse crossed with a male donkey) (Karpowicz et al.,2004).

The term "chimera" can also be used to refer to the process of transplanting cells or tissues from one person or species into a post-implantation embryo. For example, the intraperitoneal injection of hematopoietic stem cells into a sheep fetus to create a chimeric sheep that expresses human myeloid and lymphoid lineages is an example of this type of chimera. Chimeric sheep have human myeloid and lymphoid lineages (Srour, et al.,1992).

The term "chimera" shall denote the definition employed in the field of embryology. In the field of embryology, a notable instance of chimera creation dates back to the pioneering work of Hans Spemann and Hilde Mangold, wherein they transplanted a segment of an amphibian (Triturus) embryo into another embryo exhibiting diverse pigmentation levels (Le Douarin et al., 2008). Nicole Le Douarin et al. utilized chimeric embryos derived from chicken and quails for the purpose of conducting cell lineage tracing studies during the initial stages of vertebrate development. It has also been reported on natural chimeras in addition to those created by humans. As an illustration, fetal microchimerism, a situation where moms maintain some of their fetus' cells following pregnancy (Maloney et al.,1999).

II. CHIMERA CLASSIFICATION

Chimeras are divided into several types depending on several factors such as the percentage of chimera cells in the body of the organism neighborhood, origin, or other reasons.

1. Microchimeras

Numerous scholars have provided various definitions of microchimerism in the past. Galofré defined microchimerism as the existence of foreign cells with a genetically distinct background inside a single tissue (Galofré et al., 2012). It is described as the presence of cells with various genetic ancestries inside a single human by Waszak et al.

A small number of members of one population existing inside the same individual or within an organ such as the bone marrow (migration of cells from the infant to the mother). Thus, the term microchimerism describes the presence of a few cells or pieces of DNA that came from a genetically distinct person (Galofré *et al*., 2012; Nelson, 2003; Gammill and Nelson, 2010; Dawe *et al*., 2007).

Types of microchimerism:

There are two probable lineages for microchimeric cells:

1. Natural: Natural microchimerism examples include twinning, miscarriage, sexual intercourse, and pregnancy. A significant source of natural microchimerism is pregnancy.
2. Artificial: Blood transfusions and organ/tissue transplants are two instances of artificial microchimerism (Galofré *et al*., 2012; Boyon *et al*., 2011).

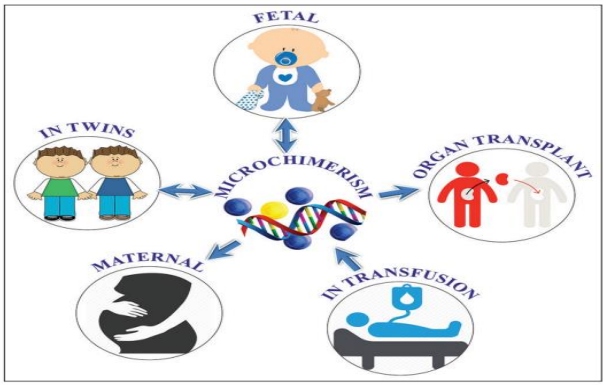

Figure 2: Types of microchimerism (Shrivastava *et al*.,2019).

1.1 Natural Human Microchimeras

Reversible transfer of maternal, fetal, and placental cells occurs during normal pregnancy (Galofré et al., 2012; Bianchi et al., 1996). (Figure 2). Most research papers about natural human microchimeras have been about mothers and their children. Transplacental cell trafficking creates natural microchimeras, most likely where the chorionic membrane of the child inside the uterus meets the decidual endometrium of the mother. The microchimera is a small cell population, thus the name. Any infant whose tissue samples show maternal cells at a frequency of less than 1% is considered to be a fetal microchimera, and any mother whose tissue samples show maternal cells at a frequency of less than 1% is considered to be a maternal microchimera (Wenk, 2018).

Figure 3: The bidirectional fetomaternal trafficking of cells across the placenta (Shrivastava *et al*.,2019).

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1- Fetal microchimeras

It is defining as small cell population of less than 1% is specified. (Some employees have utilized quantities as high as 5%.) In a typical early pregnancy, there are one to 150 fetal cells per milliliter of mother blood. Fetal cells multiply after complications such hyperemesis gravidarum, preeclampsia, premature delivery, fetal loss, and elective abortion. Fetal cells are able to migrate into and implant in the mother's tissues because pregnant women are immune to their child's antigens (Bianchi et al.,1996)

Abortion-related microchimerism in fetuses, it is more common for undifferentiated progenitor cells to be transferred from the fetus to the mother after an abortion, since the placenta is disrupted during the procedure. Women who had a surgical abortion after the first trimester had a higher level of fetal DNA identified in their bloodstreams than those who received a chemical abortion (Dawe et al., 2007) (Figure 4).

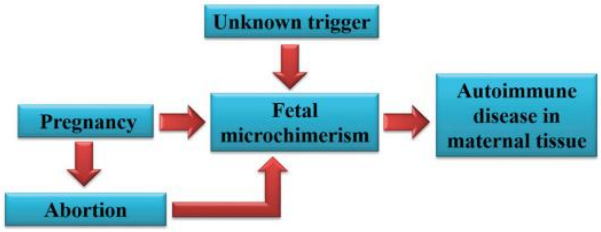

Figure 4: Elective abortion increases fetal microchimerism, which causes postabortive women to develop autoimmune disease.

