In addition, it has been reported that Treg might have an important role in diseases associated with or caused by an excessive immune response.

However, there is currently no available and efficient strategy for treating Treg associated diseases. There is still thus a great need for providing efficient therapeutic strategies targeting diseases involving Treg.

SUMMARY ~~OF THE INVENTION~~

Surprisingly, the inventors have shown that the interaction between ICOS and its ligand plays a central role in the activation, proliferation and suppressive function of Treg in some cancers through interaction with plasmacytoid dendritic cells (pDC). They then concentrated their effort to generate specific antibodies with antagonist and agonist effects.

The antagonist antibodies are efficient for treating a disease or a condition associated with Treg mediated suppression of immune response. The agonist antibodies are efficient for treating a disease or a condition associated with or caused by an excessive immune response.

The present ~~invention~~disclosure thus relates to an antibody directed against ICOS or a derivative thereof which:

- neutralizes ICOS engagement on Treg by inhibiting the fixation between ICOS and ICOS-L; and
- abrogates proliferation of Treg induced by pDC.

In the context of the present ~~invention~~disclosure, said antibody may also be called "antagonist antibody".

The ~~invention~~disclosure further relates to an antibody directed against ICOS, wherein said antibody is selected from the group consisting of Icos 145-1 and Icos 314-8, respectively obtainable from the hybridoma deposited at the "Collection Nationale de Cultures de Microorganismes" (CNCM, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris Cedex 15, France), in accordance with the terms of Budapest Treaty, on July 2, 2009 under the access accession numbers CNCM 1-4179 and CNCM 1-4180 and derivatives thereof.

The ~~invention~~disclosure also relates to an antagonist antibody directed against ICOS according to the ~~invention~~disclosure or a derivative thereof for use as a medicament. The ~~invention~~disclosure further relates to an antagonist antibody directed against ICOS according to the ~~invention~~disclosure or a derivative thereof for use for treating cancers or chronic infections.

The present ~~invention~~disclosure further relates to an antibody directed against ICOS or a derivative thereof which:

- induces IL-10 and IFNγ production;
- induces CD4+ T cells proliferation;
- reduces Tconv proliferation, and
- increases the immunosuppressive function of Treg.

In the context of the present ~~invention~~disclosure, said antibody may also be called "agonist antibody".

The ~~invention~~disclosure also relates to an antibody directed against ICOS, wherein said antibody is selected from the group consisting of Icos 53-3, Icos 88-2 and Icos 92-17, respectively obtainable from the hybridoma deposited at the "Collection Nationale de Cultures de Microorganismes" (CNCM, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris Cedex 15, France), in accordance with the terms of Budapest Treaty, on July 2, 2009 under the accession numbers CNCM 1-4176, CNCM 1-4177, CNCM I-4178 and derivatives thereof.

The ~~invention~~disclosure relates to an agonist antibody according to the ~~invention~~disclosure or a derivative thereof for use as a medicament. The ~~invention~~disclosure also relates to an agonist antibody according to the ~~invention~~disclosure or a derivative thereof for use for treating autoimmune diseases, transplantation rejection or a graft versus host disease.

According to one aspect, there is provided an antibody directed against ICOS, wherein said antibody is selected from the group consisting of Icos 314-8, obtainable from the hybridoma deposited at the CNCM on July 2, 2009 under the accession number CNCM I-4180, and derivatives thereof.

According to another aspect, there is provided an antibody directed against ICOS, wherein said antibody has the following 6 CDRs:

	Aminoacid sequence
H-CDR1	GYTFTTYWMH (SEQ ID NO:7)
H-CDR2	EIDPSDSYVNYNQNFKG (SEQ ID NO:8)
H-CDR3	FDY (SEQ ID NO:9)
L-CDR1	RSSKSPLHSNGNIYLY (SEQ ID NO :10)
L-CDR2	RMSNLAS (SEQ ID NO :11)
L-CDR3	MQHLEYPYT (SEQ ID NO :12)

According to another aspect, there is provided an antibody as disclosed herein for use as a medicament.

According to another aspect, there is provided use of an antibody as disclosed herein in the manufacture of a medicament for the treatment of a disease or condition selected from cancers and chronic infections.

DETAILED DESCRIPTION OF THE INVENTION

Definition

As used herein, the terms "ICOS" or **"Inductible T cell costimulator"** refer to a transmembrane homodimeric glycoprotein of 55 to 60kDa which presents an IgV type domain in its extracellular part and a tyrosine within an YMFM motif in its cytoplasmic part. It has been shown that ICOS engagement with its ligand induces the