



BIO380HF

Creating Transgenic Mice: On-Line Self-Study

Goals of this exercise

- To learn a few terms related to genetically modified organisms
- To understand the value of using genetically engineered organisms to study developmental biology
- To learn the basic approaches about how transgenic mice are produced

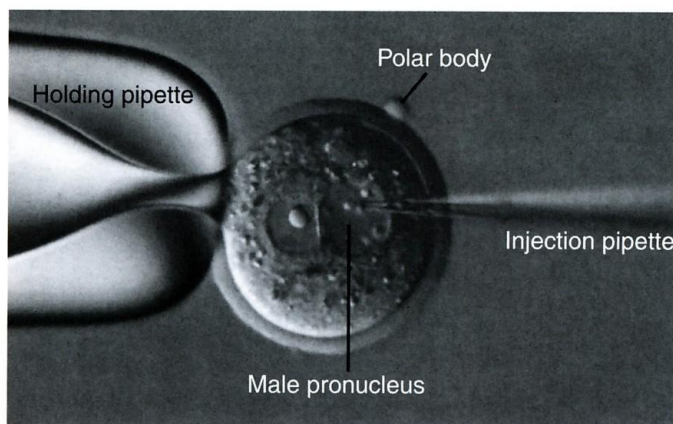
Genetically Modified Organisms

Genetically modified organisms (GMO) or genetically engineered organisms (GEO) are plants, animals, bacteria or viruses that have been altered through the transfer of new genes into or deletion of genes from that organism. These changes can be produced by a number of different methods depending on the organism. GMOs have a number of applications from their use in biomedical research to the production of pharmaceuticals. New strains of plants have been generated using this approach in agriculture.

Transgenic organisms are a group of GMOs defined by the fact that the inserted DNA originated in a different species. Transgenics are widely used in biomedical research and for other purposes (e.g., production of human insulin). Transgenic rats, goats, pigs, and primates among a longer list of mammals, have all been developed. Transgenic mice are widely used to study mutations that underlie a number of human genetic disorders. For example, the “oncomouse” has been genetically modified to carry an activated oncogene and is widely used in cancer research. Here we will look at the steps involved in producing transgenic mice.

Producing Transgenic Mice: Step by Step

Well before any mice are handled, the researcher needs to design an appropriate transgenic construct with a promoter gene and reporter gene (e.g., LacZ). This plasmid will then be purified prior to injection into the male pronucleus. The male pronucleus is chosen because it is the larger of the pronuclei.



Injection of DNA plasmid into male pronucleus (from Larsen's Embryology, 4th ed, Elsevier)