It is the most common kind of natural microchimerism, present in every pregnancy and increasing in frequency as the gestational age increases. It entails the movement of whole, living fetal cells from the fetal circulation to the maternal circulation (Galofré *et al*., 2012; Dawe et al., 2007 Miech, 2010).

The migration of pluripotent progenitor cells of fetal hematopoietic origin commences during the fourth or fifth gestational week and persists throughout the entirety of the prenatal period. It is possible to detect these microchimeric fetal cells in the postpartum blood of the mother for up to 30 days (Miech, 2010; Vogelgesang et al., 2014).

In the lungs of autopsied pregnant women, trophoblastic cells with embryonic heritage were first seen and later found in the maternal blood. Recent efforts to do noninvasive prenatal genetic diagnosis and prenatal paternity testing relied on the collection of a variety of fetal cell types from maternal blood. (Cell-free DNA in maternal plasma collected between 8 and 10 weeks of gestation is now being used in prenatal tests.) Fetal cells, including lymphocytes and multipotent mesenchymal cells, may be found in the mother's blood.

The fetal cells may have advantageous benefits, such as enhanced maternal immunity, greater tissue repair and wound healing, and higher cancer resistance.

However, some research on fetal microchimeras indicates that fetal cells may be harmful and increase the risk of cancer and other maternal "autoimmune" illnesses that including Sjogren's syndrome, Type 1 diabetes mellitus, systemic sclerosis, lupus, mixed connective tissue disease, rheumatoid arthritis, and dermatomyositis (Jeanty, 2014).

2- Maternal microchimeras

Ancient research revealed that babies have maternal cells amongst their blood white blood cells, however not as frequently as mothers do (Loubière et al., 2006). Recent research, however, indicates that all human female babies are microchimeras (Dierselhuis and Goulmy, 2013).

Microchimerism (the existence of circulating fetal cells in mothers during and after pregnancy) is widely known (Bianchi et al., 1996; Gammill et al., 2010). However, nulliparous women also have male microchimeric cells (Yan et al., 2005).

Male microchimerism has been linked to a number of things, including missing male twins, (un)known male pregnancies, male leukocytes found in semen that reach a woman's bloodstream, and transmaternal transit of cells from older brothers (de Bellefon et al., 2010; Ariga et al., 2001; Moldenhauer et al., 2009; Bucher et al., 2007)

Future microchimerism research should pinpoint an individual's whole microchimeric repertoire, which is likely to include maternal, fetal, fraternal, grandmaternal, and other genetic material. While the microchimeric repertory in healthy males can alter with time.

Future microchimerism research should pinpoint an individual's whole microchimeric repertoire, which is likely to include maternal, fetal, fraternal, grandmaternal, and other genetic material. While the microchimeric repertory in healthy males can alter with time, While in women, the microchimeric repertoire can alter during pregnancy in addition to fluctuating over time. As a result, the female immune system faces more challenges and a greater risk of dysregulation. This might help to explain why more women are affected by autoimmune illnesses (Gammill et al., 2010; Dierselhuis and Goulmy, 2013).

Male white blood cells (WBCs), presumably inherited from mothers, have been detected in studies of cord blood from newborn females. The first entry point for male cells into the mother's blood remains a mystery. One possible explanation for the phenomenon is because it originated in a male fetus that was carried during a previous pregnancy. The procedure known as transplacental trafficking involves the transfer of a limited quantity of a pregnant woman's cells to the developing baby. Cells from the mother are able to implant themselves in various tissues of the developing fetus, where they may continue to live and carry out their duties. All of a newborn's organs and tissues, including the lungs, blood, spleen, heart, thymus, skin, and thyroid

ISSN: 2583-4053

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https://doi.org/10.55544/jrasb.2.2.37

gland include cells from the mother (Srivatsa et al., 2003).

Congenital primary biliary atresia and other illnesses have been linked to maternal T cells, but few studies have looked at the potential benefits or risks of these cells after they have been transferred to the child (Suskind et al., 2004).

3- Twin microchimeras

There are various speculative ways that dizygotic (DZ) twin microchimeras could develop. First, to create natural twin chimeras, cells from one twin might be directly transferred to the other by vascular anastomoses, and some stem cells may survive to reach the bone marrow of the blood recipient. Second, a recipient chimera's bone marrow may receive a large number of donor cells from a twin donor. Over time, the quantity of donor cells may decrease until it falls below the 1% microchimeric threshold. As a third point, transplacental cell trafficking may have allowed for the transfer of cells from one DZ twin to the other (Wenk, 2018).

1.2 Artificial microchimerism

1- Microchimerism and blood transfusion

Blood transfusion complications known as transfusion-associated microchimerism (TA MC) seem to be widespread and newly discovered (Knippen, 2011). It has been discovered that microchimerism from nonleukoreduced cellular blood products can persist for months to years following transfusion (Lee et al., 2005). It is now generally acknowledged that the transfusion-related response is probably caused by antigen antibody reactivity between the recipient's blood cells and the donor's plasma, or the other way around. Human leukocyte antigen (HLA) Class I and Class II antigens are examples of targets on the recipient's white blood cells that the antibodies may identify (Lee et al., 2005). TA MC has so far been identified after a blood transfusion for a patient who had sustained serious injuries. Injury creates an inflammatory and immunosuppressive environment where new blood components with replication-capable leukocytes can occasionally result in TA MC (Knippen, 2011).

