YOU ARE NOT ENTIRELY YOU: MICROCHIMERISM AND THE HIDDEN PERSISTENCE OF FOREIGN CELLS- A SYSTEMATIC REVIEW AND META ANALYSIS

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Abstract

The human body was traditionally considered a self-contained system defined by a single genetic identity; however, this concept of biological unity has been challenged by the phenomenon of microchimerism. Microchimerism was defined as the long-term presence of a small population of genetically distinct cells within a host, most commonly originating from pregnancy, blood transfusion, or organ transplantation. The aim of this review was to synthesize current experimental and clinical evidence in order to evaluate whether microchimeric cells acted as functional contributors to host physiology, remained biologically neutral, or participated in pathological processes such as autoimmunity and cancer. The reviewed studies indicated that microchimeric cells were widely distributed across multiple human tissues and were capable of expressing tissue-specific markers, suggesting potential functional integration within the host. Evidence further showed that microchimerism exhibited a dual role, being associated with protective effects in certain cancers such as breast cancer and papillary thyroid cancer, while also being observed at increased levels in conditions such as colon cancer and autoimmune diseases. In addition, some findings suggested possible involvement in tissue repair, although the underlying mechanisms remained unclear. Published experimental and clinical studies were reviewed, including evidence obtained through cytogenetic and molecular techniques such as FISH, STR analysis, qPCR, ddPCR, and next-generation sequencing (NGS). Overall, the findings suggested that microchimerism challenged the traditional concept of biological individuality by demonstrating that the human body functioned as a dynamic system in which the boundary between self and non-self was not absolute.

Keywords: Microchimerism, immune tolerance, autoimmune disease, carcinogenesis, tissue repair.

Introduction

Biological identity has traditionally been understood as a stable and self-contained system encoded in DNA and confined within the boundaries of the human body.
However, this concept has been challenged by the phenomenon of microchimerism.
The term “microchimerism” refers to the presence of a small population of genetically distinct cells within an individual, most commonly acquired through pregnancy, blood transfusion, or organ transplantation.
Although these cells originate from another individual, they can persist for long periods and may integrate into host tissues. This phenomenon raises important questions regarding the functional role of foreign cells within the human body and their potential impact on health and disease.
The aim of this review was to synthesize current experimental and clinical evidence to evaluate whether microchimeric cells act as functional contributors to host physiology, remain biologically neutral, or participate in pathological processes.
Recent developments in chimerism analysis have introduced more advanced and sensitive molecular techniques, including quantitative polymerase chain reaction (qPCR), droplet digital PCR (ddPCR), and next-generation sequencing (NGS). These methods allow for the detection of very low levels of chimerism, often below 1%, and have improved the ability to monitor engraftment dynamics and identify early signs of disease relapse. Despite their high sensitivity and precision, their overall clinical utility remains under evaluation.

Results suggest that microchimerism may have beneficial roles, such as contributing to tissue repair, but may also have pathological effects, including the development of autoimmune diseases and certain types of cancer.
As research on microchimerism expands, it becomes increasingly important to bring this phenomenon into broader scientific and intellectual discussion because it shows that foreing cells can persist and even function within us.

Origins and types of microchimerism

Microchimerism is a phenomenon which originates from:
Pregnancy
Twin pregnancies
Organ transplantation
Blood transfusion

Pregnancy as a Source of Microchimerism

In 1893, the German pathologist Georg Schmorl became one of the first scientists to propose that fetal cells could enter the maternal body while studying eclampsia in Leipzig. During autopsies of women who died during pregnancy or childbirth, he identified unusual multinucleated giant cells in the lungs. Since these cells are typically associated with bone marrow and placental tissue, and no skeletal damage was observed, Schmorl concluded that they most likely originated from the placenta. Decades later, in 1959, researchers in New York demonstrated that trophoblast cells could also be detected in the blood of healthy pregnant women as early as the eighteenth week of gestation. (Barnéoud, 2025)
Pregnancy-related microchimerism can be further classified into two subtypes based on the direction of cell transfer:
Fetal microchimerism
Maternal microchimerism

Fetal Microchimerism

Fetal microchimerism refers to the long-term persistence of a small population of fetal cells within the maternal body after pregnancy has ended. This phenomenon arises when cells from the developing fetus cross the placental barrier during gestation and enter the maternal circulation. These fetal-derived cells can survive in various maternal tissues, organs, and blood for many years or even decades. The passage of fetal cells into the mother is thought to occur mainly through transcytosis, a process by which cells move across the placental barrier. (Avery, 2026)

