Notice of Reasons for Refusal

Application number: Japanese Patent Application No. 2017-093750
Date of Drafting: Reiwa 1(2019) June 11
Patent examiner: FUKAKUSA, Ako 9548 4U00
Representative/Applicant: ONDA, Makoto (and 3 others)
Applied Provisions: Article 17bis(3), Article 29(2)

This application should be refused for the reason mentioned below. If the applicant has any opinion(s) against the reason, a written opinion should be submitted within 3 months from the date on which this notification was dispatched. Reason

1. (New Matter) The amendments which were conducted in the Amendment dated 1/9/Heisei31(2019) does not satisfy the requirements specified in Article 17-2, Paragraph 3 of the Patent Act on grounds that they are not made within the scope of the matters described in the description, scope of claims, or drawings originally attached to the present application.
2. (Inventive step) The claimed invention(s) listed below of this patent application shall not be granted a patent under the provision of Patent Act Article 29 (2) for the reason that the claimed invention(s) could have easily been made by persons who have common knowledge in the technical field to which the claimed invention(s) pertains, on the basis of the invention(s) described in the distributed publication listed below or made available to the public through electric telecommunication lines in Japan or other foreign countries prior to the filing of the patent application.
Note (For the cited documents, please refer to the list of cited documents below.)
- Reason 1
- Remarks
According to the written amendment dated January 9, 2019, the specification of "having an average diameter of the 80nm-150nm " was added to Claim 1. In the paragraph 0947 mentioned as a basis of correction in the attachment written opinion on the same day, "using lipidide, may have a mole ratio of 50/10/38.5/1.5 to 200 / distearoylphosphatidyl (disteroylphosphatidyl) choline / PEG-DMG. 7 Weight ratio of a total lipid to a tumor related to a total lipid of 1, a primary construct, or mmARNA [1, 2006.01] It originates in the size of that and the intravenous pharmaceutical preparation which has the mean particle diameter of 80 nm is effective in delivering oncology related polynucleotide, a primary structure, or mmRNA to hepatocytes, and it obtains", and "inner-bark window (fenestrae), Although the particle size of less than 150 nm can be expected to be effective for the delivery of an effective hepatocyte, none of them is a statement concerning the lipid nanoparticle according to the Invention, nor does it indicate the range of the average particle size of the 80nm-150nm . In addition, even if the table 56,57,146,147,158,159,164,165 is referred to, the boundary values of 80 nm and 150 nm are not clearly specified, and if the average particle diameter of the 80nm-150nm is particles, the boundary values are not explicitly specified. It cannot be said that the particles have an effect superior to that of particles having an average particle size, and it is not recognized that the average particle diameter of the 80nm-150nm

is preferable. In addition, there is no other statement that serves as a basis for the range of the average particle size of the 80nm-150nm . Therefore, the matter of "having an average particle diameter of the 80nm-150nm " is not found to be within the scope of the matters described in the Originally Attached Description, etc. of the present application.

Note that it should be noted that the "average diameter of the 80nm-160nm " in Claim 9 before the Amendment is not recognized to be also within the scope of the matters described in the original description, etc. of the present application.

- Reason 2

- Claim 1-11

- Cited Document, etc. 6

- Remarks
Regarding the specification of "having an average particle size of 80nm-150nm " in Claim 1, it is not recognized that it is within the scope of the matters described in the Description, etc. of Japanese Patent Application No. 2015 - 504571, which is an original application. Therefore, the present application is not found to satisfy the substantial requirements for division, and is treated as an application filed on May 10, 2017, which is a real application date.

Regarding lipid nanoparticles described in Cited Document 6, which is the original application of the present application, it is a mere exercise of ordinary creativity by a person skilled in the art to make the average particle size of the lipid nanoparticles be a 80nm-150nm . Further, even referring to the table 56,57,146,147,158,159,164,165 of the present application Since it cannot say that the effect superior to the particles which have the other mean particle diameter is produced if it is the particles which have the mean particle diameter of 80nm-150nm , it is not admitted that it is shown that the present invention produces the prominent effect which a person skilled in the art cannot predict. In the written opinion, the applicant has a composition containing lipid nanoparticles having an average particle size smaller than 80 nm or a composition containing lipid nanoparticles having an average particle size larger than 150 nm, based on the table 56,57,146,147,158,159,164,165 of the present application. It is alleged that the expression of the polypeptide encoded by the enclosed modified mRNA is less than in the case of the composition containing lipid nanoparticles having an average particle size of the 80nm-150nm . However, for example, in Table 7, NPA-3 - 1 and NPA-3 - 072 to NPA-3 - 1 are compositions containing lipid nanoparticles having an average particle size of less than 80 nm, and 075 It cannot be said that the applicant's allegation is supported, such as showing expression lower than that of NPA-3 - 1 having an average diameter of the 80nm-150nm , and it is not recognized that a remarkable effect that could not be predicted by a person skilled in the art can be achieved. 074.