2- Microchimerism in organ transplantation

According to a new theory put up by Starlz et al., the establishment of long-term tolerance is caused by the interchange of migratory leukocytes between the organ transplant recipient and donor. Microchimerism is the name for this occurrence. The idea is that the existence of donor cells in organ transplant recipients corresponds with tolerance and permits stopping or reducing immunosuppression. Some researchers think that transplantation will be profoundly impacted by this form of cell transfer between host and donor. It was hypothesized that cell migration may speed up graft-versus-host disease (GVHD), trigger rejection, or lay the groundwork for tolerance. In any case, it is not out of the possibility that these cells are only a harmless observer (Jindal and Sahota, 1997).

3- Microchimerism and bone marrow transplantation

The graft versus host disease that affects bone marrow transplant patients can result in severe harm and even death. It is generally accepted that organ transplantation involves the incorporation of "passenger" leukocytes from the donor into the organs or tissues of the recipient in order to establish a "microchimerism" state that is stable over time. Another important activity is the migration of circulating recipient leukocytes back and forth into the interstitial space of whole organ allografts. This refills the interstitial space. Following an organ transplant, the bidirectional exchange and interaction of bone marrow-derived cells is considered a significant event in the establishment of donor-specific tolerance and the acceptance of allografts (Perico and Remuzzi, 1997).

2. Natural human macro-chimeras

The scholarly discourse surrounding natural chimeras has predominantly centered on a pair of chimeric classifications, namely twin chimeras and fusion chimeras. The genotypes of cells in both sets can be identified in separate dizygotic twin pairs, who are considered full siblings. Chimeras with a minority cell population exceeding 1% of their total cell population are referred to without the prefix "micro" in their nomenclature. Despite the fact that natural macrochimeras are more precisely referred to as such, the term "chimera" continues to be employed due to its historical usage predating the discovery of microchimeras. Twin and fusion chimeras are characterized by the presence of embryonic cells originating from two distinct zygotes, which subsequently divide into two distinct populations as the embryo undergoes development. DZ cells have the potential to manifest in varying quantities across multiple organs.

2.1 Twin chimeras

A twin chimera is the offspring that is born as a consequence of a DZ twin pregnancy. fetal and embryonic hematopoietic cells are transfused from one DZ twin to the other via evident anastomoses in the placental blood vessels. It is possible that either one or both of the twins may get donated stem cells. These cells, once received, go to the bone marrow of the person receiving the blood transfusion and proliferate there. Either during the pregnancy itself (with the use of ultrasound tests), or after delivery, twins may be seen. Vascular anastomoses may form in DZ twins whose placentas have either entirely combined into one or have only partly integrated into a monochorionic placenta (Boklage, 2009).

Blood chimeras and 'blood group chimeras' are other names for twins with MFA in their RBCs. Since other names may be confused with chimeras made intentionally via therapeutic transfusion, the term "twin chimera" was used instead. Most, if not all, reported human "blood chimeras" have not had their extravascular tissues analyzed for DZ cell populations.

Journal for Research in Applied Sciences and Biotechnology

www.jrasb.com

ISSN: 2583-4053

Volume-2 Issue-2 || April 2023 || PP. 259-267

https://doi.org/10.55544/jrasb.2.2.37

That DZ cells persist in blood for a lengthy time is the only fact that the term "blood chimera" alludes to.

It is well-known that the proportion of donor cells in the blood of a twin chimera recipient varies widely. Less than 1% to 50% of the minor cell population may be microchimeric. The life duration of minor cell populations in extravascular tissues is almost completely unknown, although it most likely varies widely as well (Wenk, 2018).

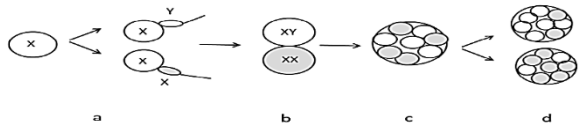

Figure 5: possible mechanism of formation of chimeric twins (souter et al., 2007)

a) The female pronucleus divides parthenogenetically, and then two spermatozoa, one with an X chromosome and the other with a Y chromosome, fertilize the two daughter cells.
b) The fusion of two zygotes.
c) Chimeric trigamete consisting of chromosomes 46, XX, and 46, XY.
d) Twinning occurrence in which the XX and XY cells were not distributed evenly, resulting in the birth of twins: one male (the one on top), and one real hermaphrodite.

2.2 Fusion chimeras

A human fusion chimera with two eye colors (brown and hazel) and one ovary and one ovotestis was described in 1962, created from dual-haploid cell lines (Gartler et al.,1962, Giblet et al., 1963).

Dizygotic twins or natural fusion chimeras are the potential result of the fertilization event involving two sperm cells and two female germ cells that are in close proximity to each other within the confines of the ovarian follicle and enclosed by the same zona pellucida. The theory presented challenges the commonly accepted notion that DZ twins are produced from ova that are released from distinct follicles. Additionally, it provides an explanation for why both MZ and DZ twins experience similar issues with embryonic asymmetry during development (Boklage, 2009).

