allograft survival has been prolonged and T cell infiltration in the graft was decreased compared with controls (J Immunol. 1990, 144:4604-4612). Enlimomab also had been proved to be beneficial in depressing disease activity in patient with rheumatoid arthritis (Arthritis Rheum. 1994, 37:992-999; J Rheumatol. 1996, 23:1338-1344). However, enlimomab induction therapy after renal transplantation in a randomized multicenter study was not able to reduce the rate of acute rejection or the risk of delayed onset of graft function (Transplantation. 1999, 67:729-736). Moreover, clinical trial in acute ischemic stroke patient revealed that anti-ICAM-1 therapy with enlimomab was not an effective and indeed significantly worsen stroke outcome and induced more adverse effect, primarily infections and fever compared with placebo (Neurology. 2001, 57:1428-1434). The enlimomab functions by blocking the adhesion of T cells as wells as neutrophils to the vascular endothelial cells and thus it has been suggested that interfering with neutrophil emigration potentially increases the susceptibility to infection (J Immunol. 1999, 162:2352-2357).

Another anti-ICMA-1 monoclonal antibody, MD-3, has been known to suppress transplantation rejection (US Patent Publication No. 2010-0168394-A1). Unlike R6-5-D6, this antibody binds the domain of ICAM-1 and does not block the interaction between ICAM-1 and LFA-1. Rather then, this antibody suppresses T cell function via modulating the development and function of dendritic cells.

SUMMARY OF THE INVENTION

An embodiment of the present invention relates to an antibody binding to the domain 2 of human intercellular adhesion molecules-1 (ICAM-1) where the antibody is able to modulate the differentiation and function of dendritic cells and induce antigen-specific T cell tolerance, thereby being effective in the prevention and/or treatment of T cell-mediated immune disorders, such as transplantation rejection, graft-versus-host disease, and autoimmune disease. In addition, the present invention provides a pharmaceutical composition comprising the antibody. The present invention further provides a pharmaceutical composition comprising the antibody for treating the T cell-mediated immune disorders, the antibody for use in treating the T cell-mediated immune

WHAT IS CLAIMED IS:

1. An monoclonal antibody designated MD-3 produced by the hybridoma cell deposited as accession number of KCLRF-BP-00264.

2. An monoclonal antibody binding to human ICAM-1 comprising a heavy chain and a light chain, the heavy chain comprising three complementary determining regions (CDRs) from the heavy chain of an antibody produced by a hybridoma deposited as an accession number of KCLRF-BP-00264 and the light chain comprising three CDRs from the light chain of an antibody produced by a hybridoma deposited as an accession number of KCLRF-BP-00264.

3 The antibody according to Claim 2, wherein the antibody is a chimeric or humanized form from designated MD-3 produced by the hybridoma cell deposited as accession number of KCLRF-BP-00264.

4. A hybridoma cell deposited as accession number of KCLRF-BP-00264.

5. A pharmaceutical composition comprising the monoclonal antibody of any one of claims 1 to 4.

6. The pharmaceutical composition according to claim 5, wherein the monoclonal antibody is in isolated form.

7. A pharmaceutical composition for modulating the differentiation and functions of dendritic cells via binding the domain 2 of ICAM-1 and inducing antigen-specific T cell tolerance, comprising the monoclonal antibody according to any one of claims 1 to 4 as an active ingredient.

8. A pharmaceutical composition for the prevention or treatment of T cell-mediated immune disorders, comprising the monoclonal antibody according to any one of claims 1 to 4 as an active ingredient.

9. The pharmaceutical composition according to Claim 8, wherein the T cell-mediated immune disorders is transplantation rejection, graft-versus-host disease, or autoimmune disease.

10. A method of modulating the differentiation and functions of dendritic cells via binding the domain 2 of ICAM-1 and inducing antigen-specific T cell tolerance, comprising the step of administering the monoclonal antibody according to any one of claims 1 to 4 to a patient in need thereof.

11. A method of the prevention or treatment of T cell-mediated immune disorders, comprising the step of administering the monoclonal antibody according to any one of claims 1 to 4 to a patient in need thereof.

12. The method according to Claim 11, wherein the T cell-mediated immune disorders is transplantation rejection, graft-versus-host disease, or autoimmune disease.

13. A monoclonal antibody for use in modulating the differentiation and functions of dendritic cells via binding the domain 2 of ICAM-1 and inducing antigen-specific T cell tolerance, wherein the monoclonal antibody is according to any one of claims 1 to 4.

