

"Interspecific Chimeras in Mammals: Successful Production of Live Chimeras Between *Mus musculus* and *Mus caroli*" (1980), by Janet Rossant and William I. Frels ^[1]

By: Newkirk, Nicole Keywords: [Mice](#) ^[2] [Chimeras](#) ^[3]

In 1980 [Janet Rossant](#) ^[5] and [William I. Frels](#) ^[6] published their paper, "Interspecific Chimeras in Mammals: Successful Production of Live Chimeras Between *Mus musculus* and *Mus caroli*," in *Science*. Their experiment involved the first successful creation of [interspecific mammalian chimeras](#) ^[7]. Mammalian [chimeras](#) ^[8] are valuable for studying early embryonic development. However, in earlier studies, [clonal analysis](#) ^[9] was restricted by the lack of a cell marker, present at all times, that makes a distinction between the two parental cell types *in situ*. To battle this limitation, Rossant and Frels decided to make [chimeras](#) ^[8] from embryos of two different species in order to have sufficient genetic differences so that, in any tissue type, the two cell types could be clearly identified. In their paper Rossant and Frels describe the successful creation of live [chimeras](#) ^[8] between *Mus musculus* and *Mus caroli*. These two species of mice are more closely related than [chimeras](#) ^[8] produced previously. The [chimeras](#) ^[8] created in the experiment showed no sign of selection against one cell type or the other. Therefore, they are valuable for [clonal analysis](#) ^[9] of development. Rossant and Frels were the first to successfully produce an interspecific mammalian chimera that experienced normal development.

Previously, [chimeras](#) ^[8] had been created between [rat](#) ^[10] and [mouse](#) ^[11] and between bank [vole](#) ^[12] and [mouse](#) ^[11]. Scientists had seen successful [implantation](#) ^[13] in mice uteri, but limited development after [implantation](#) ^[13] and no live births. Better results were obtained when creating [rat](#) ^[10]-[mouse](#) ^[11] [chimeras](#) ^[8] by [blastocyst injection](#) ^[14]. The resulting mixed [rat](#) ^[10] and [mouse](#) ^[11] embryonic tissues existed at least until the midpoint of [gestation](#) ^[15]. However, these experiments produced few offspring with stunted growth, along with insignificant proof of [rat](#) ^[10] tissue, suggesting selection against the [rat](#) ^[10] cells had occurred during development.

In their experiment, Rossant and Frels worked with *M. musculus*, a laboratory [mouse](#) ^[11], and *M. caroli*, a wild species originating from Southeast Asia. These two species show multiple genetic differences and do not usually interbreed in nature. The two species differ in pre-[implantation](#) ^[13] development with *M. caroli* being complete sixteen to twenty hours earlier than *M. musculus*. *M. caroli* also has a shorter [gestation](#) ^[15] period. The two species share similar morphological changes in relation to [embryogenesis](#) ^[16]. Rossant and Frels created [chimeras](#) ^[8] by injecting the inner cell masses of *M. caroli* into *M. musculus* blastocysts. They used *M. musculus* blastocysts retrieved on the afternoon of the fourth day after the mating of albino, non-agouti mice that were homozygous for the *b* allele of the glucose phosphate isomerase (GPI) gene (*Gpi-1b/Gpi-1b*). *M. caroli* females were super-ovulated and bred with males. Seventy-six hours after a [human chorionic gonadotropin](#) ^[17] (hCG) injection, Rossant and Frels rid the uteri of blastocysts with cell numbers close to those of *M. musculus* blastocysts. Rossant and Frels dissected the inner cell masses from *M. caroli* blastocysts and then injected them into *M. musculus* blastocysts.

On the third day of artificial [pregnancy](#) ^[18] these embryos were transferred into uterine horns of albino, non-agouti mice homozygous for the *b* allele of the GPI gene. Right before the birth of the fetuses, nine were dissected to study fetal tissues and extra-embryonic structures. Six out of the nine were determined, by GPI analysis and eye pigmentation, to be chimeric. Each chimera showed *M. musculus* and *M. caroli* GPI enzymes in every tissue that was analyzed. Rossant and Frels noted that the proportions of the enzymes varied from tissue to tissue, similar to that observed in *M. musculus*-*M. musculus* [chimeras](#) ^[8].

During the experiment Rossant and Frels found a hybrid GPI enzyme present in the skeletal muscles of the [chimeras](#) ^[8]. From this they concluded that normal interaction between *M. musculus* and *M. caroli* cells had occurred. The myoblasts from both *M. musculus* and *M. caroli* fused to create myotubes with normal function. Five other females were allowed to give birth. Out of forty-eight offspring, thirty-eight were determined to be chimeric by hair and eye pigmentation and GPI analysis. Coat and eye pigmentation, as well as the percentage of *M. caroli* GPI enzyme in the blood, varied in each chimera. Of those [chimeras](#) ^[8] brought to term, twenty-seven were male and nine were female. Similar to previous findings with *M. musculus*-*M. musculus* [chimeras](#) ^[8], there were more phenotypic males. Rossant and Frels found that *M. musculus*-*M. caroli* [chimeras](#) ^[8] and *M. musculus*-*M. musculus* [chimeras](#) ^[8] showed striking similarities in their somatic tissue [organization](#) ^[19]. They concluded that there was no evidence to suggest that *M. caroli* cells were selected against.

Rossant and Frels were the first to successfully create an interspecific mammalian chimera. Unlike in previous experiments, the *M. musculus*-*M. caroli* chimera survived after birth and developed normally. Such [chimeras](#) ^[8] may be valuable for studying early embryonic development. Rossant and Frels indicate that the creation of species-specific antisera, or the identification of genetic differences between the two species in order to provide an *in situ* cell marker, would make interspecific [chimeras](#) ^[8] more valuable for further studies of mammalian development. Rossant and Frels state that interspecific [chimeras](#) ^[8] may also be beneficial for studying interactions between mother and [fetus](#) ^[20] and the genetic control of mating behavior.

Sources

1. Rossant, Janet, and [William I. Frels](#) ^[6]. "Interspecific Chimeras in Mammals: Successful Production of Live Chimeras Between *Mus musculus* and *Mus caroli*." *Science* 208 (1980): 419–21.

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