A fusion chimera occurs when DZ embryonic cells admix to form a single embryo between the zygote and early blastocyst stages of development. Fusion chimeras were initially called "dispermic chimeras," a term that alluded to the fact that they were created from two different spermatozoa, but the role of maternal germ cells in their development was not recognized. Fertilization of an ovum and the first polar body, an ovum and the second polar body, or two secondary oocytes might have resulted in the formation of a fusion chimera. The term "tetragametic" was created when it was found that many distinct ova's genomes were present (Chapelle et al.,1974; Strain et al.,1998). The term "primary" (of unknown origin) chimera has also been used since the creation of a fusion chimera has never been directly seen. All chimeras, even those who have undergone organ transplantation, contain four gamete genomes, hence the term "tetragametic" is misleading.

Mice embryos between the zygote stage and early blastocysts may be used to create fusion chimeras for experimental purposes (Tarkowski, 2004). Human fusion chimeras might theoretically originate from the same processes. Although close implantation of two blastocysts is unlikely to occur naturally in humans (Miura and Niikawa, 2005), it is possible to occur after in vitro fertilization. Morulas making contact with one another prior to the implantation of embryonic cell masses into the endometrium.

The three most common ways they take shape are as follows: (Figure 1)
1) Tetragametic chimeras are produced through the fusion of two zygotes, each resulting from the fertilization of an ovum by a spermatozoon.
2) Tetragametic chimeras are created when a fertilized ovum and a fertilized second polar body fuse together.
3) Parthenogenetic chimeras, also known as trigametic chimeras, are formed when a female pronucleus undergoes a process of parthenogenetic division, and the resulting two daughter cells are subsequently fertilized by two separate spermatozoa.

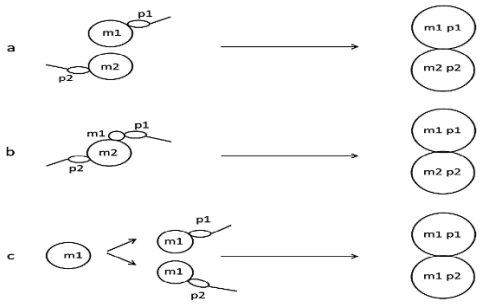

Figure 1: Fusion chimera genesis. a) The fusion of two fertilized eggs. b) Fusion of a fertilized 2nd polar body with a fertilized egg. c) Duplication of the female pronucleus followed by fertilization of the two female pronuclei by two spermatozoa.

3 Man-Made chimeras

Patients who have had successful transplants retain donor cells that are viable and have nuclei for extended periods of time. All recipients of transplanted cells, tissues, or organs are artificial chimeras, meaning they are made up of cells from two or more different species (Race, 1975). All the cells in a population share the same nuclear genome with a single representative cell. Some transplant recipients become iatrogenic chimeras when doctors make a mistake during the procedure that leaves them with donor cells instead of recipient cells. In vitro fertilization (IVF) chimeras are another kind of iatrogenic chimera.

ISSN: 2583-4053
Volume-2 Issue-2 || April 2023 || PP. 259-267
https://doi.org/10.55544/jrasb.2.2.37

3.1 Therapeutic chimeras

There may be two or more cell types present in human chimeras since they include cells from many donors. Similar to DZ cells in natural chimeras, donor and recipient cells fight for survival in transplant chimeras. Potentially, certain cell populations may gradually expand at the expense of others. Immunologically tolerant chimeras include those created by in vitro fertilization (IVF), natural twin and fusion chimeras, and natural maternal microchimeras. However, a transplanted child or adult will often reject an allogeneic graft. Therefore, donor-derived cells have an immunological disadvantage when competing with endogenous cells.

Graft survival is decreased when xenogeneic cells or tissues are engrafted instead of allogeneic ones. However, in some medical situations, transient xenografts are allowed as lifesavers. In the case of burn victims, porcine skin engraftment has the potential to reduce the risk of infections, fluid loss, and electrolyte imbalance in the short term. In addition, new technology is anticipated to extend xenografts' usefulness. Islet transplants from pigs have great potential as long-term grafts for people with Type 1 diabetes because to a lack of human pancreatic islet cell donors, provided that endogenous pig retroviruses can be removed using CRSPR-Cas9 technology (Park and Hawthorne, 2015; Puga et al., 2017).

3.2 Iatrogenic transplant chimeras

Unintentional transplantation of allogeneic cells may result in the creation of man-made chimeras. It is a well-established fact that trauma patients who have undergone multiple transfusions are capable of accepting granulocytes and lymphocytes from a donor, even in cases where the donor blood has undergone leukoreduction (Bloch et al., 2013). As "transfusion-associated microchimeras," the latter cells may live for decades. The implantation of lymphocytes in patients during solid organ transplantation has been observed to result in immunological hemolysis in individuals who have received transplanted blood stem cells, livers, kidneys, lungs, and intestines. The phenomenon known as "passenger lymphocyte syndrome" is a self-limiting condition that pertains to the issues that arise after a transplant procedure (Peck et al., 2015).

3.3 In vitro fertilization chimeras

In vitro fertilization (IVF) involves the mechanical manipulation of human ova three times: first, during the selection of ova for fertilization; second, during fertilization (especially intracytoplasmic sperm injection); and third, during the transfer of two or more embryos to the uterus 1–5 days after fertilization.

