1995

Non-patent document 5: Bianco et al., Science, 16:294, 1540-1543, 2001

Non-patent document 6: Ju et al., Gene. 2004 Apr 28; 331: 159-64.

Non-patent document 7: Colonna M et al., Seminars in Immunology 12: 121-127, 2000.

Non-patent document 8: Nakajima H. et al., J. Immunology 162: 5-8. 1999

Non-patent document 9: Wilson LE et al, Semin Arthritis. Rheum. 32, 163-173, 2002

Non-patent document 10: Nestle FO et al., J. Exp. Med. 202, 135-143, 2005

Patent-document 1: WO03/12061 (U.S. Patent Published Application No. 2003-148316)

Disclosure ~~of the Invention~~

[Problems to be Solved by the ~~Invention~~Disclosure]

[0007]

An objective of the present ~~invention~~disclosure is to provide an antibody binding to Immunoglobulin-Like transcript-7 (ILT7), and to detect, identify, or isolate IPCs. Another objective of the present ~~invention~~disclosure is to regulate the activity of IPCs.

[Means for Solving the Problems]

[0008]

In order to regulate activity of a humoral factor such as IFN, administration of antibodies, which recognize the factor, is effective. For example, the attempt to treat autoimmune diseases by antibodies against interleukin (IL)-1 or IL-4 have been realized (Guler et al., Arthritis Rheum., 44. S307, 2001). Further, it is assumed that neutralizing antibodies can serve as therapeutic agents of autoimmune diseases as with interferon (Stewart, TA. Cytokine Growth Factor Rev. 14; 139-154, 2003). It can be predicted that the same approach as described above is effective on IFN produced by IPCs. However, such an approach is based on the inhibition of effect of humoral factor after production of the factor. If the production of the desired humoral factor can be directly controlled, more substantial

[0015]

The partial amino acid sequence of natural protein is often tried to be used as an immunogen in order to obtain a protein antibody. However, there are few amino acid sequences specific to human ILT7 in proteins since homology to the amino acid sequences is extremely high in ILT family. In addition, it is necessary to select the region constituted of the portion that is recognized as an epitope by antibodies on the surface of cells for the purpose of allowing antibodies to recognize molecules on the surface of cells. Therefore, it has been considered that formation of an antibody which is specific to ILT7 by using a fragment amino acid sequence as an immunogen is not realistic.

[0016]

The present inventors showed that an antibody, which binds to IPCs, could be obtained by using a special immunogen under such conditions. Further, the present inventors found that the antibody thus obtained specifically recognized human IPCs and further had an effect of regulating the activity and thereby succeeded in completing the present ~~invention~~disclosure. That is, the present ~~invention~~disclosure relates to the following anti-ILT7 antibody, production method thereof, and use thereof.

[Effects of the ~~Invention~~Disclosure]

[0016a]

In one aspect, there is provided a monoclonal antibody which binds to human ILT7, binds to none of human ILT1, human ILT2 and human ILT3, and suppresses interferon-α (IFNα) production from ILT7-expressing cells, or a fragment comprising its antigen binding region.

[0017]

The present ~~invention~~disclosure provides an immunogen useful in producing an antibody which recognizes human ILT7 and a production method of anti-human ILT7 antibody using the immunogen. ILT7 is a membrane protein belonging to ILT family. Particularly, the amino acid sequence of the extracellular region is highly conserved among ILT families. Therefore, it is extremely difficult to produce an antibody which distinguishes between ILT families by general immunization methods. The present inventors showed that the antibody, which recognizes human ILT7, can be easily obtained by using animal cells in which ILT7 is coexpressed with cell membrane protein. Anti-ILT7 antibody, which can be obtained by the present ~~invention~~disclosure, has a high specificity which distinguishes cells expressing other ILT families from those expressing human IPCs.

[0018]

In one aspect, there is provided a method for detecting an interferon producing cell, comprising the steps of:
contacting the monoclonal antibody as defined above with a test cell; and detecting the monoclonal antibody or the fragment comprising its antigen binding region which is bound to the cell.

In a preferred embodiment, anti-human ILT7 antibody provided by the present ~~invention~~disclosure binds to human IPCs. In addition, the antibody of the present ~~invention~~disclosure specifically recognizes human IPCs. Therefore, it is useful in detecting and isolating IPCs. IPC is a cell which produces most of the type 1 interferon. Therefore, the detection and isolation are important in diagnosis and study of diseases that involve IPCs such as autoimmune diseases. Particularly, according to the findings of the present inventors, the expression of ILT7 in IPCs is not reduced under the presence of IFNα. IFNα expression is often facilitated in patients with autoimmune diseases. This means that anti-ILT7 antibody of the present ~~invention~~disclosure can be used for the detection and isolation of IPCs as to the patients with autoimmune diseases in which the expression of IFNα is facilitated.

[0019]

Anti-ILT7 antibody provided by the present ~~invention~~disclosure has an effect which regulates the activity of human IPCs in a preferred embodiment. Therefore, the anti-ILT7 antibody of the present ~~invention~~disclosure can be used to inhibit the activity of IPCs. As described previously, the expression of ILT7 in IPCs is not reduced under the presence of IFNα. Therefore, if the inhibition of the activity of IPCs by the antibody of the present ~~invention~~disclosure is used, a therapeutic effect on the patients with autoimmune diseases in which the expression of IFNα is facilitated may be expected.

[0020]

Scant IPCs produce a large amount of IFN. Antibodies as many as IFN molecules are necessary for neutralization of IFN. However, producing cell activation is directly inhibited in the present ~~invention~~disclosure. As a result, a strong inhibitory effect on IFN can be expected even if smaller amount of antibodies are used compared with neutralization by anti-IFN antibody. Furthermore, in the case where IFN is continuously produced, it is predicted that neutralization by IFN antibodies is transient inhibition. In the present ~~invention~~disclosure, since the activity of IPCs is inhibited, IFN production inhibiting effect can be expected over a long period of time.

[0020a]

In one aspect, there is provided an interferon a (IFNα)-suppressing agent comprising the monoclonal antibody as defined above as an active ingredient.

Brief Description of the Drawings