ESTABLISHMENT OF A TRANSGENIC MOUSE-PRODUCING SYSTEM AND ANALYSIS OF TRANSGENE INTEGRATION

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The introduction of foreign genes into mouse embryos offers a powerful approach for studying gene regulation throughout normal growth and development and the function of gene products within the body. In spite of these advantages, few laboratories have established transgenic mouse-producing systems because the running of such a system is costly, requires extensive space for breeding, and involves highly technical procedures. The author established a transgenic mouse-producing system with the microinjection of foreign genes into mouse embryos. Human thyroid stimulating hormone (TSH)-related genes and mouse hepatitis virus (MHV)-related genes were introduced into transgenic mice. The former was aimed at establishing model animals which would develop TSH-producing cell-specific tumors or TSH deficiencies. The latter was aimed at establishing MHV resistant mice.

A significant relationship was found between the number of fertilized eggs obtained and the temperature and / or relative humidity in the mouse breeding room. A relatively large number of fertilized eggs were obtained when the temperature ranged from 22℃ to 24℃ and / or relative humidity ranged from 45 % to 65 %. Thus, strictly controlled temperature and humidity are important for obtaining large numbers of fertilized eggs.

Optimum conditions for the efficient introduction by microinjection of foreign DNA into the mouse genome were selected. Embryo-manipulation techniques proved to be effective since both the survival rate of microinjected embryos and the birthrate of non-injected embryos resulted in about 70 %. A transgenic mouse-producing system has thus been established.

The integration form of transgenes was analyzed by Southern hybridization. Most of the mice were found to have integrated the transgenes in a head-to-tail direction. However, some transgenic mice showed band patterns which were not expected from their sequences, suggesting that rearrangements of the genes such as deletion, might have occurred in transgenes during the process of integration.

Transgenes were transmitted from founder mice to their F1 pups. Certain transgenes were not transmitted to their offspring. These results suggest that the construction of transgene might determine their germ line integration in founder mice and affect the transmission rate of the transgenes from founder mice to their offspring.