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Lentivirus-mediated expression following intramuscular injection

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Elvire Gouze,[Aff1]

Aff1 Harvard Medical School, Boston, MA, USA

Keywords

Erythropoietin, gene therapy, lentivirus

Context

HIV-1-based lentiviral vectors have the advantage over oncoretrovirus of enabling provirus integration into nondividing cells. These vectors successfully transduce a variety of human cells including muscle cells. Lentiviral vectors are often pseudotyped with vesicular stomatitis virus G (VSV-G) coat protein increasing their host cell range and allowing their concentration by ultracentrifugation.

Recombinant erythropoietin (EPO) has been widely used for treatments of anemia associated with chronic renal failure, cancer chemotherapy, and HIV infections. Persistent delivery of EPO by gene transfer rather than repeat injections would provide clinical and economic benefits. The authors investigated whether a self-inactivating lentiviral vector encoding rat EPO was able to mediate long-term expression after a single administration to rat muscle.

Significant findings

VSV-G pseudotyped, lentiviral vector encoding rat EPO was administered to rat skeletal muscle. Following a single intramuscular injection of lentivirus encoding EPO, the hematocrit levels increased in a dose-dependent manner reaching a plateau at 35 days that was maintained for at least 14 months. Following the injection of a plasmid containing the same coding sequence, hematocrit levels were not increased. The authors confirm the presence of the vector sequences in genomic DNA by PCR analysis of muscle tissues. No viral sequences were recovered in liver, spleen, kidney and lung. These data show that VSV-G pseudotype, lentiviral vectors can mediate long-term transgene expression after single administration to rat muscle.

Comments

This paper reports long-term transgene expression following intramuscular injection of lentivirus in the rat. While the article itself does not directly relate to the field of arthritis, it provides a striking demonstration of the potential of this emerging gene transfer technology.

Indeed, while it has been possible to achieve therapeutic levels of certain proteins in animal models of arthritis using systemic and intra-articular gene transfer approaches, persistent expression of the transgene has not been reliably achieved. Another advantage of this system is that, like HIV-based retroviral vectors, lentiviral vectors have the capability of integrating their genetic material into the genome of both dividing and nondividing target cells. To date, however, there have been no published reports of the use of this vector system in arthritis related research. Given the clinical effectiveness of systemic administration of recombinant soluble TNF receptors, gene delivery to muscle using a lentiviral vector may, on the one hand, provide an avenue for persistent, systemic delivery of these and other anti-arthritic proteins. On the other hand, uncontrolled and sustained expression of some transgenes using a similar approach could pose a problem in the clinic with respect to toxicity, or untoward side effects. Regulated systems, such as those utilising tetracycline promoters, provide an alternative strategy that addresses this particular issue.

Methods

Lentivirus production, hematocrit, PCR

Additional information

References

1. Seppen J, Barry SC, Harder B, Osborne WRA: Lentivirus administration to rat muscle provides efficient sustained expression of erythropoietin. Blood. 2001, 98: 594-596.