"IVF-associated chimeras" are iatrogenic and created by humans. Their number, the location of DZ cells in tissues, or the survival of the DZ cells have not been the subject of any systematic research. To increase the likelihood of a successful pregnancy, two or more embryos are delivered to the uterus during IVF. Multiple births and MZ and DZ twinning are both significantly increased. Some twin chimeras created using IVF. Others are singletons, which might be fusion chimeras or twin chimeras that overcame sibling loss during pregnancy. The "vanished twin syndrome" refers to the possibility of an ultrasound absence of a twin after its death. Serial ultrasound investigations have shown that 18% of multiple babies in IVF pregnancies seem to "disappear." Gross placenta inspection after delivery may reveal signs of a missing twin (Steptoe and Walters, 1986; Shinnick et al., 2017).

Mosaic

It's important to distinguish between a genetic mosaic, which also contains two cell populations, and a genetic chimera, which is the result of random genetic mutations. A chimera develops from the combination of two zygotes, whereas a mosaic develops from a single one. A mosaic develops when a single cell suffers a heritable alteration during embryogenesis, when cells with identical nuclear DNA reproduce fast. The variation may take the form of either a change in the number of chromosomes in a cell or a mutation in its genetic code. A new cell population forms when offspring of a changed cell also inherit the modification. Molecular biology labs can typically tell the difference between genetic chimerism and genetic mosaicism.

Mosaicism typically involves modification of a limited number of chromosomal locations, often only one or two. One common type of mutation at a "short tandem repeat" (STR) locus in DNA can result in an increase in the size of an allele by one repeating base sequence. Assuming a "repeat" of four nucleotide bases, it can be inferred that the resulting offspring of the mutant cell will possess an allele that is four bases larger. The preservation of STR loci that did not undergo mutation is observed in the progeny of non-mutating cells, wherein both the original STR alleles are retained. All chromosomes seem to be affected by genetic chimerism in STR testing. Both cell populations have normal genomes, but when their DNA is combined, several locations show evidence of having more than two copies of the DZ allele.

To complicate matters, clinicians have historically used the word “mosaic” to describe two-toned skin patterns that sometimes occur in natural chimeras (Kouzak et al., 2013)

Within the field of dermatology, the term "mosaic" denotes a perceived pattern or arrangement present on the surface of the skin. The design exhibits similarities to artistic mosaics. According to Thomas et al. (1989), research on individuals who exhibit skin mosaicism has revealed that certain cases are indeed genetic mosaics, while others are natural chimeras, and some do not fall into either category.

Genetic ‘hybrid’

Another way in which a natural chimera and a genetic hybrid are different is in their parentage. A hybrid results when two species with differing

ISSN: 2583-4053

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https://doi.org/10.55544/jrasb.2.2.37

evolutionary histories mate (genera, species, or subspecies). Like a mosaic, a hybrid has just one set of chromosomes (MZ). When an ovum from one animal class is fertilized by sperm from another animal class, the resulting zygote will have two sets of identical genomes in its two diploid daughter cells. The "modern" human race is a combination of Neanderthals and our own ancestors, who bred to create them. In a hybrid, a single cell's worth of DNA comes from both parent species, whereas in a chimera, it comes from only one (Prüfer et al., 2014).

REFERENCES

[1] Ando, T., & Davies, T. F. (2004). Self-recognition and the role of fetal microchimerism. *Best Practice & Research Clinical Endocrinology & Metabolism*, *18*(2), 197-211.

[2] Kouzak, S. S., Mendes, M. S. T., & Costa, I. M. C. (2013). Cutaneous mosaicisms: concepts, patterns and classifications. *Anais Brasileiros de Dermatologia*, *88*, 507-517.

[3] Thomas, I. T., Frias, J. L., Cantu, E. S., Lafer, C. Z., Flannery, D. B., & Graham Jr, J. G. (1989). Association of pigmentary anomalies with chromosomal and genetic mosaicism and chimerism. *American journal of human genetics*, *45*(2), 193.

[4] Aoki, R., Honma, Y., Yada, Y., Momoi, M. Y., & Iwamoto, S. (2006). Blood chimerism in monochorionic twins conceived by induced ovulation: case report. *Human Reproduction*, *21*(3), 735-737.

[5] Ariga, H., Ohto, H., Busch, M. P., Imamura, S., Watson, R., Reed, W., & Lee, T. H. (2001). Kinetics of fetal cellular and cell-free DNA in the maternal circulation during and after pregnancy: implications for noninvasive prenatal diagnosis. *Transfusion*, *41*(12), 1524-1530.

[6] Barton, L. J., LeBlanc, M. G., & Lehmann, R. (2016). Finding their way: themes in germ cell migration. *Current opinion in cell biology*, *42*, 128-137.

[7] Bianchi, D. W., Flint, A. F., Pizzimenti, M. F., Knoll, J. H., & Latt, S. A. (1990). Isolation of fetal DNA from nucleated erythrocytes in maternal blood. *Proceedings of the National Academy of Sciences*, *87*(9), 3279-3283.

[8] Bianchi, D. W., Zickwolf, G. K., Weil, G. J., Sylvester, S., & DeMaria, M. A. (1996). Male fetal progenitor cells persist in maternal blood for as long as 27 years postpartum. *Proceedings of the National Academy of Sciences*, *93*(2), 705-708.

