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A Note on Germline Transgenesis in Animals

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About the Study

It became possible to incorporate exogenous DNA constructions into higher eukaryotic cells in vitro during the 1970s. The first mammalian (germline) transgenesis was achieved in the early 1980s, with mice as the test subject. Amphibians, cattle, chickens, fish, insects, nematodes, pigs, rabbits, and sea urchins are only a few of the animal (and plant) types and species that have been transgenic.

Since 1990, gene transfer technologies have been used in human gene therapy attempts. So far, gene therapy has mostly targeted monogenic diseases and malignancies. Clinical success has been limited at this point. Gene therapy, on the other hand, is still in its early stages and has a lot of potential for the future.

Gene transfer methods, as mentioned above, can be utilized to create transgenic animals. In theory, such animals may be used in one of two ways: as models for basic or practical scientific research, or as new sources of pharmacological drugs or human-compatible organs for xenotransplantation. In theory, gene transfer in higher eukaryotes might be used to treat humans in one of two ways: (a) somatic gene therapy, which involves genetic manipulation of a subset of cells in the body, or (b) germline gene therapy, which involves altering genetic information in germ cells. Because human germline gene therapy has never been done (unless it includes the transfer of foreign mitochondria during fertilization) and is fraught with serious ethical considerations, there is a dearth of scientific literature on the subject.

Types of cells

Transgenesis must take place early in the development process to achieve germline changes. Somatic cell changes, on the other hand, such as somatic gene therapy, affect a wide spectrum of cell types. Throughout this study, many somatic cell types are described at various stages. The cell types that can be employed for germline transgenesis are described in this section.

Embryonic stem cells, genetic manipulation of a recently fertilized single-cell egg (zygote) should result in the development of an organism in which the (same) alteration is present in all or a large number of cells. As a result, transgenic engineering has mostly focused on the zygote. In this study, the term 'egg' refers to all developmental stages from the oocyte through the unhatched blastocyst, in keeping with standard usage.

Pre-fertilization eggs could be good candidates for transgenesis. However, fundamental practical issues have prevented their deployment thus far. After transgenic alteration, eggs taken after ovulation would have to be fertilized. In vitro fertilization would be used in this case. As a result, potentially modified eggs would have to go through another lengthy ex vivo treatment. Because this may only harm the eggs, it's difficult to understand how transgenesis directed at this stage, rather than the zygote, could be useful.

On masse transgenic manipulation of pre-ovulatory oocytes in vivo, for example, may theoretically be undertaken. The resulting 'proto-transgenic' creature would be expected to produce transgenically altered eggs ready for fertilization with each subsequent ovulation. However, the underlying technology has not yet matured enough to support this type of in vivo technique, and no transgenic animals have been reported as a result of this method.

Eggs that have been cleaved are not appropriate for transgenesis. When only one cell is transgenically modified, the ensuing creature is most likely to be a genetic mosaic.

The organism would be made up of two types of cells: (a) cells with the transgene and (b) cells without the transgene. Indeed, the lower the number of changed cells in the transgenic, the more rounds of cleavage there have been prior to transgenesis. It's technically impossible to manipulate more than one cell in an egg. More importantly, each altered cell would not have the same change, for reasons that will be discussed later. The resulting organism would be a mosaic, despite the fact that it merely comprised of changed cells.

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