Decision of Refusal

Application number: Japanese Patent Application No. 2017-093750
Date of Drafting: Reiwa 2(2020) January 10
Patent examiner: FUKAKUSA, Ako 9548 4U00
Title of the invention:Modified polynucleotides for the production of oncology related proteins and peptides.
Applicant: ModernaTX, Inc.
Representative: ONDA, Makoto (and 3 others)

This application should be refused for the reason 1. and 2. mentioned in the Notice of Reasons for Refusal dated 6/11/Reiwa 1. Although the contents of the written opinion were examined, there is no sufficient evidence to reverse the reasons for refusal.

Remarks
- About Reason 1 (Patent Law Article 17bis(3))
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 written opinion dated December 18, Reiwa 1(2019), the values of "80 nm" and "150 nm" described in paragraph [0947] of the specification of the present application are values. When considered in combination with the contents of the examples in the specification of the present application, it is alleged that the limitation in Claim 1 of the present application, in which the lipid nanoparticles have an average particle size of 80nm-150nm , is clearly supported. However, the description in paragraph 0947 relates to the particle diameter in the Publicly Known Document, and it cannot be understood that it means the boundary value concerning lipid nanoparticles in the Invention in question, in combination with the contents of the Examples in the specification of the present application. 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 there is no other statement that serves as a basis for the range of the average particle diameter 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.

- Reason2 (Patent Act Article 29 (2))

- Claim 1-11

- Cited Document, etc. 6

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 . In the written opinion, the applicant indicates tables A-D prepared by combining parts of the in the description of the present application. It is alleged that when the average particle size is less than 80 nm and more than 150 nm, the expression level of the protein encoded by the polynucleotide contained in the lipid nanoparticle is significantly reduced. However, for example, such a trend cannot be found from the results of NPA-3 - 072, NPA-3 - 074, NPA-3 - 1, and NPA-3 - 076, which were not extracted in Table B in the data in Table 57. 1 1 It cannot be recognized that a person skilled in the art would have a prominent effect that could not be predicted by a person skilled in the art solely by specifying the average particle diameter of lipid nanoparticles.

- Reason2 (Patent Act Article 29 (2))

- Claim 1-11

- Cited Document, etc. 1-5

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 described above, the applicant's allegation on the effect cannot be accepted, and it is not recognized that a person skilled in the art would have a prominent effect that could not be predicted by a person skilled in the art by adopting an average particle size 90nm-130nm among the particles described in cited document 2. In the written opinion, the applicant indicates a reference document in which it is found that the delivery of mRNA is significantly improved by

using optimized lipid nanoparticles, whereas the delivery of siRNA does not provide any improvement in the delivery of siRNA. Cited Document 2, which relates to siRNA encapsulated with lipid nanoparticles, alleges that it is not a guide to the delivery of mRNA. However, in the cited document 2, various nucleic acids, such as polynucleotides encoding polypeptides, in addition to siRNA are assumed as the nucleic acids to be delivered (Claim 15, etc.), and it cannot be said that the guide is a guide to optimize the transmission propagule in the description of the cited document 1. 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

The applicant who is dissatisfied with the examiner's decision, may file a request for a trial against examiner's decision of refusal to the Commissioner of the Japan Patent Office within three months (where overseas resident, within four months) from the date when the copy of the examiner's decision has been served (refer to Patent Act Article 121 (1)).
<Explanation based on the Administrative Case Litigation Act Article 46 (2)>
The applicant may not file an action for the revocation of an administrative disposition against the examiner's decision. The applicant may file a suit against the trial decision regarding the demand for the trial of this examiner's decision (refer to Patent Act Article 178 (6)).

<Things to be considered in amending for filing a demand for trial>
(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) The amendment shall be made within the scope of the matters described in the translation of the document in the foreign language (or the description after the amendment of the translation of the translation, the scope of claims, or drawings). In addition, when amending the scope of claims, the amendment should be limited to deletion of the claimed invention, restriction of the scope, correction of errors, and clarification of ambiguous statements (i.e., only those specified in the notification of reasons for refusal). And also, in the written demand for trial, allege the legality of each amendment with clear indications of the corresponding parts in the translation (or the description, scope of claims, or drawings in the correction of mistranslation after the amendment) for the evidence of the legality.
(3) When you correct about a scope of the claim, please correct by making the full

text of a scope of the claim into a unit (Regulations-under-the-Patent-Act Form No. 13 Remarks 7).
(4) 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.

A Director General(p.p.), a Director(p.p.), an examiner, an assistant examiner, MATSUNAMI, Yumiko, FUKAKUSA, Ako, and 9261 9548