other signaling cascades in cells of the immune system have not yet been fully elucidated.

WO2010/017468 discloses antibodies that bind to an epitope of human CD-127 (IL-7Rα) and methods of treating multiple sclerosis (and other autoimmune diseases) comprising the neutralization of the biological activity of IL-7 by the binding of isolated binding proteins to CD127 or IL-7. The therapeutic benefits of these antibodies in autoimmune disorders such as type I diabetes and multiple sclerosis are also demonstrated. Chung et al "Prevention of graft-versus-host disease by anti-IL-7Rα antibody" In the Journal 'BLOOD', (Vol 110 No.8 {15/10/2007} pages 2803-2810) its authors also a method of disease prevention (graft-versus-host disease) through the use of an anti-IL-7Rα and WO2010/085643 discloses antibodies which bind to or interact with IL-7R and/or IL-7Rα and inhibits IL-7Rα mediated signaling for the treatment of autoimmune disorders such as multiple sclerosis, type I diabetes and graft-versus-host disease.

From the information available in the art, and prior to the present invention, it remained unclear whether the introduction of an antagonist IL-7R antibody into the blood circulation to selectively antagonize IL-7R would be effective to treat type 2 diabetes, type 1 diabetes, GVHD, lupus and rheumatoid arthritis, and, if so, what properties of an IL-7R antibody are needed for such *in vivo* effectiveness.

Summary

Antagonist antibodies that selectively interact with and inhibit IL-7R function are provided. It is demonstrated for the first time that certain antagonist IL-7R antibodies are effective *in vivo* to treat type 1 diabetes, type 2 diabetes, rheumatoid arthritis, GVHD and lupus.

In some embodiments, antagonist antibodies that selectively interact with and inhibit IL-7R function are provided. In some embodiments, the antibody specifically binds to IL-7R and comprises an antigen binding region that competes with a monoclonal antibody selected from the group consisting of C1GM, C2M3, P3A9, P4B3, P2D2, P2E11, HAL403a and HAL403b, for binding to IL-7R. In some embodiments, the antibody comprises a polypeptide having the amino acid sequence shown in SEQ ID NO: 42 or SEQ ID NO: 43. In other embodiments, the antibody specifically binds to IL-7R and recognizes an epitope which overlaps an epitope of IL-7R that is recognized by a monoclonal antibody selected from the group consisting of C1GM, C2M3, P3A9,

P4B3, P2D2, P2E11, HAL403a and HAL403b. In some embodiments, the antibody the antibody binds to an epitope comprising residues I82, K84, K100, T105, and Y192 of interleukin-7 receptor alpha (IL-7Rα). In some embodiments, the epitope further comprises one or more additional residues selected from the group consisting of residues D190, H191, and K194 of human IL-7Rα.

In some embodiments, the IL-7R is human IL-7R.

In some embodiments, the antibody specifically binds to interleukin-7 receptor alpha (IL-7Rα) and comprises a heavy chain variable region (VH) complementary determining region one (CDR1) having the amino acid sequence X_1X_2VMH, wherein X_1 is D or N; X_2 is S or Y (SEQ ID NO: 50), a VH CDR2 having the amino acid sequence $X_1X_2X_3X_4X_5GX_6X_7$TYYADSVKG, wherein X_1 is L or A; X_2 is V or I; X_3 is G or S; X_4 is W

~~It is claimed:~~ Claims

1. An isolated interleukin-7 receptor (IL-7R) antibody which specifically binds to an epitope comprising residues I82, K84, K100, T105, and Y192 of human interleukin-7 receptor alpha (IL-7Rα), wherein the epitope does not include residues V58, E59, R66, K77 or L80 of IL-7Rα.

2. The antibody of claim 1, wherein the epitope further comprises one or more additional residues selected from the group consisting of residues D190, H191, and K194 of human IL-7Rα.

3. An isolated antibody which specifically binds to interleukin-7 receptor alpha (IL-7Rα), wherein the antibody comprises three complementarity determining regions (CDRs) from a heavy chain variable region (VH) comprising the amino acid sequence shown in SEQ ID NO: 40, or CDR variants thereof having one, two or three conservative amino acid substitutions; and three CDRs from a light chain variable region (VL) comprising the amino acid sequence shown in SEQ ID NO: 41, or CDR variants thereof having one, two or three conservative amino acid substitutions.

4. The antibody of claim 3, wherein the VH region comprises the amino acid sequence shown in SEQ ID NO: 40 and the VL region comprises the amino acid sequence shown in SEQ ID NO: 41.

5. The antibody of claim 4, wherein said antibody comprises a light chain having the amino acid sequence shown in SEQ ID NO: 43 and a heavy chain having the amino acid sequence shown in SEQ ID NO: 42, with or without the C-terminal lysine of SEQ ID NO: 42.

6. The antibody of any one of claims 1 to 4, wherein the antibody further comprises a constant region.

7. The antibody of claim 6, wherein the antibody is of the human IgG1 or IgG2Δa subclass.

8. A pharmaceutical composition comprising the antibody of any one of claims 1 to 7.

9. A cell line that recombinantly produces the antibody of any one of claims 1 to 7.

10. A nucleic acid encoding the antibody according to any one of claims 1 to 7.

11. The antibody of any one of claims 1 to 7 for use in treating and/or preventing an autoimmune disorder in an individual, thereby ameliorating and/or preventing one or more symptoms of the autoimmune disorder.

12. The ~~use~~ antibody of claim 11, wherein the autoimmune disorder is selected from the group consisting of type 1 diabetes, rheumatoid arthritis, lupus and multiple sclerosis.

13. The ~~use~~ antibody of claim 11, wherein use of the antibody results in reduced naïve and activated T cell populations in the individual compared to before its use.

14. The ~~use~~ antibody of claim 13, wherein the reduced T cell populations in the individual comprise T_H1 and/or T_H17 cells.

15. The antibody of any one of claims 1 to 7 for use in treating and/or preventing type 2 diabetes in an individual suffering from or at risk for type 2 diabetes, thereby ameliorating and/or preventing one or more symptoms of type 2 diabetes.

16. The antibody of any one of claims 1 to 7 for use in treating and/or preventing graft-versus-host disease (GVHD) in an individual suffering from GVHD, thereby ameliorating one or more symptoms of GVHD.