Maternal Microchimerism

Maternal microchimerism refers to the presence of maternal cells within the fetal circulation. This phenomenon was first described in the 1960s by Desai et al., who identified maternal leukocytes in the umbilical cord blood of newborns. Further studies have shown that during fetal and early neonatal life, maternal-derived cells can be detected in multiple organs, including the skin, thymus, spleen, liver, and thyroid. These maternal cells have also been implicated in certain pathological processes, including the possible transmission of cancer from mother to fetus. Historical reports of transplacental metastasis involving various maternal

malignancies further support the existence of maternal microchimerism. (Shrivastava, Naik, & Suryawansh, 2019)

Twin Pregnancies as a Source of Microchimerism

The concept of chimerism in pregnancy was first identified in animals in 1916. It had long been observed that when cattle twins consist of one male and one female, the female is typically infertile and is referred to as a freemartin. This condition arises due to vascular connections between the twins in the placenta, allowing the transfer of anti-Müllerian hormone (AMH) from the male to the female fetus, which disrupts normal development of the female reproductive organs. In contrast, the transfer of female hormones to the male twin has no significant effect. In addition to hormonal exchange, cellular transfer between twins can also occur, resulting in XX/XY chimerism. Similar freemartin phenomena have also been documented in other species, including sheep, goats, and llamas. (Draper, 2018)

Monozygotic twins share genetically identical DNA profiles. At specific genetic loci, homozygosity is indicated by a single detectable DNA fragment, while heterozygosity produces two distinct fragments. In a study conducted at the Perinatology and Gynaecology Clinic of the Medical University of Poznan between 2007 and 2009, cord blood samples were collected from 50 consecutive pairs of twins immediately after birth. Analysis of peripheral blood lymphocytes revealed additional DNA fragments in four pairs of monozygotic twins (8%), observed at loci D7S21 and D12S11. (LeBlanc , Cheever, MacPherson, Taft, & Vichinsky, 2013)

Organ Transplantation as a Source of Microchimerism

Starzl et al. proposed that long-term tolerance after organ transplantation may be explained by the exchange of migratory leukocytes between the donor organ and the recipient. According to this hypothesis, the persistence of donor-derived cells in the recipient is associated with immune tolerance and may allow reduction or withdrawal of immunosuppressive therapy. This bidirectional movement of cells between host and graft is considered to have significant implications for transplant outcomes, as cellular migration may contribute to the development of:

Speed up rejection

Graft versus host disease (GVHD)

The basis of tolerance (Saboowala, 2020)

A study was made in Pomeranian Medical University in Szczecin in an attempt to determine the impact of post-transplant microchimerism on the function of the transplanted kidney. The study included 100 kidney transplant recipients, mostly women. All transplanted organs were from opposite-sex deceased donors. Microchimerism was assessed using multiplex PCR. Male DNA was detected in all urine samples from female recipients and in 13/56 blood samples from female kidney recipients. Female DNA was found in 31/44 urine samples from male recipients, but in none of the blood samples. (Brzóska, Wysocka, Mielczarek-Palacz, & Słotwiński, 2023)

Blood Transfusion as a Source of Microchimerism

Blood transfusion is the most common form of allogeneic transplantation.

Early studies in the 1970s, such as those by Schechter et al., showed short-term proliferation of donor leukocytes within days after transfusion, but later research suggested that these cells rarely persisted beyond about six days in immunocompetent recipients. However, these findings were limited by the low sensitivity of earlier detection methods.

Later studies revisited this topic and found that while most transfused donor leukocytes are rapidly cleared, some cases—particularly in trauma patients—show a transient expansion followed by, in some individuals, long-term persistence of donor cells known as transfusion-associated microchimerism (TA-MC). Research indicates that trauma recipients are at higher risk of developing durable TA-MC, possibly due to multiple transfusions and temporary immune suppression after injury.
This altered immune state, involving reduced innate and adaptive responses and changes in cytokine activity, may allow low-level donor cell survival and engraftment.
Genetic factors may also contribute to differences in susceptibility among patients. (Bloch, Jackman, Lee, & Busch, 2013)

