Chimerism: History and Implications

Prepared by : Aminah Samer Al-chakee , Afnan Ismail Shahin , Nadin Hatem Sarg **Supervised by** : Prof. Suleiman Ibrahim Sharif.
Dept. Pharmacy Practice & Pharmacotherapeutics, College of Pharmacy, University of Sharjah-UAE.

Do you know what's Chimera ?

Introduction and overview

In Greek mythology, "**chimera**" is a fire-breathing monster that is a hybrid of lion, goat and snake. Although this monster never existed beyond our collective imagination, **"Human chimeras" are quite real.**

Chimerism is a term used to describe a single organism having cells with more than one distinct genotype (carrying different sets of DNA).

Individuals can become chimeric in several ways ,summarized as **(transplantation, transfusion, or inheritance) .**

Pregnancy-related causes include the bidirectional transfer of cells between the mother and fetus or twin-to-twin transfer in utero, which can lead to chimerism of either the pregnant woman or the fetus. On the other hand, chimera can be **artificial** like in the case of Organ transplantation or blood transfusion where the recipient becomes a chimera . The former could result in a "permanent chimera" -like in the case of bone marrow transplantation- while the latter produces only a "temporary chimera".

Classification

A) Microchimerism

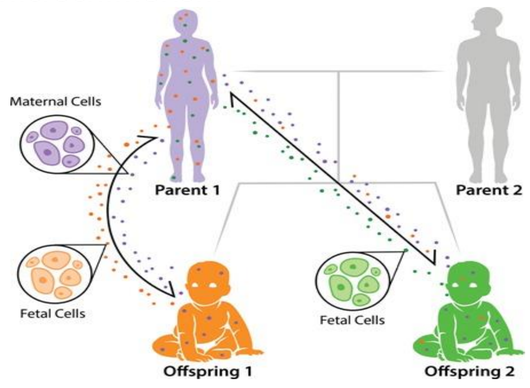


Fig 1: **bidirectional exchange of fetal and maternal cells during pregnancy.**

B) Tetragametic Chimerism

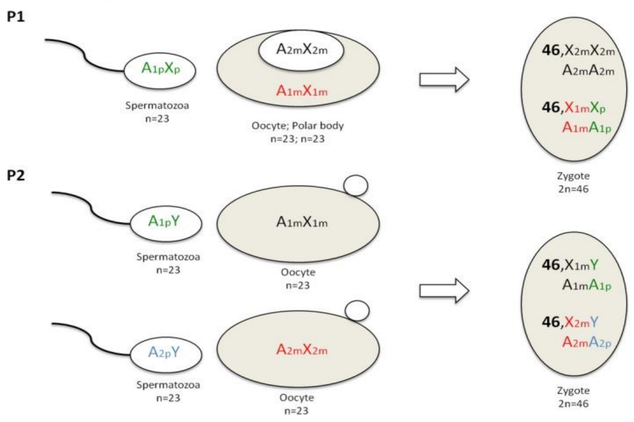


Fig 2: **P1 is normal fertilization, P2 is tetragametic chimera.**

Detection

Researchers focus mainly on finding an evidence of distinctly male Y chromosomes in females to identify it using polymerase chain reaction (PCR).

A PERSON MIGHT BE HIS OWN TWIN !

Historical background

Chimerism (Greek word magnificent monster)

The first human chimera
In 1953, Mrs. Mack donated blood and was called back and told "you carry two separate blood types.

In 2002, Keegan underwent a genetic testing for kidney transplantation. Showed her not to be the mother of her sons

In 2015, testing tissues of mothers who died after pregnancy showed fetal cells within these tissues

Microchimerism and autoimmune disease

Microchimerism is currently being investigated in a number of different diseases. In particular, autoimmune diseases that primarily affect women, producing some results supporting a potential role in the disease pathogenesis.

There are several proposed mechanisms by which chimeric cells could be involved in immune-mediated diseases. A major one is the hypothesis suggesting that microchimerism and HLA relationships of host and non-host cells are entangled.

The Role of Human Leukocyte Antigens (HLA)

HLA is one version of the major histocompatibility complex (MHC).It is a gene complex that helps the immune system distinguish the body's own proteins from foreign proteins .

The microchimerism hypothesis proposes that HLA-similar cells could result in disruption of the host immune-regulatory mechanisms. Thus, micro-chimerism could be adverse within the context of other factors, including the particular HLA genes of mother and child, the HLA relationship between them, environmental and infectious triggers.

On the other hand, It is important to remember that persistent fetal microchimerism is a common phenomenon in normal healthy women.

