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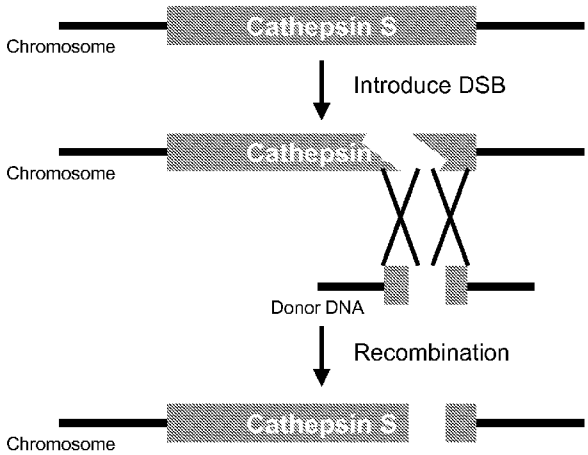
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(54) Title: HUMANIZED MODELS VIA TARGETED MTAGENESIS WITH ZINC FINGER NUCLEASE




(57) Abstract: The present invention is directed to the generation of non-human animal models of human disease via the targeted alteration of the nucleic acid sequences in genes encoding drug target proteins. The animal models of human disease may be used for the evaluation of candidate drug molecules. The present method takes advantage of engineered zinc finger nucleases to target specific regions within a gene encoding the animal homologue of a specific protein that differs from the human gene. The zinc finger nuclease introduces a DNA double-stranded break at these specific regions, which enable the introduction of exogenous nucleotide sequences by homologous recombination. The animal gene is not entirely replaced: rather, only specific regions of the animal gene are altered. Therefore, the altered gene remains under the appropriate physiological regulation.

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# INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/85 C12N15/90 A01K67/027 C12N9/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12N A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, Sequence Search

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[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

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| Date of the actual completion of the international search | Date of mailing of the international search report |
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| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | CHAMBONNET, F |

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