US009410163B2

(12) **United States Patent**
Frendewey et al.

(10) **Patent No.: US 9,410,163 B2**
(45) **Date of Patent: *Aug. 9, 2016**

(54) **PROMOTER-REGULATED DIFFERENTIATION-DEPENDENT SELF-DELETING CASSETTE**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **14/571,515**

(22) Filed: **Dec. 16, 2014**

(65) **Prior Publication Data**

US 2015/0099296 A1 Apr. 9, 2015

Related U.S. Application Data

(60) Continuation of application No. 13/934,829, filed on Jul. 3, 2013, now Pat. No. 8,946,505, which is a division of application No. 12/856,163, filed on Aug. 13, 2010, now Pat. No. 8,518,392.

(60) Provisional application No. 61/233,974, filed on Aug. 14, 2009.

(51) **Int. Cl.**

C12N 15/00	(2006.01)
C12N 5/00	(2006.01)
C12N 5/18	(2006.01)
C12N 15/85	(2006.01)
A01K 67/027	(2006.01)
C12N 15/90	(2006.01)
C12N 15/873	(2010.01)
C12N 9/12	(2006.01)

(52) **U.S. Cl.**

CPC ***C12N 15/8509*** (2013.01); ***A01K 67/0275*** (2013.01); ***C12N 9/1241*** (2013.01); ***C12N 15/85*** (2013.01); ***C12N 15/873*** (2013.01); ***C12N 15/907*** (2013.01); *A01K 2217/07* (2013.01); *A01K 2217/206* (2013.01); *A01K 2227/105* (2013.01); *C12N 2800/22* (2013.01); *C12N 2800/30* (2013.01); *C12N 2840/102* (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

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(57) **ABSTRACT**

Targeting constructs and methods of using them are provided for differentiation-dependent modification of nucleic acid sequences in cells and in non-human animals. Targeting constructs comprising a promoter operably linked to a recombinase are provided, wherein the promoter drives transcription of the recombinase in an differentiated cell but not an undifferentiated cell. Promoters include Blimp1, Prm1, Gata6, Gata4, Igf2, Lhx2, Lhx5, and Pax3. Targeting constructs with a cassette flanked on both sides by recombinase sites can be removed using a recombinase gene operably linked to a 3'-UTR that comprises a recognition site for an miRNA that is transcribed in undifferentiated cells but not in differentiated cells. The constructs may be included in targeting vectors, and can be used to automatically modify or excise a selection cassette from an ES cell, a non-human embryo, or a non-human animal.

12 Claims, 7 Drawing Sheets