Note that it should be noted that the "average particle diameter of 80nm-160nm " in Claim 9 before the amendment is not recognized to be also within the scope of the matters described in the Description, etc. of the original Application.

- Reason 2

- Claim 1-11

- Cited Document, etc. 1-5

- Remarks
Cited Document 1 describes "a modified eukaryotic mRNA molecule encoding a therapeutically relevant protein" (Claim 1), having a nucleotide sequence containing at least one chemical modification to stabilize the modified mRNA molecule. The modified mRNA is translatable (Claim 1), having an untranslated sequence (UTR) on the 5' side and 3' side (Claim 21), having a Kozak translation initiation sequence (Claim 31), and having a cap structure at the 5' end (Claim 7). 3' having a tail of poly A in the end (Claim 10), and further including intracellular delivery media such as a cation lipid, uncharged lipid, and nanoparticles (Claim 27) ; It is also described that the mRNA molecules are "expressed in cells of the subject and the disease condition of the subject is treated" (Claim 32), the disease condition is cancer (Claim 33), and 100% of uridine contained in the mRNA molecules is chemically modified ([0078]).
Cited Document 2 is a lipid nanoparticle for delivering a therapeutic agent such as a nucleic acid encoding a polypeptide to cells, (I) DIn-K-C 2 - DMA ; (ii) DSPC,POPC,DOPE ; The neutral lipids selected from SM ; (iii) cholesterol ; and (iv) PEG-lipids are described (Claims 6 8 16, and Example 16, etc.), and it is also described that the average particle size 90nm-130nm is preferable ([0187]). As the intracellular delivery member described in the cited document 1
It is recognized that it could have been appropriately performed by a person skilled in the art to adopt an average particle diameter 90nm-130nm among the particles described in the cited document 2. As mentioned above, it cannot be said that the applicant's allegation on the effect is supported, and it is not recognized that the use of the average particle size 90nm-130nm described in cited document 2 produces a prominent effect that could not be predicted by a person skilled in the art. In addition, it is a well-known problem to target cells targeted for therapeutic relevant proteins, and thus, it is a well-known problem to express them. For example, to incorporate the target sequence of miR-13, which is known to specifically inhibit expression of the transgene in the liver (if necessary, the cited document 3:[0038][0066). 122
Cited document 4:[0008][0038], a cited document
5 : See p. 31, etc., and a person skilled in the art could have easily determined as necessary. Moreover, it is not recognized that it is described in the Description of the present application that a remarkable effect cannot be achieved by a person skilled in the art by incorporating the target sequence of miR - 122.

<The list of cited documents etc.>
1.JP 2002-508299A
2.JP 2012-505250A
3.JP 2008-545406A (Document showing well-known arts)
4.JP 2009-171861A (Document showing well-known arts)
5.International Publication No. WO2011/133890 (Document showing well-known arts)
6.JP 2015-518816A (Newly cited document)

<Suggestions in amending>
(1) When making amendment to the description or the scope of claims, the amended parts should be underlined so as to be clearly identified (please refer to Note 6 and 7 of Form 13, Regulations under the Patent Act).

(2) Amendments must not go beyond the description, scope of claims, or drawings of the present application as originally filed. In addition, for the evidence of the legality of each amendment, it is advisable to allege the legality in a written opinion with clear indication of the corresponding parts in the original description, claims and drawings.
(3) One should make sure not to perform any corrections that invoke a violation against Patent Act Article 17-2(4) when amending the scope of claims.

If you have any question or are willing to make an interview with the examiner to discuss issues on this notification of reasons for refusal, please contact us at:
Examination No. 3, Medical (Biomedicine) Fukakusa (******)
TEL. 03 (3581) 1101 Extension 3438
FAX.03(3585)2088

A Director General(p.p.), a Director(p.p.), an examiner, an assistant examiner, MAEDA, Hitoshi, FUKAKUSA, Ako, and 9157 9548