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What is Chimera ? how it can be useful ?

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Abstract

Chimeras are individuals with tissues derived from more than one zygote. Interspecific chimeras have tissues derived from different species. The biological consequences of human-animal chimeras have become an issue of ethical debate. Ironically, human-animal chimeras with human blood, neurons, germ cells, and other tissues have been generated for decades. This has facilitated human biological studies and therapeutic strategies for disease, the primary goal of human-animal chimera research is to produce human cellular characters in animals. The animal carrying the human tissue can then be examined or treated to investigate human-specific biological processes and disease without experimentation on human individuals in this report different aspects about chimera and how it can be useful medically will be discussed

Introduction

A chimera is an individual composed of somatic and, in certain cases, germline tissues derived from more than one zygote. There are different ways to generate tissue chimerism, including mixing embryonic cells from two individuals, transplanting fetal or adult tissues from one individual into another individual, or grafting embryonic stem (ES) cells or their differentiated products into another individual. For example, two genetically distinct 8 cell mouse preimplantation embryos whose zona pellucidae have been removed can be pushed together in a tissue culture dish and then grown in vitro to form a single blastocyst. Transfer of this blastocyst into the uterus of a foster mother often results in a mouse with somatic and germ cells of both genotypes, a so-called aggregation chimera. Tissue chimerism can also result from clinical treatments of disease. A patient who receives a successful tissue or organ transplant (e.g., bone marrow) would likely have the adult donor tissues obtained from a genetically distinct individual, i.e., such a patient would be a bone marrow chimera. If the donor tissue and recipient are of different species, then an interspecific or cross-species chimera is generated. Human-animal interspecific chimeras have been created by grafting human cells and tissues into the embryos, fetuses, or adults of vertebrate model organisms. The derivation of human embryonic stem (hES) cells has created the opportunity to use these pluripotent cells to generate human-animal chimeras.[1,2,3]

Aim

This report is made in order to define what is chimera and how it can be useful in medical experimental practice

Methods

Laboratory animals are routinely used to model human biology and disease but are not human and therefore cannot fully replicate human physiology. The general public and most scientists may not realize that human-animal chimeras have been routinely produced for decades and are generated daily in biomedical research laboratories

throughout the world. Here we review different types of human-animal chimeras that have been used in biomedical research. We focus our review on human-animal chimeras generated by transplanting human tissues into vertebrates, predominantly rodent models. [1,2]

Results

Human-animal chimeras are typically generated by grafting human cells or tissues orthotopically or heterotopically into an immune-deficient animal. The host may be a fetus whose immune system is immature and has yet to establish "self" or a postnatal animal with a genetic mutation that causes the loss of specific immune system components. Engraftment of human cells into wild-type postnatal animals whose immune systems have been established can also be accomplished by immunosuppression with drugs (e.g., cyclosporin).[3,4]

Classically, the immune-deficient athymic nude mouse has been used for decades as a recipient for human tissue grafts to generate human-mouse chimeras. Nude (Foxn1) is a recessive mutation that results in, among other phenotypes, loss of T cells. This T cell deficiency in the nude mouse is sufficient to allow many types of xenograft tissues to survive and grow, including different types of normal fetal and adult human tissues.[4,5,6]

Discussion

Abnormal or diseased human tissues can also be transplanted into animals. The successful growth of human tumors in animals was pioneered by transplantation into immune-privileged sites (e.g., the rabbit or guinea pig anterior chamber of the eye or Syrian hamster cheek pouch). The advent of the nude mouse greatly facilitated these types of studies, and indeed, this in vivo assay is one of the fundamental experimental paradigms for cancer research[2,3]

Pieces of human tumors are grafted under the skin of nude mice providing a bioincubator for tumor growth. The mouse essentially becomes a cancer patient whose tumor can then be manipulated in various ways to understand cancer mechanisms and to test therapeutic protocols for human cancer.[3,4,5]

Another general approach to generate human-animal chimeras is to add other mutations to or chemically treat or irradiate immune-compromised (e.g., nude,) animals to make them also deficient for nonimmune system tissues. The deficient or absent tissue opens a niche for the engrafted human nonimmune system cells. For example, sublethal irradiation of NOD- mice is necessary to "knock down" host hematopoiesis for engraftment of human hematopoietic stem cells. Using this general approach, human tissues can contribute significantly or completely to a specific tissue or organ in the animal. Many of the grafted human tissues have significant regenerative potential and long-term colonizing ability (i.e., stem cells).[4,5]

This field was enabled by the discovery that the expression of an albumin-urokinase plasminogen activator (Alb-uPA) transgene in the mouse is hepatotoxic, resulting in the progressive destruction of the mouse liver. Transplantation of primary mouse hepatocytes into immune-compatible Alb-uPA transgenic mice was found to be capable of reconstituting the host liver, highlighting the tremendous regenerative capacity of hepatocytes. It was subsequently shown that rat hepatocytes could also successfully reconstitute the liver of nude Alb-uPA transgenic mice. This liver reconstitution mouse model has led to the development of mice with livers reconstituted by engrafted human hepatocytes. Another strategy to generate human-mouse chimeras is to place primary human hepatocytes in a matrix followed by engraftment under the mouse kidney capsule. These human-mouse chimera models have been useful for studying human hepatitis virus infections and human liver-specific metabolic responses to drugs.[7,8,9]

Conclusion

Chimera, in genetics, an organism or tissue that contains at least two different sets of DNA, most often originating from the fusion of as many different zygotes ,different types of human-animal chimeras have provided important insights into fundamental biological mechanisms and the development of therapeutic protocols for human disease.

Future work

More researches should be done to get more information as well as, to capture the exact pathophysiological changes in chimeric people at the molecular level, which would give us an introduction regarding the understanding of many diseases for example autoimmune diseases.

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