

# Intraspecies Chimeras Produced in Laboratory Settings (1960-1975) <sup>[1]</sup>

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When cells—but not DNA—from two or more genetically distinct individuals combine to form a new individual, the result is called a chimera. Though [chimeras](#) <sup>[2]</sup> occasionally occur in nature, scientists have produced [chimeras](#) <sup>[2]</sup> in a laboratory setting since the 1960s. During the creation of a chimera, the DNA molecules do not exchange genetic material (recombine), unlike in sexual reproduction or in hybrid organisms, which result from genetic material exchanged between two different species. A chimera instead contains discrete cell populations with two unique sets of parental [genes](#) <sup>[3]</sup>. Chimeras can occur when two independent organisms fuse at a cellular level to form one organism, or when a population of cells is transferred from one organism to another. Chimeras created in laboratories have helped scientists to identify developmental mechanisms and processes across species. Some experiments involving [chimeras](#) <sup>[2]</sup> aim to provide further knowledge of immune reactions against disease or to create animal models to understand human disease.

There are many different ways genetic material can combine to form a new organism, not all of which are [chimeras](#) <sup>[2]</sup>. Sexual reproduction occurs when a female [egg](#) <sup>[4]</sup> ([oocyte](#) <sup>[5]</sup>) and a male [sperm](#) <sup>[6]</sup> cell combine. The DNA of oocytes and of [sperm](#) <sup>[6]</sup> cells combine to make an embryo in which every cell in that organism has the same DNA. A hybrid, on the other hand, is an organism that results from the recombined DNA of individuals from two different species. Hybrid individuals receive their genetic material through the [fertilization](#) <sup>[7]</sup>, whether natural or artificial, of an [egg](#) <sup>[4]</sup> from one species by the [sperm](#) <sup>[6]</sup> of another. That genetic material then combines and is uniform throughout the hybrid organism. Hybrids are intraspecies organisms. In contrast with hybrids, transgenic organisms may be intraspecies or interspecies. Transgenic organisms are created when a gene or specific piece of DNA from one animal is inserted into the DNA of another. Chimeras differ from both hybrids and transgenic organisms in that they exhibit at least two sets of genetically distinct cells. In other words, not all individual cells of a chimeric organism contain the same DNA. Cells in a chimera work together as a whole organism.

Scientists typically create [chimeras](#) <sup>[2]</sup> in laboratories through the transfer of organs, tissues, cells, or parts of cells, from one organism to another. The cells used to create a chimera may come from an organism at any stage of development: gametes (sex cells, or oocytes and [sperm](#) <sup>[6]</sup>), zygotes, embryos, fetuses, or adults (somatic cells). In a laboratory setting, researchers generate many [chimeras](#) <sup>[2]</sup> on a cellular level using only a small number of cells. Scientists often terminate the resultant [chimeras](#) <sup>[2]</sup> during their development, and do not permit the [chimeras](#) <sup>[2]</sup> to result in live offspring.

Researchers can create [chimeras](#) <sup>[2]</sup> from the [nucleus](#) <sup>[8]</sup> (the part of the cell that contains its DNA), a cell whose [nucleus](#) <sup>[8]</sup> has been removed (enucleated), or whole cells. For example, scientists may create a chimeric embryo by injecting undifferentiated [stem cells](#) <sup>[9]</sup> into a blastocyst—a stage of early embryonic development—and allowing the two to fuse. Each of the cells retains its original genetic characteristics, resulting in organisms with tissue from two previously independent organisms that exist side by side. When undifferentiated cells from one organism fuse with the [blastocyst](#) <sup>[10]</sup> of another, a chimeric organism develops with genetic material from eight haploid cells.