Surprisingly, many mothers have reported relief from some diseases during pregnancy. Microchimerism may be the underlying explanation. **The hypothesis" chimeric cells may play in repair mechanisms by having stem-cells-like properties."**

Applications

1. DNA testing, (paternity or Forensic testing)

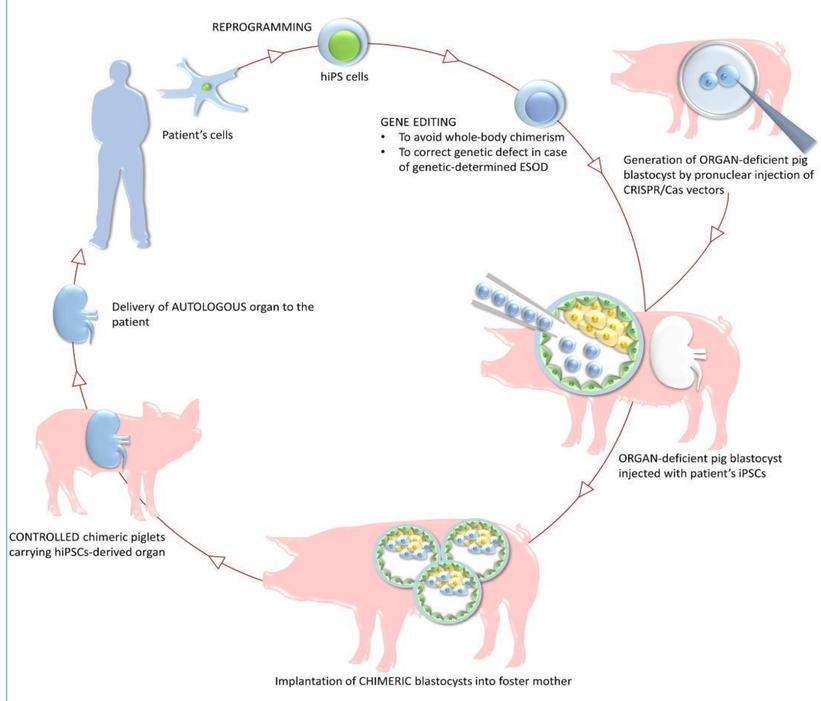
2. Creating 'humanized' animal models with cells from the liver and pancreas of human donors.

3. The generation of CNS, (forebrain, chimeras).

4. Creating chimeras as in-vivo systems to test the potential of human pluripotent cells

5. Creating Interspecies Chimera

(for Xenotransplantation)



Although the previously mentioned applications have great potential for both basic and translational science, they also raise unique ethical issues that must be considered.

Conclusion

To sum up, the precise scope and extent of chimerism is still a topic of considerable research. New genetic discoveries and diseases will initiate a need to rethink since it relates to education, practice, and research. The research into microchimerism is expected to flourish and prove therapeutically promising.

References:

Boddy, A. M., Fortunato, A., Wilson Sayres, M., & Aktipis, A. (2015). Fetal microchimerism and maternal health: A review and evolutionary analysis of cooperation and conflict beyond the womb. Bioessays, 37(10), 1106–1118. https://doi.org/10.1002/bies.201500059

Bottega, R., Cappellani, S., Fabretto, A., Spinelli, A. M., Severini, G. M., Aloisio, M., Faleschini, M., Athanasakis, E., Bruno, I., Faletra, F., & Pecile, V. (2019). Could a chimeric condition be responsible for unexpected genetic syndromes? The role of the single nucleotide polymorphism-array analysis. Molecular Genetics & Genomic Medicine, 7(3). https://doi.org/10.1002/mgg3.546

DNA At the Fringes: Twins, Chimerism, and Synthetic DNA. (n.d.). Retrieved February 18, 2020, from https://www.thedailybeast.com/dna-at-the-fringes-twins-chimerism-and-synthetic-dna?ref=scroll

Garry, D. J., & Garry, M. G. (2019). Interspecies Chimeras and the Generation of Humanized Organs. Circulation Research, 124(1), 23–25. https://doi.org/10.1161/CIRCRESAHA.118.314189

Hermeren, G. (2015). Ethical considerations in chimera research. Development, 142(1), 3–5. https://doi.org/10.1242/dev.119024

Knippen, M. A. (2011). Microchimerism: Sharing Genes in Illness and in Health. ISRN Nursing, 2011, 893819. https://doi.org/10.5402/2011/893819

Kremer Hovinga, I. C. L., Koopmans, M., de Heer, E., Bruijn, J. A., & Bajema, I. M. (2007). Chimerism in systemic lupus erythematosus—Three hypotheses. Rheumatology, 46(2), 200–208. https://doi.org/10.1093/rheumatology/kel379

Nelson, J. L. (2016). Microchimerism and human autoimmune diseases: Lupus. https://doi.org/10.1191/0961203302lu271oa

Rettner,LiveScience, R. (n.d.). 3 Human Chimeras That Already Exist. Scientific American. Retrieved February 18, 2020, from https://www.scientificamerican.com/article/3-human-chimeras-that-already-exist/