14. The monoclonal antibody for use in preventing or treating T cell-mediated immune disorders, wherein the monoclonal antibody is according to any one of claims 1 to 4.

15. The monoclonal antibody according to Claim 14, wherein the T cell-mediated immune disorders is transplantation rejection, graft-versus-host disease, or autoimmune disease.

allograft survival has been prolonged and T cell infiltration in the graft was decreased compared with controls (J Immunol. 1990, 144:4604-4612). Enlimomab also had been proved to be beneficial in depressing disease activity in patient with rheumatoid arthritis (Arthritis Rheum. 1994, 37:992-999; J Rheumatol. 1996, 23:1338-1344). However, enlimomab induction therapy after renal transplantation in a randomized multicenter study was not able to reduce the rate of acute rejection or the risk of delayed onset of graft function (Transplantation. 1999, 67:729-736). Moreover, clinical trial in acute ischemic stroke patient revealed that anti-ICAM-1 therapy with enlimomab was not an effective and indeed significantly worsen stroke outcome and induced more adverse effect, primarily infections and fever compared with placebo (Neurology. 2001, 57:1428-1434). The enlimomab functions by blocking the adhesion of T cells as wells as neutrophils to the vascular endothelial cells and thus it has been suggested that interfering with neutrophil emigration potentially increases the susceptibility to infection (J Immunol. 1999, 162:2352-2357).

Another anti-ICMA-1 monoclonal antibody, MD-2, has been known to suppress transplantation rejection (US Patent Publication No. 2010-0168394-A1). Unlike R6-5-D6, this antibody binds the domain of ICAM-1 and does not block the interaction between ICAM-1 and LFA-1. Rather then, this antibody suppresses T cell function via modulating the development and function of dendritic cells.

SUMMARY OF THE INVENTION

An embodiment of the present invention relates to an antibody binding to the domain 2 of human intercellular adhesion molecules-1 (ICAM-1) where the antibody is able to modulate the differentiation and function of dendritic cells and induce antigen-specific T cell tolerance, thereby being effective in the prevention and/or treatment of T cell-mediated immune disorders, such as transplantation rejection, graft-versus-host disease, and autoimmune disease. In addition, the present invention provides a pharmaceutical composition comprising the antibody. The present invention further provides a pharmaceutical composition comprising the antibody for treating the T cell-mediated immune disorders, the antibody for use in treating the T cell-mediated immune

WHAT IS CLAIMED IS:

1. An monoclonal antibody designated MD-3 produced by the hybridoma cell deposited as accession number of KCLRF-BP-00264.

2. An monoclonal antibody binding to human ICAM-1 comprising a heavy chain and a light chain, the heavy chain comprising three complementary determining regions (CDRs) from the heavy chain of an antibody produced by a hybridoma deposited as an accession number of KCLRF-BP-00264 and the light chain comprising three CDRs from the light chain of an antibody produced by a hybridoma deposited as an accession number of KCLRF-BP-00264.

3 The antibody according to Claim 2, wherein the antibody is a chimeric or humanized form from designated MD-3 produced by the hybridoma cell deposited as accession number of KCLRF-BP-00264.

4. A hybridoma cell deposited as accession number of KCLRF-BP-00264.

5. A pharmaceutical composition comprising the monoclonal antibody of any one of claims 1 to 4.

6. The pharmaceutical composition according to claim 5, wherein the monoclonal antibody is in isolated form.

7. A pharmaceutical composition for modulating the differentiation and functions of dendritic cells via binding the domain 2 of ICAM-1 and inducing antigen-specific T cell tolerance, comprising the monoclonal antibody according to any one of claims 1 to 4 as an active ingredient.

8. A pharmaceutical composition for the prevention or treatment of T cell-mediated immune disorders, comprising the monoclonal antibody according to any one of claims 1 to 4 as an active ingredient.

9. The pharmaceutical composition according to Claim 8, wherein the T cell-mediated immune disorders is transplantation rejection, graft-versus-host disease, or autoimmune disease.

10. A monoclonal antibody for use in modulating the differentiation and functions of dendritic cells via binding the domain 2 of ICAM-1 and inducing antigen-specific T cell tolerance, wherein the monoclonal antibody is according to any one of claims 1 to 4.

11. The monoclonal antibody for use in preventing or treating T cell-mediated immune disorders, wherein the monoclonal antibody is according to any one of claims 1 to 4.

12. The monoclonal antibody according to Claim 11, wherein the T cell-mediated immune disorders is transplantation rejection, graft-versus-host disease, or autoimmune disease.