

What is claimed is:

1. A rodent, comprising a replacement of a genomic fragment of a rodent IL-4R α gene at an endogenous rodent IL-4R α locus with a genomic fragment of a human IL-4R α gene to form a humanized IL-4R α gene comprising the ATG initiation codon of coding exon 1 through coding exon 5 of the human IL-4R α gene, and coding exons 6-9 of the rodent IL-4R α gene, wherein the genomic fragment of the rodent IL-4R α gene comprises the ATG initiation codon of coding exon 1 through coding exon 5 of the rodent IL-4R α gene, and the genomic fragment of the human IL-4R α gene comprises the ATG initiation codon of coding exon 1 through coding exon 5 of the human IL-4R α gene, and wherein expression of the humanized IL-4R α gene is under control of rodent IL-4R α regulatory elements at the endogenous rodent IL-4R α locus.
2. The rodent of claim 1, wherein the rodent is a mouse or a rat.
3. The rodent of claim 1, wherein the rodent is a mouse that is incapable of expressing a mouse IL-4R α protein.
4. The rodent of claim 1, wherein the rodent expresses a human or humanized IL-4 protein.
5. The rodent of claim 4, wherein the rodent is a mouse that does not express a mouse IL-4 protein.
6. The rodent of claim 1, wherein the rodent comprises a replacement of a genomic fragment of a rodent IL-4 gene at an endogenous rodent IL-4 locus with a genomic fragment of a human IL-4 gene to form a humanized IL-4 gene, wherein the genomic fragment of the rodent IL-4 gene comprises the ATG initiation codon of exon 1 through exon 4 of the rodent IL-4 gene, and the genomic fragment of the human IL-4 gene comprises the ATG initiation codon of exon 1 through exon 4 of the human IL-4 gene, and wherein expression of the humanized IL-4 gene is under control of rodent IL-4

regulatory elements at the endogenous rodent IL-4 locus.

7. The rodent of any one of claims 1-2, 4 and 6 which is a mouse.

8. A method for making a humanized rodent, comprising replacing a genomic fragment of a rodent IL-4R α gene at an endogenous rodent IL-4R α locus with a genomic fragment of a human IL-4R α gene to form a humanized IL-4R α gene comprising the ATG initiation codon of coding exon 1 through coding exon 5 of the human IL-4R α gene, and coding exons 6-9 of the rodent IL-4R α gene, wherein the genomic fragment of the rodent IL-4R α gene comprises the ATG initiation codon of coding exon 1 through coding exon 5 of the rodent IL-4R α gene, and the genomic fragment of the human IL-4R α gene comprises the ATG initiation gene of coding exon 1 through coding exon 5 of the human IL-4R α gene, and the humanized IL-4R α gene is operably linked to rodent IL-4R α regulatory elements at the endogenous rodent IL-4R α locus.

9. The method of claim 8, wherein the rodent is a mouse or a rat.

10. The method of claim 8 or 9, wherein the rodent is a mouse.

11. A method of screening for a human-specific IL-4 or IL-4R α antagonist, comprising:

providing a doubly humanized IL-4 and IL-4R α rodent as defined in claim 6,
inducing pulmonary inflammation in said rodent,
administering an agent to said rodent,
determining whether pulmonary inflammation is reduced by the agent, and
identifying the agent as a human specific IL-4 or IL-4R α antagonist based on its ability to reduce pulmonary inflammation, optionally wherein the extent of pulmonary inflammation is determined by measuring mucus accumulation in the airway, eosinophilic infiltrating cells in bronchoalveolar lavage fluid, and/or total circulating IgE.

12. A method of screening for a human-specific IL-4 or IL-4R α antagonist, comprising:
- providing a doubly humanized IL-4 and IL-4R α rodent as defined in claim 6,
 - inducing skin inflammation in said rodent,
 - administering an agent to said rodent,
 - determining whether skin inflammation is reduced by the agent, and
 - identifying the agent as a human specific IL-4 or IL-4R α antagonist based on its ability to reduce skin inflammation.