

CLAIMS

1. A genetically modified rodent whose genome comprises a replacement of a genomic fragment comprising exons 2-5 and the coding portion of exon 6 of an endogenous rodent *AProliferation-Inducing Ligand (April)* gene with a human genomic fragment comprising exons 2-6 of a human *APRIL* gene to form a humanized *April* gene, wherein the replacement is at an endogenous rodent *April* locus, wherein the humanized *April* gene is under control of a rodent *April* promoter at said endogenous rodent *April* locus, and encodes a humanized April protein comprising an extracellular portion of the human APRIL protein encoded by said human *APRIL* gene linked to an intracellular portion of the rodent April protein encoded by said rodent *April* gene, and wherein said genetically modified rodent expresses said humanized April protein.
2. The genetically modified rodent of claim 1, wherein said rodent does not detectably express a full-length endogenous rodent April protein.
3. The genetically modified rodent of claim 1 or claim 2, wherein said rodent is a mouse or rat.
4. The genetically modified rodent of claim 3, wherein said rodent is a mouse.
5. The genetically modified rodent of claim 4, wherein the humanized April protein comprises amino acids 87 to 250 of SEQ ID NO: 5.
6. The genetically modified rodent of claim 4, wherein the humanized *April* gene comprises exon 1 of said endogenous mouse *April* gene.
7. The genetically modified rodent of claim 6, wherein said humanized April protein comprises the amino acid sequence as set forth in SEQ ID NO: 12.
8. The genetically modified rodent of claim 1, wherein the coding exons of the humanized *April* gene consist of exon 1 of said endogenous rodent *April* gene, and exons 2-6 of said human *April* gene.

9. An isolated cell or tissue of a genetically modified rodent according to any one of the preceding claims.
10. A rodent embryonic stem (ES) cell, whose genome comprises a replacement of a genomic fragment comprising exons 2-5 and the coding portion of exon 6 of an endogenous rodent *April* gene with a human genomic fragment comprising exons 2-6 of a human *APRIL* gene to form a humanized *April* gene, wherein the replacement is at an endogenous rodent *April* locus, wherein the humanized *April* gene is under control of a rodent *April* promoter at said endogenous rodent *April* locus, and encodes a humanized April protein comprising an extracellular portion of the human APRIL protein encoded by said human *APRIL* gene linked to an intracellular portion of the rodent April protein encoded by said rodent *April* gene.
11. A rodent embryo generated from the ES cell of claim 10.
12. The rodent (ES) cell of claim 10, or the rodent embryo of claim 11, wherein the rodent is a mouse or rat.
13. A method of making a rodent that expresses a humanized April protein from an endogenous *April* locus, the method comprising the steps of:
- (a) replacing a genomic fragment comprising exons 2-5 and the coding portion of exon 6 of an endogenous rodent *April* gene at an endogenous *April* locus in a rodent embryonic stem (ES) cell with a genomic fragment comprising exons 2-6 of a human *APRIL* gene to form a humanized *April* gene at the endogenous rodent *April* locus, wherein the humanized *April* gene is under control of the rodent *April* promoter at said endogenous rodent *April* locus and encodes a humanized April protein comprising an extracellular portion of the human APRIL protein encoded by said human *APRIL* gene linked to an intracellular portion of the rodent April protein encoded by said rodent *April* gene;
 - (b) obtaining a modified rodent ES cell comprising said humanized *April* gene at the endogenous rodent *April* locus; and,
 - (c) creating a rodent using the modified ES cell of (b).

14. The method of claim 12, wherein the rodent is a mouse or rat.
15. The method of claim 13 or 14, wherein said rodent does not detectably express a full-length endogenous rodent April protein.
16. A method of engrafting human cells into a mouse, the method comprising steps of:
 - (a) providing a mouse whose genome comprises a replacement of a rodent fragment comprising exons 2-5 and the coding portion of exon 6 of an endogenous mouse *April* gene with a human genomic fragment comprising exons 2-6 of a human *APRIL* gene to form a humanized *April* gene, wherein the replacement is at an endogenous mouse *April* locus, wherein the humanized *April* gene is under control of the mouse *April* promoter at said endogenous mouse *April* locus and encodes a humanized April protein comprising an extracellular portion of the human APRIL protein encoded by said human *APRIL* gene linked to an intracellular portion of the mouse April protein encoded by said mouse *April* gene; and
 - (b) transplanting one or more human cells into the mouse, optionally; wherein the human cells are human hematopoietic stem cells.