Vanishing Twin Syndrome as a Source of Microchimerism

Vanishing twin syndrome refers to the spontaneous loss of one embryo or fetus during the first trimester in a twin or multiple pregnancy.
In most cases, the exact cause of this phenomenon, as well as later reductions in multiple pregnancies, is not well understood.
The outcome of fetal demise depends on when death occurs and how long the tissue remains in the uterus. When loss occurs early in pregnancy, the affected twin may disappear completely without leaving visible structural remnants. However, genetic traces of the lost twin may sometimes be detected as limited placental chimerism. (Creasy, Resnik, Iams, Lockwood, Moore, & Greene, 2022)
A collaborative study conducted by researchers at the Université libre de Bruxelles and INSERM UMR639 described a case of long-term microchimerism originating from a vanished twin, where fetal-derived cells persisted for decades after gestation. The study involved a 40-year-old man with a scleroderma-like condition, whose symptoms resembled graft-versus-host disease, prompting chimerism analysis using fluorescence in situ hybridization (FISH). Female cells were identified in his peripheral blood mononuclear cells, initially suggesting maternal cell origin.
However, further investigation using HLA-specific quantitative PCR excluded maternal microchimerism and instead detected a paternal HLA haplotype that the patient had not inherited. Since the patient had no history of blood transfusion, the researchers proposed that the most plausible explanation was the presence of cells from an unrecognized vanished twin. This case supports the possibility that vanished twins can be a source of long-term microchimerism, although its frequency and any potential link to autoimmune-like disease remain uncertain. (Bianchi, Zickwolf, Weil, Sylvester, & DeMaria, 2010)

Detection and Methodologies

Chimerism analysis involves identifying and measuring genetic variations, such as polymorphic markers, that can differentiate donor-derived cells from those of the recipient. This approach is used to determine the proportion of donor and recipient hematopoietic cells present in samples such as peripheral blood, bone marrow, and other tissues. Monitoring changes in these proportions over time allows clinicians to assess and track donor engraftment. Although different techniques are available for chimerism monitoring, they are all based on the same fundamental principle of detecting informative genetic polymorphisms that distinguish between donor and recipient cells. (Blouin, Ye, Williams, & Askar, 2021)
Non-molecular methods
Initial non-molecular approaches to chimerism analysis included red blood cell phenotyping and cytogenetic techniques such as fluorescence in situ hybridization (FISH). FISH was

commonly used to detect genetically distinct cell populations by targeting sex chromosomes. Although these methods provided early insights into chimerism, their sensitivity and quantitative accuracy were limited. (Blouin, Ye, Williams, & Askar, 2021)

Classical molecular methods

Classical molecular techniques significantly improved the detection and quantification of chimerism. These methods included restriction fragment length polymorphism (RFLP), variable number tandem repeats (VNTR), and short tandem repeat (STR) analysis. STR analysis, performed using polymerase chain reaction (PCR) followed by fragment analysis, became the most widely used method due to its higher sensitivity (approximately 1–5%), improved reproducibility, and strong clinical applicability. Over time, STR analysis largely replaced earlier molecular techniques in both research and clinical practice. (Blouin, Ye, Williams, & Askar, 2021)

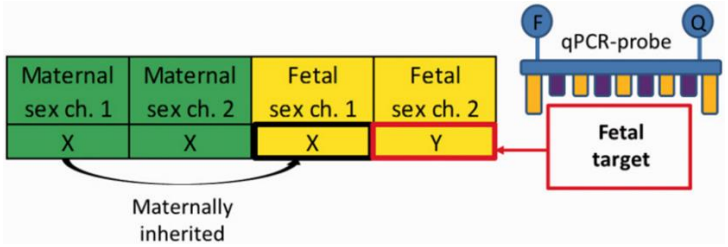

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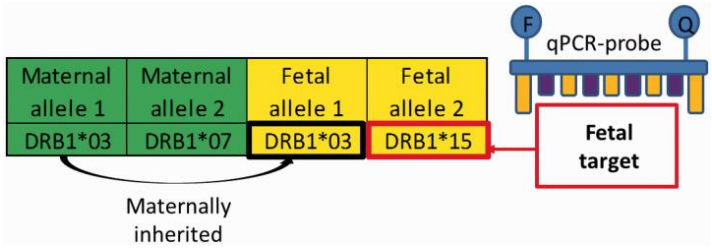
Figure 1- Fetal Y-chromosome is commonly used as a marker for detecting microchimerism. The pregnant woman has two X-chromosomes, whereas the male fetus has one maternally inherited X-chromosome and one paternally inherited Y-chromosome. This genetic difference enables the identification of fetal cells using techniques such as FISH or qPCR that specifically target Y-chromosome sequences. (Fjeldstad, Johnsen, & Staff, 2020)

Advanced molecular methods

More recently, advanced molecular techniques such as quantitative polymerase chain reaction (qPCR), droplet digital PCR (ddPCR), and next-generation sequencing (NGS) have been developed. These highly sensitive methods allow detection of very low levels of chimerism, often below 1%, and are particularly useful for monitoring engraftment dynamics and identifying early disease relapse. However, despite their increased sensitivity and precision, their overall clinical utility and cost-effectiveness in routine practice are still being evaluated. (Blouin, Ye, Williams, & Askar, 2021)



Reproduced from Fjeldstad H.E.S. et al. 2020. Journal of Reproductive Immunology, 139, 103119.

