Appeal decision

Appeal No. 2014- 17732

Hiroshima, Japan
Appellant HIROSHIMA UNIVERSITY

Tokyo, Japan
Patent Attorney KATSUNUMA, Hirohito

Tokyo, Japan
Patent Attorney NAKAMURA, Yukitaka

Tokyo, Japan
Patent Attorney ASANO, Makoto

Tokyo, Japan
Patent Attorney SORIMACHI, Hiroshi

Tokyo, Japan
Patent Attorney OMORI, Michiko

The case of appeal against the examiner's decision of refusal of Japanese Patent Application No. 2010-510175, entitled "Anti-Sweat Antigen Monoclonal Antibody" [the application published on November 5, 2009, WO2009/133951, number of claims: 15] has resulted in the following appeal decision:

Conclusion

The examiner's decision is revoked.

The invention of the present application shall be granted a patent.

Reason

No. 1 History of the procedures, The Invention

The present application was originally filed on May 1, 2009 (priority dates: May 2, 2008, December 26, 2008) as an International Patent Application, an examiner's

decision of refusal was issued on May 29, 2014, an appeal against the examiner's decision of refusal was made on September 5, 2014, a notice of reasons for refusal was issued on November 9, 2015 by the body, and a written opinion and a written amendment were submitted on January 5, 2016.

The inventions according to Claims 1 to 15 of the present application are acknowledged as follows, as specified by the matters described in Claims 1 to 15 according to the scope of claims amended by the written amendment submitted on January 5, 2016:

[Claim 1]

A method of producing an antibody or an antigen-binding fragment thereof which can react with a sweat antigen composition and inhibit histamine release, induced by the composition, from a sweat antigen stimulation-responsive cell, comprising the steps of:

subjecting secretions from a human sweat gland to anion-exchange column chromatography, thereby obtaining a fraction with histamine releasing activity which is eluted in a salt concentration range of 0.25 to 0.3 mol/L NaCl with an NaCl concentration gradient of 0 to 1.0 M;

subjecting the obtained fraction to reverse-phase column chromatography, thereby obtaining a fraction with histamine releasing activity which is eluted in an acetonitrile range of 30 to 35 v/v% with a concentration gradient from 0.1 v/v% TFA/distilled water to 0.1 v/v %TFA/acetonitrile;

subjecting the obtained fraction to gel filtration column chromatography, thereby obtaining a fraction with histamine releasing activity at an elution position ranging from 15 to 60 kD;

subjecting the obtained fraction to anti-human cystatin A antibody affinity chromatography, thereby obtaining an anti-human cystatin A antibody-non-absorbed fraction;

screening a hybridoma using, as an index, an amount of histamine release from a sweat antigen stimulation-responsive cell, by using the anti-human cystatin A antibody-non-absorbed fraction used as an antigen; and

producing an antibody from the hybridoma.

[Claim 2]

An antibody or an antigen-binding fragment thereof, wherein the antibody is produced from a hybridoma deposited under accession No. FERM BP-11110 or FERM BP-11111.

[Claim 3]

An antibody or an antigen-binding fragment thereof, wherein the antibody is produced from a hybridoma deposited under accession No. FERM BP-11110, FERM BP-11111, or FERM BP-11112.

[Claim 4]

An antibody or an antigen-binding fragment thereof, wherein the antibody is produced from a hybridoma deposited under accession No. FERM BP-11113.

[Claim 5]

A method of assisting determination of a sweat antigen-associated disease or a risk of development thereof, comprising a step of detecting a sweat antigen in a test sample using an antibody according to Claim 2 or 3,

wherein the sweat antigen-associated disease is selected from the group consisting of atopic dermatitis, urticaria, miliaria, and dyshidrosis.

[Claim 6]

The method according to Claim 5, further using an antibody according to Claim 4.

[Claim 7]

An agent or kit of diagnosing a sweat antigen-associated disease or a risk of development thereof, comprising an antibody or an antigen-binding fragment thereof according to Claim 2 or 3 and/or an antibody or an antigen-binding fragment thereof according to Claim 4,

wherein the sweat antigen-associated disease is selected from the group consisting of atopic dermatitis, urticaria, miliaria, and dyshidrosis.

