

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : The Trustees of Columbia University in the City  
of New York

Inventors : Jingyue Ju et al.

Serial No.: 16/150,185 Examiner: Jezia Riley

Filed : October 2, 2018 Art Unit: 1637

Conf. No.: 9501

For : MASSIVE PARALLEL METHOD FOR DECODING DNA AND RNA

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May 13, 2019

BY EFS

Commissioner for Patents  
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SUPPLEMENTAL COMMUNICATION SUPPLEMENTING COMMUNICATION IN RESPONSE TO  
FEBRUARY 15, 2019 FIRST ACTION INTERVIEW PILOT PROGRAM PRE-INTERVIEW  
COMMUNICATION FILED FEBRUARY 26, 2019

This Supplemental Communication is submitted to supplement the Communication In Response To February 15, 2019 First Action Interview Pilot Program Pre-Interview Communication filed February 26, 2019 in connection with the above-identified application.

Illumina Ex. 1136

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REMARKS

I. STATUS OF CLAIMS

The claims pending in this application are previously pending claims 1-2.

II. INTERVIEW SUMMARY

On May 1, 2019 the undersigned participated in a telephonic Interview with Primary Examiner Jezia Riley in connection with related U.S. Application No. 16/150,191. Ms. Brittany Internoscia, an associate of the undersigned, also participated.

Applicant acknowledges with appreciation the courtesy that Examiner Riley extended during the May 1, 2019 interview.

During the May 1, 2019 interview, the Examiner requested that applicant file a Supplemental Communication in Response to the First Action Communications mailed in connection with each of related U.S. Applications Nos. 16/149,098; 16/149,114; and 16/150,185 to address in the same way all of the issues addressed in the April 12, 2019 Communication in Response to the March 12, 2019 First Action Communication issued in U.S. Application No. 16/150,191, even though certain of these issues were inadvertently not raised in those First Action Communications. The issues not included in those First Action Communications include issues relating to 35 U.S.C. §112(a) and 35 U.S.C. §112(b) which were raised in U.S. Application No. 16/150,191. Subject to addressing in each of these three applications, each of these issues in the same way as they were addressed in connection with U.S. Application No. 16/150,191 Examiner Riley indicated the claims pending in those applications would be allowable.

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### III. OBVIOUSNESS-TYPE DOUBLE PATENTING

In response to the obviousness-type double patenting rejection of pending claims 1-2 over claim 1 of U.S. Patent No. 9,719,139 set forth in the February 15, 2019 First Action Interview Pilot Program Pre-Interview Communication, applicant, without conceding the correctness of the Examiner's rationale for this rejection, filed a Terminal Disclaimer with respect to U.S. Patent No. 9,719,139, the reference patent cited in the rejection. That Terminal Disclaimer was approved on February 26, 2019.

Accordingly, applicant maintains this rejection should be withdrawn.

### IV. REJECTION FOR INDEFINITENESS

Although claims 1-2 were not rejected under 35 U.S.C. §112(b) as indefinite applicant responds as if such a rejection had been and the same issues had been raised as were raised in U.S. Application No. 16/150,191. Applicant's response follows:

#### A. The term "small"

The Examiner indicated that the term "small" in the claims is a relative term which renders the claim indefinite; that the term "small" is not defined by the claim; that the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The Examiner further stated that the specification does not define "small" and provides only two examples, MOM ether and allyl, and a skilled artisan would not know which other groups meet the limitation "small".

Applicant notes that a relative term is not automatically indefinite [MPEP 2175.05(b)]. More importantly, applicant maintains that the specification of the subject application at page 4, lines 10-32; page 5, lines 1-32; page 6, lines 1-27; and page 13, lines 3-11, taken together

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with FIG. 1 referred to at page 4, line 31 of the application, set forth a standard for assessing whether a 3'-O capping group is "small" based on its ability to fit into the active site of a polymerase. As of October 6, 2000, the person of ordinary skill in the art ("POSA") reading the specification would have understood that "small" referred to the ability to fit into the active site of the polymerase defined by reference to the three-dimensional structure shown in FIG. 1. The POSA would have further understood that FIG. 1 corresponds to FIG. 6 of previously published Pelletier et al. (*Science*, Vol. 264, June 24, 1994, 1891-1903) cited at page 4, line 30 of the application. The POSA would also have understood that Pelletier et al. disclosed, on page 1903, the precise coordinates of the structure of the polymerase in "References and Notes" 101 and, in Table 3 on page 1897, the distances between the sugar of the nucleotide analogue and the key amino acids in the active site of the polymerase. See also paragraphs 11-13 of the accompanying Declaration of Jingyue Ju, Ph.D. signed May 2, 2017 and submitted in connection with U.S. Application No. 15/380,311, now U.S. Patent No. 9,719,139. A copy of this Declaration is attached hereto as **Exhibit 1**, including copies of **Exhibits A-E** referred to therein and attached hereto. **Exhibit B** is a copy of Pelletier et al.

With the benefit of applicant's specification, a POSA in October 2000 could have readily determined whether any given R when present as OR (a 3'-O capping group) was small by this standard using the published coordinates and available software such as Chem3D Pro. More specifically, using this approach the POSA would have known that the space available around the 3' position of a deoxyribose in the active site of the polymerase was approximately 3.7Å in diameter. By this standard, R when present as OR would need to be less than 3.7Å in diameter. Consistently, the POSA would have known that the two examples in the application, MOM and Allyl with diameters of 2.1Å and 3.0Å, respectively, would fit in the active site of the polymerase and would be "small". [See also paragraphs 14-16 of the Declaration of Jingyue Ju, Ph.D. and the Analysis discussed therein and attached to the Declaration as **Exhibit C**.]



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Using this standard the POSA also would have known which other 3'-O capping groups meet the definition "small" and have the other features recited in the claims and would, for example, have readily determined that groups such as Methylthiomethyl and Azidomethyl were "small" and would fit in the active site while a group such as a 2-Nitrobenzyl group which has a diameter of 5Å was not "small" and would not fit into the active site of the polymerase. [See also paragraph 17 of the Declaration of Jingyue Ju, Ph.D. and the Analysis attached thereto as Exhibit C.]

As Dr. Ju opines, the POSA reading the subject application and relying on information publicly known as of October 2000 would have known that the standard for assessing whether any specific 3'-O capping group in a nucleotide analogue was "small" was whether it has a diameter less than 3.7Å so that it would fit into the active site of the polymerase. [See also paragraph 18 of the Declaration of Jingyue Ju, Ph.D.]

Therefore, the meaning of "small" would not have been indefinite to the POSA. To the contrary, its meaning would have been reasonably certain to the POSA to the extent required by 35 U.S.C. §112.

#### B. The term "R"

The Examiner indicated that the definition of R in the claims is unclear. The Examiner acknowledged that the claims recite some functional characteristics of R but asserted that these functional limitations do not set forth well-defined boundaries of the invention because they only state a problem solved or a result achieved.

As an initial matter applicant points out that in the claims: (1) R is further defined as a small, chemically cleavable, chemical group capping the 3' oxygen of the sugar of a nucleotide analogue, (2) R does not contain a ketone group, or a -CH<sub>2</sub>CH=CH<sub>2</sub> group, and (3) OR is not a methoxy group, an ester group, or an allyl ether group. Further, in the structures in the claims, R is shown as covalently bound to the 3' oxygen. With the meaning of "small" defined as indicated in the preceding section and the

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