[9] Bianchi, D. W., Zickwolf, G. K., Weil, G. J., Sylvester, S., & DeMaria, M. A. (1996). Male fetal progenitor cells persist in maternal blood for as long as 27 years postpartum. *Proceedings of the National Academy of Sciences*, *93*(2), 705-708.

[10] Bianchi, D. W., Zickwolf, G. K., Weil, G. J., Sylvester, S., & DeMaria, M. A. (1996). Male fetal progenitor cells persist in maternal blood for as long as 27 years postpartum. *Proceedings of the National Academy of Sciences*, *93*(2), 705-708.

[11] Boklage, C. E. (2009). Traces of embryogenesis are the same in monozygotic and dizygotic twins: Not compatible with double ovulation. *Human Reproduction*, *24*(6), 1255-1266.

[12] Burastero, S. E., Galbiati, S., Vassallo, A., Sabbadini, M. G., Bellone, M., Marchionni, L., ... & Cremonesi, L. (2003). Cellular microchimerism as a lifelong physiologic status in parous women: an immunologic basis for its amplification in patients with systemic sclerosis. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *48*(4), 1109-1116.

[13] CHAPELLE, A. D. L., Schröder, J. I. M., RANTANEN, P., THOMASSON, B., NIEMI, M., TIILIKAINEN, A., ... & ROBSON, E. B. (1974). Early fusion of two human embryos?. *Annals of Human Genetics*, *38*(1), 63-75.

[14] Chung, Y. N., Chun, S., Phan, M. T. T., Nam, M. H., Choi, B. M., Cho, D., & Choi, J. S. (2018). The first case of congenital blood chimerism in two of the triplets in Korea. *Journal of Clinical Laboratory Analysis*, *32*(8), e22580.

[15] Davies, A. J. (2012). Immigration control in the vertebrate body with special reference to chimerism. *Chimerism*, *3*(1), 1-8.

[16] Dawe, G. S., Tan, X. W., & Xiao, Z. C. (2007). Cell migration from baby to mother. *Cell Adhesion & Migration*, *1*(1), 19-27.

[17] Dierselhuis, M. P., & Goulmy, E. (2013). We are all born as microchimera. *Chimerism*, *4*(1), 18-19.

[18] Dunsford, I., Bowley, C. C., Hutchison, A. M., Thompson, J. S., Sanger, R., & Race, R. R. (1953). Human blood-group chimera. *British medical journal*, *2*(4827), 81.

[19] Eikmans, M., & Claas, F. H. (2011). HLA-targeted cell sorting of microchimeric cells opens the way to phenotypical and functional characterization. *Chimerism*, *2*(4), 114-116.

[20] Evans, P. C., Lambert, N., Maloney, S., Furst, D. E., Moore, J. M., & Nelson, J. L. (1999). Long-term fetal microchimerism in peripheral blood mononuclear cell subsets in healthy women and women with scleroderma. *Blood, The Journal of the American Society of Hematology*, *93*(6), 2033-2037.

[21] Ford, C. E. (1969). Mosaics and chimaeras. *British Medical Bulletin*, *25*(1), 104-109.

[22] Furst, D. E., Clements, P. J., Graze, P., Gale, R., & Roberts, N. (1979). A syndrome resembling progressive systemic sclerosis after bone marrow transplantation. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *22*(8), 904-910.

[23] Gammill, H. S., Guthrie, K. A., Aydelotte, T. M., Waldorf, K. M. A., & Nelson, J. L. (2010). Effect of parity on fetal and maternal microchimerism: interaction

ISSN: 2583-4053

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https://doi.org/10.55544/jrasb.2.2.37

of grafts within a host?. *Blood, The Journal of the American Society of Hematology*, *116*(15), 2706-2712.

[24] Gartler, S. M., Waxman, S. H., & Giblett, E. (1962). An XX/XY human hermaphrodite resulting from double fertilization. *Proceedings of the National Academy of Sciences*, *48*(3), 332-335.

[25] Giblett, E. R., Gartler, S. M., & Waxman, S. H. (1963). Blood group studies on the family of an XX/XY hermaphrodite with generalized tissue mosaicism. *American Journal of Human Genetics*, *15*(1), 62.

[26] Golubovsky, M. D. (2003). Postzygotic diploidization of triploids as a source of unusual cases of mosaicism, chimerism and twinning. *Human Reproduction*, *18*(2), 236-242.

[27] Hadjiathanasiou, C. G., Brauner, R., Lortat-Jacob, S., Nivot, S., Jaubert, F., Fellous, M., ... & Rappaport, R. (1994). True hermaphroditism: genetic variants and clinical management. *The Journal of pediatrics*, *125*(5), 738-744.

[28] Hong, X., Ying, Y., Xu, X., Liu, Y., Chen, Z., Lan, X., & Yan, L. (2013). A dispermic chimera was identified in a healthy man with mixed field agglutination reaction in ABO blood grouping and mosaic 46, XY/46, XX karyotype. *Transfusion and Apheresis Science*, *48*(2), 223-228.

[29] Jacobson, D. L., Gange, S. J., Rose, N. R., & Graham, N. M. (1997). Epidemiology and estimated population burden of selected autoimmune diseases in the United States. *Clinical immunology and immunopathology*, *84*(3), 223-243.

[30] Jeanty, C., Derderian, S. C., & MacKenzie, T. C. (2014). Maternal-fetal cellular trafficking: clinical implications and consequences. *Current opinion in pediatrics*, *26*(3), 377.