[Claim 8]

A hybridoma producing an antibody according to Claim 2 or 3.

[Claim 9]

The hybridoma according to Claim 8, which is deposited under accession No. FERM BP-11110, FERM BP-11111, or FERM BP-11112.

[Claim 10]

A hybridoma producing a sweat antigen-specific antibody which can detect a sweat antigen composition using a sandwich method in combination with an antibody or an antigen-binding fragment thereof according to Claim 2 or 3.

[Claim 11]

The hybridoma according to Claim 10, which is deposited under accession No. FERM BP-11113.

[Claim 12]

A method of detecting an index for determining a sweat antigen-associated

disease or a risk of development thereof, comprising a step of detecting a sweat antigen in a test sample using an antibody according to Claim 2 or 3,

wherein the sweat antigen-associated disease is selected from the group consisting of atopic dermatitis, urticaria, miliaria, and dyshidrosis.

[Claim 13]

The method according to Claim 12, further using an antibody according to Claim 4.

[Claim 14]

A method of screening a hybridoma producing an antibody which can react with a sweat antigen composition and inhibit histamine release, induced by the composition, from a sweat antigen stimulation-responsive cell, comprising the steps of:

subjecting secretions from a human sweat gland to anion-exchange column chromatography, thereby obtaining a fraction with histamine releasing activity which is eluted in a salt concentration range of 0.25 to 0.3 mol/L NaCl with an NaCl concentration gradient of 0 to 1.0 M;

subjecting the obtained fraction to reverse-phase column chromatography, thereby obtaining a fraction with histamine releasing activity which is eluted in an acetonitrile range of 30 to 35 v/v% with a concentration gradient from 0.1 v/v% TFA/distilled water to 0.1 v/v %TFA/acetonitrile;

subjecting the obtained fraction to gel filtration column chromatography, thereby obtaining a fraction with histamine releasing activity at an elution position ranging from 15 to 60 kD;

subjecting the obtained fraction to anti-human cystatin A antibody affinity chromatography, thereby obtaining an anti-human cystatin A antibody-non-absorbed fraction;

obtaining a hybridoma producing an antibody using the anti-human cystatin A antibody-non-absorbed fraction as an antigen; and

selecting a hybridoma producing an antibody having a histamine release inhibiting effect using, as an index, an amount of histamine release from a sweat antigen stimulation-responsive cell.

[Claim 15]

A method of producing a hybridoma producing an antibody which can react with a sweat antigen composition and inhibit histamine release, induced by the composition, from a sweat antigen stimulation-responsive cell, comprising the steps of:

subjecting secretions from a human sweat gland to anion-exchange column chromatography, thereby obtaining a fraction with histamine releasing activity which is

eluted in a salt concentration range of 0.25 to 0.3 mol/L NaCl with an NaCl concentration gradient of 0 to 1.0 M;

subjecting the obtained fraction to reverse-phase column chromatography, thereby obtaining a fraction with histamine releasing activity which is eluted in an acetonitrile range of 30 to 35 v/v% with a concentration gradient from 0.1 v/v% TFA/distilled water to 0.1 v/v %TFA/acetonitrile;

subjecting the obtained fraction to gel filtration column chromatography, thereby obtaining a fraction with histamine releasing activity at an elution position ranging from 15 to 60 kD;

subjecting the obtained fraction to anti-human cystatin A antibody affinity chromatography, thereby obtaining an anti-human cystatin A antibody-non-absorbed fraction;

obtaining a hybridoma producing an antibody using the anti-human cystatin A antibody-non-absorbed fraction as an antigen;

(i) selecting a hybridoma producing an antibody having a histamine release inhibiting effect using, as an index, an amount of histamine release from a sweat antigen stimulation-responsive cell; and

(ii) cloning the hybridoma obtained in step (i).

No. 2 Reasons for refusal notified by the body

An outline of reasons for refusal notified by the body is as follows:

[Reason 1] The description of the scope of claims of this application does not meet the requirement stipulated in Article 36(6)(ii) of the Patent Act in the following points.

