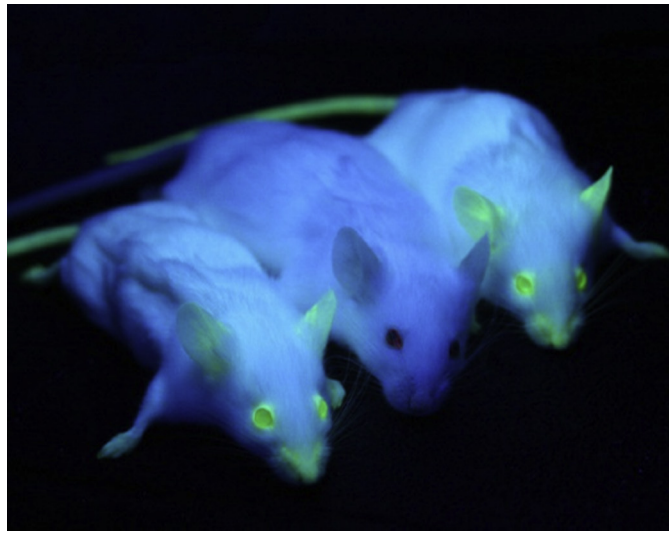

FIGURE 2.10 Transgenic insertion of the gene responsible for the production of green fluorescent protein (GFP) results in mice that fluoresce when exposed to ultraviolet light. The GFP gene has been successfully expressed in bacteria, fungi, plants, insects, and mammalian cells. Martin Chalfie, Osamu Shimomura, and Roger Y. Tsien were awarded the Nobel Prize in Chemistry in 2008 in acknowledgement of their work on GFP technology. *Source: Moen, I.; Jevne, C.; Wang, J.; Kalland, K. H.; Chekenya, M; Akslen, L. A.; Sleire, L.; Enger, P.; Reed, R. K.; Yan, A. M.; Stuh, L. E. B. Gene expression in tumor cells and stroma in dsRed 4T1 tumors in eGFP-expressing mice with and without enhanced oxygenation. BMC Cancer 2012, 12:21.* http://doi:10.1186/1471-2407-12-21.

In their seminal experiments, they were able to eliminate functional hypoxanthine-guanine phosphoribosyl transferase genes (*hprt*) in mouse embryonic stems cells using either a sequence replacement targeting vector or a sequence insertion targeting vector (Figure 2.11). In both cases, the insertion of foreign DNA into the otherwise functional DNA segment led to the suppression of the *hprt* gene in viable embryonic stem cells, which were then implanted into the uterus of a healthy mouse and progressed to birth. In the following years, thousands of knockout mouse models have been developed to study a wide range of disease states. The p53 knockout mouse, for example, has been an important model in the study of cancer progression and therapy. The absence of functional p53 tumor suppressors, encoded by the TP53 gene, provides a mouse strain that mimics Li-Fraumeni syndrome. The resulting mice are far more susceptible to tumor formation.[37] Additional examples include the Fmr1 knockout mouse that serves as a model for Fragile X-related mental retardation,[38] the nescient helix loop helix 2 (Nhlh2) knockout mouse that decreases the levels of α-melanocyte-stimulating hormone and thyrotropin-releasing hormone, providing a model for the study of obesity,[39] and the ApoE knockout mouse in which the expression of Apolipoprotein E is suppressed, leading to the formation of vascular plaques similar to those found in humans suffering