Creating Transgenic Mice

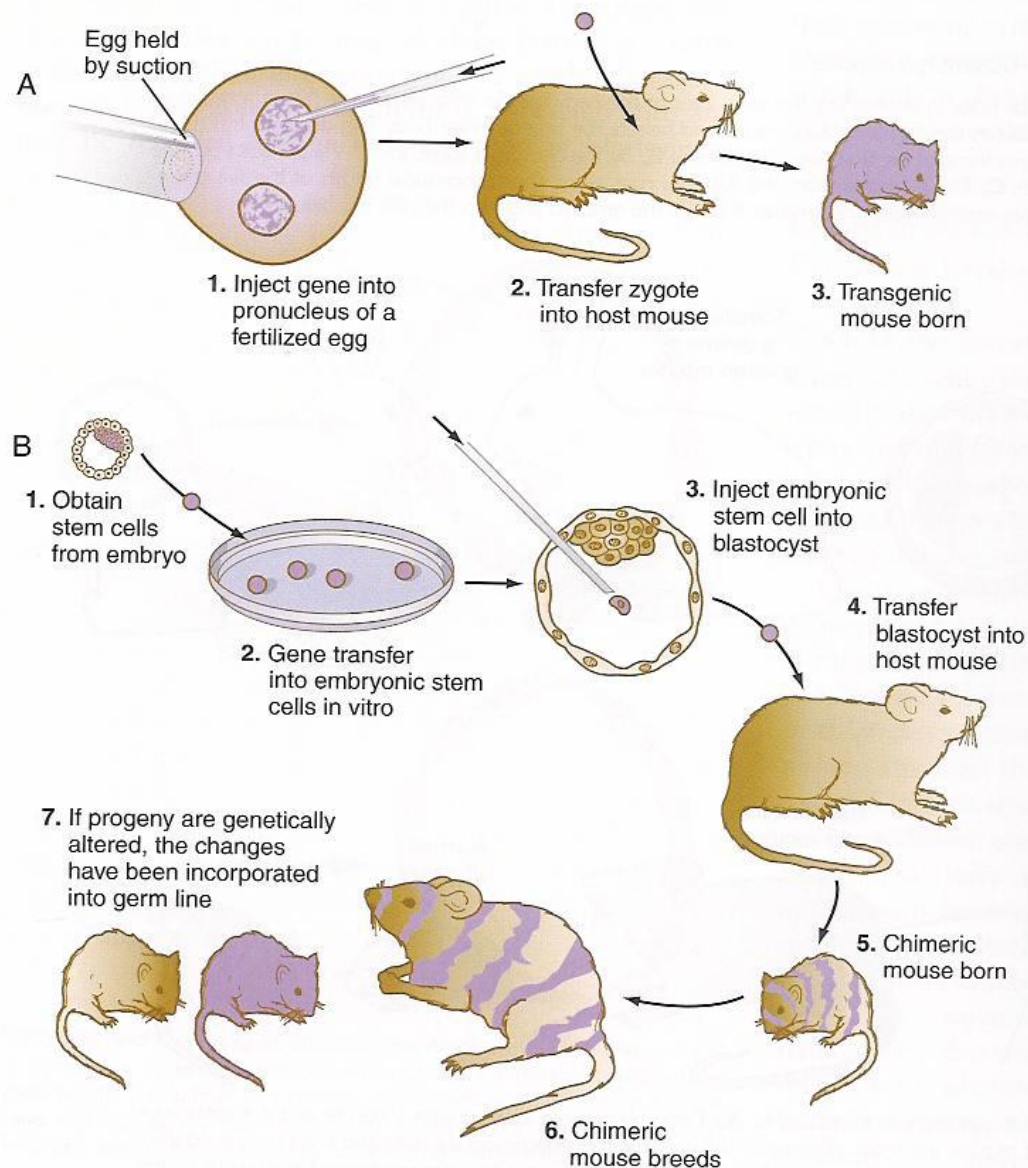
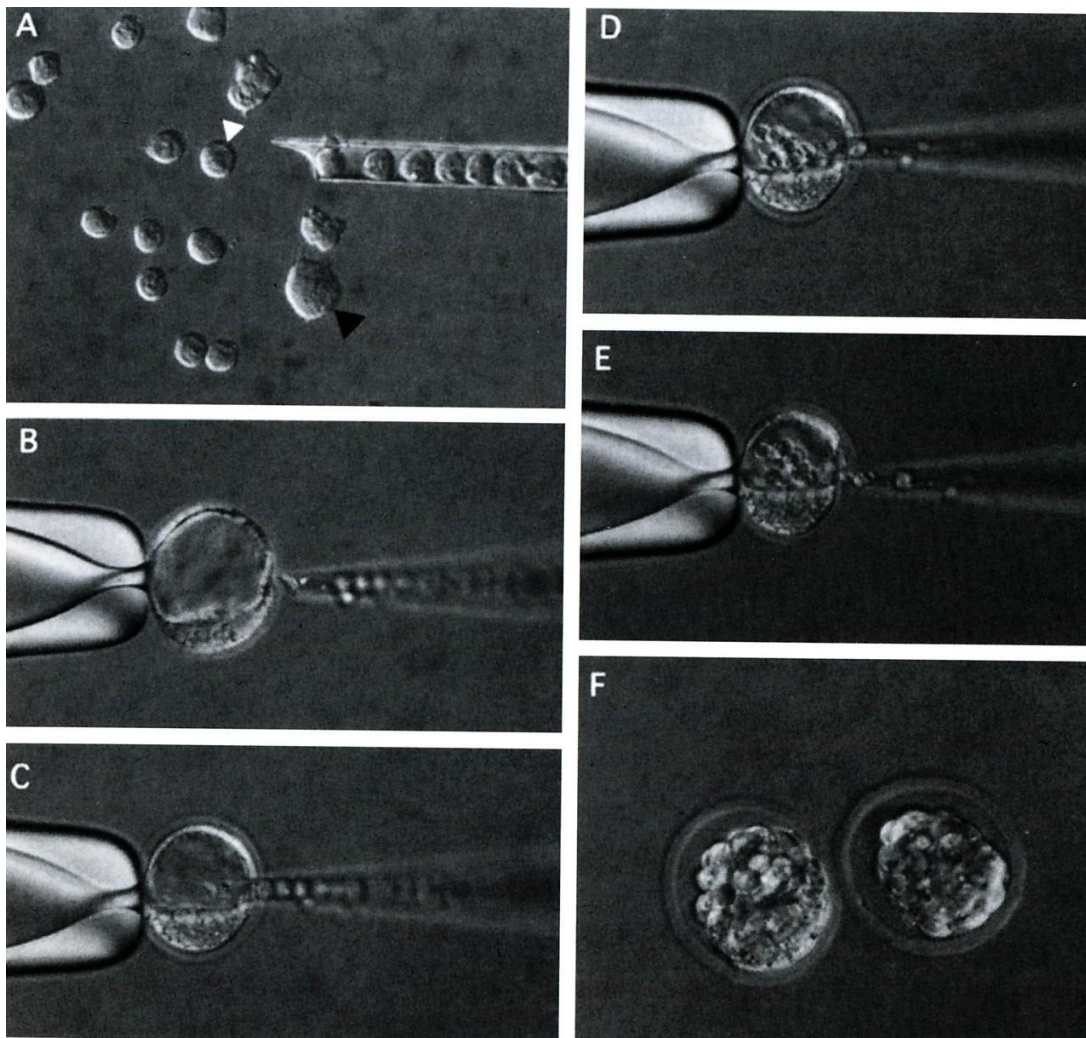


Figure 3-10 from *Human Embryology and Developmental Biology*, 3rd Ed. by B.M. Carlson

The figure shows the two approaches to producing a transgenic mouse. A. The gene of interest (in a plasmid) is injected into the male pronucleus. If all goes well after the zygote is transferred to a host mouse, a transgenic mouse will be born with the gene defect or altered gene. B. Embryonic stem cells are isolated from a trophoblast after which a plasmid containing the gene of interest is transfected into the stem cells (i.e., isolated cells from the inner cell mass) by various methods (e.g., electroporation). The transfected stem cells are then injected into a blastocyst which is placed in a receptive female mouse uterus. This will lead to a chimeric mouse from which later progeny can be selected which have incorporated the genes into their genomic DNA. Clearly this is a simplification of a complex process but it reveals how the method is carried out. You will learn more about the technique in the tutorial.

Creating Transgenic Mice



A procedure used to generate chimeric mice. A. Blastocysts are dissociated into individual cells and injected into another blastocyst B-E. to generate chimeric blastocysts which will be inserted into host uteri. (from Larsen's Embryology, 4th ed, Elsevier)

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