Approaches to Improving Production Efficiencies of Transgenic Animals

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Transgenic animals are very useful for scientific, pharmaceutical, and agricultural purposes. In livestock, transgenic technology has been used forthe genetic alteration of farm animals, the production of human proteins inlarge quantities in the milk of transgenic farm animals, and the generation of animals with organs suitable for xenotransplantation. To date, the transfer of foreign genes into farm animals has been performed mainly by microinjection of DNA into the pronuclei of fertilized eggs. However, the overall success rate of transgenic animals in livestock so far has been disappointingly low, eg., the efficiency is 0～5% in swine, and less than 1% in sheep and cattle, compared with the rate in mice where 5% microinjected develop into transgenic animals.

Recently, McGreath et al. (2000) have succeeded in producing the gene targeted sheep by the use of nuclear transfer from cultured somatic cells transfected with a foreign gene *in vitro*. However, we may need plenty of time until currently employ this method for gene transfer to farm animals. We have been studying to exploit the method for improving production efficiencies of transgenic animals with emphasis of its application to farm animals. The present paper describes three approaches that we have made in our laboratory to improve production

efficiencies of transgenic animals, based on the DNA microinjection method.

1. Co-injection of restriction enzyme with foreign DNA into the pronucleus for elevating production efficiencies of transgenic animals.
2. Efficient selection of transgenic mouse embryos using EGFP as a marker gene.
3. Phenotypes of tansgenic mice expressing WAP/hGH-CAG/EGFP fusion gene produced by selecting transgenic embryos.
4. Efficient site-specific integration of the transgene targeting an endogenous lox like site in early mouse embryos.