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Molecular Genetic Factors Affecting Gene Regulation in Transgenic Mice

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Transgenic animals have been provided as a powerful model for regulating gene expression and/or understanding gene function. We have produced some transgenic mice until now. The transgenic mice expressing human lactoferrin(hLf) and growth hormone(hGH) in their mammary glands have been developed. Expression of hLf was achieved by placing its cDNA under the control of bovine β-casein gene. To improve the hLf expression level, two artificial introns were introduced into the expression vector. Twenty lines of transgenic mice were produced. hLf was expressed in the mammary gland and secreted into the milk of transgenic mice. hLf RNA was only specifically detected in the mammary gland of transgenic mice. The expressed RNA was correctly spliced at the exon/intron junctions. For the production of hGH in the mammary glands of transgenic mice, hybrid genes (pBCN1GH and pBCN2GH) consisting of the rat β-casein and hGH genes were constructed. Totally six lines of transgenic mice were generated and the highest expression level of hGH in milk was 5.2 mg/ml in the transgenic mouse with BCN1GH transgene. In hGH transgenic mice, the 3'-flanking sequence of hGH played an important role in the efficient expression. To determine whether matrix attachment regions sequence(MARs) can confer position independent expression of transgene, we generated transgenic mice with whey acidic protein(WAP)-human Lf hybrid gene(pWL) or WAP-human Lf hybrid gene with MARs(pMWL). The results showed that the transmission and expression frequency in transgenic mice with pMWL transgene were improved more than those with pWL transgene. According to our studies on the production of transgenic mice, we could find out that gene regulatory sequences such as enhancer, promotor, hybrid intron, 3'-flanking sequence and MARs may affect the regulation of transgene in transgenic mice.