In the 1960s, [Beatrice Mintz](#) <sup>[11]</sup> created a chimera from mice in her laboratory <sup>[11]</sup> at the Fox Chase Cancer Center in Philadelphia, Pennsylvania. She researched genetic factors linked to cancer development, [sex hormones](#) <sup>[12]</sup> and [sex determination](#) <sup>[13]</sup> in [amphibians](#) <sup>[14]</sup>, and the development of reproductive cells and systems. In 1960, while investigating mutations of the *T12* gene and its lethal effects on an organism's blood, she developed a strain of mice (*Mus musculus* <sup>[15]</sup>) with two different genomes to study mutant cell behavior. Mintz genetically manipulated two groups of mice to exhibit the characteristics she was investigating. One group of mice had normally functioning gametes, while the gametes of the mutant group of mice did not properly divide after [fertilization](#) <sup>[7]</sup>.

Mintz synthesized the first laboratory chimera by fusing two embryos. The result was one mosaic [mouse](#) <sup>[16]</sup> with dual characteristics, representing both sets of DNA. To create a chimeric [mouse](#) <sup>[16]</sup>, Mintz exposed two embryos of eight to ten cells to a protease, which is a type of enzyme that removed the embryos' protective outer layers called the [zona pellucida](#) <sup>[17]</sup>. Without the barrier of the [zona pellucida](#) <sup>[18]</sup>, the two embryos fused together without additional intervention. The resulting [mouse](#) <sup>[16]</sup> displayed physical traits of both embryos, for instance a white [mouse](#) <sup>[16]</sup> chimerized with a black [mouse](#) <sup>[16]</sup> displayed black and white banding. Mintz referred to these mice as allophenic, because she found the name chimera a distasteful reference to the terrifying Greek monster.

In the late 1960s and early 70s, work on [chimeras](#) <sup>[2]</sup> occurred at the bench of [Nicole Marthe Le Douarin](#) <sup>[19]</sup>. While working at the University of Nantes in Nantes, France, Le Douarin grafted together [germ layers](#) <sup>[20]</sup>, which are the first cell layers generated in

embryonic development, of [chick](#)<sup>[21]</sup> and quail embryos to investigate cell communication and migration as embryonic tissues grow. In her studies, she used a type of cell stain called a Feulgen stain to identify the quail cells. When the [germ layers](#)<sup>[20]</sup> from the [chick](#)<sup>[21]</sup> and the quail successfully fused and began to develop into an embryo, Le Douarin distinguished which cells originated from the [chick](#)<sup>[21]</sup>, and which came from the quail. Le Douarin published her experiment in 1973. Le Douarin's work with chimeric embryos, though terminated before fully developed, helped show how cells communicate with each other and differentiate into more advanced cell types in embryonic development.

In 2012, the first interspecies chimeric monkeys were born at the Oregon National Primate Research Center in Beaverton, Oregon. Three rhesus macaque monkeys ([Macaca mulatta](#)<sup>[22]</sup>) were born sharing genetic material from six different parental monkeys. In the early decades of the twenty-first century, researchers have created [chimeras](#)<sup>[2]</sup> using human genetic material, but they did not allow inter-species [chimeras](#)<sup>[2]</sup> involving human cells to mature for more than a few weeks. Scientists conduct chimera research with the hope that perhaps a non-human–human chimera, for example a [mouse](#)<sup>[16]</sup> with human cells, could provide an improved model for human disease research and therapy.

European and American governments have created definitions, new classifications, and laws to guide the use of embryonic cells and chimeric research. In the United Kingdom as of 2013, the Human Fertilization and Embryology Authority, in London, a branch of the Health and Social Services department, regulates and oversees the use of [chimeras](#)<sup>[2]</sup> for research purposes. The United States developed the Embryonic Stem Cell Research Oversight Committee to review human [embryonic stem cell research](#)<sup>[23]</sup>, including part-human chimera research. Researchers have noted that a human harboring a donor kidney, for example, is not a topic of ethical or political debate despite the fact that he or she could be considered a chimera. Scientists consider experimental [chimeras](#)<sup>[2]</sup>, on the other hand, as [chimeras](#)<sup>[2]</sup>.

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## Subject

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