(1) Regarding the invention according to Claim 1, which is an invention of a product relating to "an antibody or a functional fragment thereof", it is acknowledged that a process for producing "an antibody or a functional fragment thereof" is described in Claim 1, from the description that secretions from a human sweat gland are subjected to anion-exchange column chromatography, reverse-phase column chromatography, gel filtration column chromatography, and anti-human cystatin A antibody affinity chromatography to obtain a fraction as an antigen, and a hybridoma producing an antibody is screened using, as an index, an amount of histamine release from a sweat antigen stimulation-responsive cell, by using the antigen.

It is reasonable to understand that when a claim of a patent for an invention of a product recites a process for producing the product, the recitation of the claim should be held to meet the requirement that the claimed invention is clear as prescribed in Article

36(6)(ii) of the Patent Act, only if there are circumstances where it was impossible or utterly impractical to directly define the product subject to the invention by means of its structure or characteristics at the time of the filing of the application (impossible or impractical circumstances) (Judgment of the Supreme Court, June 5, 2015, 2012 (Ju) 1204, (Ju) 2658).

However, there is no reason for acknowledging the existence of impossible or impractical circumstances, since there is no description about the existence of impossible or impractical circumstances in the description and other materials and the applicant does not allege and prove it.

Further, "A functional fragment thereof" is described in Claim 1; however, this term is unclear. Claims 2 to 7, 10 to 13, 19, and 20 are similar to Claim 1 on this point.

Therefore, the invention according to Claim 1 is not clear. Claims 2 to 18 which are dependent on Claim 1 are similar to Claim 1.

(2) Regarding an invention of a product of "an antibody", "the antibody is produced from a hybridoma" is described in Claim 2.

As described in (1) above, since there is no description about the existence of impossible or impractical circumstances in the description and other materials, it cannot be said that the description of Claim 2 should be held to meet the requirement that "the claimed invention is clear" as prescribed in Article 36(6)(ii) of the Patent Act.

Further, Claims 3 and 6 in which an antibody produced from a hybridoma is described are similar to Claim 2.

(3) It is acknowledged that Claim 19 is an invention of "a method of screening a hybridoma"; however the whole description of Claim 19 is unclear as Japanese and "a method of screening a hybridoma" cannot be clearly understood since there is a technically incorrect matter such that a hybridoma produces a fragment of an antibody.

(4) It is acknowledged that Claim 20 is an invention of "a method of producing a hybridoma"; however, similar to Claim 19, "a method of producing a hybridoma" cannot be clearly understood.

[Reason 2] The appellant should not be granted a patent for the invention according to the following claims of this application in accordance with the provisions of Article 29(2) of the Patent Act, since the invention would have been easily made by a person ordinarily skilled in the art prior to the filing of the patent application, on the basis of

inventions that were described in a distributed publication, or inventions that were made publicly available through an electric telecommunication line in Japan or a foreign country, prior to the filing of the patent application.

It is described in Cited Document 1 that an antigenic substance having histamine release activity comprises a fraction obtained by fractionating sweat using an anion-exchange resin column and reverse-phase column chromatography. It is acknowledged that this antigenic substance comprises "a sweat antigen which reacts with an antibody or a functional fragment thereof according to Claims 1 to 4" of Claim 5 of the present application.

Since it is described in Cited Document 2 that an antibody of an antigenic substance having histamine release activity is produced to be used for diagnosis of atopic dermatitis, producing an antibody of an antigenic substance having histamine release activity derived from sweat, which is described in Cited Document 1, could be easily implemented by a person ordinarily skilled in the art.

Further, it is not acknowledged that the antibody specified by Claim 5 is different from an antibody which is produced by such process.

Claims 7, 9, 12, which are dependent on Claim 5, are similar to Claim 5.

List of Cited Documents, etc.

1. Research report for research project of prevention and treatment of immunological and allergic disease, part 1 for 2002, 2003, pp. 100-102 (Document 5 in the examiner's decision of refusal)
2. International Publication No. WO03/084991 (Document 4 in the examiner's decision of refusal)

[Reason 3] In the following point, the description of the scope of claims does not meet the requirement stipulated in Article 36(6)(i) of the Patent Act.
[Reason 4] In the following point, the description of the detailed description of the invention does not meet the requirement stipulated in Article 36(4)(i) of the Patent Act.