[31] Jindal, R. M., & Sahota, A. (1997). The role of cell migration and microchimerism in the induction of tolerance after solid organ transplantation. *Postgraduate medical journal*, *73*(857), 146-150.

[32] Johnson, K. L., McAlindon, T. E., Mulcahy, E., & Bianchi, D. W. (2001). Microchimerism in a female patient with systemic lupus erythematosus. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *44*(9), 2107-2111.

[33] Karpowicz, P., Cohen, C. B., & Van der Kooy, D. (2004). It is ethical to transplant human stem cells into nonhuman embryos. *Nature medicine*, *10*(4), 331-335.

[34] Kelkar, R. L., Meherji, P. K., Kadam, S. S., Gupta, S. K., & Nandedkar, T. D. (2005). Circulating auto-antibodies against the zona pellucida and thyroid microsomal antigen in women with premature ovarian failure. *Journal of reproductive immunology*, *66*(1), 53-67.

[35] Knippen, M. A. (2011). Microchimerism: sharing genes in illness and in health. *International Scholarly Research Notices*, *2011*.

[36] Le Douarin, N., Dieterlen-Lièvre, F., Creuzet, S., & Teillet, M. A. (2008). Quail–Chick Transplantations. *Methods in cell biology*, *87*, 19-58.

[37] Lee, T. H., Paglieroni, T., Utter, G. H., Chafets, D., Gosselin, R. C., Reed, W., ... & Busch, M. P. (2005). High-level long-term white blood cell microchimerism after transfusion of leukoreduced blood components to patients resuscitated after severe traumatic injury. *Transfusion*, *45*(8), 1280-1290.

[38] Lepez, T., Vandewoestyne, M., Hussain, S., Van Nieuwerburgh, F., Poppe, K., Velkeniers, B., ... & Deforce, D. (2011). Fetal microchimeric cells in blood of women with an autoimmune thyroid disease. *PLoS One*, *6*(12), e29646.

[39] Lissauer, D. M., Piper, K. P., Moss, P. A., & Kilby, M. D. (2009). Fetal microchimerism: the cellular and immunological legacy of pregnancy. *Expert Reviews in Molecular Medicine*, *11*.

[40] Loubière, L. S., Lambert, N. C., Flinn, L. J., Erickson, T. D., Yan, Z., Guthrie, K. A., ... & Nelson, J. L. (2006). Maternal microchimerism in healthy adults in lymphocytes, monocyte/macrophages and NK cells. *Laboratory investigation*, *86*(11), 1185-1192.

[41] Machin, G. (2009, May). Non-identical monozygotic twins, intermediate twin types, zygosity testing, and the non-random nature of monozygotic twinning: a review. In *American Journal of Medical Genetics Part C: Seminars in Medical Genetics* (Vol. 151, No. 2, pp. 110-127). Hoboken: Wiley Subscription Services, Inc., A Wiley Company.

[42] Maloney, S., Smith, A., Furst, D. E., Myerson, D., Rupert, K., Evans, P. C., & Nelson, J. L. (1999). Microchimerism of maternal origin persists into adult life. *The Journal of clinical investigation*, *104*(1), 41-47.

[43] Miech, R. P. (2010). The role of fetal microchimerism in autoimmune disease. *International Journal of Clinical and Experimental Medicine*, *3*(2), 164.

[44] Miura, K., & Niikawa, N. (2005). Do monochorionic dizygotic twins increase after pregnancy by assisted reproductive technology?. *Journal of human genetics*, *50*(1), 1-6.

[45] Moldenhauer, L. M., Diener, K. R., Thring, D. M., Brown, M. P., Hayball, J. D., & Robertson, S. A. (2009). Cross-presentation of male seminal fluid antigens elicits T cell activation to initiate the female immune response to pregnancy. *The Journal of Immunology*, *182*(12), 8080-8093.

[46] Mueller, U. W., Hawes, C. S., Wright, A. E., DeBoni, E., Jones, W. R., Firgaira, F. A., ... & Turner, D. R. (1990). Isolation of fetal trophoblast cells from peripheral blood of pregnant women. *The Lancet*, *336*(8709), 197-200.

[47] Mujahid, A., & Dickert, F. L. (2015). Blood group typing: from classical strategies to the application of synthetic antibodies generated by molecular imprinting. *Sensors*, *16*(1), 51.

ISSN: 2583-4053

Volume-2 Issue-2 || April 2023 || PP. 259-267

https://doi.org/10.55544/jrasb.2.2.37

[48] Niu, D. M., Pan, C. C., Lin, C. Y., Hwang, B., & Chung, M. Y. (2002). Mosaic or chimera? Revisiting an old hypothesis about the cause of the 46, XX/46, XY hermaphrodite. *The Journal of pediatrics*, *140*(6), 732-735.

[49] O'donoghue, K., Choolani, M., Chan, J., De la Fuente, J., Kumar, S., Campagnoli, C., ... & Fisk, N. M. (2003). Identification of fetal mesenchymal stem cells in maternal blood: implications for non-invasive prenatal diagnosis. *Molecular human reproduction*, *9*(8), 497-502.

[50] Owen, R. D., Davis, H. P., & Morgan, R. F. (1946). Quintuplet calves and erythrocyte mosaicism. *Journal of Heredity*, *37*(10), 291-297.

