DELINEATION OF DUCHENNE MUSCULAR DYSTROPHY GENE THERAPY USING GENETICALLY ENGINEERED MICE

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ABSTRACT

Duchenne muscular dystrophy (DMD) is an X-linked disease that elicits severe skeletal and cardiac muscle degeneration. Currently there is no cure. Gene therapy has shown great promise. However, many fundamental issues related to the development of gene therapy are unclear. Here I have addressed four of these issues. Specifically, (1) I clarified the relationship between skeletal muscle and cardiomyopathy and demonstrated that dystrophic heart disease is independent of skeletal muscle disease; (2) I determined an effective long-term DMD therapy required persistent dystrophin expression in both skeletal muscle and the heart; (3) I identified dystrophin spectrin-like repeats 16-19 as a putative heart protection domain; and (4) I demonstrated that uniform dystrophin expression at ~3.3% of the wild type level can partially preserve heart function.