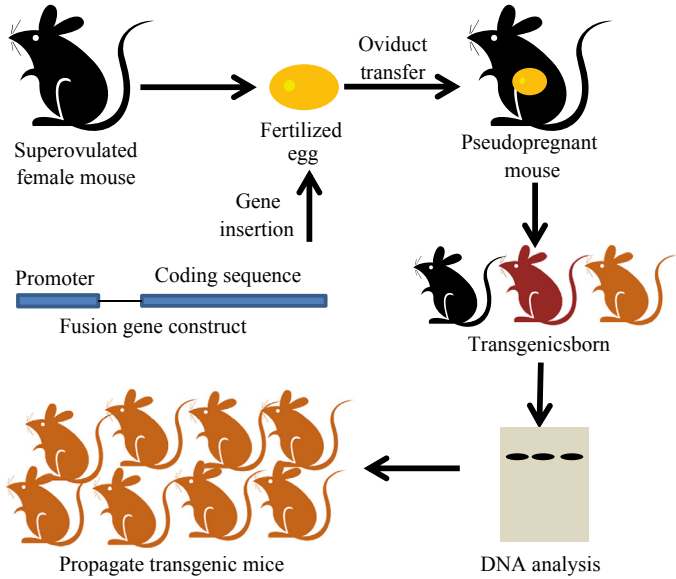

FIGURE 2.9 Transgenic animal models are developed through a combination of selective breeding and genetic manipulation. A gene construct suitable for insertion into an organism's DNA is prepared and then inserted into a fertilized egg via microinjection. The altered embryos are then implanted into a suitably pseudo-pregnant female and carried to term. After birth, genetic profiling is employed to identify offspring that are carriers of the transgene. Identification of transgene positive progeny is then followed by selective breeding to further the germ line.

have all been studied through the development of transgenic models through expression of either the human receptor for the virus or viral proteins important for pathogenesis.[31] Production of therapeutically relevant biomolecules has also been accomplished through the generation of transgenic animals.[32] Human antithrombin,[33] fibrinogen,[34] and monoclonal antibodies[35] have all been produced via transgenic science. It is well beyond the scope of this text to describe the wide array of transgenic animal models that has been developed since these initial experiments, but the impact of transgenic animals has been significant (Figure 2.10).

Knockout Animal Models

The advent of transgenic technology in animal models opened the door to knockout animal models. By the late 1980s, it had been well established that new animal models could be developed through the insertion and expression of foreign DNA in animal models. The next logical step, the suppression of normal gene function, was addressed by Capecchi, Evans, and Smithies in 1989 when they introduced the first knockout mouse.[36]