(1) "A step of detecting an IgE antibody specific to a sweat antigen in a test sample using an antibody according to Claims 1 to 4" is described in Claim 8, and it is acknowledged that detecting an IgE antibody specific to a sweat antigen using an antibody reacting with a sweat antigen is specified.

On the other hand, it is not acknowledged that it is described in the detailed

description of the invention that only using an antibody reacting with a sweat antigen could detect an IgE antibody specific to a sweat antigen.

Measurement of an IgE antibody specific to an anti-sweat antigen in the serum of cholinergic urticaria patents is described in Example 8 of the present application. It is also described that a smith-2 antibody was immobilized to an ELISA plate, a QRX fraction was blocked thereto, a test subject's serum (cholinergic urticaria patent's or healthy individual's serum) is reacted therewith, and an anti-sweat antigen IgE antibody was detected using peroxidase-labeled goat anti-human IgE antibodies; however, this detection is not a process for using only an antibody reacting with a sweat antigen.

Thus, the invention according to Claim 8 is not described in the detailed description of the invention. Claim 9, which is dependent on Claim 8, is similar to Claim 8.

Further, "a step of detecting an IgE antibody specific to a sweat antigen in a test sample using an antibody according to Claims 1 to 4" is also specified in Claim 17. As described above, the invention according to Claim 17 is not described in the detailed description of the invention. Claim 18, which is dependent on Claim 17, is similar to Claim 17.

Therefore, the inventions according to Claims 8, 9, 17, and 18 are not described in the detailed description of the invention.

(2) An invention of a pharmaceutical composition which comprises an antibody reacting with a sweat antigen and is used for the prevention or treatment of a sweat antigen-associated disease selected from the group consisting of atopic dermatitis, urticaria, miliaria, and dyshidrosis is described in Claim 10.

Regarding an invention of medicinal use, since it is difficult to predict that a substance described as an active ingredient can be used in medicinal use of the matters specifying the invention, medicinal data or data similar thereto in the description are required for supporting that the substance can be used for medicinal use, for making a person ordinarily skilled in the art understand that the invention which can be used is described. Further, when the invention described in the scope of claims exceeds the scope supported in the detailed description of the invention, it is not said that the description of the scope of claims is described in the detailed description of the invention.

It is described in the detailed description of the invention of the present application that an antibody reacting with a sweat antigen inhibited histamine release from basophiles of two atopic dermatitis patients of a QRX fraction; however, it is not

described that atopic dermatitis could be actually treated, and it is not acknowledged that the possibility to treat atopic dermatitis from the result of inhibiting the histamine release is not obvious.

Claim 11 is similar to Claim 10.

Therefore, it is not acknowledged that the inventions according to Claims 10 and 11 are not clearly and sufficiently described for a person ordinarily skilled in the art to carry out the invention in the detailed description of the invention of the present application. Further, inventions according to Claims 10 and 11 exceed the scope stated in the description which is described in such a way that a person ordinarily skilled in the art could recognize that a problem to be solved by the invention would be actually solved.

No. 3 Judgment by the body

Of the reasons for refusal notified by the body, it is acknowledged that reasons (1), (3), and (4) in [Reason 1], [Reason 2], [Reason 3], and [Reason 4] are solved by the written amendment submitted on January 5, 2016.

Thus, of the reasons for refusal notified by the body, reason (2) in [Reason 1] will be examined as follows:

Claim 2 of the present application is "An antibody or an antigen-binding fragment thereof, wherein the antibody is produced from a hybridoma deposited under accession No. FERM BP-11110 or FERM BP-11111", with respect to an invention of a product of "an antibody", a process for producing an antibody "which is produced from a hybridoma" is described, and it is acknowledged that a process for producing a product is described in a claim of an invention of the product.

However, according to Judgment of the Supreme Court, June 5, 2015, 2012 (Ju) 1204, (Ju) 2658, it is reasonable to understand that when a claim of a patent for an invention of a product recites a process for producing the product, the recitation of the claim should be held to meet the requirement that the claimed invention is clear as prescribed in Article 36(6)(ii) of the Patent Act, only if there are circumstances where it was impossible or utterly impractical to directly define the product subject to the invention by means of its structure or characteristics at the time of the filing of the application (impossible or impractical circumstances). We will examine as follows whether the invention according to Claim 2 falls under the above circumstances.