Figure 2- Highly polymorphic human leukocyte antigen (HLA) class II genes, particularly the DRB1 locus, are used to identify fetal-derived cells. A pregnant woman carries two DRB1 alleles, one on each chromosome, while the fetus inherits one maternal allele and one paternal

allele. When the paternal allele differs from the maternal genotype, it can serve as a unique genetic marker for detecting fetal microchimeric cells within maternal tissues. (Fjeldstad, Johnsen, & Staff, 2020)

The dual role of microchimerism in health and pathology

Accumulating evidence indicates that microchimeric cells can contribute to both protective and pathological processes.
The balance between beneficial and deleterious outcomes appears to depend on cell type, tissue localization and the interplay with host genetic and environmental factors. (Index, 2026)

Pathogenic and Protective Roles of Microchimerism in Autoimmune Diseases

Several human and animal studies have suggested that microchimerism may play a role in triggering autoimmune processes.
Early researches focused on detecting microchimeric cells in peripheral blood and examined conditions such as systemic lupus erythematosus, multiple sclerosis, primary biliary cirrhosis, thyroiditis, rheumatoid arthritis, Sjögren's syndrome, and systemic sclerosis.
Sjögren's syndrome, an autoimmune disorder affecting exocrine glands, shows a strong female predominance and often increased incidence following childbirth, which implies a possible link between pregnancy and disease development.
This has led to the hypothesis that fetal microchimerism may contribute to its pathogenesis. (Demir & Görgun, 2021)
At the same time, microchimerism may also have beneficial effects in certain autoimmune conditions, as seen in rheumatoid arthritis, which typically improves during pregnancy in many patients. (Bhattacharya & Stubblefield, 2013)

Role of Microchimerism in Tissue Repair and Regeneration

Microchimerism has been marked as both actively enhancing tissue repair and regeneration.
Fetal stem cells show substantial potential in regenerative medicine and have been investigated in the treatment of myocardial injury, hematopoietic engraftment, and necrotizing enterocolitis models. (Shangaris & El Hoss, 2023)

Pathogenic and Protective Roles of Microchimerism in Cancer

Fetal microchimerism has been reported at lower levels in certain cancers, such as breast cancer and lymphoma, while higher frequencies have been observed in colon cancer.
Microchimeric cells have also been detected in both normal and diseased tissues, as well as in healing and tumour environments.
This has led to the hypothesis that these cells may have dual roles, potentially offering protection against some malignancies while contributing to the development of others.
In humans, microchimeric cells have been found in multiple organs, including the brain, lymph nodes, thyroid, heart, skin, spleen, kidneys, pancreas, liver, gastrointestinal tract, bone marrow, and cervix.
These cells have been shown to express tissue-specific markers such as lymphocyte differentiation antigens and cytokeratins, suggesting functional integration within host tissues.
Epidemiological evidence linking microchimerism with both cancer risk and protection supports the idea that these cells may actively influence carcinogenesis.
Early observations as far back as 1960 suggested a possible role for maternal lymphocytes in Hodgkin lymphoma in offspring. Some studies have reported that women with detectable microchimerism in peripheral blood may have a reduced risk of breast cancer, and male-derived cells have been found more frequently in normal and benign breast tissue than in malignant lesions. Similarly, reduced levels of microchimerism have been associated with

papillary thyroid cancer and certain hematological malignancies, which has been interpreted as a potential protective effect.
In contrast, increased microchimerism has been observed in colon cancer, although the underlying mechanism remains unclear.
In melanoma, microchimeric cells have even been proposed to contribute to tumour progression through effects such as lymphangiogenesis.
Given the many interacting biological and environmental factors involved in cancer development, the precise role of microchimerism remains complex and not fully understood. (Gadi & Nelson, 2014)

Conclusion

Microchimerism has deeply challenged our understanding of the immune system's behavior toward foreign cells. For a long time, it was believed that the human body was determined to keep itself "clean" of them, eliminating them rapidly, if not immediately. However, to our surprise, we now know that these foreign cells can coexist within us for decades.
We know that all of us were carried by our mothers, usually for nine months. What we did not know is that they may continue to carry parts of us for the rest of their lives.
It is undeniable that microchimerism plays a dual role in the organism. It may have a healing role associated with tissue repair, a protective role in certain cancers such as breast cancer, and a pathogenic role in other cancers such as colon cancer, while also contributing to the development of autoimmune diseases.
Microchimerism offers an entirely new perspective on the human organism and the way it functions. It is extremely important for research to continue on the protective, healing, and pathogenic effects it may have within the body, so that those suffering from diseases currently considered incurable are not left without hope indefinitely. Science continuously shows us that what we deny today may tomorrow be accepted as an absolute truth. As Evelyn Fox Keller said, "To know the history of science is to recognize the mortality of any claim to universal truth."

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