

mammalian organ systems in the interpretation of data collected from these animals; animals do not passively receive experimental manipulation and endogenous gene activities may be altered in response to the introduction of exogenous DNA sequences. Therefore, in addition to technical advancement, additional basic information regarding the control of specific gene expression in animals is required in order to achieve the highest level of specificity and precision in transgenic animal experimentation.

4.2. Application of Transgenic Technology in Drug Industry

Transgenic animals are produced using molecular genetic techniques to add functional genes, to alter gene products, to delete genes, to insert reporter genes into regulatory sequences, to replace/repair genes, to make tissue/lineage-specific alteration of gene expression, and so on. These genetically altered animals provide unique tools for studying a wide range of biomedical problems *in vivo*, allowing the manifestation of specific genetic changes in a variety of biological systems to be examined. Drug development relies largely on animal systems, and several areas of research have been hindered for decades due to the lack of suitable animal models. Established transgenic techniques undoubtedly have facilitated the progress of animal experimentation for some pharmacological questions where potential target molecules have been characterized. Because this technology is evolving rapidly, it is foreseeable that future development of this technology will allow one to address some difficult pharmacological questions where no specific targets have been identified.

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REFERENCES

1. Wei L-N. Transgenic animals as new approaches in pharmacological studies. *Annu Rev Pharmacol Toxicol* 1997; 37:119–141.
2. Hofker MH, Breuer M. Generation of transgenic mice. *Methods Mol Biol* 1998; 110:63–78.
3. Bradley A, Zheng B, Liu P. Thirteen years of manipulating the mouse genome: a personal history. *Intern J Dev Biol* 1998; 42:943–950.
4. Sedivy JM, Dutriaux A. Gene targeting and somatic cell genetics—a rebirth or a coming of age?. *Trends Genet* 1999; 15:88–90.
5. Rossant J, Spence A. Chimeras and mosaics in mouse mutant analysis. *Trends Genet* 1998; 14:358–363.
6. Sauer B. Inducible gene targeting in mice using the Cre/lox system. *Methods* 1998; 14:381–392.