[51] Park, C. G., Bottino, R., & Hawthorne, W. J. (2015). Current status of islet xenotransplantation. *International Journal of Surgery*, *23*, 261-266.

[52] Perico, N., & Remuzzi, G. (1997). Acquired transplant tolerance. *International Journal of Clinical and Laboratory Research*, *27*(2), 165-177.

[53] Polejaeva, I., & Mitalipov, S. (2013). Stem cell potency and the ability to contribute to chimeric organisms. *Reproduction (Cambridge, England)*, *145*(3), R81.

[54] Prüfer, K., Racimo, F., Patterson, N., Jay, F., Sankararaman, S., Sawyer, S., ... & Pääbo, S. (2014). The complete genome sequence of a Neanderthal from the Altai Mountains. *Nature*, *505*(7481), 43-49.

[55] Puga Yung, G., Rieben, R., Buehler, L. H., Schuurman, H. J., & Seebach, J. D. (2017). Xenotransplantation: where do we stand in 2016?. *Swiss medical weekly*, *147*, w14403.

[56] Ramsay, M., Pfaffenzeller, W., Kotze, E., Bhengu, L., Essop, F., & De Ravel, T. (2009). Chimerism in black southern African patients with true hermaphroditism 46, XX/47XY,+ 21 and 46, XX/46, XY. *Annals of the New York Academy of Sciences*, *1151*(1), 68-76.

[57] Repas-Humpe, L. M., Humpe, A., Lynen, R., Glock, B., Dauber, E. M., Simson, G., ... & Eber, S. (1999). A dispermic chimerism in a 2-year-old Caucasian boy. *Annals of hematology*, *78*(9), 431-434.

[58] Ron-El, R., Nachum, H., Golan, A., Herman, A., Yigal, S., & Caspi, E. (1990). Binovular human ovarian follicles associated with in vitro fertilization: incidence and outcome. *Fertility and sterility*, *54*(5), 869-872.

[59] Schlitt, H. J., Ko, S., Deiwick, A., & Hundrieser, J. (1998). Microchimerism in organ transplantation. *Organ Transplantation in Rats and Mice*, *1*, 285-98.

[60] Shin, S. Y., Yoo, H. W., Lee, B. H., Kim, K. S., & Seo, E. J. (2012). Identification of the mechanism underlying a human chimera by SNP array analysis. *American Journal of Medical Genetics Part A*, *158*(9), 2119-2123.

[61] Shrivastava, S., Naik, R., Suryawanshi, H., & Gupta, N. (2019). Microchimerism: A new concept. *Journal of oral and maxillofacial pathology: JOMFP*, *23*(2), 311.

[62] Srivatsa, B., Srivatsa, S., Johnson, K. L., & Bianchi, D. W. (2003). Maternal cell microchimerism in newborn tissues. *The Journal of pediatrics*, *142*(1), 31-35.

[63] Srour, E. F., Zanjani, E. D., Brandt, J. E., Leemhuis, T., Briddell, R. A., Heerema, N. A., & Hoffman, R. (1992). Sustained human hematopoiesis in sheep transplanted in utero during early gestation with fractionated adult human bone marrow cells.

[64] Strain, L., Dean, J. C., Hamilton, M. P., & Bonthron, D. T. (1998). A true hermaphrodite chimera resulting from embryo amalgamation after in vitro fertilization. *New England Journal of Medicine*, *338*(3), 166-169.

[65] Suskind, D. L., Rosenthal, P., Heyman, M. B., Kong, D., Magrane, G., Baxter-Lowe, L. A., & Muench, M. O. (2004). Maternal microchimerism in the livers of patients with biliary atresia. *BMC gastroenterology*, *4*(1), 1-7.

[66] Tanaka, A., Nakamura, H., Kumasawa, K., Tsutsui, T., Furuya, K., Kim, N., ... & Kimura, T. (2016). A case report of conjoined oocytes with independent zona pellucida from polycystic ovary syndrome. *J Gynaecol Obstet*, *4*(5), 25-29.

[67] Tarkowski, A. K. (2004). Mouse chimaeras revisited: recollections and reflections. *International Journal of Developmental Biology*, *42*(7), 903-908.

[68] Van Dijk, B. A., Boomsma, D. I., & de Man, A. J. (1996). Blood group chimerism in human multiple births is not rare. *American journal of medical genetics*, *61*(3), 264-268.

[69] Viëtor, H. E., Hallensleben, E., van Bree, S. P., van der Meer, E. M., Kaal, S. E., Bennebroek-Gravenhorst, J., ... & Claas, F. H. (2000). Survival of donor cells 25 years after intrauterine transfusion. *Blood, The Journal of the American Society of Hematology*, *95*(8), 2709-2714.

[70] Wang, L., Wang, F. S., & Gershwin, M. E. (2015). Human autoimmune diseases: a comprehensive update. *Journal of internal medicine*, *278*(4), 369-395.

[71] Wenk, R. E. (2018). A review of the biology and classification of human chimeras. *Transfusion*, *58*(8), 2054-2067.

[72] Yan, Z., Lambert, N. C., Guthrie, K. A., Porter, A. J., Loubiere, L. S., Madeleine, M. M., ... & Nelson, J. L. (2005). Male microchimerism in women without sons: quantitative assessment and correlation with pregnancy history. *The American journal of medicine*, *118*(8), 899-906.