First, as described in paragraphs [0127] and [0153] in the detailed description of

the invention, "a hybridoma" described in Claim 2 is a typical "hybridoma" obtained by the fusion between "lymphocytes obtained by immunization with a sweat antigen composition" and "myeloma cells". It is clear that "an antibody" (monoclonal antibody) produced from a specific "hybridoma" is unique for a person ordinarily skilled in the art on the basis of common general technical knowledge (if necessary, see "Keyword Book of Gene Engineering" Yodosha, published on April 25, 1996, p. 299 "hybridoma", and "Encyclopedia of biochemistry (2nd Edition)", Tokyo Kagaku Dojin, published on November 22, 1990, p. 993 "hybridoma").

Further, "a hybridoma" described in Claim 2 is "deposited under accession No. FERM BP-11110 or FERM BP-11111", and "an antibody" according to Claim 2, "an antibody produced from a hybridoma" is obtained and can be used by acquiring the hybridoma under accession No. FERM BP-11110 or FERM BP-11111 from a depositary institution, and producing an antibody. Thus, even though a chemical structure (such as an amino acid sequence) is not described in Claim 2 regarding "an antibody", when "an antibody produced by a hybridoma" is specified, "an antibody" (monoclonal antibody) produced is unique and it is acknowledged that the "antibody" can be produced and used. In this point, the appellant alleges in the written opinion submitted on January 5, 2016 that "an antibody that a hybridoma produces is one, and when the hybridoma is specified, the antibody is unambiguously specified.

On the other hand, when specifying the chemical structure of "an antibody produced from a hybridoma", the "antibody" is protein with high molecular weight having a three-dimensional structure, not a compound with low molecular weight, and as alleged by the appellant in the written opinion submitted on January 5, 2016, it is thought that time, effort, and costs are spent to determine the chemical structure of "an antibody".

Therefore, on the basis of the above common general technical knowledge, regarding an antibody that it is clear that enablement requirements ("a product can be produced" and "a product can be used", regarding an "invention of the product") are met, it is "utterly impractical" to spend time, effort, and costs only to determine a chemical structure of the "antibody". Further, delaying the application with the reason is "utterly impractical" in terms of first-to-file system. Since a field of biotechnology to which an invention of the present application relates is a globally competitive field whose technology is rapidly inventive, and it is very important to rapidly file a patent application, there is a circumstance which is "utterly impractical".

It is described in the concurring opinion of Judgment of the Supreme Court that "the term 'utterly impractical' assumes the case where, rather than from a technical perspective, the work to define the product could force a person ordinarily skilled in the art at the time of the filing of the application to spend time and costs to an extent that is impractical in terms of profitability and therefore it would be too cruel to require such person to perform such work while trying to obtain a patent in the face of the rapid advancement of technology and fierce competition on a global scale." It is acknowledged that the above circumstances fall under "utterly impractical circumstances" which is described in the concurring opinion.

Thus, it is acknowledged that there are circumstances where it was impossible or utterly impractical to directly define the product subject to the invention by means of its structure or characteristics at the time of the filing of the application (impossible or impractical circumstances) in the description of Claim 2, and Claim 2 falls under the requirements that "the claimed invention is clear" of Article 36(6)(ii) of the Patent Act.

Further, for the same reasons, it is said that Claim 3 and Claim 4 fall under the requirements that "the claimed invention is clear".

Therefore, it is acknowledged that the description of the scope of claims of the present application complies with the requirements of Article 36(6)(ii) of the Patent Act.

No. 4 Closing

As described above, it cannot be decided that the present application shall be rejected based on the reasons for refusal notified by the body.

Further, no reasons for refusal were found.

Therefore, the appeal decision shall be made as described in the conclusion.

March 2, 2016

Chief administrative judge: TAMURA, Akiteru
Administrative judge: NAKAJIMA, Yoko
Administrative judge: TAKA, Miyoko